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Editorial Board

NESOG Executive Committee 2015-2017

Journal Contact

Mailing Address

Nepal Society of Obstetricians and Gynaecologists (NESOG)
Maternity Hospital,
Thapathali,
GPO : 23700,
Kathmandu,
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Principal Contact

Prof. Ganesh Dangal
Editor-in-Chief

Nepal Society of Obstetricians and Gynaecologists (NESOG)
Maternity Hospital,
Thapathali,
GPO : 23700,
Kathmandu,
Nepal

Phone: +977 1 4252315
Fax: +977-1-4215175
Email: njogeditor@gmail.com

Support Contact

Office of the Editorial Board

Shikha Thapa
Phone: +977 1 4252315
Email: nesog2011@gmail.com

Design and Layout
Mr. Milan Chandra Khanal (9841426101)
E-mail: milanchandra2002@gmail.com

Obstetric Fistula in 2015 and Beyond

Arrowsmith S
Medical and Programs Director, Fistula Foundation, CA, USA.

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It seems difficult for me to believe, but I first repaired an obstetric fistula in early January 1987. At that time, the landscape of the fistula world was remarkably different. Fistula effort was confined to a very few geographic areas, each of which were completely dominated by the spirit and energy of the founder of a fistula center. The list of leading surgeons contains names familiar to fewer and fewer active fistula care providers: Drs. Ann Ward, John Lawson, and Una Lister in Nigeria were all in the late prime of their lives; in the north of Nigeria, a leprosy surgeon was just getting started in fistula repair at a new center near Katsina: the founder being Dr. Kees Waaldiijk. In eastern Africa, Dr. Abbo Hassan Abbo was dominant in Sudan, the Hamlins in Ethiopia, and an odd band of travelling surgeons, including the late Dr. John Kelly, Dr. Brian Hancock, and Dr. Tom Raassen, were establishing themselves across the region. Also quite active, but completely unheralded were a cadre of non-Western surgeons just beginning long careers in fistula repair: Drs. Mulu Muleta and Ambaye w/ Michael in Ethiopia, Dr. Kalilou Ouattara in Mali, Dr. Serigne Gueye in Senegal, Dr. Khisa Wakasiaka in Kenya, Dr. Ojengbede Akanbi in Ibadan, Nigeria, and Dr. Jonathan Karshima in Jos. Meanwhile, Dr. Kundu Yangzom was quietly establishing a tradition of quality fistula care in Nepal. Of course, this listing is far from exhaustive.

Because of the huge scale of the fistula problem and all of the overwork than ensued, the isolation of these individuals from one another, difficulty in travelling between fistula endemic areas, lack of the easy communication we enjoy today via e-mail and social media, very few of these individuals had any idea of what the others were doing, how they approached fistula repair, what supportive social and preventive programs they had in place. Everyone was inventing the wheel in isolation.

Fast-forward 28 years, and the situation is unimaginably different. The Global Fistula Map[1] now lists fully 152 centers offering fistula care. Needs in areas other than Africa have been identified and are being addressed as there are now active centers in countries like Pakistan, Afghanistan, Nepal, and Bangladesh. We have a professional society for fistula surgeons, an internationally sanctioned training curriculum, and resources from an ever-growing number of governmental and non-governmental sources. The media have awoken to the fistula issue, and the thing that so many of us referred to as the "hidden epidemic" is now thoroughly out in the open. National surgeons have begun to receive their due of international recognition and lead most of the organized international efforts against fistula. Fistula survivors also have a voice, as they are being asked to provide wisdom and perspective to programmatic strategy (such as Kenya's Sarah Omega[2] of the Fistula Foundation, whom I can proudly claim as one of my bosses). In 2015, the results of the very first multi-center, prospective, randomized clinical trial will be published in a major medical journal,[3] marking a new era of transcontinental cooperation and established the developing world as a place where quality clinical research can and should be done.

But in 2015 we also face challenges that were not imaginable in 1987: First to mind is the issue of security. In 1987, there was no Boko Haram, no ISIS, no Al Shabab, AQIM, Ansaru, Taliban, or any other organized terrorist organization active in places where we fistula surgeons try to work. Add chronic conflict in Sudan and South Sudan, Afghanistan, Somalia, the DRC, Yemen, Central African Republic, among others, and there is barely a spot that one can point to in the fistula world and say with confidence that the area was "safe". Future planning must take risks of kidnapping or violent attack into consideration, both in terms of prevention and planning should such a thing happen. How does one decide when "hot" is too "hot"? If we back away from a certain area because of security, how can we decide when to return? How can we remain true to our commitment to women with fistula without assuming "undue" risk? The near-death of Dr. Denis Mukwege[4] in the

CORRESPONDENCE

Dr Steven Arrowsmith
Consultant Urologist & Fistula Surgeon, Fistula Foundation, USA.
Email: steven@fistulafoundation.org
Phone: +1-866-756-3700

DRC, and the constant exposure of others, like Dr. Sunday Lengmang in Jos, Nigeria) remind us that these risks are very real.

In 2014, a new issue exploded onto the scene with the unprecedented outbreak of the Ebola virus in West Africa. Most of us have worked in areas where Ebola, Lassa, Marburg, Dengue, resistant Malaria, and other pathogens were a nagging concern. Have we thought through a rational approach to work in areas where epidemics like this one occur? What if Lassa broke out in your post-operative ward (as it once did in mine in Nigeria)? Do you have policy in place for this possibility? Most of the fistula work in Liberia, Sierra Leone and Guinea is currently shut down. Are we prepared to rapidly and robustly resume fistula repair when the epidemic plays out? Everyone expects there to be a new "crop" of fresh fistulae resulting from the collapse of other forms of health care during this huge epidemic. Let's be ready to go, and show the world that our commitment to the poor is not diminished, even when dangerous, hideous things like this outbreak happen.

A huge "thaw" in the isolationist past of fistula centers has begun, and it is our challenge to keep this movement alive. With the International Society of Obstetric Fistula Surgeons[5], the International Obstetric Fistula Working Group[6] of the UNFPA, the collaborative training effort of FIGO[7] there are more and more opportunities for us to band and work together. Many countries now have a Fistula Task Force or Providers Group sponsored by the local Ministry of Health. My employers, the Fistula Foundation, have begun asking our funded sites in areas of geographic proximity to band together and to benefit from the collective wisdom, resourcefulness, and spirit of other provider working in each area. This is now reality in Nepal and in Kenya, and we hope to rapidly expand to other areas. EngenderHealth has made similar efforts at "community building" among their funded sites. We are stronger together than we are apart. Finally, there is a last challenge. Recent attempts to accurately define the incidence and prevalence of fistula based on real-world data have produced estimates significantly lower than the estimates of the past. Many centers seem to be working harder and harder to identify and assist new fistula clients. Some have begun to wonder that perhaps we have finished with the fistula problem and need to refocus our efforts and resources on other conditions impacting the quality of life of women in the developing world. My work takes me to fistula centers all over the world, and it is apparent that while some centers are working hard to find clients, others are seeing increasing numbers. The number of iatrogenic fistulae[8] seems to be on the rise. Are our new relationships strong enough to include an approach of professional accountability to deal with this issue? We have only just begun to explore effective and rational strategies for client recruitment.

As yet we don't know if women are staying away from us because we treat them badly, whether they stay away from irrational fear, or whether they truly no longer exist. Before we declare victory over the fistula problem, we should wait for the strong data that we have always lacked. New approaches to defining incidence and prevalence of fistula are being developed using novel statistical modeling techniques. Let's give new studies a chance to shed further light on the issue. The attention focused on fistula has been far too hard-won to give it up prematurely. It is a great pleasure to submit this editorial to a Nepali publication, knowing that the women of Nepal are in good hands with a robust cadre of committed fistula surgeons now well-united in a national treatment network. All the best in 2015 as we fight together to end fistula!

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Abortion Practices in Nepal: What does Evidence Show?

Bhandari TR[1,2], Dangal G[3]

[1]Department of Public Health, School of Health and Allied Sciences, Pokhara University, Kaski, Nepal, [2]Achutha Menon Centre for Health Science Studies, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India, [3]Department of Obstetrics and Gynaecology, Kathmandu Model Hospital, Kathmandu, Nepal

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Twenty-five years have passed since the global community agreed in Nairobi to address the high maternal mortality by implementing the Safe Motherhood Initiative. However, every year around 22 million women seek unsafe abortion in developing countries. Globally, the unsafe abortion accounts for 13% maternal deaths. Out of the total aborted women, around five million women were admitted to hospitals as a result of unsafe abortion. Similarly, more than three million women suffer from severe complications from unsafe abortion every year. In 2002, responding to the public voices and high attribution of unsafe abortion on maternal mortality, Nepal granted legal access to safe abortion introducing safe abortion act. Women can seek abortion up to 12 weeks of gestation for any indication. However, sex selective pregnancy termination is prohibited in Nepal. This study aimed to assess the results of various studies on abortion practices in Nepal. Literature published in PubMed, Lancet, Medline, WHO and Google Scholar web pages from 1990 to 2014 were used to prepare this paper. From 2004 to 2014, more than half a million women sought safe abortion care in Nepal. Despite the considerable progress, unsafe abortion is still a major issue in Nepal as it has been estimated that it constitutes half of all abortions undertaken every year. Published literature further showed that still an unmet need of safe abortion services exists in Nepal. However, the overall awareness of legal abortion was found to be high among Nepalese women. We found negative attitude of most people towards women who sought abortion care. Similarly, a large number of unmarried women were found at risk for seeking abortion care due to socio-cultural norms, values and stigmas in Nepal.

Keywords: abortion practices; legalization of abortion; medical abortion; surgical abortion; unsafe abortion.

INTRODUCTION

Globally, everyday approximately 800 women die from pregnancy related causes. In 2013, nearly 289,000 women died during and following pregnancy. Almost 99% deaths occurred in developing countries.[1] Achieving millennium development goal five still remains a challenge in most developing countries although maternal mortality reduction has been identified as a priority agenda.[2]

If a woman with an unwanted pregnancy does not have access to safe abortion care, she is at a high risk of undergoing an unsafe abortion. Every year around 22 million women seek unsafe abortion and this occurs mostly in developing countries. Unsafe abortion accounts for 13% maternal deaths. Around 5 million women admit to hospitals as a result of unsafe abortion and more than three million women who have complications following unsafe abortion do not receive skilled care each year.[3–5]

Despite various efforts and liberalization of abortion laws, unsafe abortion remains a major public health concern in developing countries. Access to safe abortion remains elusive for many women because of the urban centered health facilities, poor awareness, costs, cultural issues, and availability of skilled human resources.[6,7]

In 2002, responding to public health, human rights imperatives and the high attribution of unsafe abortion on maternal mortality, Nepal's legal code (*Muluki Ain 1854*) 11thAmendment Bill was adopted by the parliament and granted women legal access to safe abortion.[8,9] Women can seek safe abortion up to 12 weeks of gestation for any indication upon request, up to 18 weeks of gestation in case of rape or incest and at any time during pregnancy in case of mental/ physical illness or if the life of the pregnant woman is at risk as approved by a medical practitioner and at any time during pregnancy if the fetus is deformed and incompatible with life. Additional considerations

CORRESPONDENCE

Tulsi Ram Bhandari
Achutha Menon Centre for Health Science Studies,
Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India
Email: tulsib2004@gmail.com
Phone: +977-9851178182

include- only the certified providers are eligible to provide induced abortion services. The pregnant woman alone has the right to choose to continue or discontinue pregnancy, however in the case of minors (< 16 years of age) or mental incompetence; a legal guardian must give consent. Moreover, sex selective pregnancy termination is extremely prohibited in Nepal.[8–12]

Since 2002, in order to regulate abortion laws, the Government of Nepal has initiated various efforts. In 2003, Ipas for the first time conducted training for trainers on abortion care and in the same year government approved the Safe Abortion Procedural Order for establishing safe abortion care. Safe Abortion Advisory Committee allowed the commencement of safe abortion services in approved health facilities. In 2004, legal abortion services started for the first in some selected government hospitals of Kathmandu, Nepal. In the same year, manual vacuum aspiration training course was also started for service providers. The Abortion Task Force was dissolved and a technical committee for planning and implementing the comprehensive abortion care services was formed throughout the country. In 2007, government introduced second-trimester abortion services. Similarly, midlevel provider training was started and medical abortion scale of strategy was approved in 2007 and 2008 respectively.[8,9,13]

Eight hundred eight-one physicians and 371 staff nurses were trained for safe abortion care and 255 auxiliary nurse midwives received midlevel abortion training from 2002 to 2011. Similarly, 532 safe abortion care health facilities including private sectors were registered and established covering all 75 districts. At the end of 2011 throughout the country, 497,804 women sought the safe abortion.[8,9,13] Despite such considerable progress, unsafe abortions are still a major issue in Nepal as it has been estimated that they constitute only half of all the abortions undertaken every year. In Nepal, estimated 97,400 illegal abortions occurred in 2008 which was likely equal to those done by unregistered providers.[9,14] This indicates the unmet need of safe abortion services in Nepal. This paper examines the published research findings on abortion care practices in Nepal from 1990 to 2014.

METHODS

For assessing the scientific publication on abortion practices in Nepal, we searched and analyzed all available scientific writings published from 1990 to 2014. We decided to start from 1990 considering that Nepal's first National Health Policy was launched in 1991. We used the various key words such as "Nepal" and "abortion/medical abortion/unsafe abortion/ pregnancy termination/access of safe abortion/ induced abortion." We developed search strategy based on search terms and used filter to confine the publication period.

The main sources for our literature searching are PubMed, ScienceDirect, Google Scholar, Cochrane Library, World Health Organization and Ministry of Health and Population of Nepal homepages. First, we collected available literature and screened them for unrelated as well as duplicate items. Second, we classified all literature into three groups, i.e. original articles, review articles and other publications. We found 58 relevant publications, out of which we located 38 original articles, six review articles and 14 other publications such as comments, talking points, editorials, view points, working papers, conference papers, unpublished thesis, reports and case reports. We selected 38 peer-reviewed original articles to assess the abortion practices in Nepal, of which five articles were based on community based studies and the remaining articles were based on the health facilities based studies (Figure 1).

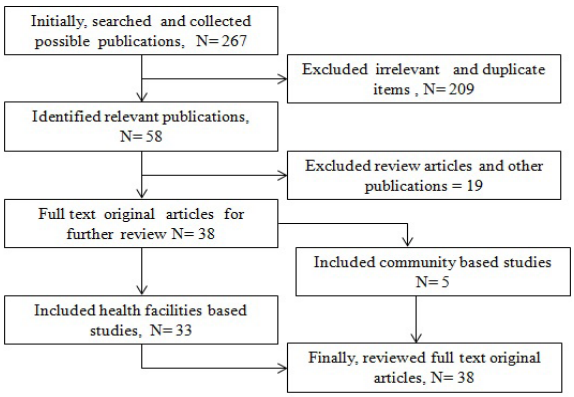

Figure 1: Flow diagram of literature search and management

RESULTS

We analyzed 38 articles considering objectives, designs, methods, study sites, sample size and major findings of the studies which are presented below (Table 1 and 2).

Table 1. Analysis of community based original articles on abortion practices in Nepal published from 1990 to 2014.

Studies	Objectives	Designs	Study sites	Sample size	Key findings
Tamang and Tamang 2005[15]	- Gauge current awareness of the availability of medical abortion drugs in Nepal, - Explore feeling of health professionals about the use of Medical Abortion (MA) to expand access to safe abortion in the country.	Community based cross-sectional survey	Across the country: urban and peri-urban areas of Terai, inner Terai and Kathamndu valley	Private obstetrician–gynaecologists 49, general practitioners 55, paramedics 168, ayurvedic and homeopathic practitioners 62 and chemists 177	- Allopathic and indigenous medicines available, knowledge of the availability of mifepristone misoprostrol was low. - Many were interested in MA themselves.
Puri et al 2007[16]	Explore factors associated with abortion decisions among young couples in the context of recently legalized abortion in Nepal.	Community based cross-sectional survey and qualitative study	Five districts of Nepal: Ilam, Morang, Chitwan, Kaski, and Lalitpur	For survey Women- 997 Men-499 For qualitative study Women -19 Men- 11	- Half had experienced an unwanted pregnancy and some attempted abortion, however only few succeeded. - In decision-making husband and providers played a major role.
Thapa et al 2009[17]	Reveal the understanding of abortion in Nepal among marginalized and underserved community.	Community based qualitative	Throughout country (selected six districts and NGO/INGOs)	FGD- 13 KII- 22	- Despite misconceptions, many consulted providers for safe abortion. - Legalization of abortion was not enough to address the unmet need.
Thapa and Sharma 2012[18]	Assesses the effectiveness of programmatic interventions in the early years of the country's abortion program.	Cross-sectional survey	DHS data 2006 which covered whole country	- 9926 (15-44 years old married women)	- 32% were aware on safe abortion and 56% knew where to go for safe abortion service (SAS). - There was variation by ecological regions, education, age and number of living children.
Hald and Sondergaard 2014[9]	Explore a local community's perception of the situation for unmarried Nepalese women wanting to practice their legal right to abortion	Cross-sectional survey / qualitative and quantitative	Makwanpur District, Nepal.	- For survey 55 - For in-depth interview 16	- Overall awareness of legal abortion was found high. - People's attitude was negative to women who sought abortion. - Unmarried women were found at higher risk to seek abortion due to socio-cultural norms, values and stigmas.

Table 2. Analysis of health facility based original articles on abortion practices in Nepal published from 1990 to 2014.

Studies	Objectives	Designs	Study sites	Sample size	Key findings
Rayamajhi et al 2003[19]	Study the reasons of abortion and outcomes of unsafe abortion.	Health facility based cross-sectional analysis	Tertiary level hospital, Dharan	877 abortion related cases	- 11% of complication was sepsis. - 2/3 abortions were performed by quacks.
Rana et al 2004[20]	Study maternal mortality and morbidity in induced septic abortions.	Retrospective record analysis	Purposively selected a teaching hospital	92 cases of induced abortion from 1992 to 1999	- Of induced abortion 6% faced life-threatening conditions and some died.
Thapa et al 2007[21]	Assess whether unsafe abortions are getting lesser after the establishment of CAC unit.	Descriptive retrospective records review	A tertiary level maternity hospital in Kathmandu	12,481women's records were reviewed who attained hospital for abortion care	- There was a decline in the admission of serious cases of induced abortion.
Duwadi and Shrestha 2007[22]	Determine the reasons that lead to choose abortion, assess the involvement of partner.	Health facilities based cross-sectional study	8 clinics of Family Planning Association of Nepal	304 women from FPAN clinics	- Maternal education was a strong predictor of SAS. - Half accompanied by husband for CAC.
Vaidya and Giri 2008[23]	Assess the morbidities as results of unsafe abortion after legalization.	Descriptive prospective study	A tertiary level maternity hospital in Kathmandu	5592 women who sought abortion related care	- Unsafe abortion was 2% . - 61% were in their second trimester and peritonitis (12%) was the major morbidity.
Karki et al 2009[24]	Assess the feasibility and acceptability of a simplified mifepristone–misoprostol regimen.	Cross-sectional prospective data collection	2 teaching hospitals and 2 family planning clinics	400 women in early pregnancy	- 91% had successful MA. - 89% preferred misoprostol at home.
Chawdhary et al 2009[25]	Compare the efficacy of mifepristone and misoprostol with misoprostol alone for MA up to 63 days	Quasi-randomized controlled trial	A public teaching hospital, Kathmandu.	Group A 50 women and group B 50 women	- Fewer side effects and a more complete abortion rate (94%) was observed in group A (mifepristone and vaginal misoprostol).
Regmi and Madison 2010[26]	Evaluate patient satisfaction with the new second-trimester abortion services in Nepal.	Purposive institutions based study	One public and one private hospital in Kathmandu	50 women who sought abortion care service	- Abortion clients were satisfied and well counselled. - There was some lack of privacy and confidentiality
Tuladhar and Risal 2010[27]	Study the level of awareness about legalization of abortion in women attending gynecology OPD.	Descriptive cross-sectional study	Purposively selected a teaching hospital in Kathmandu	200 women who sought gynecology services from OPD.	- 66% were aware of legalization. - Young women with higher education were more aware about it.
Shrivastava et al 2010[28]	Find out the profile of abortion clients	A prospective study	A tertiary level maternity hospital	57 clients who sought second trimester abortion	- Most common reason of abortion was multiparty (61%) .
Regmi et al 2010[29]	Find out the contribution of unsafe abortion to maternal mortality/morbidity.	Health facility based study	A tertiary level hospital, Dharan Nepal	70 women who sought unsafe abortion	- 52% had high grade complications. - 11% died due to unsafe abortion.
Lamichhane et al 201130	Examine provider's perspectives on sex-selective abortion on legal abortion in the public sector.	Qualitative study: in-depth interview	Four public hospitals: two in Kathmandu valley and two outside valley.	35 in-depth interview with providers and administers of hospitals.	- Despite ban, sex selective abortion as an increasing problem. - Availability of abortion, USG were contributors of sex selective abortion.
Warriner et al 2011[31]	Assess early first-trimester medical abortion provided by midlevel providers was as safe/effective.	Multicentre randomized controlled equivalence trial	Five rural district hospitals in Nepal	Assigned to doctor- 514 and midlevel providers- 518	- 1% were failed abortion in the doctor cohort and none in the midlevel provider cohort.

Bingham et al 2011[32]	Reveal results from Dialogues for Life, undertaken in Nepal from 2004 to 2006, after abortion was legalized in 2002.	Intervention study	Kathmandu Valley and Rupandehi District.	478 people were participated in Dialogue Group Sessions and 20 session were conducted	- Despite the legalization, women faced barriers. - Interpersonal communication interventions play an important role.
Andersen et al 2012[33]	Estimate the frequency and type of abortion complications arising from CAC	A prospective study and cluster sampling strategy	Sampled CAC facilities throughout the country	7386 abortion clients	- 2% had complications. - Women receiving CAC at 4-5 weeks were less likely to have complications.
Tamang et al 2012[34]	Investigate factors associated with women's choice of medical abortion (MA) or manual vacuum aspiration (MVA).	Exit interview with women who sought abortion care (1 each every 4/5 clients)	7 clinics of 3 districts of Nepal	MA clients: 499 MVA clients: 542	- Many were not aware of MA and MVA methods and the odds of choosing MA were more than 3 times high among those who knew both methods. - MA was high compared to MVA.
Khanal et al 2012[35]	Explain the perceptions, practices and factors affecting the use of family planning among abortion clients attending SAS.	Health facility based cross sectional study	A tertiary level public health facility in Kathmandu	58 women who are going to seek abortion care in the near future.	- Main reason of the abortion was unwanted pregnancy. - Knowledge of modern contraception was high 98%, knowledge of emergency contraception was low
Möller et al 2012[36]	Investigate the experiences, opinions and attitude of providers on SAS centres in the Kathmandu.	Facility based qualitative study	One hospital and four clinics from Kathmandu valley	15 doctors and nurses	- prevent abortions from being used instead of contraceptives; - stop illegal medical abortions; - deal with the dilemma of sex-selective abortions
Puri et al 2012[37]	Examine health care workers' views on abortion legalization, and changes that they have observed in their practices.	Facility based qualitative study: in-depth interview	Four tertiary level hospitals: two from Kathmandu and two from outside valley	35 in-depth interviews with doctors, nurses and other providers	- Most had positive views about abortion legalization. - The proportion of women obtaining abortion services was increasing.
Thapa and Neupane 2013[38]	Investigate similarities and differences between abortion clients.	Facility based cross-sectional study	Health facility based study	1,172 women from two clinics	- 50% of the public and 35% clients of the NGO clinic reported use of contraceptives.
Paudel 2013[39]	Assess the immediate impact of MA on women's health and clients' satisfaction.	Descriptive study	A Center in Lalitpur	100 women who sought medical abortion	- MA was successful in 91%. - 79% were satisfied with MA.
Panta et al 2013[40]	Compare efficacy and safety of MA with surgical abortion in a district hospital	Facility based observational study	Purposively selected a district level health facility	MA 48 cases and manual vacuum aspiration-35	- From MA, 95% and 97% MVA aborted completely.
Henderson et al 2013[41]	Assess the maternal health effects of unsafe abortion.	Cross-sectional study	Retrospective study from 4 public centers	23,493 women who sought abortion service	- Reductions in sepsis occurred sooner, during early implementation.
Paudel et al 2013[42]	Find out the prevalence and the pattern of abortion	Retrospective records review	A tertiary care hospital in Kathmandu	4830 records of induced abortion.	- Abortion contributed to about 1.68% of the total patient.
Rocca et al 2013[43]	Investigate abortion practices of Nepali women requiring post-abortion care	Cross-sectional study	Four major public hospitals	527 women presenting with complications	- Out of medically induced abortion, 89% took unsafe, ineffective or unknown substances.

Thapa and Neupane 2013[44]	Examine the incidence and risk factors of repeat abortion in Nepal.	Health facility based prospective survey	Two approved abortion clinics in Kathmandu	1172 women who had surgical abortions	- One-third women had repeat abortions.
Berin et al 2014[45]	Compare knowledge and attitudes about contraceptive among women seeking induced abortion	Cross-sectional cohort study with matched controls.	Kathmandu Medical College, Kathmandu	64 cases for abortion service, 89 controls (women who sought medical care)	- Women with higher education were less likely to seek an abortion than women with lower education.
Gerdts et al 2014[46]	Assess the denial of abortion in legal settings	Cross-section study	2 abortion provider clinics	300 women sought abortion	- In Nepal, 26% of women were denied abortions
Rocca et al 2014[47]	Assess contraceptive information received and methods chosen, received, and used among women having abortions.	Prospective follow –up study (base-line and end-line survey)	Two non-governmental clinics and two government hospitals from across Nepal.	830 participated from four health facilities.	- 1/3 did not receive any information on contraceptives, 56% left facilities without any method. - Depo-Provera (88%) and pills (75%).
Puri et al 2014[48]	Determine the effectiveness of engaging mid-level health workers to provide medical abortion services.	Operation research	As study site: Rupandehi district and as control site: Kailali district	16 health facilities and 126 FCHVs from study area and 8 health facilities and 96 FCHVs from control area	- MA care provided by nurses/ANM was reported to be accessible, effective, and of good quality by clients who received MA.
Puri et al 2014[49]	Assess the effectiveness of training for ANM as MA providers, and FCHV as referral agents for expanding access to MA	Intervention study (comparison between study group and control group)	As study site: Rupandehi district and as controlled site: Kailali district	16 health facilities and 126 FCHVs from study area and 8 health facilities and 96 FCHVs from control area	- ANM were confident in conducting MA safely and effectively. - FCHV were effective change agents for MA.
Conkling et al 2014[50]	Assess acceptability of self-administration of mifepristone at home.	A prospective study	Hospital based study	200 women	- For MA, 72% opted to take the mifepristone at home from which 95% succeeded, 94% succeeded in the clinic
Padmadas et al 2014[51]	Investigate timing of contraceptive use and estimate discontinuation rate of temporary methods.	Population-based cross-sectional study	Nepal Demographic and Health Survey data 2011	3190 women who had at least one pregnancy	- 43% had not initiated contraceptive use in following 12 months. - The discontinuation rate was higher in the post-abortion group.

Most scientific studies and publications on abortion practices in Nepal were conducted and published after legalization of the abortion care services since 2002. Nearly 90% studies were conducted in the health facilities of Kathmandu valley and other big cities and followed quantitative techniques. Nearly three-fourths papers were published in the last five years. Out of the total scientific publications more than two-thirds were published in international journals. Similarly, out of the total publications in national as well as international journals, the first authors of more than two-thirds of publications were also Nepalese researchers.

DISCUSSION

This study was focused to assess the abortion practices in Nepal and relevant scientific publications before and after the legalization of abortion care services. After analysis of available literature, we concluded that safe abortion practice has been increasing steeply since legalization of abortion care services in the country. However, unsafe abortions still take place in

various parts of the country, particularly in rural and remote areas.

More than two-third women were aware of legalization of abortion in Nepal. Studies showed

that the medical abortion has high successful rate and fewer side effects, even though both medical and surgical abortions are being practiced in Nepal. For seeking the abortion care husband and health service providers played a major role in the decision making process[16,25,29] which emphasizes the empowerment of women and their reproductive autonomy.

We noticed significant variation in abortion practices by ecological and development sub-regions, residence, education, household wealth quintile, age and number of living children. Merely legalization of abortion is not enough to address the unmet need of safe abortion and reduce the burden of unsafe abortion.[18,42,51]

The decision making for abortion was found to be at risk for most of the Nepalese women due to socio-cultural norms, values and stigmas; however, unmarried women were found to be at higher risk. Still, proportion of unwanted pregnancy is higher in Nepal.[9,27,32] A study showed that one-third of women did not receive any information on contraceptive methods, and 56% left facilities without any method from public health facilities.[47] Many women did not use any contraceptives before termination of pregnancy and nearly one-third women had repeated abortion[17,22,28,35] which indicates that many women sought abortion as alternative of family planning. It further gives us an idea about unmet need of family planning services in Nepal. Similarly, more than half of the women did not initiate contraceptive methods after abortion.[51]

Nearly two-third unsafe abortions were reported in second trimester and pelvic peritonitis was the major cause of morbidities. However, there was a downward trend in the proportion of serious infection, injury and systemic complications[19,21,23] which reflects the increased access of safe abortion care services in Nepal. More than two-thirds women were aware of sex-selective abortion in Nepal. Despite the strong restriction of sex selective abortion, the high sex ratio difference of the new-borne child indicates that the sex-selective abortion is being practicing consistently in Nepal. The increased access to abortion services and sex screening technology along with high value of male child in the society are contributing for sex selective abortion in Nepal.[30]

Despite the intensive review, we confined our search only on the free accessed literature and limited paid accessed WebPages from 1990 to 2014. So, this paper may not cover all the published literature on abortion care practices of Nepal. Out of the accessed literature, this paper primarily concentrated on the original articles either conducted in community or in health facility. The analysis focused mainly on objective, design, methods, sample size, study sites and major findings of the studies. However, this paper reveals the existing situation of abortion care practices in Nepal and scientific publications on this issue. For further assessment of the scientific literature on abortion practices of Nepal, we suggest more systematic reviews as well as meta-analyses studies.

CONCLUSIONS

After legalization of abortion care in Nepal, the utilization of safe abortion care was found to have increased steeply. Many abortion care health facilities were established and a large numbers of health care providers were trained in abortion care. Despite the various efforts, a significant number of unsafe abortion practices still exist in Nepal. Poor access to the abortion care services in remote and rural areas and socio-cultural norms, values, stigmas and so forth are the major contributing factors for unsafe abortion practices in Nepal. For addressing the unsafe abortion issues, state should ensure that all women should have access to the safe abortion services. The abortion should not be promoted instead of contraceptive methods and sex-selective abortion most be prohibited strictly.

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Pregnancy Induced Ocular Changes and Associated Risk of Ocular Medications

Kaur G, Isac DM, Thomas S, Koshy J
Department of Ophthalmology, Christian Medical College, Ludhiana, India

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Pregnancy is associated with various ocular changes which can be either physiological or pathological or modification in pre existing conditions. These changes are mostly transient, however some can become permanent. Physiological ocular changes include change in ocular adnexa, tear film composition, cornea, refraction and intraocular pressure. Pathological ocular changes occur as a result of pregnancy induced hypertension, pseudotumour cerebri, vascular occlusive disorders and amniotic fluid embolism. Some of the pre-existing ocular conditions worsen during pregnancy which include diabetic retinopathy, Grave's disease, toxoplasmosis, pituitary tumours, meningioma and uveal tumours. Others show improvement in pregnancy such as uveitis, optic neuritis and multiple sclerosis. Yet others are associated with exacerbations during postpartum period as optic neuritis. Knowledge of these changes is important for both ophthalmologists and gynaecologists for proper management of these patients. Also the treatment modalities for various disorders differ between pregnant and non pregnant females. The ophthalmic medications should be used cautiously during pregnancy and lactation to avoid harmful effects in the mother and the fetus. The materials published in Pubmed, Google Scholar webpages and standard books have been used for preparing this paper.

Keywords: ocular changes; ocular medications; pregnancy.

INTRODUCTION

Pregnancy is a state characterised by manyfold changes occurring in various organs of the body. Haematological, immunological and cardiovascular systems undergo the most prominent changes. These are mainly attributed to the hormones released by placenta, maternal endocrine glands and the fetal adrenal glands.[1] As with other parts of the body, eyes undergo many changes during pregnancy, which are usually transient in nature but sometimes can become permanent. Knowledge of these changes is essential for both gynaecologists and ophthalmologists. In this article, we reviewed the physiological and pathological ocular changes during pregnancy, the effect of pregnancy on pre-existing eye disorders, the ocular changes during labor and the effect of ophthalmic medications during pregnancy.

METHODS

The pregnancy induced ocular changes were assessed by reviewing the available literature. The literature published in Pubmed, Google Web pages from 1985 to 2012 were searched for this purpose. We also looked at other relevant publications like reports, training manuals and books.

CORRESPONDENCE

Dr Gurvinder Kaur
Department of Ophthalmology, Christian Medical College, Ludhiana, Punjab, India
Email: gurvinder.eye@gmail.com
Phone: +091-9872210103

THE PHYSIOLOGICAL OCULAR CHANGES

The physiological changes in the eye during pregnancy occur at both structural and functional levels.

Ocular adnexa

Chloasma manifests as increased pigmentation around the eyes and cheeks.[2] Spider angioma is a type of telangectasia which commonly develops during pregnancy on the face and upper body.[3] Ptosis has been reported during and after normal pregnancy and is usually unilateral. It is attributed to the defect developing in the levator aponuerosis because of fluid retention and hormonal changes.[4] All these changes resolve during postpartum period. Ocular motility defects can present for the first time during pregnancy for which pre-existing conditions such as Grave's disease need to be ruled out.[5]

Tear composition

Alterations in the composition of the tear film occur during pregnancy. The secretion of lysozyme, a viscous component of the tear film is increased during pregnancy.[6] Disruption of lacrimal acinar cells may lead to pregnancy induced dry eye syndrome.[7] These changes can lead to contact lens intolerance or greasy deposits on the contact lenses.

Conjunctival vessels

In the third trimester, reduced visibility of conjunctival capillaries and conjunctival arteriolar spasm may occur possibly because of the gradual decrease in blood flow rate. The conjunctival veins may take on a granular appearance. These changes reverse during post partum period.[6]

Cornea

There is an increase in both corneal thickness and corneal curvature in the third trimester and in the post partum period. This may lead to temporary alterations in refraction. Hormone induced corneal edema may be responsible for these corneal changes. These changes revert to normal after delivery.[8,9] Corneal sensitivity has been reported to decrease during pregnancy. These changes may aggravate contact lens intolerance during pregnancy.[5,10] Krukenberg spindles can develop early in pregnancy and they tend to decrease in size during the third trimester and postpartum. This is attributed to increasing levels of progesterone and aqueous outflow during pregnancy. Progesterone is known to increase stromal melanin phagocytosis leading to increased clearance of pigment.[11]

Refractive error and accommodation

Transient loss of accommodation has been seen during pregnancy and lactation.[12] The tendency of fluid retention during pregnancy and lactation affects refraction. The patient should be aware of possible fluctuations in vision and that glasses prescribed during this time may become unsuitable later**.** It is advisable that any changes in eyeglass prescriptions should be postponed until several weeks postpartum. The results of refractive eye surgery before, during or immediately after pregnancy are also unpredictable. Thus refractive surgery should be postponed until there is a stable postpartum refraction.[13]

Aqueous circulation

The intra-ocular pressure decreases steadily during pregnancy and continues for several months postpartum.[13] Thus improvement in preexisting glaucoma has been observed during pregnancy. In ocular hypertensives, pregnancy can decrease IOP up to a level of normal limit.[11] The postulated mechanisms for reduced IOP are increase in the facility of aqueous outflow because of increased levels of prostaglandins and β- human chorionic gonadotropin, decreased episcleral venous pressure related to the generalized decrease in peripheral vascular resistance and increased tissue elasticity leading to reduced scleral rigidity.[14]

Visual field changes

There are conflicting reports on changes in visual field during pregnancy. Some studies have described bitemporal contractions while others have reported concentric contraction with enlargement of the blind spot.[6] In some cases the changes begin early in pregnancy and progress until the time of delivery whereas in others the contraction occurs in the last month of pregnancy and remains unchanged. The proposed mechanism includes pituitary enlargement with mechanical compression of the chiasma.[15]

THE PATHOLOGICAL OCULAR CHANGES

There are a few pathological eye changes which are specifically related to the pregnant state of female.

Pregnancy induced hypertension

Pregnancy induced hypertension (PIH) is a systemic hypertensive disorders characterized by generalised edema and proteinuria occuring in the third trimester of pregnancy. These changes alone are termed as preeclampsia. Preeclampsia associated with seizures is termed as eclampsia. Superimposed PIH is the development of preeclampsia or eclampsia in a woman with preexisting systemic hypertension. It is postulated that the disorder results from generalized vasospasm related to increased sensitivity to circulating prostaglandins and angiotensin ll.[6] PIH has an incidence of 5%. It usually occurs after fifth month of pregnancy but may present anytime between 3rd and 9th month of pregnancy. Retinal changes are likely to occur when diastolic BP is more than 100 mm of Hg and systolic BP is above 150mm of Hg.[16]

The most common visual symptom is blurring of vision. Other symptoms reported are photopsia, scotomas, diplopia and cortical blindness. Visual disturbances may be a precursor of a seizure in preeclamptic patients. Widespread arteriolar constriction involving vessels of conjunctiva, retina, choroid, optic nerve and occipital cortex is seen in PIH. The most common vascular abnormality is seen in retinal arterioles, occurring in 40-100% of the PIH patients. Focal arteriolar narrowing is commonly seen which may progress to generalised constriction associated diffuse retinal edema, hemorrhages, exudates and cotton wool spots.[6]

Exudative retinal detachment has been reported in 1% of patients with preeclampsia and in 10% of those with eclampsia. It is usually bilateral and its pathogenesis is related to the choroidal ischemia secondary to an intense arteriolar vasospasm.[17] The patients complain of a relative central scotoma in the affected eye. The majority of patients have spontaneous reattachment with complete recovery of vision with clinical management.[6,18]

Vascular changes in optic nerve may lead to papilledema, acute ischemic optic neuropathy and optic atrophy. Cortical blindness resulting from cerebral vasospasm is a rare complication of PIH. It is usually reversible.[19]

Central serous chorioretinopathy

Idiopathic central serous chorioretinopathy (CSC) is characterized by a serous retinal detachment of the sensory retina. Pregnancy is considered a risk factor for the development of central serous chorioretinopathy.[20] Patient complains of decreased vision, central scotoma, metamorphopsia and micropsia. CSC is often associated with fibrinous subretinal exudation. It usually develops in the third trimester and resolves spontaneously within 1 to 2 months after delivery with visual functions returning to normal or near–normal. The possible mechanisms include physiologic changes in hemodynamics, vascular permeability, autonomic nervous function and hormones that occur during pregnancy.[6]

Pseudotumor cerebri

It is characterized by increased intracranial pressure, normal cerebrospinal fluid content and normal head imaging scan. It is mostly seen in obese females of child bearing age. Pregnancy does not increase the risk of development of pseudotumour cerebri. It is mostly seen during the first and second trimester.[21] It is associated with headache, visual disturbances and papilloedema. Visual field defects are the most common visual disturbances. It is a diagnosis of exclusion. Once diagnosed the decision to treat is based on visual acuity and visual field loss. Medical management is usually effective. Pregnancy is not contraindicated in women with pseudotumor cerebri, and termination of pregnancy is seldom required.[11,22]

Vascular occlusive disorders

A hypercoagulable state exists during pregnancy because of increased platelet adhesiveness, elevated levels of clotting factors, hyperfibrinogenemia, elevated fatty acid levels and reduced fibrinolytic activity. The resultant slowing of venous flow may predispose to thrombosis.[6] Retinal artery occlusion, retinal vein occlusion, disseminated intravascular coagulopathy, amniotic fluid embolism and cerebral venous thrombosis are the vascular occlusive disorders seen during pregnancy.[6]

Retinal artery occlusion

Both branch and central retinal artery occlusions have been reported in pregnancy or in the immediate postpartum period. A Purtscher-like retinopathy with occlusion of multiple retinal arterioles has been described after childbirth. Because of the hypercoagulable state and elevated levels of estrogens, pregnancy itself is a risk factor for retinal artery occlusion.[6]

Retinal vein occlusion

Retinal vein occlusions are less common than arterial occlusions. It has been associated with impaired fibrinolysis and large fluctuations in IOP. Treatment with aspirin has been suggested and the condition resolves after delivery.[6]

Disseminated intravascular coagulopathy

It is a haemorrhagic syndrome resulting from activation of clotting factors and fibrinolytic enzymes which leads to widespread thrombosis and tissue necrosis. It may develop in disorders of pregnancy such as abruptio placentae, complicated abortions, intrauterine death and preeclampsia. Visual symptoms may develop and tend to be of early and sudden onset. Extensive areas of choroidal occlusion, serous retinal detachments and choroidal haemorrhages may occur. Changes tend to be bilaterally symmetrical. Both visual acuity and retinal detachment resolve after recovery from the systemic disorder.[6,23]

Amnoitic fluid embolism

It is serious complication of pregnancy with a high mortality rate. It results in anaphylaxis and disseminated intravascular coagulopathy. Ocular manifestations include bilateral retinal arteriolar occlusions caused by embolization of particulate matter in the amniotic fluid and retinal and choroidal ischemia following massive hemorrhage.[6,24]

Cerebral venous thrombosis

It is a known complication of the post partum period. It presents with severe headache and may progress

to seizures, focal neurological deficits and visual disturbances. Visual field defects occur in 6% of cases. Cortical blindness has also been reported.[6]

EFFECT OF PREGNANCY ON PRE-EXISTING EYE DISEASES

Various pre-existing eye diseases show either worsening or improvement during pregnancy

Uveitis

Uveitis is an ocular disease characterised by inflammation of the uveal tract which include iris, ciliary body and choroid. Pregnancy is associated with lower numbers of flare-ups of non-infectious uveitis compared to the non pregnant state.[25] The immunosuppressive state and high levels of steroids present in pregnant women may have a beneficial effect on uveitis during pregnancy but there is a risk of exacerbation of the disease in the postpartum period.[26]

Uveal tumors

The occurrence of malignant melanoma of the choroid during pregnancy is rare. In contrast, cutaneous melanomas during pregnancy are frequently reported.[6] Although hormonal influence is suggested for the growth of melanomas in pregnancy, recent evidence has suggested that estrogen and progesterone do not have any role in the development or progression of uveal melanomas.[15]

Choroidal haemangiomas undergo rapid growth during pregnancy but some regress postpartum.[27]

Diabetic retinopathy

Diabetic retinopathy is the leading cause of blindness between 24 to 64 years of age. Many females of child bearing age correspond to this group. It has been well documented that pregnancy can worsen pre existing diabetic retinopathy. Diabetic changes that occur during pregnancy are similar to those seen in non pregnant diabetic patients.[28]

Pregnancy is considered as an independent risk factor for development and progression of diabetic retinopathy especially in women with insulin dependent diabetes mellitus. Also the progression of diabetic retinopathy during pregnancy is related to the degree of retinopathy prior to conception, duration of diabetes, metabolic control prior to pregnancy, adequacy of treatment and presence of additional vascular disorders like pre-existing or concomitant hypertension.[15] As the changes and progression are still strongly correlated with duration of diabetes, these females are encouraged to plan pregnancies early in life if possible.[29]

In Diabetes in Early Pregnancy Study (DIEP), progression of diabetic retinopathy was seen in 21.1% women with mild non proliferative diabetic retinopathy and 54.8% women with moderate to severe nonproliferative retinopathy. Also severe form of diabetic retinopathy is associated with higher rates of fetal deaths and congenital malformations. Thus in women with severe proliferative changes before conception; pregnancy should be deferred till the disease is treated and a good glycemic control is achieved. [15,30]

Retinopathy changes that have progressed during pregnancy have a tendency to regress after delivery.[30]

Gestational diabetes is diabetes mellitus that develops during pregnancy. Reports suggest that it has not been associated with the development of retinopathy and thus does not require regular eye examination during pregnancy.[31]

According to The American Academy of Ophthalmology recommendations, all diabetic women should have an eye examination before conception to determine the baseline severity of diabetic retinopathy. The subsequent eye examinations should be planned once in each trimester or earlier as advised by the ophthalmologist according to the severity of retinopathy.[30]

Laser photocoagulation should be considered for pregnant women with severe non proliferative diabetic retinopathy. The treatment should not be delayed till proliferative changes develop because proliferative diabetic retinopathy has a tendency to progress despite treatment. Regular follow-ups are required during pregnancy and in the postpartum period in this group of patients until the retinopathy has stabilized.[32]

Indications for surgery during pregnancy include tractional retinal detachment, non-clearing vitreous haemorrhage and neovascular glaucoma.[15]

Diabetic macular edema may develop or worsen during pregnancy. It is increased by coexisting hypertension, nephropathy and proteinuria. The treatment should be delayed until postpartum period as there is possibility of spontaneous recovery. Cases in whom clinically significant macular edema persists after delivery should be treated with focal laser photo-

coagulation.[33,34]

Grave's disease

Graves' disease is the most common cause of hyperthyroidism in pregnancy. It is an important cause of unilateral and bilateral proptosis. Graves' disease aggravates in the first trimester and after delivery but improves in the second and third trimester.[6,35] Rarely the fetus can be affected because of transplacental passage of maternal IgG. Pregnant female with Graves's orbitopathy is treated in the same manner as in a non-pregnant female. Mothers with active Graves' disease should be treated with antithyroid drugs, because in untreated cases there is high rate of abortions, intrauterine and perinatal deaths, and premature births. The lowest possible dose should be used so as to maintain maternal free thyroxine levels at or just above the upper limit of the normal non pregnant reference range. The drug of choice in pregnancy is propylthiouracil.[6,36]

Toxoplasmosis

Primary infection in mother during pregnancy can result in transplacental transmission of infection to the fetus. Latent ocular toxoplasmosis may reactivate during pregnancy in the mother. Toxoplasmosis infection typically presents as retinochoroiditis. Decreased vision and floaters are the most frequent symptoms. Active infection typically presents as grey-white retinal necrosis with choroiditis, vasculitis and vitritis. The diagnosis is based on clinical findings and can be supported by the detection of antibodies and Toxoplasma gondii DNA using polymerase chain reaction (PCR).[15] Women with active infection during pregnancy should be monitored for antibiotic levels once per trimester. If the titres increase, therapeutic abortion may be considered. If titres remain stable, pregnancy can be continued with small risk to the fetus.[6,37]

Pituitary tumours

Prolactinomas are the most common functioning tumours seen in the pregnant patients. They present a potential risk in pregnancy because pituitary gland shows physiological growth during pregnancy.[38] Adenomas less than 1.0 cm in size are defined as micro- prolactinomas and those more than 1.0 cm are macro-prolactinomas. Hormone fluctuations during pregnancy can stimulate estrogen receptors on the prolactinoma which can lead to enlargement of the tumour.[39] Patient presents with headache which may be followed by progressive visual field disturbances. Bi-temporal hemianopia is most common visual field defect seen. Homonymous hemi-anopia can also be seen in advanced cases. An untreated pituitary adenoma appears to increase the risk of miscarriage.[15,40]

Asymptomatic patients should have visual field testing every 3 months to monitor tumour growth and compression of the visual pathways. Symptomatic pituitary adenomas require the combined efforts of an ophthalmologist, obstetrician, neurosurgeon, and endocrinologist to decide upon appropriate medical, surgical, or radiation treatment. Bromocriptine, a dopamine agonist, can lower prolactin and cause shrinking of the tumor. Bromocriptine is considered safe during pregnancy. If the tumor does not respond to drugs, transsphenoidal hypophysectomy can be planned during the second trimester.[11]

Multiple sclerosis and optic neuritis

Patients with multiple sclerosis show stability or even improvement during pregnancy. But there is a significant increase in the risk of relapse in the postpartum period especially first three months after delivery.[6,41] Puerperal immune-mediated changes are responsible for activation of optic neuritis associated with relapsing multiple sclerosis. This may result in acute loss of vision in breastfeeding women and multiple sclerosis should be considered as a cause for lactation associated loss of vision when there is no other clear cause.[11,42] However studies have shown that pregnancy does not appear to exert any adverse effect on the overall course of the disease neither does multiple sclerosis has any adverse influence on fetus, pregnancy and delivery.[6]

Meningioma

Meningiomas are benign, slow growing tumors with male to female ratio of 1:3. Meningiomas may show a rapid growth during pregnancy that may be attributed to the presence of progesterone and estrogen receptors in tumour cells. The patient presents with a variety of visual disturbances like visual loss, visual field defects, diplopia, disc edema, optic atrophy, cranial nerve palsies and proptosis.[43]

Meningiomas regress postpartum but may regrow during subsequent pregnancy. Asymptomatic patients should be closely observed. The mainstay of treatment is surgical intervention. Management of meningioma in pregnancy depends on the severity

of the symptoms and stage of gestation. In patients with mild symptoms in the last trimester, surgery is deferred until postpartum period. In cases with severe visual loss in last trimester, induction of labour and intracranial surgery is advised. If a patient comes with severe symptoms early in pregnancy, therapeutic abortion can be considered. Those who want continuation of pregnancy, steroids and hyperosmotic agents can be tried to decrease cerebral edema so that surgery can be delayed till the fetus is mature enough for delivery.[6,33]

Ocular migraine

There is a greater prevalence of migraine headaches among women suggesting that hormone levels especially estrogen influence the occurrence, frequency and severity of migraine attacks. There may be a change in the frequency of migraine attacks during pregnancy. Both increased and decreased frequencies have been noted.[17]

OCULAR CHANGES DURING LABOUR

Sheehan's syndrome

Sheehan's syndrome or pituitary apoplexy occurs as a result of ischemic pituitary necrosis due to severe postpartum haemorrhage. It may be rarely seen without massive bleeding or after normal delivery. This condition may present as a sudden onset of headache, visual loss and/or ophthalmoplegia. Enlargement of pituitary gland, small sella size, disseminated intravascular coagulation and autoimmunity have been suggested to play a role in the pathogenesis of Sheehan's syndrome in women who suffer from severe postpartum hemorrhage.[11,44]

EFFECT OF OPHTHALMIC MEDICATIONS ON PREGNANCY

Little is known about the risk of ophthalmic medications in pregnant and nursing women. As a general rule, the lowest possible dosage should be used. When using topical medications, nasolacrimal compression and temporary punctual occlusion could be performed to minimize systemic drug absorption.[45]

Anti-glaucoma medications:

Topical beta blockers (e.g. timolol) come under FDA risk category C in first trimester while D in 2nd and 3rd trimester. Beta blockers can cause intrauterine growth retardation if used in 2nd and 3rd trimester and persistent neonatal blockade if used near term. They should be avoided during pregnancy and should be discontinued 2 to 3 days before delivery to avoid inhibiting uterine contractility. They should not be used during lactation also.[45,46]

Topical and systemic carbonic anhydrase inhibitors (e.g. acetazolamide, dorzolamide) are contraindicated during pregnancy because of potential teratogenic effects. They are contraindicted during lactation because of the adverse renal and hepatic effects in the infant.[45,46]

Prostaglandin analogs (e.g. latanoprost) fall in FDA risk category C. These are not well studied and the reports that do exist are conflicting. Their use is generally contraindicated in pregnant and lactating women.[45,46]

Mydriatics (dilating drops)

Use of occasional dilating drops during pregnancy for the purposes of ocular examination is safe. However, repeated use is contraindicated in pregnancy because of the potential teratogenic effects of both parasympatholytics (e.g. atropine) and sympathomimetics (e.g. phenylepinephrine).[6,33,45]

Topical corticosteroids

They come under FDA risk category B. Systemic corticosteroids are contraindicated in pregnancy because of teratogenic effects, stillbirths, intrauterine growth retardation and congenital cataract. Topical steroids have not been reported to have an adverse effect on pregnancy but the safety of their use has not absolutely been established. Therefore use with care and avoid their prolong use in pregnancy and lactation.[6,33,45]

Antibiotic eye preparations

Antibiotics which should be avoided during pregnancy are gentamycin, streptomycin, neomycin, kanamycin and fluorinated quinolones like norfloxacin and ciprofloxacin are not considered safe during pregnancy. Erythromycin and polymyxin B appears to be the safest antibiotics during pregnancy and polymyxin B and the sulfonamides are safest in lactation.[33,45]

Antiviral eye preparations (acyclovir eye ointment)

These fall under FDA risk category B. Topical acyclovir has not been studied in pregnant woman. However this medicine has been shown to be teratogenic in animal studies. Thus it should be used with caution in pregnancy and lactation.[6,33,45]

Fluorescein dye

It comes under FDA risk category B. No known teratogenic effects of fluorescein during pregnancy exist. In literature, there is evidence suggesting the use of fluorescein after due consideration of risk and benefit.[47] Still most of the retinal specialists avoid fluorescein angiography during pregnancy, especially first trimester. Effect in lactating women is not known.[6,33]

Topical anesthetic

No known contraindications exist to use of topical anesthetic drops in pregnancy.

Anti-allergic eye drops

Sodium cromoglycate 2% (FDA risk category B) eye drop is safe to use in pregnancy while antihistaminic eye drops containing naphazoline (FDA category C) should be avoided.[6,33,45]

CONCLUSIONS

Knowledge of various ocular changes in pregnancy helps to differentiate physiological changes from pathological disorders of the eye in pregnant females, in whom treatment may differ from that in non pregnant females. Care should be taken while prescribing ocular medications to pregnant and lactating females so as to maintain the health of both mother and the baby.

DISCLOSURE

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A Study of Complications following Self-administration with Medical Abortion Pills

Giri A, Srivastav VR, Suwal A, Sharma B
Department of Obstetrics and Gynecology, Nepal Medical College and Teaching Hospital, Kathmandu, Nepal

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Aims: The objective of this study was to find out the complications following self-administration with medical abortion pills.

Methods: A prospective descriptive study was conducted in Department of Obstetrics and Gynecology,Nepal Medical College over a period of two years from January 2013 to December 2014 among 48 women who were admitted with abortion complications and also gave history of self-administration of abortion pills.

Results: During the study period, 48 women with history of self-medication with abortion pills were admitted with various abortion complications. There were 60% of women who had consumed abortion pills within approved nine weeks gestation while 19% had consumed after nine weeks and 21% after twelve weeks. Majority (60%) were admitted with incomplete abortion, 4% with missed abortion, 13% with continued live pregnancy, 6.5% with septic abortion and 6.5% with ectopic pregnancy. Anemia was present in 79% of patient. More than one third of the patient had severe anemia and blood transfusion was needed in 52%. Surgical evacuation was required in 71% of patient; medical abortion with repeat doses of mifepristone and misoprostol was done in was done 13% and 6.5% needed laparotomy for ectopic pregnancy.

Conclusions: Though medical abortion is considered to be highly effective and safe procedure, unsupervised self-administration of medical abortion pills was associated with serious maternal morbidities. There should be some policy to restrict over the counter sale of this medicine.

Keywords: complications; medical abortion; self-administration.

INTRODUCTION

Each year an estimated 42 million pregnancies end in induced abortion, out of which 20 million are performed under unsafe condition. Unsafe abortion is responsible for 13% of maternal deaths worldwide.[1]

World Health Organization (WHO) recommends medical abortion using 200 mg of oral mifepristone followed by 800 mcg of misoprostol vaginally, buccally or sublingually 24-48 hours later for termination of pregnancy up to nine weeks. WHO guidelines necessitate women requesting medical abortion to confirm pregnancy, estimate correct gestational age, and locate site of pregnancy, rule out contraindications and it also recommends that the person or facility providing MA should have back up facility in case of failed or incomplete abortion.[2]

Medical abortion was approved in Nepal since 2009 with good success rate. As of September 2012, medical abortion was scaled up in all public hospitals, selected private hospitals and some non governmental organizations throughout the 75 districts of the country to make it easily accessible to all women.[3] Despite the advances in MA services in Nepal, some women still resort to pharmacies for over the counter procurement of drugs to induce abortion. Due to unrestricted availability of these drugs, women consider this to be extremely safe option and are unaware of life threatening complications like excessive hemorrhage, sepsis or undiagnosed ectopic pregnancy that are not uncommon with its unsupervised use. This study was carried out to find the consequences of self-administration of medical abortion pill by women to induce abortion.

CORRESPONDENCE

Dr Amrita Giri
Department of Obstetrics and Gynecology,
Nepal Medical College and Teaching Hospital, Kathmandu,
Email: amritatuladhar@yahoo.com
Phone: +977-9841222129

METHODS

This study was done in the Department of Obstetrics & Gynecology, Nepal Medical College over a period of two years from January 2013 to December 2014 after due permission from hospital ethical committee. All the women admitted to gynecology ward with diagnosis of any abortion and early pregnancy complications were interviewed. Among them, those

women who gave history of self-administration of medicines to induce abortion and admitted for further management of complications were identified and enrolled for the study after an informed consent. Self-administration means that these women did not visit any registered and trained medical practitioner or any health facility recognized to give medical abortion pill for consultation. Woman or her close relatives purchased MA drugs from the pharmacy over the counter without prescription. They were followed till discharge and the treatment they received were reviewed. All the relevant data were entered into specially designed proforma and the data was analysed. The data collected included age of the women, parity, gestational age at which abortion pill was taken, reason for admission to hospital, treatment received, need for blood transfusion, intensive care unit (ICU) admission and duration of hospital stay. Severity of anemia was defined according to Indian Council of Medical Research (ICMR) classification. Blood transfusion was given when hemoglobin level was less than 8 gm%.

RESULTS

During the study period of two years, 48 women who gave history of self-administration of medical abortion pills were admitted to our hospital with various complications. The demographic profile of these women are shown in Table 1.

Table 1. Age and parity of women (n=48).

Age of women	**Number**	**%**
≤19 years	2	4
20-29 years	25	52
30-39 years	21	44
Parity of women		
Primigravida	10	21
Multigravida	38	79

The abortion pills were used by women of all ages, youngest one being sixteen years of age. In this study, 79% of women were multigravida and 21% were primigravida.

The gestational age at which abortion pill was consumed is shown in Table 2. In this study, we found that 40% had done medical abortion at gestational age of more than nine weeks.

Table 2. Gestational age at consumption of medical abortion pills (n= 48).

Gestational age at which MA pills consumed	Number	Percentage
<9 weeks	29	60
9-12 weeks	9	19
>12 weeks	10	21

All of these women had confirmed their pregnancy by doing urine pregnancy test either at home or at the pharmacy. Gestational age was confirmed only by calculating months from last menstrual period and clinical bimanual examination and/or USG were not done. Among these women, only 8% could recall the name of the drug they had consumed and rest 92% did not know the name of the medicines. There were 42 (87.5%) women who agreed on consuming five pills in total but the way they had taken the pills were different. The amount of money paid for MA pills ranged from NRs 700 to 3000.

Table 3. Regimen of self administration of abortion pills (n=48).

Regimen of MA drug	**Number**	**%**
1st day one tablet orally 24 hours later 2 tablets orally 36 hours later another 2 tablets orally	14	29
1st day one tablet orally 24 hours later 4 tablets orally	16	33
1st day one tablet orally 12 hours later 4 tablets orally	4	8
1st day one tablet orally 48 hours later 4 tablets buccally	3	7
1st day one tablet orally 24 hours later 2 tablets orally 48 hours later another 2 tablets orally	5	11
Only one tablet orally	2	4
Only four tablets orally	4	8

Table 3 shows the way they have consumed the abortion pill. This table shows that only three women had taken the pills in the standard way as stated in medical abortion guideline of Nepal. They were not given any emergency contact number and did not know where to go to in case of emergency.

Twenty-nine (60%) patients presented with vaginal bleeding on and off and were diagnosed as incomplete abortion where as two patients had to be resuscitated for hemorrhagic shock (Table 4).

Table 4. Diagnosis at admission (n=48).

Diagnosis at admission	Number	%
Incomplete abortion	29 (2 with hemorrhagic shock)	60
Complete abortion	5	10
Missed abortion	2	4
Continued live pregnancy	6	13
Septic abortion	3	6.5
Ectopic pregnancy	3	6.5
Total	48	

There were 5 (10%) patients diagnosed as complete abortion with anemia, 2 (4%) as missed abortion, and 6 (13%) as continued viable pregnancy. All six patients with continued live pregnancy had taken the abortion pills after nine weeks of gestation. One patient with continued live pregnancy was diagnosed as late as twenty weeks.

There were 3 (6.5%) patients who presented with high-grade fever, abdominal pain and vaginal bleeding and were diagnosed as septic incomplete abortion. One patient with septic abortion was in septic shock and was managed in ICU. There were 3 (6.5%) patients diagnosed as ectopic pregnancy with two presenting with hemoperitoneum in shock and one as unruptured ectopic pregnancy and all of them underwent laparotomy.

Among these 48 women, 38 (79%) had varying severity of anemia, which was managed with blood transfusion in 25 women.

Table 5. Severity of anemia and need for blood transfusion (n= 48).

Severity of anemia*	Number	%
Very severe anemia Hb < 4gm%	6	12.5
Severe anemia Hb 4 – 6.9 gm%	12	25
Moderate anemia Hb 7 – 9.9 gm%	14	30
Mild anemia Hb 10 -10.9gm%	6	12.5
No anemia Hb > 11 gm%	10	20
Blood transfusion		
Two units	14	
Four units	5	
Five units	3	
Six units	3	

**ICMR classification*

Table 5 shows the severity of anemia and the need for blood transfusion in these women. It was very alarming to see that 12.5% of women presented with very severe anemia which can sometimes be a life threatening complication. All patients presenting with very severe anemia had done medical abortion after 12 weeks of gestation. There were 11 (23%) patients who needed four or more units of blood transfusion.

The management of the patients done at our hospital is shown in Table 6. All the women who had failed abortion with live pregnancy opted for termination of pregnancy. All these six women had complete abortion at our center with repeat administration of mifepristone and misoprostol. Suction evacuation was done in 34 (71%) women in this study i.e. 29 for incomplete abortion, 2 for missed abortion and 3 for septic incomplete abortion. Laparotomy was done in all three patients presenting with ectopic pregnancy. Three patients needed admission to ICU. One patient with septic abortion in septic shock and two others with very severe anemia were managed in ICU.

Table 6. Management of patients (n= 48).

Diagnosis	Number	Management	Number
Incomplete abortion	29	Suction evacuation (S&E)	29
Missed abortion	2	Suction evacuation	2
Continued live pregnancy	6	Medical abortion	6
Complete abortion with anemia	5	Correction of anemia	5
Septic abortion	2	I/V antibiotic & suction evacuation	2
Septic abortion in septic shock	1	I/V antibiotic, Inotropes, S&E	1
Ectopic pregnancy	3	Laparotomy	3

DISCUSSION

WHO defines unsafe abortion as a procedure for terminating an unintended pregnancy either by individuals without the necessary skills or in an environment that does not conform to minimum medical standard or both.[4] Unsafe abortion particularly invasive method can lead to severe maternal morbidity and mortality due to complications like sepsis and uterine perforation.[5] To decrease the incidence of unsafe abortion and thereby reduce maternal mortality ratio of country, Nepal legalized abortion in year 2002. Despite significant progress in comprehensive abortion care services in

the country, many Nepalese women continue to rely upon illegal and unskilled providers for abortion. A recent national study found that approximately 7% of maternal mortality were due to abortion between April 2008 and April 2009.[6]

WHO in the year 2003 stated that medical methods of abortion were effective and safe. Based on international evidence about its safety and efficacy and to make abortion services readily available and accessible to all women especially to poor rural women of Nepal, medical abortion using mifepristone and misoprostol was approved in Nepal since 2009. Medical abortion is even being provided at primary health center and health post of Nepal by midlevel health care providers with high success rate of 98% and low complications rate of 0.3% irrespective of doctors.[7]

Over the counter sale of MA tablets by pharmacies is not permitted in Nepal. Despite advances in facility and restrictions in sale of drugs, women still visit pharmacies to procure drugs for medical abortion as both registered and unregistered brands of abortion pills are easily available at pharmacy shops. The 2011 Nepal Demographic and Health Survey showed that among the women who had an abortion in the five years preceding the survey, 19% had used tablets for their last abortion. Moreover, 5% of them had obtained the tablets from a pharmacists or medicine shops.[8]

In our study, 83% women were multiparous which was similar to the study by Mishra et al[9] also reported that 78% of women who had self administered abortion pills were multiparous. This shows that women rely on medical abortion and consider it as a better method to space the birth rather than using contraception and preventing unwanted pregnancy in the first place.

Though the recommendation on medical abortion in Nepal has been restricted to early first trimester i.e. up to nine weeks or sixty three days from last menstrual period, 19% of the patient in our study used the pills between 9-12 weeks of gestation and another 21% used it after 12 weeks which was quite alarming. In their study, Nivedita et al[10] reported that 10% of patients had consumed abortion pills after nine weeks and 17.5% after twelve weeks which was similar to our study. Studies indicate that the complications of second trimester medical abortion when compared with first trimester medical abortion are high with an increased risk of bleeding, sepsis and surgical evacuation.[11] Here also complications were seen more in women who had attempted second trimester abortion. All six women presenting with very severe anemia were of this group. Half of the patient with continued live pregnancy had attempted abortion after twelve weeks and two out of three cases of septic abortion were of this group showing high complication rate. Thus it is very important to confirm the gestational age before prescribing the medical abortion pill which was not done here. Even the women perceived medical abortion to be extremely safe option of termination of pregnancy even in hands of untrained personnel and at any gestational age.

In our study, 60% of the patients had incomplete abortion, 13% had continued live pregnancy, 6.5% presented with septic incomplete abortion and 6.5% had ectopic pregnancy. Similar to our study, Nivedita et al[10] reported that the rate of incomplete abortion was 62.5%, septic incomplete abortion 7.5% and failed abortion 22.5% with 80% of these patient requiring surgical evacuation. In another study conducted by Thaker et al[12] 70.2% patient had incomplete abortion and 10.8% had failed abortion. In the study conducted by Bennett et al,[13] medical abortion using correct regimen of mifepristone and misoprostol was associated with high success rate of 96.5%, incomplete abortion as 1.2%, failed abortion as 1.45% and missed ectopic pregnancy as 0.08%.

The high rate of incomplete abortion and failed abortion in this study could be because the medical abortion regimen used by the pharmacist was not the ideal one recommended by WHO or government of Nepal. Moreover all six patients with failed abortion had consumed medical abortion pill after nine weeks of gestation.

The incidence of ectopic pregnancy was 6.5% in our study and similar to that reported as 5.4% by Thaker et al.[12] A recent review of the published literature about medical abortion found that ectopic pregnancy went undetected in only 10 of every 44,789 women (0.02%) undergoing medical abortion if all guidelines were followed.[14] As these women were not counseled properly regarding the possibility of extra uterine pregnancy and bimanual examination also was not

done to confirm gestational age and assess the uterine size, ectopic pregnancy went undetected. Moreover, ultrasonography was also not done in any patient if they did not expel product of conception.

In this study, because of unsupervised use of abortion pill and its erratic drug schedule, many women had excessive and prolonged vaginal bleeding leading to anemia. There were 6% women with very severe anemia and 12% with severe anemia in this study. Similarly Thaker et al[12] reported the incidence of severe anemia in their study as 13.5%. It is very alarming to see 6% of patients being admitted with very severe anemia (Hemoglobin < 4 gm %), as this could be life-threatening complication sometimes. Blood transfusions were needed in 23 (52%) of patients in our study where 11 patients required four or more unit of blood transfusions. The rate of blood transfusion is higher than that reported as 23% by Ojha et al.[15]

In this study, there were 3 (6.5%) cases of septic abortion with one patient in septic shock. Similarly Ojha et al[15] reported the incidence of infection after self administration of MA as 3.5%. In another study conducted by Bajwa et al,[16] the incidence of sepsis was 6.54% following medical abortion which was similar to our study. In a systematic review covering 46,421 women, the frequency of infection after medical abortion done in ideal condition was less than 1%.[17] The higher incidence of infection here could be because these women presented to hospital late, mostly after 14 days of termination of pregnancy and all of them had attempted medical abortion after 12 weeks.

CONCLUSIONS

Medical abortion is effective and safe when carried out under medical supervision. Unsupervised use of medical abortion pills were associated with many complications like higher chances of incomplete abortion, failed abortion, hemorrhage leading to anemia and needing blood transfusion, septic abortion and missed ectopic pregnancy. So over the counter sale of medical abortion pill should be restricted. Moreover the need to educate women regarding the use of these drugs should be emphasized.

DISCLOSURE

The authors report no conflicst of interest in this work.

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Medical and Surgical Abortion in the Second Trimester of Pregnancy

Karki A, Dangal G, Pradhan H, Shrestha R, Bhattachan K
Department of Obstetrics and Gynaecology, Kathmandu Model Hospital, Nepal

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Aims: This study was done to know the demographic profile of women undergoing second trimester abortion at Kathmandu Model Hospital. The aim was to see the success rate of combination of mifeprostone and misoprostol for the medical induction and misoprostol alone for the cervical dilation in case of surgical evacuation.

Methods: A retrospective study was done by looking at the profiles of 540 clients on whom second trimester abortion was performed during the period of October 2010 to October 2014. Twenty-nine women underwent dilatation and evacuation (D&E) with misoprostol cervical priming, and 510 underwent medical induction with mifeprostone and misoprostol whereas one client absconded. Furthermore, the reasons for seeking second trimester abortion were also investigated.

Results: It can be seen that the age of women undergoing second trimester abortion at Kathmandu Model Hospital was greatest (33.33%) for the age group of 26-30 years. Most women were illiterate (31.67%) and a majority of the women were housewives (89.81%). A greater proportion of the women had never undergone abortion. Mental cause appeared to be the major reason for abortion constituting 82.04%. Success was 90.58%, expulsion with total five doses of misoprostol. The median induction to abortion time was 4-7 hours. The expulsion hours increased as the gestational age increased. The median number of dose of misoprostol required was two for medical induction and three for surgical abortion.

Conclusions: Mifeprostone and misoprostol, as combination was a good method for the medical induction of second trimester pregnancy and misoprostol alone for the cervical preparation in surgical evacuation was promising.

Keywords: dilation and evacuation; medical induction; mifeprostone; misoprostol; second trimester abortion.

INTRODUCTION

More than one third of the approximately 205 million pregnancies that occur each year worldwide are unintended and about 20% of them end in induced abortion.[1] A vast majority (90%) of these abortions take place during the first trimester of pregnancy. In spite of legalizing abortion and making safe abortion available at an affordable price at accessible distance to almost everyone, unsafe abortion, especially second trimester abortion is still a major health problem in Nepal. Through past studies, it has been established that second trimester abortions carry higher risks of complications than first trimester abortions.[2,3] Even though second trimester abortion constitutes only 10-15 % of all induced abortions globally, they are the cause of a vast proportion of abortion related complications.[4] In an effort to reduce the complications brought forth by surgery, the administration of mifeprostone and misoprostol is now considered to be a successful and effective method for second trimester abortion.[4] The advantages of administering these drugs are two-fold: reduction in unwanted surgical evacuation and a cheaper cost than the former, which can be especially useful in a developing country like Nepal.[4] In the past years, several studies have shown that misoprostol is an effective means in the termination of pregnancy in the first trimester.[5,6] More recently, it has been shown that misoprostol has also proven successful in the termination of pregnancy in the second trimester.[7-9]

We intended to see the success rate of combination of mifeprostone and misoprostol for the medical induction, median time required for expulsion and misoprostol alone for the cervical dilation in case of surgical evacuation. Furthermore, the reasons for seeking second trimester abortion were also investigated.

CORRESPONDENCE

Dr Aruna Karki
Department of Obstetrics and Gynaecology
Kathmandu Model Hospital, Nepal
Email: aruna.karki@gmail.com
Phone: + 977-9851042579

METHODS

This is a retrospective study done at Kathmandu Model Hospital (KMH). Five hundred and forty clients

(Medical Induction- 510 and D & E- 30) had second trimester abortion performed from October 2010 to October 2014. Institutional review committee approval was taken for this study. Proper counseling was done and an informed consent was taken from all women before performing the procedures.

For medical induction clients were given tablet mifeprostone 200 mg under supervision at abortion service room and asked to return after 36 hours. On the day of the second visit, misoprostol 800 mcg as loading dose was administered by buccal or vaginal route as per client's choice followed by four hourly misoprostol 400 mcg until complete expulsion or total five doses. In case of buccal route, after thirty minutes the remainder of the medicine was asked to swallow with water. In high risk clients like previous caesarean section and grand multigravida the loading dose was 400 mcg and interval was six hourly or total of five doses. In case of repeat cycle a 24 hours gap was maintained. For surgical method, only misoprostol was used for cervical priming. Misoprostol was administered via buccal or vaginal route 400 mcg four hourly and in high risk as mentioned earlier six hourly until cervix becomes favourable a total of not more than five doses. The client's personal record form was filled properly. Structured questionnaires given to the clients were used for this study and this data were further analyzed.

RESULTS

The study showed that the age group of women undergoing second trimester abortion at KMH was greatest in the age group 26-30 years (n=180; 33.33%). Majority of them were housewives (n= 485; 89.81%) and illiterate (n= 171; 31.67%). Most of the women seeking abortion were from Kathmandu (n=290; 53.70%) and 202 clients (37.41%) were from outside Kathmandu, Lalitpur and Bhaktapur. Majority of the clients (n=438; 81.11%) never experienced abortion in the past. Mental ill-health constituted the major proportion (n=443; 82.04%) of reason for abortion followed by unmarried status (n=64; 11.85%) and fetal malformation (n=26; 4.81%). Minor reasons encountered were maternal co-morbid conditions, rape and incest (Table 1).

Table 1. Demography and clinical features of clients (n=540).

Characteristics	Number (%)
Age	
16-20 yrs	79 (14.63)
21-25 yrs	130 (24.07)
26-30 yrs	180 (33.33)
31-35 yrs	90 (16.66)
36-40 yrs	42 (7.77)
Above 40	19 (3.52)
Education	
Illiterate	171 (31.67)
Primary education	65 (12.04)
Secondary education	122 (22.59)
Higher secondary	101 (18.70)
Bachelor	61 (11.29)
Master	20 (3.70)
Profession	
Housewife	485 (89.81)
Student	52 (9.63)
Service holder	3 (0.56)
Area	
Kathmandu	290 (53.70)
Lalitpur	18 (3.33)
Bhaktapur	30 (5.55)
Outside Kathmandu, Lalitpur and Bhaktapur	202 (37.41)
Parity	
Nullipara	157 ((29.07)
Multipara	383 (70.93)
Past abortions	
No abortion	438 (81.11)
1 abortion	69 (12.77)
>1 abortion	33(6.11)
Causes of Abortion	
Unmarried	64 (11.85)
Fetal malformation	26 (4.81)
Mental causes	443 (82.04)
Maternal illness	3 (0.56)
Rape	3 (0.56)
Incest	1 (0.19)
Others	
History of previous caesarian section	28(5.19)

The gestational age of the clients were tabulated in Table 2, which depicts that most of the clients were in early gestational age of 12-14 weeks (n=283; 52.40%).

Table 3 illustrates the type of contraception used by the clients before and after abortion. Most of

them did not use contraceptives before abortion and refused after abortion too. They postponed choice of contraception for the time of follow up after consulting with husbands.

Table 2. Gestational age of clients (n=540).

Gestational age	Clients (%)
12-14 weeks	283 (52.41)
15-17 weeks	193 (35.74)
18-20 weeks	66 (12.22)
21-23 weeks	25 (4.63)
24 weeks and above	23 (4.26)

Table 3. Type of contraception used by clients before and after abortion (n=540).

Contraception Type	Number (before abortion)	Number (after abortion)
No contraceptives	459	505
Implant	1	0
Depo Provera	30	7
Vasectomy	1	1
Minilap	1	1
OCP	28	14
Condom	13	8
IUCD	7	4

Out of the 540 clients, 510 (94.44%) clients had medical induction and 29 (5.37%) clients had surgical evacuation whereas one absconded. Thirty-four clients (6.67%) of medical induction were converted to surgical evacuation.

Table 4. Misoprostol dose for medical induction.

Number of dose	Number of clients
Mifeprostone only	1
1	74
2	219
3	169
4	44
5	22
Repeat cycle	14

In medical induction, as shown in Table 4, one client expelled with mifeprostone alone and 74 expelled with the loading dose only. Highest number of clients expelled with two doses. Fourteen clients required repeat cycle of misoprostol. Exploration was required in 42 clients. The mean expulsion hours according to gestational age is given in the Table 5.

Table 5. Mean expulsion hours in medical induction according to gestational age.

Gestational age	Mean expulsion hours
12-14 weeks	5 hours
15-17 weeks	6 hours
18-20 weeks	7 hours
21-23 weeks	7 hours
24 weeks and above	9 hours

The expulsion hour increased in higher gestational age. Most of the clients (n=245) expelled within 4-7 hours (Table 6).

Table 6. Expulsion hours for medical induction (n= 510).

Expulsion Hours	Number (%)
1-3 hours	99 (19.41)
4-7 hours	245 (48.04)
8-10 hours	64 (12.55)
More than 11 hours	54 (10.59)
Repeat doses	14 (2.75)
Medical induction converted to D&E	34 (6.67)

In surgical method, out of thirty planned clients one absconded. In most of the clients cervix was well prepared in 2 (n=10) or 3 (n=12) doses (Table 7).

Table 7. Misoprostol dose for surgical abortion (n=29).

Number of dose	Clients (%)
1	4 (13.7)
2	10 (34.4)
3	12 (41.3)
4	2 (6.8)
5	1 (3.4)

DISCUSSION

Misoprostol with or without mifeprostone has been investigated for medical abortion in the second trimester. This study used both mifeprostone and misoprostol for medical induction and only misoprostol for dilatation and evacuation.

In our study one patient absconded after taking

mifeprostone and one patient had ruptured uterus. Both were excluded from analysis. The age of the clients ranged from 16-46 years out of which 31.67% (n=171) were illiterate, 89.81% (n=485) were housewives. Around seventy one percent (n=383) were multipara, gestational age ranged from 12-24 weeks and 52.41% (n=283) were between 12-14 weeks. The commonest reason for abortion was mental ill-health 82.04% (n=443). In a study from Nepal, the age range was 14-45 years, and 50% were illiterate. In that study 84% were multipara, gestational age range was 12-24 weeks and 56% were between 12-14 weeks.[10]

In our study success was 90.58% (n=462), expulsion with total five doses of misoprostol which is comparable to 91.4% in a study from Hong Kong[11] and 97% in a study from Scottland.[7] There were 70.93% (n=383) clients who were multiparous, 82.04% (n=443) wanted abortion due to mental ill-health and 11.85% (n=64) were unmarried in comparison to a study from Nepal where multiparity was 61.4% and 5.26% were unmarried.[10] The median induction to abortion time was 4-7 hours. The expulsion hours increased, as the gestational age increased as the study showed median induction to abortion time for more than 24 weeks was 9 hours. The median induction to abortion time was 6.7 hours in study of Ngai et al[12] and 7 hours in study of Elami-Suzin et al[13] which are comparable to our study.

In this study, 7.78% (n=42) required exploration of uterine cavity due to retained placenta or bleeding, whereas 5% in a study of Goh et al[14] and 8.1% in a study of Rose et al[15] required exploration.

Surgical evacuation was done in 29 cases. The median number of dose of misoprostol required was three whereas in the study from Nepal, the median number of dose of misoprostol was two.[10] In our study, 6.67% (n=34) of medical abortion were converted to surgical abortion, but none of the surgical abortion was converted to medical abortion. But Shrivastava et al[10] reported a 5% conversion of surgical abortion to medical abortion.

Out of the total 2298 cases of abortion performed during the study period, 24% were for second trimester abortion, 22% were for medical abortion up to 9 weeks and 54% were surgical abortion below 12 weeks. In the survey of Health Ministry of Nepal as cited by Thapa[16] 3% were for second trimester abortion, 74% were medical abortion and 23% were for surgical abortion. The difference might be due to not including the data of private centers that give abortion service in greater number.

CONCLUSIONS

The combined use of mifeprostone and misoprostal had a good outcome in medical induction of second trimester abortion. Misoprostal only can be used for the cervical preparation in case of surgical abortion for second trimester.

DISCLOSURE

The authors report no conflicts of interest in this work.

No violation of human rights and safety.

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Near-miss Obstetric Events in a Tertiary Care Teaching Hospital in Nepal: An Audit

Gurung BS[1], Koju RB[2], Dongol Y[3]

[1]Department of Obstetrics and Gynaecology, KIST Medical College, Lalitpur, Nepal, [2]Department of Anaesthesia and Critical Care, KIST Medical College, Lalitpur, Nepal, [3]Department of Biochemistry, KIST Medical College, Lalitpur, Nepal

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Aims: This study aims to determine the frequency of near-miss obstetric events and analyze its nature such as reasons for near-miss, organ dysfunction associated and critical management required among pregnant women managed over a 3-year period in a Tertiary Care Teaching Hospital in Nepal.

Methods: This hospital based prospective, descriptive study was done from August 2011 to February 2015. Case eligibility was defined by WHO Near-Miss Guidelines. Medical records of the patients and the interview with the patient, accompanying family members and health workers from referral centres were used to generate the data which were filled in the pre-designed questionnaire. The data generated and analyzed included age and gestation weeks, parity, mode of intervention, associated organ dysfunctions, reasons for near-miss and critical intervention accompanied to manage the near-miss cases. Results were presented in mean ± SD and percentages, wherever applicable.

Results: There were 4617 deliveries with 28 near-miss cases. The major factors contributing near-miss events were obstetric haemorrhage followed by hypertensive disorder. Three fourth (n=21) of cases required blood transfusion and almost all cases (n=26) required ICU management. Coagulation disorder was observed in majority of cases (n=23) followed by cardiovascular, respiratory and uterine atony.

Conclusions: In this study, maternal near-miss event was mainly attributable to obstetric haemorrhage followed by hypertension and sepsis. Major organ-system disorders observed were coagulation disorder, cardiovascular, respiratory and uterine disorders. Almost all the cases were managed in ICU and majority of them required blood transfusion.

Keywords: maternal mortality; obstetric haemorrhage; obstetric near miss.

INTRODUCTION

Maternal near-miss case is defined as "a woman who nearly died but survived a complication that occurred during pregnancy, childbirth, or within 42 days of termination of pregnancy".[1] Until few years ago, there were no set criteria for identification of these cases for routine implementation, and application of this concept was limited.[2] But in 2009, WHO has come up with clinical, laboratory, and management criteria for the identification of these cases.[1]

A review of near-miss cases highlighted the shortcomings and positive elements of the quality of maternal and newborn healthcare, and these cases of near-misses demonstrated similar characteristics to those of maternal death.[3,4] Clinical audit of these cases can help to identify preventable factors that, if addressed, would improve the quality of services offered.[5] A clinical audit also identifies the determinants of near misses and contributes to improving the management of a mother's severe life-threatening complications.[6-8]

In this medical audit, we analyze and present the various determinants and complications associated with the near-miss events encountered at KIST Medical College Teaching Hospital.

METHODS

This hospital based prospective descriptive study was done from August 2011 to February 2015. Case eligibility was defined by WHO Near-Miss Guideline.[1] A questionnaire was designed to collect the information of the cases. In-patient medical records of the patients verified with the treating physicians were used as the primary source of information. However, in order to complete the information gaps in the patient's files as well as to facilitate the institutional

CORRESPONDENCE

Dr Bandana Sharma Gurung
Department of Obstetrics and Gynaecology
KIST Medical College, Lalitpur, Nepal
Email: drbandanamd@gmail.com
Phone: +977-9841341744

audit in near-miss cases, an interview was conducted with the patient and accompanying family members, health workers from referral centre relevant person involved in her care.

Near-miss cases were identified by trained nurses or attending gynaecologist according to the WHO 2009 criteria[1] and approved by the principal investigator or the second gynaecologist and the intensive care specialist.

Data generated and analyzed primarily included age and gestation weeks, parity, mode of intervention, associated organ dysfunction, reasons for near miss and critical intervention accompanied to manage the near-miss cases. Results were presented in mean ± SD and percentages, wherever applicable.

RESULTS

There were 4617 deliveries with 28 near-miss cases (i.e., 6.06 per 1000 births).

Table 1. Age and Gestation Week of Near-miss Cases (n = 28).

Age	**Mean ± SD: 24.29 ± 5.36 years**	**Range: 17-36 years**
	Gestation Week	
Live Birth(n = 25)	Mean ± SD: 37.68 ± 1.44 weeks	Range: 35-40 weeks
Abortion (n=1)	16 weeks	
Still Birth (n=1)	36 Weeks	
Ectopic Pregnancy (n=1)	6 weeks	

Table 1 depicts the age and gestation week distribution of the near-miss cases along with the frequency of live birth, abortion, still birth and ectopic pregnancy. Figure 1 illustrates that 46.43% of near-miss cases were multigravida whereas 53.57% cases were primigravida. Similarly, table 2 enlists the identified reasons for near-miss cases – obstetric haemorrhage comprising the maximum cases (50%) followed by hypertension (32.14%).

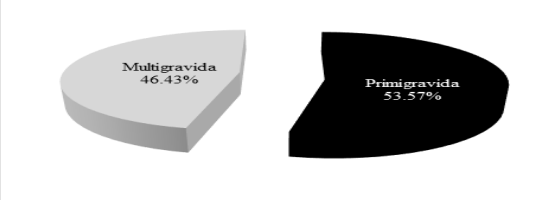

Figure 1. Parity of Near-miss Cases.

Likewise, figure 2 demonstrates the percentage of associated organ dysfunction encountered in near-miss events.

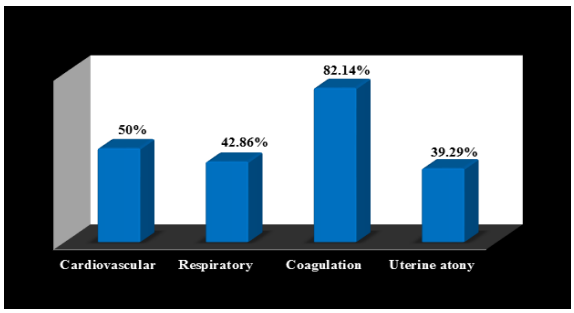

Figure 2. Associated Organ Dysfunction in Near-miss Cases.

Coagulation disorder was observed in maximum cases followed by cardiovascular disorder, respiratory disorder and uterine atony. Renal and hepatic dysfunctions were the least observed each contributing only one case (3.57%).

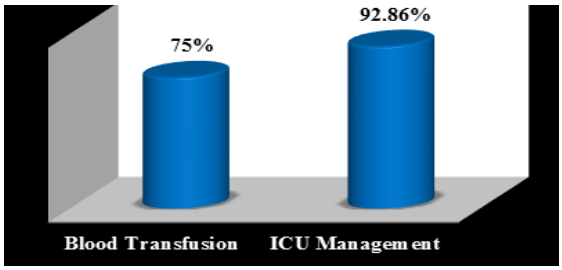

Figure 3. Critical Intervention.

As depicted in figure 3, 75% (n=21) cases required blood transfusion, 92.86% (n=26) cases were managed in ICU, 3.57% cases needed haemodialysis support and 3.57% cases were managed with condom tamponade.

Table 2. Reasons for Near-miss (n = 28).

Reasons for Near-miss	**Percentage**
Obstetric haemorrhage	50%
Hypertension	32.14%
Sepsis	10.71%
Cardiac cause	3.57%
Spinal shock	3.57%

DISCUSSION

We observed a near-miss event rate of 6.06 per 1000 birth compared to 3.8 per 1000 births in a national multicentre surveillance led by Rana et al[9] and between 3.8 – 12 per 1000 births in high income countries.[10] Our study shows that obstetric haemorrhage was the most common cause of obstetric near-miss event being the commonest followed by hypertensive disorders

during pregnancy. Similar results were observed in a study done at Kathmandu Medical College Teaching Hospital (KMCTH) where haemorrhage (41.66%) was the commonest cause for obstetric near-miss event followed by hypertensive disorder of pregnancy (27.77%).[11] Likewise, in 2012, a big multicentric study done in Nepal by Rana et al also highlighted PPH (40%) as the commonest cause for maternal near-miss event followed by hypertensive disorders of pregnancy (17%).[9] Similarly, the study also depicts that major organ-system dysfunction associated with obstetric near-miss event includes coagulation, cardiovascular, respiratory and uterine atony with almost all patients requiring ICU management and three fourth of cases demanding blood transfusion. Complications observed in near-miss cases were as per the expectation and included PPH, pre-eclampsia and sepsis in common.

Obstetric deaths represent the quality of maternal care. But for the present scenario it may not reflect the global situation with regard to obstetric care. Hence, new "near miss" criteria take over maternal mortality ratio. Although near-miss criteria were in vogue for some years, lack of uniformity was the hindrance. WHO criteria, 2009[1] are unique in considering not only clinical but also laboratory and management-based criteria. Hence, it incorporates both Mantel's[12] and Waterston's criteria.[13] So, if one of the criteria fails to pick the case, the other makes it up, thus minimizing the chance of missing the case.

CONCLUSIONS

This study highlights obstetric haemorrhage as the most common serious obstetric complication leading to near-miss event followed by hypertension during pregnancy. Almost all the patients were managed in ICU and majority of them required blood transfusion. There were various other reasons noted for near-miss events with lesser frequencies and several different complications observed which were managed accordingly. Therefore, reduction of maternal mortality may best be achieved by developing evidence-based protocols and improving the resources for managing severe morbidities.

DISCLOSURE

The authors report no conflicts of interest in this work.

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Puerperal Sepsis and its Cause in Patan Hospital

Pradhan B[1], Duwal Shrestha S[1], Singh A[1], Bhandary S[2], RC L[1], Shrestha R[1]
[1]Department of Obstetrics and Gynaecology, Patan Academy of Health Sciences, [2]Department of Community Health Science, Patan Academy of Health Sciences, Lalitpur

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Aims: This study was done to find out morbidity related with puerperal pyrexia/sepsis and its risk factors.

Methods: This was retrospective study conducted from January 2011 to December 2012 at Department of Obstetrics and Gynaecology, Patan Hospital, Kathmandu, Nepal. All women who delivered in this hospital within 42 days of delivery with puerperal pyrexia/sepsis diagnosed on clinical examination and relevant investigations were included in the study. Women with malaria, typhoid fever and ??other fever were excluded. The data was recorded in predesigned proforma and analyzed.

Results: During this period, there were 122 cases of puerperal pyrexia. Puerperal pyrexia accounted for 6.28% of 1945 admissions. Most of the women were aged between 20-29 years, primiparous and booked cases with absent membranes. The causes of puerperal pyrexia in our study were urinary tract infection (47.5%), wound infection (20.5%), endometritis (19.7%) retained product of conception (8.2%), pyoperitoneum (2.5%) and septicemia (1.6%).

Conclusions: Puerperal pyrexia/sepsis is one of the causes of preventable maternal morbidity and mortality though in our study it was not proved to be very high in number. Optimal aseptic measures during labour can prevent most of the cases.

Keywords: Nepal; Patan Hospital; puerperal sepsis.

INTRODUCTION

Puerperal sepsis is defined as the infection of the genital tract occurring at labour or within 42 days of the postpartum period. It presents commonly with fever and abdominal pain, foul smelling vaginal discharge and sub involution of the uterus.[1] According to the study done in Nigeria, puerperal sepsis is second leading cause of death accounting for 26.3% of maternal deaths.[2] WHO reported 358,000 maternal deaths occurring during childbirth and 15% are associated with puerperal sepsis.[3] Puerperal pyrexia and sepsis are among the preventable conditions in both developing as well as developed countries.[4] It usually occurs after discharge within 24 hours of delivery. The predisposing factors are anemia, low socioeconomic condition, prolonged labour, frequent vaginal examinations in labour, premature rupture of membranes for prolonged period.[5] Puerperal sepsis remains the common cause of maternal morbidity and mortality in developing countries and delay in detection and treatment may lead to obstetric shock and even death. Oliver Holmes, in 1843, was the first to establish that puerperal fever was contagious. Proper drug and better technology needs to be combined with effective health system intervention to reduce infection.[6] The main focus is on infection control measures and hand hygiene, and staff to bed ratios. These have been the product of work done which targeted hand hygiene as a flagship campaign.[7] The main aim of this study was to know the causes of puerperal pyrexia/sepsis and its morbidities so as to take the necessary action for its prevention.

CORRESPONDENCE

Dr Binita Pradhan
Department of Obstetrics and Gynaecology
Patan Academy of Health Sciences
Lalitpur, Nepal
Phone: +977- 9841587001
Email: binitapatan@gmail.com

METHODS

This was a retrospective study done after reviewing the charts between January 2011 and December 2012. These women were diagnosed on basis of clinical examination and relevant investigations. Women having medical diseases like malaria, typhoid fever were excluded from the study. The data were kept in predesigned proforma. The variables included were age, parity, booking status, onset of labour, status of the membranes, mode of delivery, duration of labour, haemoglobin level and the morbidity. The data entry

and analysis was done in SPSS and the result was presented in terms of percentage/proportions. Ethical approval was taken from the hospital.

RESULTS

Over the study period 122 patients presented with puerperal pyrexia representing 6.27% of 1945 admissions in Gynaecology ward of Patan Hospital. About thee out of five patients with puerperal pyrexia were aged 20-29 years whereas around one out of five was below 20 years (Table 1).

Table 1. Sociodemographic characteristics of the patients (n=122).

Variables	Frequency	Percentage
Age in years		
< 20	23	18.9
20-29	74	60.7
30+	25	20.5
Parity		
1	63	51.6
2	39	32
3+	20	16.4
Booking status		
Booked	80	65.6
Unbooked	42	34.4

Table 2. Obstetric Profile of the patients (n=122).

Variables	Frequency	%
Mode of delivery		
SVD	76	62.3
LSCS	46	37.7
Duration of labor		
<12 hours	52	42.6
>12 hours	70	57.4
Membrane status		
Present	51	41.8
Absent	71	58.2
Hemoglobin level (gm%)		
<10	66	54.1
>10	56	45.9

Table 2 illustrates the obstetric profile of the patients. Around two-third of the cases with puerperal pyrexia/ sepsis delivered through vaginal delivery. Further, nearly two out of five women had less than 12 hours of labour and membrane was present. Nearly one out of two women (45.9%) developing puerperal sepsis had haemoglobin level less than 10 mg/dl.

Table 3. Morbidities of the patients (n=122).

Morbidities	Frequency	Percentage
Urinary tract infection	58	47.5
Wound infection	25	20.5
Endometritis	24	19.7
Retained poc	10	8.2
Pyoperitoneum	3	2.5
Septicemia	2	1.6

Table 3 shows that around half of the women had urinary tract infection whereas one in five had wound infection and endometritis. Further, nearly one in 10 had retained product of conception.

DISCUSSION

Puerperal pyrexia and sepsis is an important public health problem and one of the leading causes of maternal morbidity and mortality. Due to the advent of antibiotics and proper aseptic technique there has been significant reduction of these cases in both developed as well as developing countries. This study includes more of puerperal pyrexia cases and the actual puerperal sepsis was only seen in 19.7% cases. In this study the mothers with puerperal pyrexia was younger (60.7%) and with lower parity (51.6%) which was similar to the study by Shamshad.[8] The reason behind that could be lack of education relating with unhygienic conditions. Another study showed age and parity tend to be younger 70% of less than 30 years and 30% less than parity two.[9] Khaskheli reported puerperal sepsis more in un-booked grand multiparous patients[10] but in our study booked cases were more (65.6%) which may be because booked cases were aware of seeking health care.

Our study revealed 62.3% cases of puerperal pyrexia with normal vaginal delivery that may be due to frequent vaginal examination along with neglect regarding the six 'c' (clean hands, clean delivery surface, clean cord cutting instrument, clean perineum and clean cutting surface). In developed countries the main contributing factor for puerperal sepsis is caesarean section.[11] There is more tissue trauma and manipulation than in vaginal delivery. There is increased rate of puerperal pyrexia with prolonged labor in our study (57.4%). Duration of labor directly contributes to development of postpartum sepsis as prolonged labor with frequent vaginal examinations lead to sepsis as a result of

prolonged state of an open cervix often with ruptured membranes impairing natural mechanical barrier to ascending infection from vagina.[12] Majority of these women (58.2%) had rupture of membrane at the time of labor. Vacca reported that operative delivery was significantly associated with sepsis especially when followed by prolonged labour.[13] In a study at Ife Hospital Nigeria, the predisposing factor associated with sepsis was anemia in 69.2% of cases[5] while it is 54.1% in our study. The most frequent morbidity was urinary tract infection (47.5%) and wound infection (20.5%). This may be attributed to improper asepsis during catheterization in labour. In three of the cases patient had abdominal distension along with fever. Exploratory laparotomy was performed and around 500 ml of pus was drained. The serious complication was septicemia, which was seen in two of the cases. One patient of urinary tract infection had acute renal failure needing intensive care unit admission. Shamshad reported 14.2% mortality related to sepsis but there was no mortality seen in our study. An estimated 15% of all maternal deaths are due to sepsis.[14] Mortality depends on proper management of sepsis and its complications.

CONCLUSIONS

Puerperal pyrexia is a preventable and treatable illness, however timely recognition is very important for the preventive management. The risk factors like mode of delivery, status of membranes and duraiton of labour leading to this condition is of prime importance as it can cause serious maternal morbidity and mortality and proper aseptic measures during labour including catheterization can prevent most of the cases.

DISCLOSURE

The authors report no conflicts of interest in this work.

No violation of human rights and safety.

Funding: Nil

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Spinal Anaesthesia Failure among Women Undergoing Caesarean Section in Kirtipur Hospital

Rajbhandari PK[1], Pradhan P[2], Dangal G[3]

[1]Department of Anaesthesiology, Kirtipur Hospital, Kathmandu, [2]Department of Obstetrics and Gynaecology, Kirtipur Hospital, Kathmandu, [3]Department of Obstetrics and Gynaecology, Kathmandu Model Hospital, Kathmandu

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Aims: This study was done to find out the spinal anaesthesia failure rate necessitating the conversion to general anaesthesia and use of intraoperative supplemental analgesia.

Methods: This was a retrospective study undertaken in Kirtipur hospital in 660 patients. Spinal anaesthesia (0.5% heavy bupivacaine 2.2 ml) was given to women who had undergone elective or emergency caesarean section from January 2009 to December 2013.

Results: In this study spinal anaesthesia failure rate was 1.66% (n=11/660). Among them complete failed spinal anaesthesia rate was 0.75% (n=5/660) requiring conversion to general anaesthesia. Intraoperative supplemental analgesic and sedation like pethidine, ketamine or midazolam was required in 0.90% (n=6/660).

Conclusions: The failure rate of spinal anaesthesia given for caesarean section was low (1.66%) and it was within the acceptable range.

Keywords: caesarean section; failure rate; spinal anaesthesia.

INTRODUCTION

Spinal anaesthesia was introduced in 1899 to clinical use by August Bier. In the last five decades it has gained its popularity. "Experienced professional, healthy patient, correct technique, single puncture, adequate cerebrospinal fluid back flow, effective anaesthetic agent so, why did it fail? was the expression used by August Bier.[1] It is frequently used anaesthetic technique and success rate and patient satisfaction are generally high.[2] The use of regional anaesthesia has been increasing in obstetrics recently because it gives better maternal and fetal outcomes compared with general anaesthesia. Most women also prefer to be awake during caesarean delivery and women want to hear the first cry of their babies at birth.[3] The nearly no existing risk of systemic toxicity to the mother and fetus from the small dose of local anaesthetic used has endeared it to obstetric anaesthetists.[4]

There are reports of failed spinal anaesthesia and published failure rates range from 0.46%-17%.[5,6] In some cases of spinal anaesthesia failure supplemental analgesic is sufficient but some requires conversion to general anaesthesia. A spinal anaesthesia is considered to have failed if anaesthesia and analgesia have not taken effect within 10 minutes of successful intrathecal deposition of heavy bupivacaine and 25 minutes for plain bupivacaine.[7,8] Technical errors are common causes of failed spinal anaesthesia like: drug deposition at lower spinal level than surgical site, improper rate of injection, failure to recognize dural puncture, needle partly inside/ outside dural sac, needle in ventral epidural space and lateral horizontal position. Chemical interactions are also contributory like bloody tap cause hydrolysis of ester type anaesthetic by pseudocholinestarage, concentration errors, loss of potency by prolonged exposure to light, high cerebrospinal fluid PH, glucose causes hyperalgesia and spotty anaesthesia.[8] In some patients the onset of spinal anaesthesia is rapid, but it can be slow in some patients, so " tincture of time" should always be allowed.[9] If block has not developed within 15 minutes some additional maneuver is needed. Repeating the procedure or conversion to general anaesthesia is the only option.[10]

CORRESPONDENCE

Dr Pradeep Kumar Rajbhandari
Department of Anaesthesiology
Kirtipur Hospital, Kathmandu, Nepal.
Email: prakura@gmail.com
Phone: +977-9851058958

METHODS

Six hundred and sixty women who underwent caesarean section under single shot spinal anaesthesia in the Kirtipur Hospital from January 2009 to December 2013 were studied retrospectively. Approval for this study was taken from the instutional review committee. Age, weight of the parturient, types and indications of caesarean section and American society of anaesthesiologists (ASA) physical status were analyzed. Contraindication to spinal anaesthesia such as coagulopathy, septicaemia, known spinal pathology, history of antepartum haemorrhage, allergy to local anaesthestic agents and patient refusal were excluded. After coming to operation theatre all parturient were preloaded with 500 ml Ringer lactate solution. The parturients were kept in sitting position and after all aseptic precaution 27-gauge pencil point spinal needle (whitarche) was inserted at third or fourth lumber space. After free flow of cerebrospinal fluid 2.2 ml (11 mg) of 0.5% bupivacaine heavy was administered. Patients were immediately kept on supine position with a wedge under right buttock and vitals were monitored. Effects were noted after 5 minutes, those who did not show effect in 5 minutes were watched for another 5 minutes and then they were tested for temperature sensation, pain at incision site, level of block and motor response by asking them to raise their legs. Parturients who felt pain after being pricked by a pin at the site of incision or could move her legs were considered as failed spinal anaesthesia, so general anaesthesia was given. Those who developed motor block of lower limbs but had pain sensation during surgery were supplemented with intravenous analgesia like pethidine or ketamine or midazolam. After the completion of surgery, the parturient were shifted to postoperative ward and observed for residual effects of anaesthesia and postoperative nausea and vomiting.

RESULTS

In our study six hundred and sixty caesarean sections were performed under spinal anaesthesia. The age of patients ranged from 19 years to 40 years. Five hundred and five (73.4%) were ASA physical status I and 155 (26.6%) were ASA physical status II. The patients weighed from 49 Kg to 88 Kg. There were 248 (37.5%) elective and 412 (62.5%) emergency caesarean sections. The main indication of caesarean section was fetal distress 265 (40.2%) followed by previous caesarean section 89 (13.5%). There were 11 cases with failed spinal anaesthesia among which 5 women had complete failure and were converted to general anaesthesia. Out of 5 complete failure spinal anaesthesia, 2 were performed by an anaesthesiologist and 3 by a nurse anaesthetist. Six cases had partial failure of spinal anaesthesia that required intraoperative supplementation of analgesia and sedation.

Table 1. Demographic characteristics (n=660).

Age	Number (%)
<19	31 (4.7)
20-24	186 (28)
25-29	293 (44.4)
30-34	116 (17.6)
35-39	31 (4.7)
> 40	3 (0.4)

Table 2. ASA physical status (n=660).

ASA Status	Number (%)
I	505 (73.4)
II	155 (26.6)

DISCUSSION

True failure of spinal anaesthesia should be differentiated from failure to depositing the drug in the subarachnoid space. The word failure implies that a spinal anaesthesia was attempted but no block resulted or a block that resulted was inadequate for that surgery. Due to concern about the potential risk associated with general anaesthesia, some of our patients were distressed when informed the need for conversion to general anaesthesia following the failure of the spinal anaesthesia. In our study the incidence of total failed spinal anaesthesia for caesarean section was 1.66% which was lower than 6%, 6% and 2.5% reported by Shrestha and collegue,[11] Adenekan et al,[16] Olateju SO and Abraham et al[17] respectively. In our study complete spinal failure necessitating conversion to general anaesthesia was 0.75%, which was higher than 0.5% reported by Sng et al[13] and lower than 2.5% to 17% reported by different authors.[4,10,11,16,]

If the patient could not move her lower limbs but felt pain over the incision site during surgery after having spinal anaesthesia then intravenous analgesia was supplemented. In our study 6 (0.9%) patients needed supplemental analgesia which was lower than 1.8% reported by Shrestha and his collegues,[11] 10.9% reported by Garry et al,[14] 6.4% reported by Adenekan et al[16] and 11.9% reported by Abraham and Jacob.[17]

In the United Kingdom, higher volume of hyperbaric bupivacaine is used for spinal anaesthesia and this has happened without higher incidence of complication. Immediate conversion to general anaesthesia after a single failed spinal anaesthesia can be safely avoided.

CONCLUSIONS

Spinal anaesthesia is a centenary technique, which is used universally by specialists and non-specialists and considered easy to execute by the majority of the professionals. It is subjected to occasional failure due to one of the several factors mentioned. Therefore, proper evaluation of the anatomy of the patient related to the procedure, judicious choice of needle and punctured site, careful storage of anaesthetic agents, selection of the dose and baricity, correct positioning of the patient during the puncture and shortly after the administration of the anaesthetic agent and until it is fixed to the tissue should be done to achieve better results.

DISCLOSURE

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No violation of human rights and safety.

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An Insight to Burn Related Maternal Morbidity and Mortality in Pregnancy

Rijal H, Rana A, Chalise G
Department of Obstetrics and Gynecology, Tribhuvan University Teaching Hospital, Institute of Medicine, Kathmandu, Nepal.

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Aims: The aim of this study is to study morbidity and mortality of burn cases during pregnancy and postpartum period.

Methods: This is a retrospective study conducted at Tribhuvan University Teaching Hospital from April 1998 to July 2014. The data were retrieved from the records in burn ward, intensive care unit and emergency unit. Pregnant women with burn were studied for the nature, degree and the percentage of burn in relation to pregnancy outcome and mortality.

Results: There were 32 cases of burn patients with pregnancy. The most common source of burn was kerosene-induced flame (23) followed by domestic firewood (7), boiling water (1) and lightening (1).There were 25 cases of accidental burn and seven were suicidal burn. The age of the patients was ≤19 years in 7, 20-24 in 13, 25-29 in 6 and 30-34 in 6 patients. Except for two cases of postpartum burn , all the others occurred during pregnancy between 6-40 gestational week{<12weeks =5, 13-27 weeks =10, 28-36 weeks=4, 37-42 weeks =6 and unknown =7}. There was only one cesarean and three vaginal births and most resulting in stillbirth owing to higher percentage of burn above second degrees. The percentage of burn was <30% in 13, 30-39% in 3, 40-59 % in 6, 60-69% in 5 and 70-90% in 2 patients. There were nine mortality (28.1%) in women above 30% burn.

Conclusions: The most common cause of burn in pregnancy was flame burn. Pregnant women need to be cautioned against flame burn and avoid using kerosene cooking stove to prevent themselves from burn, genuinely necessary steps to be propagated by all healthcare providers and also at the same time counseling against suicide to be done.

Keywords: maternal mortality; suicidal burn; wood fire burn.

INTRODUCTION

Maternal mortality is a priority research subject in Nepal. Upcoming studies have shown suicide as one of the few important contributes to the maternal mortality issues.[1] Burning themselves to death has also been implicated as a suicidal motive.[2] Significant female population in reproductive age group are being subjected to death due to burn in Nepal.[3]While we commonly witness more incident within households, females are more prone as they are engrossed in domestic cooking using firewood.[4] Burn acquired at domestic cooking using firewood in squatting position, a normal norm of rural lifestyle that results in extensive scarring in perineum, has been the cause of obstructed labor.[5]

This study values the role of multidisciplinary approach through a specialized team of anesthetist/ intensivist, physicians, plastic surgeons and obstetricians for management of these patients. This study also helps to recognize, understand and educate us regarding current status of burns in pregnancy employing hospital-based data.

CORRESPONDENCE

Dr Hima Rijal
Department of Obstetrics and Gynecology,
Tribhuvan University Teaching Hospital, Maharajgunj,
Kathmandu, Nepal.
E-mail: rizhima@hotmail.com
Phone: +977-9841456576

METHODS

This was a retrospective study conducted at Tribhuvan University Teaching Hospital between

15th April 1998 – July 2014 from burn ward, intensive care unit and emergency unit. Data source was the record book in burn ward, emergency, intensive care unit, and medical record section. Pregnant women with burn were studied to establish relationships between maternal age, nature of burn (homicidal, suicidal or accidental) including the degree and the percentage of total body surface (TBSA) area burn, source and intentionality of the burn and trimester of pregnancy at the time of the burn. Perinatal and maternal outcome were also studied. A fixed questionnaire was created and filled up. Informed consent was obtained from all the women. Approval from the Intitutional Review Committee of the hospital was also taken.

RESULTS

During last 16-years, 32 married women of reproductive age group were admitted with burn

during pregnancy. Among them, thirty patients were pregnant and two were in puerperium. The intent of burn was accidental in 25 (78.1%) and suicidal in 7 (21.8%) patients (Table 1). Most of the suicidal burns were attempted by using kerosene and three of them succumbed to death. Among the accidental burn, 23 were flame burn, one due to hot water and one due to lightening.

Table 1. Nature of burn, accidental/suicidal (n=32).

Cause of burn	Accidental	Suicidal
kerosene	0	4
Kerosene stove	4	0
Gas stove	2	0
Wood	5	0
Flame	3	0
Makal	3	1
Scald	1	0
lightening	1	0
Unspecified	6	2

Majority were second degree burn (n=28, 87%) and the deeper to dermis or third degree burn were four in number (13%). Among the patients with third degree burn, two survived while two died, all four having had 60% burn. Burned out total body surface area (TBSA) ranged from 1 to 90%. Higher percentage total body surface area affected by burn was noted to produce grave results in terms of maternal and fetal wellbeing. There was no mortality less than 30% burn {(n=10, (31.2%)}, more than 30% (n =22, 68.7%). Nine out of the twenty-two patients (40%) with greater than 30 % burn (Figure 1).

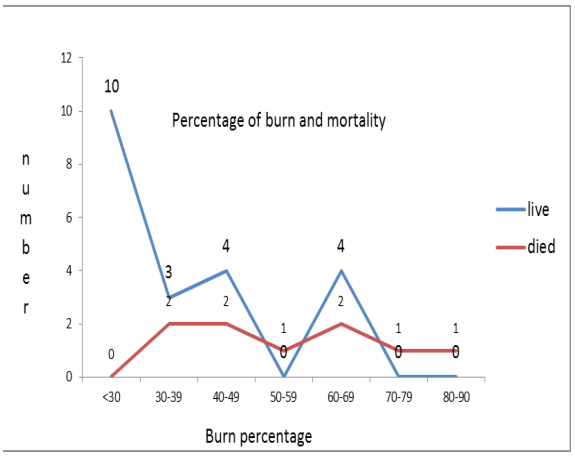

Figure 1. Burn and mortality (n=32).

Among the maternal death that occurred in 9/32 women who sustained burn injury, 3(9.3%) of them were suicidal and 6 (18.7%) were accidental. The age of the women ranged from 18-34 years and the pregnancy varied from 16-40 weeks. Five of the pregnancy being above 30 weeks period of gestation and two of them being 40 weeks with the record of one fresh stillbirth.

The maternal complications that led to mortality were shock, respiratory distress and sepsis with one sustaining corneal abrasions/perforation. The seriousness of the condition indicated by death within one day in three cases and three days in another, while women were kept alive up to 53 days in one case (Table 2).

Table 2. Summary o f maternal mortality due to burn (n=9).

Age (years)	Gestational age (weeks)	Burn %	Type/cause of burn	Burn to mortality interval (days)
18	35	75	Accidental (Kerosene stove)	1
26	16	55	Suicidal (kerosene)	29
18	*	60	Accidental (Kerosene stove)	53
31	40	37	Accidental (woodfire)	31
20	27	30-35	Suicidal (kerosene)	17
19	40	60	Accidental (flame burn)	36
20	*	40	Suicidal	1
18	30	90	Accidental	3
20	36	40	Accidental	1

Note : * Gestational age not known

The pregnancy ranged from G1-G6. Age of the patients ranged from 18-34 years, less than 19 (n=7, 22%); 20-24(n=13, 40.6%); 25-29 (n=6, 18.7%) and 30-34 (n=6,18.7%). with the mean age of the burn affected pregnant women being 23.4 years (Figure 2).

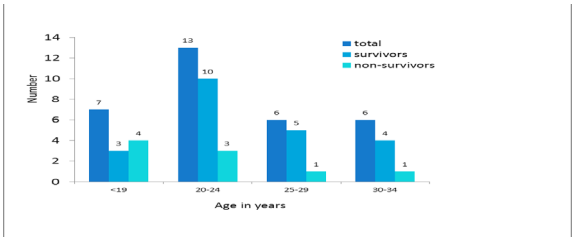

Figure 2. Age in years (n=32).

Two postpartum cases, one who caught fire on saree end while lactating. Period of gestation was less than 12 weeks (n=5, 15.6%); 13-27 weeks (n=10, 31.2%); 28-36 weeks (n=4, 12.5%) and 37-42 weeks (n=6,

18.7%) with dates not verified in five cases (Figure 3).

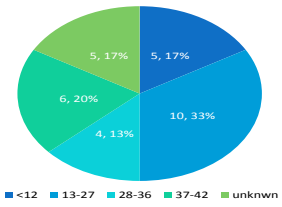

Figure 3. Period of gestation in weeks (n=32).

Labor was induced but failed to progress in one and needed cesarean section. Hospitalization period was 1-66 days (mean =26 days). Hospitalizations in for those who expired were 1- 51days

(mean =19 days) and who survived were 2-66 days (mean= 33 days) (Figure 4).

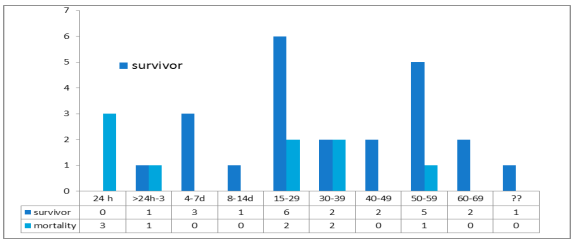

Figure 4. Length of hospitalization (n=32).

DISCUSSION

This retrospective study showed that burn injury during pregnancy is seldom met in our hospital.

Review of hospital records revealed that hardly two cases of burn in pregnancy are admitted per annum with four thousands deliveries and about 250 mixed pregnancies ending uneventfully. And this finding is similar to the other studies reporting incidence of small number of cases of burn in pregnancy.[6-9] Burn injuries during pregnancy have adverse effects on maternal and fetal outcome with high incidence of IUD, abortion and premature labor. Pregnancy itself does not alter the maternal survival.[10]

The possibility of pregnancy must be considered when any woman of reproductive age sustains a burn injury. Although rare, an extensive burn during pregnancy is a serious complication. In the study done by Agrawal et al[11] reported 12.29% of all women of reproductive age admitted with burns were pregnant. Because pregnancy tests were not done routinely the true incidence of pregnancy associated with burn injuries, especially in the first trimester, remains unknown. Burn can happen accidentally during pregnancy, fetal wellbeing need special attention.

There are specific physiological changes that occur during pregnancy that may have an impact after thermal injury on maternal and fetal well-being. Burns causes many maternal physiological changes and places additional stress on systems that are already highly modified. Pregnancy is associated with hyperdynamic cardiovascular state. After burns there is increased capillary permeability and third space loss leading to hypovolemia, which may in turn lead to hypotension if the patient is inadequately resuscitated leads to placental insufficiency, fetal ischemia, hypoxia and acidosis leading to premature birth. Thus aggressive fluid resuscitation, upright posture and oxygen supplementation should be provided to the mothers even in the absence of smoke inhalation.[12,13] And fetus in utero calls for extra caution.[14-16]

In this study women of reproductive age group have got burn injuries mostly while doing household tasks. Although most of them were accidental, some were intentional and maternal mortality was more in intentional burns. Most of the maternal mortality (40%) had TSAB above 30%. Kamini et al[9] also showed in their study that the maternal and fetal mortality rates were higher when the burn was suicidal. Higher degree of burn is directly proportionate to severity of outcome.All third degree burn (n=4) resulted in poor outcomes in our study. Prevention of hypovolemic shock by adequate early fluid therapy is required to maintain the uterine blood flow, which in turn maintains fetal tissue pO2 levels within the normal range. It is recommended to maintain the mother's blood pressure within the normal range and a urine output of 30-60 ml/h. Ventilatory support should be initiated when maternal pO2 is less than 60 mm Hg as inhaled carbon monoxide can cross the placental barrier to compete for binding sites on fetal hemoglobin, provoking fetal cardiac edema, and affecting cardiac development.[17]

There have been concerns of perineal burns posing a difficulty for vaginal birth or cesarean delivery with respect to abdominal burn injuries imparting situational challenges. This runs everywhere even in the best of the hospital, equipped with burn care facilities or having guiding protocol for the management.[18,19] Women in developing countries typically squat around cooking fires and perineal

burns result in scarring of genitalia leading to obstructed labour and abdominal burn scar may sometimes interfere in abdominal incision while performing cesarean sections. However, in our study spontaneous labor occurred in most cases, while induction was done in one case and resulted in fresh stillbirth.

Our study showed comparable figures of the nature and type of burn, most common being accidental flame burn. This study also showed the maternal mortality comparable to the figures mentioned in most literature as 39% -68.6%.[7,9,13,20] Despite of sustaining large body surface destruction by burn and long period of hospitalization many patients were successfully sent home after wound management with skin graft.

CONCLUSIONS

Pregnancy does not influence maternal outcome after thermal injury and best chance for fetal survival is to ensure maternal survival. Pregnant women need to be cautioned against flame burn and avoid using kerosene-cooking stove to prevent them from burn. Maternal survival is less likely if the burn wound exceeds 30% total body surface area. Thermal injury does increase the risk of spontaneous abortion and premature labour and foetal survival depends upon foetal maturity. Urine pregnancy test should be done to all women in reproductive age group admitted in burn ward.

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Pregnancy Related Acute Kidney Injury at a Tertiary Care Center in Nepal

Paudyal P, Pradhan N, Bista KDB, Rawal S
Department of Obstetrics and Gynaecology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal

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Aims: This was performed to study the characteristics of Pregnancy Related Acute Kidney Injury (PRAKI), its management and outcome in patients at a tertiary level referral centre.

Methods: A hospital based prospective observational study was conducted in Tribhuvan University Teaching Hospital (TUTH) over a period of 18 months. All patients diagnosed with PRAKI were included in the study. Patient profiles in terms of age, parity, gestational age were studied along with time of occurrence of PRAKI, preceding event, etiology, management and maternal outcome. Descriptive and univariate analyses were conducted and qualitative variables were expressed as percentages while quantitative variables as means.

Results: There were fifteen cases of PRAKI during the study period with incidence of 2.1 per 1000 deliveries. The average age was 25.23± 3.8 years and 9(60%) were primipara. Fourteen (93.3%) developed PRAKI in the postpartum period with 10(66.6%) cases following Lower Segment Caesarian Section (LSCS). The commonest etiology of PRAKI was severe preeclampsia/ Hemolysis, Elevated Liver enzymes, Low Platelet (HELLP) syndrome and pregnancy hemorrhages each consisting 4(26.6%) cases. The stage of Acute Kidney Injury (AKI) according to RIFLE (Risk, Injury, Failure, Loss, ESRD-End Stage Renal Disease) criteria was as follows: risk in 1(6.6%), injury in 3(20%) and failure in 11(73.3%) cases. Hemodialysis was necessary in 12(80%) cases while 3 cases (20%) improved with medical management only. The average duration of hospital stay was 25.2±14.7 days and 7(46.6%) needed ICU admission. Twelve (80%) cases recovered completely while two patients were dialysis dependent at the time of evaluation. There was one death.

Conclusions: PRAKI occurred mainly in the postpartum period with severe preeclampsia/HELLP syndrome and hemorrhages as the most common causes. It is associated with high maternal morbidity, prolonged hospital stay and even mortality. Multidisciplinary team management is essential.

Keywords: acute kidney injury; postpartum; PRAKI; pregnancy.

INTRODUCTION

Acute kidney injury (AKI) is a clinical syndrome denoted by an abrupt decline in glomerular filtration rate (GFR) sufficient to decrease the elimination of nitrogenous waste products (urea and creatinine) and other uremic toxins.[1] Pregnancy Related Acute Kidney Injury (PRAKI), though uncommon, causes significant maternal and fetal morbidity and mortality. New cases of PRAKI have declined from approximately 1/3000 in the 1960s to 1/15,000 – 20,000 in recent times.[2] Two main factors may be responsible for the overall decline in the incidence of PRAKI: improvement in pre-natal care and a decrease in the rate of illegal, septic abortions in developed countries.

CORRESPONDENCE

Dr Pooja Paudyal
Department of Obstetrics and Gynaecology, Tribhuvan University Teaching Hospital. Maharajgunj, Kathmandu.
Email: paudyalpooja@yahoo.com
Phone: +977-9841526853

Usually, the development of AKI during pregnancy follows a bimodal distribution with two incidence peaks: one in the first trimester, caused by septic abortion and the other in the third trimester, due to late obstetric complications such as uterine hemorrhages, preeclampsia, hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome, acute fatty liver of pregnancy, and Thrombotic Thrombocytopenic Purpura-Hemolytic Uremic Syndrome(TTP-HUS).[3,4] AKI is reported in approximately 1% of women with severe preeclampsia and 3 to 15% of women with HELLP syndrome.[5,6]

Despite a favorable trend in incidence rates worldwide, maternal and perinatal morbidity and mortality remain significant problems in developing countries and management of PRAKI is extremely challenging in low resource settings. There is no published data on this problem in Nepal. Ours being a referral centre with dialysis and renal transplant facilities, we do see such cases with increased morbidity and mortality. This study was therefore done to assess the

problem, its causes and outcome so that we can better understand and care for these patients.

METHODS

This hospital based prospective observational study was conducted in the Tribhuvan University Teaching Hospital, Kathmandu, Nepal over a period of 18 months from 1st Baisakh 2070 to 31st Asoj 2071 (April 14, 2013 to October 17, 2014). Ethical clearance was obtained from the Institutional Review Board (IRB) of Institute of Medicine. All pregnant and postpartum patients who developed PRAKI were included in the study. Patients with preexisting renal disease or renal insufficiency before pregnancy were excluded. Patients were enrolled in this study once PRAKI was diagnosed according to the definition given below and after taking informed consent from the patient. Patients were classified during analysis into stages of RIF (Risk, Injury, Failure) according to the maximum stage reached. The causes of AKI, its characteristics, need for dialysis, and the outcome (improved, partial recovery/loss of renal function, ESRD) were examined prospectively. For this study, data was collected regarding different aspects; (i) Population: age, parity, follow up status (ii) AKI: time of occurrence, preceding event, biochemical parameters, management, time to start of diuresis, hospital stay, need for intensive care, RIFLE stage and etiology (iii) Maternal outcome in the form of complete recovery of kidney function, partial recovery of kidney function, dialysis dependence and death.

Descriptive and univariate analyses were conducted using the SPSS 17 software. Qualitative variables were expressed as percentages and quantitative variables as means.

Definitions

(i) Acute kidney injury was defined as an abrupt (within 48 h) reduction in kidney function defined as at least one of the following: (*i*) an absolute increase in the serum level of creatinine of 26.4 µmol/L (0.3 mg/dL) or more; (*ii*) a percentage increase in the serum level of creatinine of more than 50% (a 1.5-fold increase from baseline); or (*iii*) a reduction in the volume of urine output (oliguria < 0.5 mL/kg hourly for > 6 h).[7]

(ii) AKI was classed according to risk of renal dysfunction; injury to the kidney; failure of kidney function, loss of kidney function, and end-stage kidney disease (RIFLE) criteria based on changes in serum creatinine or changes in urine output, or both. RIFLE criteria include three levels of renal dysfunction and two clinical outcomes: "loss" and "end-stage renal disease" (ESRD).[8]

RIFLE criteria for AKI

Class	Glomerular filtration rate criteria	Urine output criteria
Risk	Serum creatinine x 1.5	< 0.5 ml/kg /hr x 6 hrs
Injury	Serum creatinine x 2	< 0.5 ml/kg/ hr x 12 hrs
Failure	Serum creatinine x3 or serum creatinine ≥4 mg/dl with an acute rise >0.5 mg/dl_	<0.3 ml/kg/ hr x 24 hrs or anuria x12 hrs
Loss	Persistent acute renal failure=complete loss of kidney function > 4 weeks	
End stage renal disease (ESRD)	End stage kidney disease > 3 months	

(iii) PRAKI was defined as development of AKI at any time during pregnancy and postpartum period.

(iv) Maternal Outcomes:

Complete recovery- Patient recovered complete kidney function

Partial recovery- partial recovery of kidney function to make the patient dialysis free for some time.

ESRD- no recovery of kidney function, patient is dialysis dependent and requires kidney transplantation.

Death

RESULTS

Fifteen cases of PRAKI were admitted to the hospital during the study period. Incidence was 2.1 per 1000 deliveries (15 out of 7108 deliveries). Their ages varied from 20 to 33 years, with an average of 25.23± 3.8 years (Table 1). Parity ranged from 1-4 and primipara were 9(60%) while multipara were 6(40%) with an average parity of 1.5±0.91 (Table 1).

Table 1. Age and Parity of PRAKI patients (n=15).

Age (yrs)	N (%)	Parity	N (%)
16-20	1(6.6)	P1	9 (60)
21-25	9 (60)	P2	4(26.6)
26-30	4(26.6)	P3	1 (6.6)
31-35	1 (6.6)	P4	1 (6.6)

Of the 15 cases, 11(73.3%) were referred cases whereas 4(26.6%) patients were our booked (having previous antenatal visit in our hospital) cases. Most patients, 14(93.3%) developed PRAKI in the postpartum period while 1 was after a late first trimester abortion (Table 2).

Table 2. Time of occurrence of PRAKI and preceding event (n=15).

Occurrence of PRAKI	N	%	Preceding event	N	%
Antepartum	1	6.6	Septic abortion	1	6.6
Postpartum	14	93.3	Vaginal delivery	4	26.6
			LSCS	10	66.6

Of the 14 postpartum cases, 4(26.6%) were following vaginal delivery [1-stillbirth, 2-Intra Uterine Fetal Death (IUFD) expulsion, 1-Normal Vaginal Delivery] and the rest, 10(66.6%) cases were following Lower Segment Caesarian Section (2-elective, 8-emergency) (Table 2). Mean gestational age at termination of pregnancy was 35.8±7.1 weeks. Twelve cases (80%) developed AKI early in the postpartum period i.e. first to second postpartum/post-operative day while 1 patient developed AKI as late as 20th post-operative day. Of the 15 patients, all had raised serum creatinine levels, 12(80%) were anemic; 6 of them severe and 11(73.3%) had thrombocytopenia (Table 3).

Table 3. Biochemical parameters in PRAKI patients (n=15).

	Creatinine (mmol/l)	Hb (gm/dl)	Plateletes (/mm^3)
Mean	707.3±400	7.96±2.75	86200±7357
Minimum	220	3.5	26000
Maximum	1607	14.8	277000

The commonest etiology of PRAKI was severe preeclampsia and HELLP syndrome along with pregnancy hemorrhages consisting of 4(26.6%) cases each (Table 4).

Table 4. Causes of PRAKI (n=15).

Cause	N	Percent
Severe preeclampsia, HELLP	4	26.6
Pregnancyhemorrhage(APH,PPH)	4	26.6
PROM with sepsis	2	13.3
Obstructed labour with sepsis	2	13.3
Septic abortion	1	6.6
Sepsis with IUFD	1	6.6
Hemolytic Uraemic Syndrome	1	6.6

Hemodialysis was necessary in 12 (80%) cases while 3(20%) cases improved with medical management consisting of volume resuscitation, appropriate antimicrobials, avoidance of nephrotoxic drugs and other supportive measures. Average days to go into diuresis were 10.25±5.1 days. In one patient, plasmapheresis was attempted on suspicion of Thrombotic Thrombocytopenic Purpura (TTP) but there was no response. The average duration of hospital stay was 25.2±14.7 days with range of 14 to 71 days. The number of patients needing Intensive Care Unit (ICU) admission were 7(46.6%), 4(26.6%) required mechanical ventilation.

The stage of AKI according to RIFLE criteria was as follows: risk in 1(6.6%), injury in 3(20%) and failure in 11(73.3%). Overall 12(80%) patients had complete recovery in our study with recovery rates of 100% each for stages of risk and injury while those in the failure stage at diagnosis had a lower recovery rate of 73% only. Two patients were dialysis dependent at the time of evaluation and there was one mortality due to intractable pulmonary edema (Table 5).

Table 5. Outcome of PRAKI according to RIFLE stage (n=15).

Outcome according to stage				
	RIFLE			
OUTCOME	RISK	INJURY	FAILURE	Total
Complete recovery	1	3	8	12 (80%)
Partial recovery	0	0	1	1 (6.6%)
ESRD	0	0	1	1 (6.6%)
Mortality	0	0	1	1 (6.6%)
Total	1 (6.6%)	3 (20%)	11 (73.3%)	15

DISCUSSION

PRAKI has become a rare entity in the West. New cases of PRAKI have declined from approximately 1/3000 in the 1960s to 1/15,000 – 20,000 in recent times.[2] In France, the incidence of AKI in pregnancy has decreased from 40% in 1966 to 4.5% in 1978.[9] On the other hand, PRAKI is still common during pregnancy in developing countries, being responsible for a high maternal morbidity and mortality.[10,11] In the Moroccan study by Arrayhani M et al with sample size of 37(n=37) incidence was 6.6 per 1000 deliveries (0.66%) while in our study incidence was approximately 2.1 per 1000 deliveries (0.22%).[10]

In our series, PRAKI was more frequent in the postpartum period (93.3%). This is probably a reflection of reduction in cases in early pregnancy due to legalization of abortion and improving antenatal care. Similar results were obtained in India in a study carried out over two years with a sample size of 40 by Najar et al, where PRAKI occurred during the postpartum in 75.6% of cases (n=40) while in a study done by Ansari et al over one year with a sample of 42 in Pakistan (n=42), the majority of PRAKI occurred in the 3rd trimester (86%).[12] In our study PRAKI was seen more following emergency LSCS probably due to the indications for LSCS like HELLP or preeclampsia and contributed also by inadequate infection control leading to sepsis.

In most studies from developed countries, preeclampsia/eclampsia was reported to be a major cause of AKI during pregnancy. Pregnancy toxemia was the most common cause of PRAKI (66.6%), followed by pregnancy hemorrhages (25%) in a Moroccan study.[10] Septic abortion was the main cause of PRAKI in a series from Kashmir(n=40) accounting for 20 (50%) cases, 8 hemorrhage (20%) cases and 6 toxemia (15%) cases.[11] In our study, the main cause of AKI associated with pregnancy was preeclampsia and HELLP syndrome along with pregnancy hemorrhages in 4(26.6%) cases each, followed by PROM with sepsis and obstructed labor in 2(13.3%) cases each while septic abortion was seen in only 1 case, probably reflecting the legalization of abortion in our country.

The stage of AKI according to RIFLE criteria in our study: risk in 1(6.6%), injury in 3(20%) and failure in 11(73.3%) cases whereas in the Moroccan study - risk in 40%; injury in 27%; and failure in 33% of cases was seen; probably due to early recognition of kidney injury in their study. Most of our patients were referred cases from outside the Kathmandu valley and that explains the higher stage.[10] Among the four booked cases in our study, 2(50%) were in the stage of risk at diagnosis of PRAKI and improved with medical management only, probably because of earlier recognition. In the study by Najar et al 60% needed dialysis while in our study 80% needed dialysis likely due to delayed recognition and late stage of presentation of referred cases.[11]

The overall recovery rate of 80% in our study is comparable with the Moroccan study in which 72.5% patients recovered completely and in the study by Najar et al in Kashmir, recovery was obtained in 76%.[10,11] There was one (6.6%) maternal mortality in our study compared to 2.7% in the Moroccan study and 20% in the study by Najar et al.[10,11]

CONCLUSIONS

The incidence of PRAKI was higher in our hospital compared to developed countries. Most patients 14 (93.3%) developed PRAKI in the postpartum period and majority 10 (66.6%) were following LSCS. The commonest etiology of PRAKI was severe preeclampsia and HELLP syndrome along with pregnancy hemorrhages consisting of 26.6% cases each. Most of the cases were in the failure stage reflecting the late referral of cases to our institute. PRAKI resulted in prolonged hospitalization, ICU

admission and need for dialysis/transplantation. One patient died. Therefore early recognition of signs and symptoms, close vigilance in high risk cases, early referral and a multidisciplinary team management could potentially prevent progression to higher stages of PRAKI and reduce morbidity and mortality.

DISCLOSURE

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Relationship between Amniotic Fluid Index and Perinatal Outcome

Pradhan S[1], Adhikari A[2], Pradhan P[2], Pradhan Sunil[1]
[1] Department of Radiodiagnosis, [2] Department of Obstetrics and Gynaecology, Nepal Medical College Teaching Hospital, Kathmandu, Nepal

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Aims: This study was done to evaluate the predictive value of low amniotic fluid index (AFI) of < 5 cm for adverse perinatal outcome in term of caesarean section for fetal distress, birth weight, meconium stained liquor and APGAR scores.

Methods: This was a prospective study of 200 antenatal women booked at Nepal Medical College Teaching Hospital during the year 2013-2014 with gestational age between 34 and 41 weeks. Patients history and clinical examination were recorded and AFI was measured and the perinatal outcome was compared between two groups i.e AFI <5 cm and >5 cm.

Results: The caesarean section (C/S) rate for fetal distress and low birth weight babies (<2.5 kg) was higher in patients with low AFI (p=0.048, 0.001 respectively). There was no significant difference in meconium staining, APGAR score at 5 minutes between the two groups (p=0.881, 0.884 respectively).

Conclusions: Caesarean section for fetal distress and low birth weight babies was significantly associated with low amniotic fluid index. There was no significant difference in meconium staining liquor, APGAR score at 5 minutes between the two groups.

Keywords: amniotic fluid index; birth weight; caesarean delivery; meconium-stained liquor.

INTRODUCTION

Amniotic fluid provides a protective milieu for the growing fetus cushioning it against injury.[1,2] Although the clinicians were readily able to recognize the development of acute and excess of amniotic fluid in their patients, it is often difficult to recognize low amniotic fluid volume (AFV). Sonography is well suited to this task on a large scale and can be used frequently for repeat AFV determination. Phelan et al[3] and subsequently Rutherford et al[4] and Moore et al[5] developed a semi-quantitative sonographic assessment of the AFV that has come to be known as the amniotic fluid index (AFI). This measurement is based on the division of the gravid uterus into four quadrants using the external maternal landmarks of the umbilicus and linea nigra. These four measurements are added together and the sum is referred to as AFI. Most examiners[6] use an AFI of 5 cm as the threshold for oligohydramnios. Regardless of the causes many investigators have noted increased perinatal morbidity and mortality in the presence of oligohydramnios.[1,2,6] In our study, amniotic fluid quantification was done by four quadrant technique as described by Phelan et al[3] to determine AFI and we sought to determine if an antepartum AFI of 5 cm or less is a predictor of adverse perinatal outcome in terms of meconium stained liquor, caesarean section rate for fetal distress, birth weight and low APGAR scores.

METHODS

This was a prospective study carried out at Nepal Medical College Teaching Hospital, Kathmandu. The participants included 200 booked women with gestational age between 34 and 41 weeks admitted for delivery over a two-year period from January 2013 to December 2014. We included all eligible women for the study who attended our hospital during the study period. Records were maintained of meconium stained liquor, mode of delivery, birth weight and APGAR score at 1 and 5 minutes. Demographic profile, obstetric characteristics and perinatal outcome are also noted (Table 1-3). Inclusion criteria were women with singleton, non-anomalous fetus with intact

CORRESPONDENCE

Dr Sujan Pradhan
Department of Radiodiagnosis
Nepal Medical CollegeTeaching Hospital, Kathmandu, Nepal
Email: sujanpradhan@ hotmail.com
Phone: +977-9843108655

membrane at the time of antepartum testing. Women with premature rupture of membranes, with known fetal or chromosomal anomalies, gestational diabetes, Rhesus incompatibility, placental anomalies and multiple pregnancies were excluded from the study. On admission, a detail history was taken and clinical examination was performed and the gestational age was assessed. Amniotic fluid index was determined using the Phelan's technique[3] at admission and whenever seemed necessary after informed verbal consent. Non-stress Test (NST) was performed for all patients. Women were divided into two groups based on their AFI (within 48 hours of admission): group 1- AFI of ≤ 5 cm; group 2 AFI of >5 cm. Statistics was analyzed using Chi square (X^2) test and p value less than 0.05 was taken as significant. Informed consent was obtained from all the women. Approval from the Intitutional Review Committee of Nepal Medical College was also taken.

RESULTS

Out of 200 women the mean maternal age was 27.04 years in group 1 and 27.95 years in group 2. Gestational age was less than 37 weeks in 14/25 (46%) in group 1 as compared to 60/175 (34.3%) in group 2. Maternal weight gain during pregnancy was less than 10 kgs in 9 (36%) in group 1 as compared to 15 (8.6%) in group 2. Eighteen (72%) patients were induced in group 1 and 89 (50.9%) in group 2. Obstetrics and perinatal outcomes were studied in both the groups (Table 1).

Table 1. Maternal demographic and obstetric characterstics (n=200).

	AFI ≤ 5 (n=25)	AFI>5 (n=175)	p value
Maternal age (mean)	27.04 yrs	27.95 yrs	0.34
Nulliparity	17 (68%)	103 (58.9%)	0.22
Gestational age <37 weeks at delivery	14 (56%)	60 (34.3%)	0.35
Weight gain <=10 kg	9 (36%)	15 (8.6%)	0.001
Induction of labour	18 (72%)	89 (50.9%)	0.043

Four (16%) women in group 1 and 26(14.9%) women in group 2 had meconium stained liquor. The difference was not significant (p=0.881). Caesarean section was performed in 14(56%) women in group1 and 62 (35.4%) in group 2 (p=0.047). Caesarean section for fetal distress was higher in women with oligohydramnios (57.1%) as compared to women with AFI of >5 cm (38.7%){p=0.048}. Birth weight <2.5 kgs was found in 14 (56%) patients in group 1 and 38 (21.7%) in group 2.In group 1 the APGAR score at 1 minute was of <7 in 9 women (36%) and 19 (10.9%) in group 2 (p=0.001). APGAR score of <7 at 5 minutes was noted in 1(4%) in group 1 and 6 (3.4%) women in group 2 (p=0.884) and the difference was not statistically significant (Table 2).

Table 2. Obstetric and perinatal outcome (n=200).

	AFI ≤ 5 (n=25)	AFI>5 (n=175)	p value
Meconium stained liquor	4 (16%)	26 (14.9%)	0.881
Cesarean delivery	14 (56%)	62 (35.4%)	0.047
Cesarean for non-reassuring fetal status	8 (57.1%)	24 (38.7%)	0.048
Birth weight	<2.5 kg	38 (21.7%)	0.001
Apgar score	14 (56%)		
1 min<7	9 (36%)	19 (10.9%)	0.001
5 min<7	1(4%)	6 (3.4%)	0.884

In group 1, 17 (70%) had normal and 5 (20%) had pathological cardiotocography (CTG). In group 2 out of 175 patients, 146 (83.4%) had normal CTG and 9 (5%) had pathological CTG. The rate of pathological CTG in group 1 was statistically significant (Figure 1).

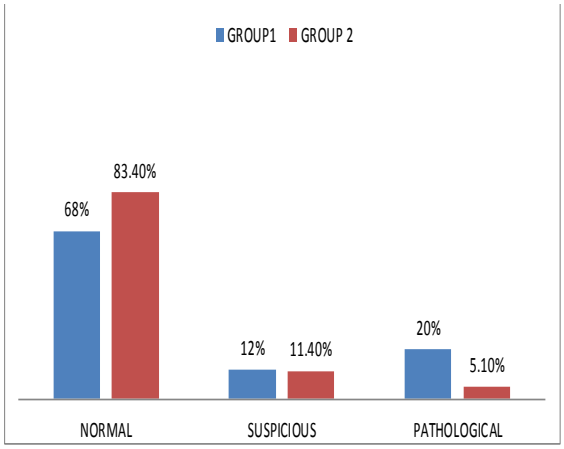

Figure 1. Intrapartum CTG.

Non-reactive NST was present in a significant number of patients in group 1, 8 (32%) compared to 17 (9.7%) in group 2 {p=0.0002}. Twenty-three babies (92%) were admitted to the neonatal intensive care unit (NICU) in group 1. In group 2, 125 (71.4%) babies were admitted to the NICU. Duration of NICU stay of more than two days was found in 9 (36%) in group 1 and 42 (24%) in group 2 (p=0.198). Therefore the two groups were comparable with regard to NICU stay (Table 3).

Table 3. Secondary outcome measures (n=200).

	AFI ≤ 5 (n=25)	AFI>5 (n=175)	p value
Non-Reactive NST	8 (32%)	17 (9.7%)	0.002
Admission to NICU	23 (92%)	125 (71.4%)	0.028
NICU stay > 2 days	9 (36%)	42 (24%)	0.198

DISCUSSION

In the present study, meconium stained liquor was present in 4(16%) of the patients in group 1 and 26 (14.9%) in group 2, the difference was not significant (p=0.881). The caesarean section rate was higher in group 1, 56% as compared to 35.4% in group 2,the difference was statistically significant (p=0.047). Caesarean section for fetal distress was also higher in patients with oligohydramnios as compared to group with normal AFI (57.4 vs 38.7%). A study conducted by Baron et al[7] showed that the meconium stained liquor occurred significantly less often in the oligohydramnios group as compared to normal AFI group. A study by Voxman et al[8] concluded that there were no difference between the groups with regard to meconium stained liquor, which was comparable to our study. Chauhan et al[9] in their meta analysis found that intrapartum AFI of ≤ 5 cm was associated with increased risk of Caesarean section for fetal distress which was similar to our study. Rutherford et al [10] found an inverse relationship between amniotic fluid index and caesarean section for fetal distress. In the current study, birth weight of <2.5 kg was found in 14 (56%) in group 1 vs 38 (21.7%) in group 2 and the difference was statistically significant (p=0.001). Locatelli et al[11] reported that in an uncomplicated term pregnancy with hydramnios the presence of AFI of <5cm independently increased the risk for small for gestational age babies Morris et al[12] found that 60 % of babies were low birth weight in the group with the AFI of <5 cm indicating that oligohydramnios had an association with growth restriction. A study by Rutherford et al[10] showed that when the AFI was < 5 cm (36%) pregnancies resulted in infants with intrauterine growth restriction (IUGR). In the present study, the 1 min APGAR score was <7 in 9 (36%) in group 1, whereas only 10.9% babies in group 2 had 1 min APGAR score <7 and this difference was statistically significant (p=0.001). However the 5 min APGAR score <7 was almost equal in both the groups (4 vs 3.4%). Chauhan et al[9] reported in the meta analysis that antepartum AFI of ≤ 5 cm was associated with a 5 min APGAR score of <7. A study by Driggers et al[13] reported at 5 min APGAR score of <7 in 3.8 % patients in an oligohydramnios group vs 4.6 % in a normal AFI group and concluded that there was no significnant difference. A study by Grubb et al [14] was found that 1 min APGAR score of <7 in 84% of patients with AFI of <5 as compared to 14 % in normal AFI groups which was highly significant (p=0.01). In the same study, 5 min score of <7 was seen in 13% patients with AFI of ≤ 5 cm vs 5% in normal AFI group.

CONCLUSIONS

In this study antepartum oligohydramnios (AFI≤5) was associated with increased caesarean section delivery particularly for fetal distress. A significant positive correlation was found between oligohydramnios and low birth weight babies. However there was no difference in perinatal outcome in terms of meconium staining liquor and 5 minute APGAR score between the two groups. When the secondary outcomes were measured, significant correlation was found in term of non-reactive NST and admission to NICU. Therefore, patients with severe oligohydramnios with AFI of ≤ 5 cm should undergo strict antepartum and intrapartum management and/or timely caesarean caesarean to improve their perinatal outcome.

DISCLOSURE

The authors report no conflicts of interest in this work.

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Obstetric Referrals to a Tertiary Teaching Hospital of Nepal

Maskey S
Department of Obstetrics and Gynaecology, Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal

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Aims: This study was done to review the primary reasons and pattern of obstetric cases referred to Tribhuvan University Teaching Hospital, and to identify the clinical course, mode of management, maternal and perinatal outcomes.

Methods: This prospective observational study reviewed 112 obstetric cases referred from various centers. Thorough history was taken; complete physical and obstetric examination and relevant investigations were done. Management of the patient, clinical course, mode of delivery, both maternal and perinatal outcomes were documented.

Results: Most common diagnosis at referral was medical disorders complicating pregnancy (38%) among which cardiac disease accounted for 20%, followed by hypertensive disorder (17%). Unavailability of perinatal facility was the most frequent reason (24%) for referral. Twenty seven percent of the patients were in serious or critical condition on arrival, 52% patients required surgical intervention, 19% received intensive care management and there were mortalities of 2 women (1.8%). Total number of live births were 70 (62.5%) among which 28 (42%) required neonatal admission and 3 (4% of live birth) had early neonatal death.

Conclusions: Wide spectrum of complicated obstetric cases were referred to this hospital. Unavailability of perinatal facility was the most common reason for referral followed by unavailability of physician. Most common diagnosis at the time of referral was medical disorders complicating pregnancy.

Keywords: eclampsia; obstetrics; referred cases.

INTRODUCTION

The referral system is an essential component of any health systems which is particularly important in pregnancy and childbirth for providing access to essential obstetric care. Even though pregnancy and childbirth are physiological processes bringing happiness to a couple these are associated with risks and complications, sometimes taking life of a woman and her baby if they are not taken care of in time. Especially in developing country like Nepal, major population lives in rural areas lacking access to essential obstetric facilities. In such areas timely referral and intervention of high risk and complicated obstetric cases can reduce maternal morbidity and avoid maternal deaths. However lack of structured referral system is a major hurdle in Nepal that delays proper management of such cases.

CORRESPONDENCE

Dr Suvana Maskey
Department of Obstetrics and Gynaecology;
Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal.
E mail: suvanashrestha@yahoo.com
Phone: +9779851139574

Tribhuvan University Teaching Hospital (TUTH) is a tertiary care hospital, located in Kathmandu, which receives and manages a wide spectrum of complicated obstetric cases that are referred from different centers from all over Nepal and from India. This study was done as there is minimum or no data available concerning the varieties of referred obstetric cases managed in TUTH.

The objective of the study was to review the reasons for referral and patterns of obstetric cases referred to our hospital, to study the clinical course and management of women during the hospital stay and to study the maternal and perinatal outcomes (in terms of live birth or stillbirth, intrauterine fetal death, and neonatal admission).

METHODS

This was a prospective observational study carried out from 1st October 2011 to 30th September 2012. All referred obstetric cases that were managed in emergency or admitted to the Department of Obstetrics and Gynaecology of TUTH during the study period were included. Permission from the

Department of Obstetrics and Gynaecology was taken before starting the study. Patients were explained about the purpose of the study and were included only after taking informed written consent.

Those cases that required admission and immediate management were taken. Thorough history of the patients who had been referred from different centers in Nepal was taken, taking note of the referring center and reason for referral. All collected data was filled in a predefined proforma. Complete physical and obstetric examination was done. Patient's clinical condition on arrival was classified - according to American Hospital Association.[1] Basic investigations like complete blood count, urine routine and obstetric ultrasonography as well as case specific investigations were carried out as mandated by the clinical condition of the patient. Management of the patient (whether conservative or interventional) and mode of delivery (whether vaginal or operative) were noted. Fetal outcome parameters like abortion, live/still birth, intra uterine fetal death (IUFD), Apgar score at 5 minute, neonatal admission and mortalities were noted. Patient was followed up until discharge and condition of mother on discharge, any maternal morbidity or catastrophe were also noted.

RESULTS

TUTH received and managed 112 women with various obstetric as well as associated medical and surgical conditions referred during the study period which constitutes 2.6% of total admission. Among them 58 (51.8%) came from rural area and 54 (48.2%) from urban area. Sixty four (57.14%) of the patients were referred from various centers outside Kathmandu and 48 (42.86%) from within Kathmandu Valley. Maximum cases (48, 42.86%) were referred from government hospitals (Table 1).

Table 1. Distribution of centers from where patients were referred (n=112).

Referring Center	Outside KTM	KTM	Total
Medical college	12	20	32 (28.57%)
Private hospital	10	10	20 (17.86%)
Government hospital	35	13	48 (42.86%)
Zonal hospital	2		
Regional hospital	2		
District hospital	10		
Healthpost/SHP/PHC	10		
Other government hospital	11		
Cardiac Hospital	-	5	5 (4.46%)
Private Clinic	3	-	3 (2.68%)
India	4	-	4 (3.57%)
Total	64 (57.14%)	48 (42.86%)	112 (100%)

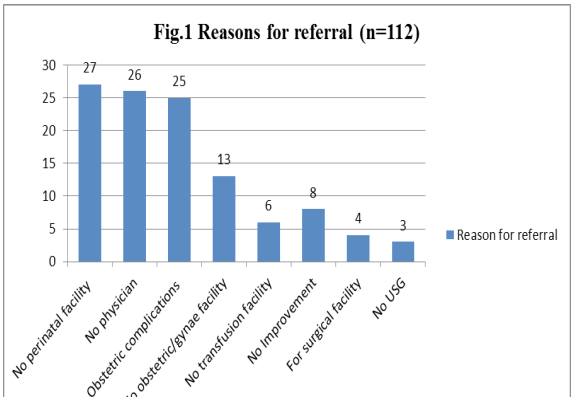
Ninety eight patients (87.5%) arrived directly to TUTH whereas 14 (12.5%) patients went to other hospitals and were then referred to TUTH. Ninety seven patients (86.6%) were referred by doctor, and rest by nurse, health workers and paramedics. Referral slip was not available in 13 (11.6%) cases and prior information via phone call was received only in 8 (7%) cases.

The mean age of the patients was 25.2 years while age ranged from 15 years to 40 years. Mean period of gestation was 34.35 weeks and 70 (62.5%) cases were < 37 weeks. Concerning pregnancy status 62 (55.35%) patients were antepartum, 32 (28.57%) were intrapartum, 8 (7.14%) postpartum, 10 (9%) early pregnancy. Most common diagnosis for referral was medical disorders complicating pregnancy (42, 37.5%) among which cardiac disease accounted for 22 cases (19.64%), followed by hypertensive disorder which was 18 (16%) as shown in (Table 2).

Table 2. Patterns of different conditions among referred cases (n=112).

Diagnosis			No	Total (%)
Medial disorders complicating pregnancy (42, 37.5%)	Hypertensive disorder	Eclampsia	5	18 (16)
		Severe Pre-eclampsia	12	
		Chr. HTN	1	
	Cardiac disease	RHD	18	22 (19.64)
		Cong HD	3	
		Peri Partum DCM	1	
	Pancytopenia			2 (1.79)
Obstetric hemorrhage	Antepartum hemorrhage		6	9 (8)
	Secondary PPH		3	
Labor abnormalities	Obstructed labor leading to bladder rupture		1	8 (7.14)
	Prolonged labor		5	
	Preterm Labour		2	
Early pregnancy conditions				10 (8.9)
PROM	Term PROM		3	8 (7.14)
	Preterm PROM		5	
Infective conditions				5 (4.46)
Mal presentation				4 (3.57)
Pregnancy with surgical conditions				7 (6.25)
Miscellaneous				19 (17)

Unavailability of perinatal facility was the most frequent reason for referral (Figure1).



Eighty six patients (76.79%) had done antenatal checkup. According to American Hospital Association's Classification, 5 (4.46%) patients were in critical condition, 25 (22.32%) in serious and rest (82, 73%) were in good condition at the time of admission. Fifty eight (51.79%) patients required surgical intervention and 21 patients (18.75%) received intensive care management. In addition to obstetric management nonobstetric management from other specialties (physician, surgeon) was required in 36 (32.14%) patients (Table 3).

Table 3. Distribution of patients according to modes of management required.

Mode of management			No	No %	Total %
Surgical inter vention	LSCS		40	42 (37.5)	58 (51.79)
	Lapa rotomy	With CS hystere-ctomy	1	9	
		With B-lynch/ Uterine artery ligation	1		
		With salping-ectomy	8		
		Hyste-rotomy	1		
	Uterine exploration/MVA			2	
	Surgical indications			5	
ICU care	Ventilator used			8	21 (18.75)
	Not used			13	
Nonobstetric management					36 (32.14)
Blood and blood product transfusion					29 (25.89)
Hemodialysis					1 (0.89)

*The same patient had received multiple modalities of treatment (eg. Same patient had received blood transfusion, ICU care and surgical intervention)

Majority of patients (69, 61.61%) stayed for < 7 days but 13 (11.61%) patients were treated for >21 days (maximum 66 days). The mean duration was 10.54 days.

There were 2 mortalities during the study period among which one was in 34 year Para4+1 woman because of secondary post partum hemorrhage (PPH) with sepsis following vaginal delivery at home. Another was in a 28 years Para1 woman due to acute renal failure (ARF) following lower segment caesarian section (LSCS) for severe preeclampsia with

abruptio placenta. Total number of live births (LB) were 70 (62.5%) among which 28 (40%) required neonatal admission and 3 had early neonatal death (NND) (Table 4).

Table 4. Maternal and perinatal outcome.

Maternal and Perinatal Outcome		Delivered at TUTH	Delivered outside	Total %
Maternal Outcome	Patients Improved	104	6	110 (98.22)
	Maternal mortality	-	2	2 (1.78)
Pregnancy /Perinatal outcome	Live birth (LB)	66	4	70 (62.5)
	Still birth	2	2	4 (3.5)
	IUFD	15	2	17 (15.17)
	Not delivered	11	-	11 (9.82)
	Ectopic. Abortus	10		10 (9)
	Neonatal admission	28	-	28 (40% of LB)
	APGAR <7 in 1 min	20	-	20(29% of LB)
	NND	3	-	3 (4.28% of LB)

DISCUSSION

In the present study obstetric referred cases accounted for 2.6% of the total admissions in the Department of Obstetrics and Gynaecology which was consistent with the study conducted by Ohn et al.[2] Fifty one percent came from rural area and 48.2% from urban area whereas Rathi et al reported 67% of the referrals from urban areas.[3] Most common diagnosis among the referrals was medical disorders complicating pregnancy (37.5%) among which cardiac disease accountted for 19.64%, followed by hypertensive disorder which was 16% in the present study. This is comparable to results reported by Ohn et al in which gestational hypertention was the most common indication (18.5%) for referral.[2] In another study done by Rathi et al 26% were referred for hypertensive disorders of pregnancy, 26% for preterm labour and 21% medical disorders complicating pregnancy.[3] Hypertensive disorder was main indication of referral in another study also done by Shilpa and Anand.[4] However, leading conditions of referral were different in other studies such as premature rupture of membranes, non progress of labour and grand multipara.[5-10] The disparity from these studies might be because TUTH being the tertiary multidisciplinary hospital received medical disorder (heart disease) complicating pregnancy the maximum. Presence of a cardiac centre with intensive care facilities results in many referrals for pregnancy with cardiac diseases at this institute. Lack of advanced cardiac facility or physicians, lack of tertiary level care with multidisciplinary facility might be the possible reasons for referrals to this institute from the various centers especially from outside Kathmandu.

In present study, majority of referrals were during antenatal period (55.35%), followed by

intranatal (28.57%), early pregnancy (9%) and postnatal (7.14%) which is similar to Ohn et al.[2] However, another study done by Patel et al found that majority of referrals were during intranatal period (64.5%), followed by antenatal (23.9%).[10] They had done the study in rural area where women seeking obstetric care directly in intranatal period was more common where as both Ohn et al and present study was done in urban hospital area which received patients in antenatal period more than in intranatal period.

In this study, 25.89% required blood and blood products transfusion whereas according to Rathi et al, 42% patients required blood or blood product transfusion. Higher incidence of PPH in her study was responsible for this high percentage of transfusion.[3] In another study done by Khatoon et al, the figure was 35%.[11] In contrast, only 2.2% of patients, required transfusions in a study done by Ohn et al.[2]

Intensive care management was required in 18.75% of cases in present study. However, in a study done by Rathi et al and Sabale and Patankar, only 8% and 0.79% patients respectively required intensive care,[3, 12] possible explanation again being TUTH a tertiary referral hospital which received more cardiac patients (19.64%), and 26.78% of patients were serious or critical on arrival requiring intensive monitoring.

There were 2 mortalities during the study period. One was in 34 year Para4+1 woman because of secondary PPH with sepsis following home delivery and managed conservatively by health worker at home which was later on taken to nearby health post on 10th post partum day and then ultimately referred to

TUTH. She arrived after 10 days of starting problems. Family members' lack of awareness, poor financial status, arriving TUTH late are the contributing factors for the mortality. Another was in 28 years Para1 woman due to ARF following LSCS for severe preeclampsia with abruptio placenta, referred from medical college outside Kathmandu after no sign of improvement despite their management for few days. Whether early referral could have saved this woman or not is still an unanswerable query. Obstetric haemorrhage, sepsis and toxaemia- the main three components of classic triad of causes of maternal mortality in developing countries- were reasons of mortality of these two women too. The percentage of mortality of present study (1.73%) is comparable to Khatoon et al (2.55%).[11]

In this study total number of live births were 70 (62.5%), intra uterine fetal death 17 (15.17%). while 4 (3.5%) were still births. Among these live births 28 (40%) required neonatal admission and 3 (4.29%) had NND. The percentage of nursery care and NND is quite high in other studies.[3,10] This might reflect that the perinatal facility is probably better in this hospital for which most of the patients (24%) were referred from other centers.

CONCLUSIONS

Wide spectrums of complicated obstetric cases were referred to this hospital. Unavailability of perinatal facility was the most common reason for referral followed by unavailability of physician. Most common diagnosis at the time of referral was medical disorders complicating pregnancy (37.5%). Fifty two percentage patients required surgical management and 19% required intensive care management. Twenty seven percentages of cases were in serious or critical condition on admission and 98% improved and were discharged. Timely referrals with detailed referral slips or prior information of referred cases might help in early and optimal intervention so that both major morbidities and mortalities can be avoided. A structured referral system would help both patient and doctor in providing essential life saving care.

DISCLOSURE

The authors report no conflicts of interest in this work.

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Effectiveness of Intrathecal Morphine for Analgesia following Elective Caesarean Section

Koju RB[1,2], Gurung BS[3], Dongol Y[4]

[1]Department of Anaesthesia and Critical Care, KIST Medical College, Lalitpur, Nepal, [2]Department of Anaesthesia and Critical Care, Nagarik Community Teaching Hospital, Bhaktapur, Nepal, [3]Department of Obstetrics and Gynaecology, KIST Medical College, Lalitpur, Nepal, [4]Department of Biochemistry, KIST Medical College, Lalitpur, Nepal

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Aims: This study evaluates the effectiveness of usage of 0.2 mg intrathecal morphine as post-operative analgesia and its effect on activity of mother after elective cesarean section.

Methods: This hospital based prospective, randomized, double-blinded and placebo controlled study was carried out at Nagarik Community Teaching Hospital, Bhaktapur between 2012 January to 2014 November after the approval was taken from the hospital authority and the written informed consent from the participating patients. Fifty women of ASA I or II physical status undergoing cesarean section under sub-arachnoid block was randomized into two groups – P group (placebo group, n = 25) and M group (Treatment group, n = 25). P Group received hyperbaric bupivacaine 2.3ml, 0.5% bupivacaine (11.5 mg) and M Group received morphine 0.2 ml (0.2 mg) plus bupivacaine 2.3ml, 0.5% (11.5 mg) intrathecally. All subjects received 8 mg ondansetron intravenously 30 minutes before surgery to prevent possible drug-induced pruritus and post-operative nausea and vomiting. 1000 mg rectal acetaminophen suppository was given at the end of the surgery. Pain, nausea and pruritus during the first 24 hours using visual analog scale were recorded by a trained nurse or attending doctor who was not involved in the study.

Results: Duration of complete analgesia and the time to request for additional analgesics was longer in M Group than in P Group. Similarly, the active movement is earlier in M Group than in P Group. There were no significant differences in adverse effects between the groups.

Conclusions: Addition of morphine 0.2 mg to heavy bupivacaine intrathecally reduced post-operative pain and analgesic requirements without any significant difference in adverse effects.

Keywords: caesarean section; intrathecal morphine; post-operative pain.

INTRODUCTION

It is a great challenge to all anaesthetics in providing optimal analgesia. The main purpose of any anaesthesiologist is to provide satisfactory pain relief with a minimal cost. Now-a-days, there are many post-operative pain controlled methods, such as patient controlled analgesia (PCA) or patient controlled epidural analgesia (PCEA), which are more expensive and may not be appropriate because of lack of knowledge among the patients. On the other hand, the sedative effects of the opioids and motor blockade due to local anaesthetics may limit the mother's ability to care for her child shortly after delivery.[1] Administration of intravenous PCA with pethedine to breast feeding mother after caesarean section may cause neonatal neurobehavioral depression.[2]

CORRESPONDENCE

Dr Ram Bhakta Koju
Department of Anaesthesia and Critical Care
KIST Medical College, Lalitpur, Nepal
Email: dr.koju@gmail.com
Phone: +977-9841113271

Sub-arachnoid block (SAB) is very popular for caesarean section because this technique is very easy and provides adequate muscle relaxation of abdominal muscles and adequate intra and post-operative analgesia.[3] Single dose of intrathecal morphine decreases post-caesarean opioid requirements and may reduce or prevent neonatal neurobehavioral depression due to maternal analgesia.[2]

The addition of intrathecal morphine to local anaesthetics provide an effective and prolonged post-operative analgesia but has been associated with incidence of pruritus.[4] Acetaminophen, when given along with opioids, potentiates the effect of opioid analgesia. Hence, small dose of intrathecal morphine combined with acetaminophen per rectally, antiemetics and medications for prutitus is clinically relevant to study post-caesarean delivery analgesia.[5-7]

In our clinical setting, we undertook a prospective, randomized, double blinded and placebo controlled study to assess the effectiveness of 0.2 mg intrathecal

injection of morphine along with 0.5%, 2.3 ml heavy bupivacaine on post-operative analgesia and activity of mother after elective caesarean section.

METHODS

This prospective, randomized, double blinded and placebo controlled study was conducted in Nagarik Community Teaching Hospital, Bhaktapur between 2012 January to 2014 November. The hospital authority approved the study protocol and written informed consent was taken from each patient. Parturients of American Society of Anesthesiologists (ASA) I or II physical status scheduled for caesarean section under spinal anaesthesia were recruited in the study. Term size was 37 completed gestation weeks with singleton or post term cases. All subjects weighed between 50-100 kgs. Parturients with history of heart disease, respiratory insufficiency, known allergy to any of the study drugs and foetal compromises for example malfunction, underweight and cardiorespiratory insufficieny were excluded from the study. Similarly, patients with any contraindication for spinal anaesthesia or those who refused to participate in the study were also excluded.

Fifty patients were randomly divided into two groups – P group (placebo group, n = 25) and M group (Treatment group, n = 25). All patients received 0.5%, 2.3 ml (11.5 mg) preservative free heavy bupivacaine. P group received 0.2 ml of normal saline and the M group received 0.2 ml (0.2 mg) morphine, for a total volume of spinal injection of 2.5 ml. The study drug and the placebo were prepared by an anesthetic nurse. She also assisted in maintaining the randomization of sample in a double-blinded fashion, using a simple lottery method. She was oriented of the study procedure but neither involved in the study nor in the patient care. Therefore, both the patients and the anaesthesiologists performing the spinal anaesthesia and collecting the post-operative data were blinded as to the study drugs.

Following fluid preload of 1000 ml crystalloid solution, spinal anaesthesia was performed using a 25 gauze Whitacre or Quincke needle with the patient in left lateral or sitting position, at the level of L3-L4 or L4-L5. 8 mg ondansetron intravenous was given to all patients in both the groups 30 minutes before SAB. ECG, NIBP, SpO_2 and heart rate were continuously monitored. 1000 mg rectal acetaminophen suppository was given at the end of the surgery to both of the groups. A visual analog scale (VAS) was used to assess post-operative pain with anchor point at 0 mm and 100 mm marked scale (0 = No pain and 100 mm = worst pain).

The surgery was started when the sensory block reached the level of T4, as detected by the loss of cold sensation. The end point of this study was 24 hours post-operative period. Post-operative care was provided as per the institutional monitoring protocol. Our post-operative ward is well equipped with monitors, 24-hours on duty doctors, experienced nurses and bed-side availability of naloxone. Staffs were instructed to be aware of the study patients who may become drowsy due to intrathecal morphine, monitor SpO_2, respiratory rate, send ABG if needed and report to anesthesiologist. Attending doctors or nurses– who were blinded observers – were involved in the patient care and data collection in the format provided.

From the study of Terajima et al.,[8] we used the standard deviations of pain at rest during 24 hours to detect the difference of 18 units in average pain score between two groups, with 80% power and at 5% level of significance. The minimum sample size calculated was 24 in each group.

Statistical analysis was performed using chi square test and data were presented in mean with standard deviation and the percentage. P-value less than 0.05 was considered to be significant.

RESULTS

All the enrolled patients participated until the completion of the study. Demographic characteristics, as shown in table 1,

Table 1. Demographic Characteristics of the Patients *(Mean ± SD)*

Variables	Study Group Placebo (P); n=25	Treatment (M); n=25	p-value
Age (years)	25.2 ± 3.27	24.2 ± 3.56	0.859
Height(Cm)	157.4 ± 4.77	155 ± 4.12	0.895
Weight(Kg)	69.2 ± 9.96	70 ± 8.56	0.845

were similar in both groups. The new born characteristics in both the groups were also similar and the APGAR Score in 1 minute and 5 minutes

were similar and within normal limits, which was shown in Table 2.

Table 2. New Born Baby Characteristics *(Mean ± SD).*

Variables	Study Group: Placebo (P); n=25	Treatment (M); n=25	p-value
Weight (gms)	3100 ± 300	3110 ± 250	0.857
APGAR score			
1 minute	8.7 ± 0.6	8.7 ± 0.6	0.999
5 minute	9.0 ± 0.5	9.1 ± 0.5	0.857

Table 3 illustrates the VAS pain score within 24 hours in the two groups at two different situations; namely, at rest and during movement. At rest, M Group (30 ± 10 mm) have significantly lower pain score than P Group (70 ± 20 mm). During movement as well, the pain score between the two groups are statistically significantly – 60 ± 20 mm in M group whereas 80 ± 10 mm in P group.

Table 3. Maximum Pain Score within 24 hours Post-operation scored in VAS *(Mean ± SD).*

Variables	Study Group: Placebo (P); n=25	Treatment (M); n=25	p-value
At rest (in mm)	70 ± 20	30 ± 10	<0.0001
During Movement (in mm)	80 ± 10	60 ± 20	<0.0001

The duration of complete analgesia and time of first request for additional analgesia were longer in M group than in P group with p-value less than 0.0001 (statistically significant), as shown in table 4.

Table 4. Time of Request of Additional Analgesia *(Mean ± SD).*

Variables	Study Group: Placebo (P); n=25	Treatment (M); n=25	p-value
Time of first additional analgesia request (in hours)	5.0 ± 2	24.0 ± 0	<0.0001

In M group request for first additional analgesia was after 24 ± 0 hours whereas in P Group it was 5 ± 2 hours. 90% of the patients requested for analgesia within 24 hours in P group whereas no patient had requested for additional analgesia in M group (table 5). The opioid used in cases of additional analgesia was tramadol injection.

Table 5. Use of Additional Analgesia to manage the Post-caesarean Pain.

Variables	Study Group: Placebo (P); n=25	Treatment (M); n=25	p-value
Analgesic requested within 24 hrs	90%	0%	<0.0001
Total tramadol dose (mg/pt) at 24 hours	50 ± 25mg	0 ± 0.0	<0.0001

Regarding the adverse effects, the incidence of pruritus was same (5%) in both the groups and was cured without any medication. Similarly, the incidence of nausea was also same (3%) in both the groups and was treated by injection metoclopramide intravenous, if needed (table 6).

Table 6. Adverse Effects observed in the Patients under SAB.

Variables	Study Group: Placebo (P); n=25	Treatment (M); n=25
Pruritus	5%	5%
Antipruritic use	0%	0%
Nausea	3%	3%

The significant decrease in the incidence of pruritus and nausea might be due to prophylactic administration of ondansetron. There was no question of retention of urine because all patients were catheterized with foley's catheter.

DISCUSSION

Morphine, an opioid, is an alkaloid constituent of opium. It is dried latex obtained as natural product in opium poppy (Papaver Somniferum). Morphine is an archetypal opioid which, in clinical medicine, is still considered as a gold standard of analgesic therapy used to relief intense pain. It elicits analgesia by stimulating the opioid receptors, a G protein coupled receptor (GPCR) highly expressed in the CNS.[9] Morphine-6 beta-glucronide is a major metabolite of morphine with potent analgesic effect and is 5 fold

more effective at the level of the spinal cord than supra-spinally.[10]

This study shows that additional intrathecal morphine 0.2 mg with 0.5% heavy bupivacaine for elective caesarean section is highly effective in reducing post-operative pain and analgesic requirement. These findings are very much similar to other studies.[8,11] Intrathecal morphine provides very effective analgesia after caesarean delivery even when administered in very small doses (25-200mcg).[12] Intrathecal morphine when combined with other analgesia such as ketorolac and other NSAIDs for post-caesarean pain management are found to be very effective.[6,13] NSAIDs and intrathecal morphine seems to act synergistically.[4,5,13] Similarly, acetaminophen is well known to potentiate opioid analgesia.[7] Multi classes of analgesic administration simultaneously to the same patient produces competitive, additive or synergistic effects resulting into powerful analgesic effects and also decreases side effects due to the use of minimal doses in such scenario.[8]

SAB induced prior to surgical incision attenuates peripheral and central sensitization.[14] On the other hand, pain is also induced by uterine contraction due to involvement of several chemical nociceptive pathways,[15] which is mediated by prostaglandin cascade.[16] This theory postulates the effectiveness of intrathecal morphine and NSAIDs combination therapy for post-caesarean pain management but it may concern post-operative platelet dysfunction. So, this study explores the effectiveness of intrathecal morphine and the rectal acetaminophen suppository. Small dose of intrathecal morphine if used along with other analgesia provide adequate pain relief after caesarean delivery without respiratory depression or compromising mothers ability in caring her new born baby.[8] Early mobilization also decreases complications such as deep vein thrombosis (DVT).[17]

Pruritus and nausea are common and troublesome side effects of neuraxial opioid administration after caesarean section. Intravenous droperidol,[18] ondansetron[19] and dexamethasone[20] all are found to be effective to decrease nausea and pruritus after caesarean delivery. Activation of opioid receptor and 5-HT3 receptors in the dorsal part of spinal cord and the nucleus of the spinal tract of the trigeminal nerve in the medulla by neuraxial opioid administration or by circulating oestrogen in the parturients result into neuraxial opioid-induced pruritus.[21] In this study, the incidence of puritus and nausea are similar in both the groups because of prophylactic administration of 8 mg ondansetron 30 minutes before surgery. Intrathecal morphine is safe for new born baby as the APGAR score in 1 minute and 5 minutes are similar and within normal limits in both the groups because of very minimal systemic absorption of intrathecal morphine. The onset of intrathecal morphine is 30-60 minutes,[22] so baby can be delivered before the occurrence of effect of intrathecal morphine.

This study suggests that intrathecal morphine in very small dose 0.2 mg has an effective role in post-caesarean delivery pain management. The results of this study are in good agreement with the work of Rosaeg et al[23] who have shown that intrathecal morphine is effective as part of multimodal pain management after caesarean delivery.

CONCLUSIONS

Very small doses of intrathecal morphine added to bupivacaine for spinal anaesthesia for caesarean delivery provides effective analgesia to mothers at rest and during activity such as breast feeding, locomotive activities in the ward etc, up to 24 hours and reduced intravenous opioid requirements. Similarly, it also does not pose the adverse effects to the newborn since it has lesser and delayed systemic absorption.

DISCLOSURE

The authors report no conflicts of interest in this work.

No violation of human rights and safety.

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Cornual Ectopic Pregnancy: Case Series

Baral G, Shakya B, Silwal J
Department of Obstetrics and Gynaecology, Paropakar Maternity and Women's Hospital, Kathmandu.

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Three cases of cornual pregnancies encountered within three weeks at Paropakar Maternity and Women's Hospital had diverse presentations. Fortunately, in all three case series, cornual resection was performed successfully. Cornual pregnancy is difficult to diagnose preoperatively with low ultrasonographic sensitivity and is easily confused with tubal ectopic pregnancy or a normal intrauterine pregnancy. Diagnosis before rupture is essential to prevent mortality and potential loss of fertility. The surgical management of diagnosed cornual pregnancy consists of hemostasis, resection, repair and reconstruction.

Keywords: cornual ectopic; cornual pregnancy; cornual resection.

INTRODUCTION

Cornual pregnancy is a rare subtype of ectopic pregnancy, resulting when implantation occurs in the most proximal part of the fallopian tube. It occurs in approximately 2-4 percent of ectopic pregnancies or one in every 2500 to 5000 pregnancies.[1] Cornual pregnancies are life-threatening conditions with an associated mortality rate of 2-2.5% compared to the overall 0.14% mortality rate for ectopic pregnancy.[1,2]

CASE 1

Forty years old gravida-2 para-1 was admitted on 30th May 2014 at 9 pm with suspicion of ectopic pregnancy at 9 weeks and 2 days of amenorrhoea. She had pain abdomen and mild vaginal bleeding seven hours prior to emergency visit. She was hemodynamically stable- pulse 78 bpm, blood pressure 120/80 mmHg, hemoglobin 11.9g/dl, soft abdomen and brownish vaginal discharge. Urine for pregnancy test was positive with serum β-hCG 34,401 mIU/ml and there were subserous fibroid with heterogenous lesion at right adnexa sized 3.2x2.5 cm in ultrasonography. She was kept under conservative management. Repeat serum β-hCG after 48 hours was 31,000m IU/ml and ultrasonography revealed gestational sac of seven weeks with fetal pole and cardiac activity at cornual junction suggesting cornual pregnancy. Emergency laparotomy was done with right cornual resection and repair with left tubal ligation under subarachnoid block. There was hemoperitoneum of about 50 ml, left cornual pregnancy sized 6x4 cm with trickling blood, and round ligament was in the middle at its base. There were multiple subserous fibroids 3x3 cm near cornual ectopic area and another one 4x4 cm at anterior wall of uterus. Uterus was soft and enlarged. Left tube and both ovaries were normal. Total blood loss was 200 ml. Her post-operative period was uneventful and discharged on 7th postoperative day. Histopathology was reported as cornual ectopic pregnancy.

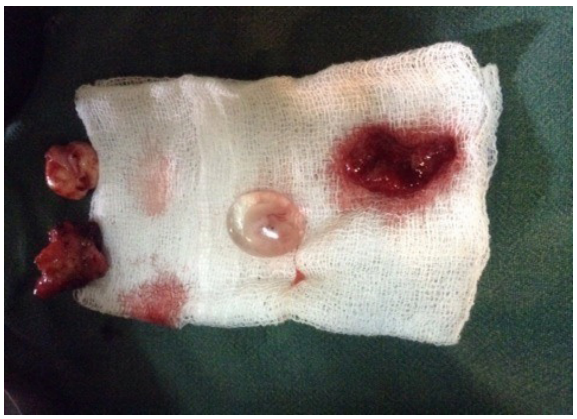

Figure 1. Case 1: Intact gestational sac of cornual ectopic pregnancy.

CORRESPONDENCE

Dr Gehanath Baral
Department of Obstetrics and Gynaecology,
Paropakar Maternity and Women's Hospital, Kathmandu.
Email: gehanath@gmail.com
Phone: +977-9841228829

CASE 2

Thirty three years old gravida-2 para-1 at seven weeks of amenorrhoea was admitted on 7th June, 2014 at 8.15 PM who had vaginal bleeding following failed surgical termination one week ago at health post and pain abdomen 17 hours prior to emergency visit which was severe and sudden in onset. This was a referred case from Bir Hospital as ultrasonogaphy revealed mixed echogenic lesion of 8.6x5.7 cm with minimal vascularity at left adnexa and anterior to uterus, and moderate amount of collection in peritoneal cavity. Patient was pale, pulse 110 bpm, blood pressure 140/70 mmHg. Abdomen was tender with rebound tenderness without vaginal beeding on speculum examination. Urine for pregnancy test was positive. Patient underwent emergency laparotomy with left cornual resection under subarachnoid block. There was hemoperitoneum of about 2000 ml (600 ml blood + 1400 ml clots). There was ruptured left cornual pregnancy just lateral to the round ligament. Uterus was bulky, right tube and bilateral ovaries were normal. Patient received 2 units blood transfusion intra-operatively and 2 units post-operatively. Her post-operative period was uneventful except for low-grade fever on first and second postoperative day and was discharged on seventh post-operative day. Histopathology report revealed cornual ectopic pregnancy.

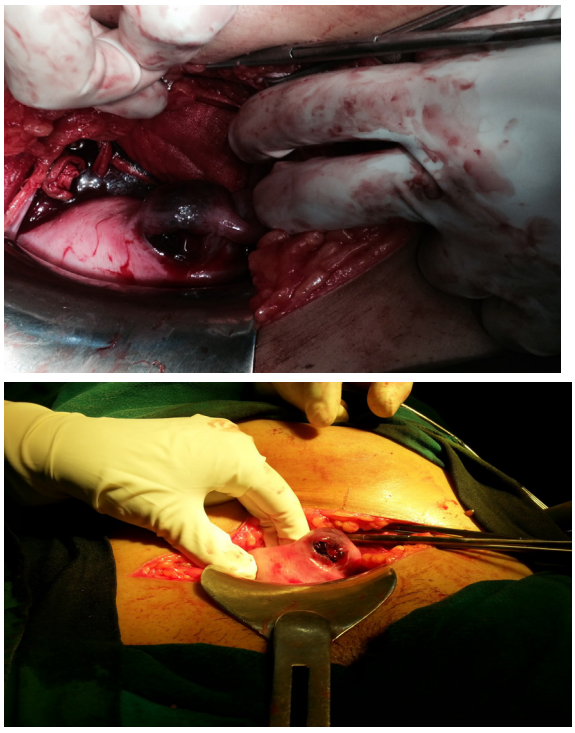

Figure 2-3. Case 2: Cornual ectopic pregnancy.

CASE 3

Twenty years old primigravida of around 16 weeks of amenorrhoea was admitted through emergency department on 18th June, 2014 at 8 pm as she had history of fall from stairs and vaginal bleeding three hours prior to admission. Her pulse was 78 bpm, blood pressure 90/60mmHg. Abdomen was soft, mild tender and uterus was 14-16 weeks size. There was no vaginal bleeding, cervical os was closed and no forniceal tenderness. Patient was managed conservatively. Ultrasonography revealed 17 weeks intrauterine fetal death, fetal ascites and anteriorly situated placenta. The management plan decided as medical termination of pregnancy with misoprostol 200 mcg vaginally 4 doses 6 hours apart. Since she did not respond, she again received 400 mcg misoprostol 4 doses 6 hours apart. Next day, manual vacuum aspiration was tried in operation theatre and no tissue was obtained. Pelvic examination under anesthesia revealed separate mobile mass next to the uterus of equal size. Then with the suspicion of abdominal pregnancy, emergency laparotomy was done under general anesthesia. Per operative finding revealed right cornual pregnancy with engorged vessels over its surface lateral to round ligament and a short pedicle, 50 ml of hemoperitoneum, enlarged uterus with perforation (3x2 cm) at anterior uterine wall of corpus (iatrogenic) and normal tubes and ovaries. Right cornual resection and repair along with repair of uterine perforation performed. Cut section revealed dead macerated male fetus and intact sac with about 50 ml of amniotic fluid. Operative blood loss was 200 ml. Her post-operative period was uneventful and was discharged on seventh postoperative day. Histopathology report revealed cornual ectopic pregnancy.

In all of the case series, the known risk factors like pelvic inflammatory disease, previous ectopic or tubal/pelvic surgery, use of IUCD, artificial reproductive technique or smoking habit were absent.

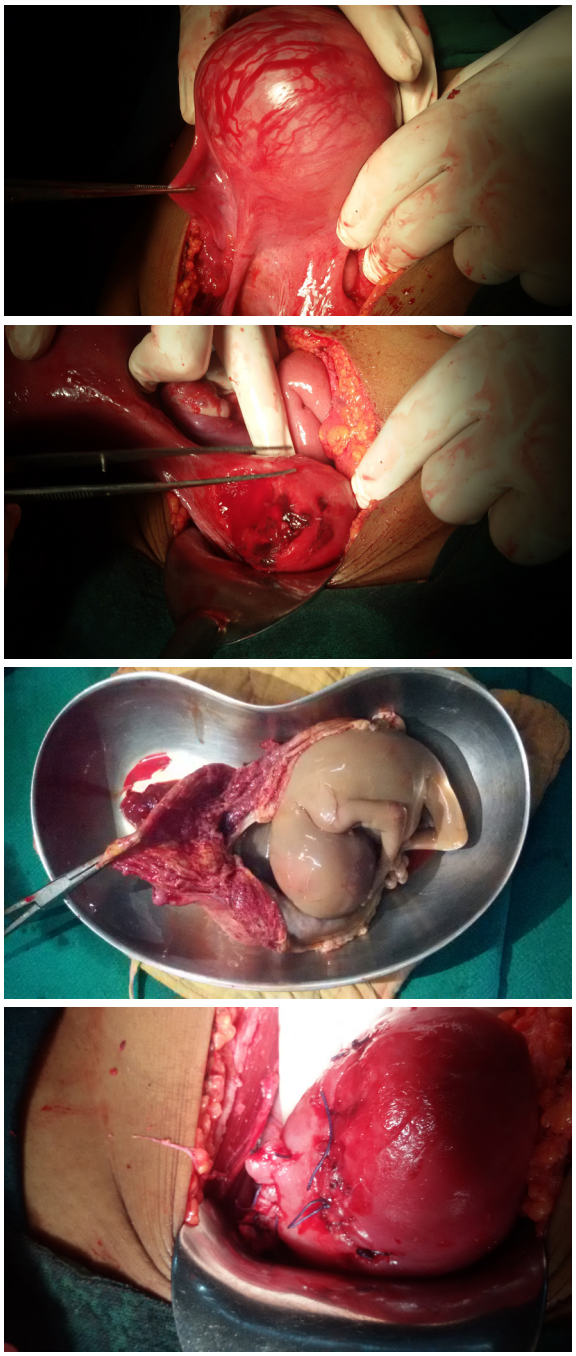

Figure 4-7. Case 3: 16 weeks cornual ectopic pregnancy.

COMMENT

Each of the case series of cornual pregnancy had diverse presentations. Women over 40 years of age have a 3 – 4 fold increase in the risk for developing an ectopic pregnancy compared to women aged 15-24 years.[3] In our study, case 1 was 40 years the other two were 33 and 20 years.

The ultrasound picture of cornual ectopic can be very similar to that of an early pregnancy in a bicornuate uterus or a fibroid uterus.[3] In case 1, it was associated with fibroid uterus missing the cornual pregnancy. Even with a high index of suspicion and advances in sonography, including transvaginal sonography and serum β-hCG, cornual pregnancy remains the most difficult type of ectopic pregnancy to diagnose due to the low sensitivity and specificity of symptoms and imaging.[1]

Cornual pregnancies show fewer early symptoms due to the stretching potential of the uterine wall.[4] The site of implantation also makes the pregnancy difficult to differentiate from an intrauterine pregnancy on ultrasound.[3,5] Moreover, the assessment of the uterine size is rarely helpful and cervical excitation is not a specific sign in cornual ectopic.[3] As was seen in our third case, 16 weeks cornual pregnancy was missed by clinical and ultrasonography examination as the pregnancy may appear to be in an intrauterine location. Further the clinical examination was limited by abdominal wall tenderness due to fall injury.

Cornual ectopics are associated with high risk of rupture that could occur as late as 10 –16 weeks gestation.[3] Rupture of a cornual ectopic at that late gestation can cause profuse intraperitoneal bleeding which can be life threatening. As contrast to case 2 in which rupture occurred at seven weeks gestation requiring four units of blood transfusion, patient had presented late to our hospital and moreover, patient was even tried for surgical termination of pregnancy. Fortunately in case 3, there was no rupture of 16 weeks cornual pregnancy despite being tried for misoprostol induction.

Overall, cornual pregnancy is one of the most dangerous type of ectopic pregnancies with high maternal mortality and cannot be solely relied on findings of abdominal ultrasound. Diagnosis is done with transvaginal ultrasound: 1) an empty uterine cavity, 2) a chorionic sac seen separately and > 1cm from most lateral edge of uterine cavity, and 3) a thick myometrial layer surrounding the chorionic sac. Laparoscopy may be needed to confirm diagnosis but in case of massive intraperitoneal bleeding immediate laparotomy must be done. The surgical principle for the management of diagnosed cornual pregnancy can be described by mnemonic HR3,

which stands for *Hemostasis, Resection, Repair and Reconstruction*. The management of cornual ectopic pregnancy depends upon extent of trauma and desire of patient to preserve fertility. It can be done with systemic methotrexate or conservative laparoscopic technique in selected cases. Cornual resection and repair of the defect by laparotomy remains the standard conservative surgical procedure for many surgeons. In some cases, where uterine rupture had occurred or a very large cornual pregnancy is present hysterectomy may be required. A cornual resection and salpingectomy is done by first ligating the ascending uterine vessels where they approach the cornua. The pregnancy site is excised in a V-shaped manner, and the myometrium is approximated with figure of eight closure using no. 0 delayed absorbable suture. The round ligament is cut and resutured to the cornu and the uterine serosa by use of interrupted sutures. The round and broad ligaments are brought over the incision with mattress suture (the modified Coffey Suspension), and an additional interrupted sutures of no. 2-0 or no. 3-0 delayed absorbable sutures can be used to secure the serosa of the round ligament to the serosa of uterus to maintain the operative site in a permanent retroperitoneal position.

Traditionally, cornual ectopic pregnancies were treated with hysterectomy. The current gold standard for a cornual pregnancy is a diagnostic laparotomy followed by a cornual wedge resection. Recent surgical advances have demonxstrated that operative laparoscopy is a possible alternative in a stable patient with no suspicion of rupture.[6] Fortunately, in all three case series, cornual resection was performed successfully.

Repeat sonographic assessment is essential even in light of a "normal" intrauterine pregnancy if a patient's symptoms are consistent with ectopic pregnancy. Diagnosis before rupture is essential to prevent mortality and potential loss of fertility.[7]

CONCLUSIONS

Clinical differentiation of cornual pregnancy from tubal ectopic pregnancy or a normal intrauterine pregnancy is often difficult due to low ultrasonographic sensitivity. Since, symptoms are often nonspecific and diagnostic imaging inconclusive, correct diagnosis of an advanced extrauterine pregnancy warrants a high index of suspicion.

DISCLOSURE

The authors report no conflicts of interest in this work.

No violation of human rights and safety.

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Lymphoma of Ovary: A Primary Extra-nodal Manifestation

Joshi AP, Chitrakar NS, Shrestha I
Department of Obstetrics and Gynaecology, Civil Service Hospital of Nepal, Minbhawan, Kathmandu, Nepal

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Involvement of the ovary by malignant lymphoma is a well-known manifestation of disseminated nodal disease. But, lymphoma as primary manifestation is extremely rare. Here, we report a case of malignant lymphoma which presented as ovarian cancer and managed with surgery and subsequent chemotherapy. A lady of thirty two years presented with features of malignant ovarian tumor. The diagnosis of malignant ovarian lymphoma was made after surgery and histological and immunohistochemical study of the excised tumor. The tumor was classified as diffuse large B-cell lymphoma. The patient was put on chemotherapy and she is on follow-up in disease free-state for last two years.

Keywords: lymphoma; ovary; primary.

INTRODUCTION

Ovary is the site of pluripotency. So, ovaries are very susceptible to various malignant and benign histopathological tumors. One of the rare forms of tumor that arise in ovary is lymphoma. Lymphoma can arise de novo or as a part of systemic disease. Common form of lymphoma in ovary is non-Hodgkin's type. Primary ovarian non-Hodgkin's lymphoma is very rare accounting 0.5% of all non-Hodgkin's lymphomas and 1.5% of all ovarian neoplasms.[1,2] We present a case of non-Hodgkin's lymphoma of the ovary which was managed with surgery and chemotherapy.

CASE

A lady of thirty two years with two children, regularly menstruating, presented to emergency with complaints of pain lower abdomen for one month which had increased for four days and fever with chills and rigors also for the same duration. There was no significant past medical and surgical as well as family history. Her examination revealed generalized abdominal and fornicial fullness with tenderness however there was no lymphadenopathy.

Her blood investigation including complete blood counts showed no abnormality. Among the tumor markers Cancer Antigen-125 (CA-125) was 236 and Lactate Dehydrogenase (LDH) was 1636. Contrast enhanced Computerised-Tomography revealed large heterogenously enhancing soft tissue density masses in bilateral parauterine region with ascitis, enhancing omental thickening and retroperitoneal lymphadenopathy. The ascitic fluid for cytology was negative for malignancy and fine needle aspiration cytology of tumor deposit showed chronic inflammatory lesion.

She underwent staging laparotomy with total abdominal hysterectomy, bilateral adnexectomy, omentectomy and peritoneal biopsy and staged as IIIc.

She was found to have straw coloured ascitic fluid around 1000ml with bilateral ovarian solid tumors, right sided measuring 7x5 cm and left 5x4cm with intact capsule (Figure 1).

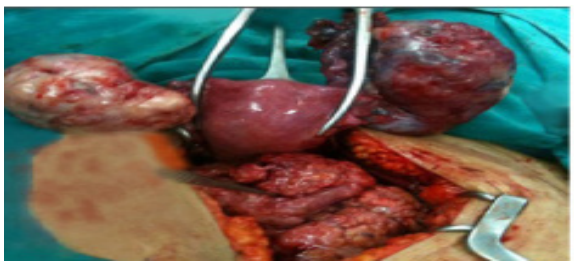

Figure 1. Intra operative finding of uterus bilateral ovarian tumor with involved omentum.

The Omentum was thickened and studded with miliary like deposits and similar deposits were present in bowel, bladder, liver, under surface of diaphragm. Both parietal and visceral peritoneum were thickened.

On gross examination, there were bilateral solid ovarian tumors with areas of cystic degeneration and omental caking (Figure 2 and 3).

CORRESPONDENCE

Dr Arun Prasad Joshi
Department of Obstetrics and Gynaecology,
Civil Service Hospital of Nepal, Minbhawan
Email: e_apj2000@yahoo.com
Phone: +977-9841341723

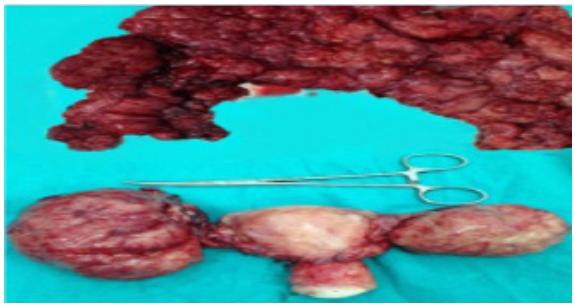

Figure 2. Excised tissue of bilateral ovarian tumor with omentum.

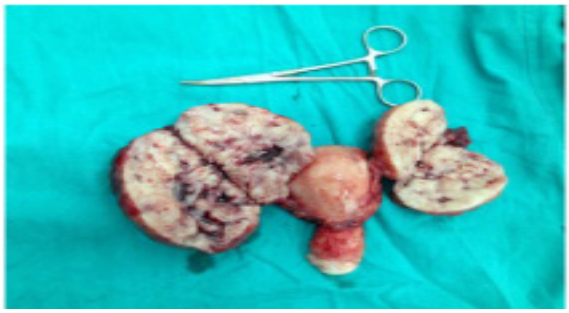

Figure 3. Cut section of bilateral ovarian tumor.

The excised tissue sent for histopathological examination was consistent with bilateral ovarian non-Hodgkin's lymphoma with extragonadal involvement (peritoneal biopsy and omentum were positive for tumor). Immunohistochemistry of the same showed Leucocyte common antigen (LCA), CD20 and Bcl-6 being positive favoring diffuse B-cell non-Hodgkin's lymphoma.

Her bone marrow aspiration done after surgery showed normal hematopoiesis with no abnormal cells.

The patient received six cycles of Cyclophosphamide, Hydroxydaunorubicin (doxorubicin or adriamycin), Oncovin (vincristine), Prednisone (CHOP) regimen. Follow-up Computerised Tomography (CT) scan done after six months of treatment showed no signs of recurrence.

COMMENT

Lymphoma is a rare tumor of the ovary and its presence most commonly represents involvement in overt systemic disease, almost always of non-Hodgkin's type.[3,4] The diffuse large B-cell lymphoma appears to be the most common one.[2] Lymphoma of ovary can be divided into primary and secondary. It is important to separate one from the other because there is considerable evidence that primary extra-nodal lymphoma tends to run a less aggressive course than does the nodal one.[5,6] The 5 year survival for extra-nodal is 80% whereas secondary malignant lymphoma is only 33%.[7] Fox et al[8] suggested criteria for diagnosing primary ovarian lymphoma 1) Tumor is confined to ovary, regional lymph nodes or adjunctive organs at the time of diagnosis 2) the peripheral blood and the bone marrow should not contain any abnormal cells 3) The lymphomateous lesions that occur at the sites remote from the ovary, at least several months should have elapsed between appearance of ovarian and extra ovarian lesions. In our case there was no obvious lymphadenopathy (except retroperitoneal) and no atypical cells in peripheral blood at presentation and post-treatment follow-up CT scan favoring the diagnosis of primary ovarian lymphoma. However, there is always an argument regarding this when there is involvement of omentum and peritoneum at the time of surgery as seen in our case.[1,9]

Majority of primary ovarian lymphomas present with pelvic complaint; some cases present with ascitis and raised CA-125[10] which were also present in this case.

The use of chemotherapy is based on the principle that ovarian lymphoma must be considered as a localized manifestation of systemic disease.[8] The appropriate chemotherapy regimen is CHOP as similar to nodal non-Hodgkin's lymphomas.

Our patient was also treated with total abdominal hysterectomy and bilateral adnexectomy and omentectomy followed by six cycles of CHOP regimen. At present she is doing well. Considering the way she presented to us, findings at surgery, blood and bone marrow investigations and respond to the treatment modalities, primary ovarian lymphoma is more likely entity rather than secondary to systemic nodal non-Hodgkin's lymphoma of ovary.

In conclusion, lymphoma of ovary is a rare manifestation. Primary extra-nodal manifestation in ovary lymphoma should also be considered as a differential diagnosis when a middle aged lady presents with features of advanced ovarian cancer.

DISCLOSURE

The authors report no conflicts of interest in this work.

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Posterior Reversible Encephalopathy Syndrome due to Eclampsia in Term Pregnancy

Gurung T, Shrestha AB, Shrestha S
Department of Anaesthesia, Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu, Nepal

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We report a 30 years primigravidae presented in term pregnancy with eclampsia with intrauterine foetal death and underwent instrumental delivery. Peripartum management of eclampsia is always challenging for anaesthesiologist and obstretrician. The case was managed under general anaesthesia and kept on mechanical ventilation for three days. Postpartum cranial computed tomography revealed low attenuated area in right basal ganglia. Low attenuated area in bilateral frontal and parietal lobes with subtle gyral high density in bilateral frontal lobes. Report was suggestive of posterior reversible encephalopathy syndrome. Clinical improvement was observed with supportive treatment and extubated on the third postpartum day. Posterior reversible encephalopathy syndrome is a cliniconeuroradiological syndrome associated with the various conditions including severe hypertension and seizures. Eclampsia is one of the most important causes of posterior reversible encephalopathy syndrome.

Keywords: eclampsia; posterior reversible encephalopathy syndrome; preeclampsia.

INTRODUCTION

Preeclampsia is a multi-organ system disorder that occurs after the 20th week of gestation and is characterised by hypertension and proteinuria with or without oedema.[1] When the diastolic blood pressure is more than 110 mmHg and protein is above 3 gm/day, the condition is called severe preeclampsia. Preeclampsia and its variants affect approximately 5% of the pregnancies and remain the leading causes of both maternal and foetal morbidity and mortality worldwide.[2] The incidence of eclampsia occurs in approximately 0.5% of the patients with mild preeclampsia and 2% to 3% of those with severe preeclampsia. Depending on the systemic involvement, several other symptoms such as coagulopathy, renal or liver failure, HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome also complicate the clinical picture and recent entity of posterior reversible encephalopathy syndrome (PRES).

PRES was first described in 1996 by Hinchey et al[3] and was named as reversible posterior leukoencephalopathy syndrome. It is a transient clinicoradiological syndrome, first noted in patients with hypertensive encephalopathy. PRES has been associated with many conditions including eclampsia, severe hypertension, autoimmune disease, immunosuppressive agents and sepsis. It can be reversible with prompt diagnosis and treatment without any residual neurological deficit. Delay in diagnosis and management can result in permanent damage to brain tissues. The incidence of PRES in association with eclampsia is still unknown. We presented one case of term pregnancy associated with eclampsia with PRES and completely recovered without any neurological deficits.

CORRESPONDENCE

Dr Tara Gurung
Department of Anaesthesia
Paropakar Maternity and Women's Hospital
Thapathali, Kathmandu, Nepal
Email: grgtara@hotmail.com
Phone: +977-9841379504

CASE

A 30 years primigravidae was referred from Jiri Hospital, with the diagnosis of term pregnancy with eclampsia. She was managed there conservatively with loading dose of magnesium sulphate 4 gm intravenous slowly and 5 gm intramuscular in each buttock, paracetamol 300 mg intramuscular, diazepam 5 mg intravenous, nifedepine 10 mg per oral and referred to our hospital for better management on the same day. She had severe headache for three days and multiple episodes of loss of consciousness followed by generalised seizures, initially in every 2-3 hours, later every half hourly and lasted for one minute on average. Her personal and past history was not significant.

On our emergency room, patient's general condition was poor, pulse rate was 110 beats/min, blood

pressure was 80/40 mmHg, and respiratory rate was 20/min. On neurological examination, her Glasgow Coma Scale was 4/15 (E1M2V1), pupil was bilaterally equal and reacting to light, and bilateral plantar reflexes were absent. On chest auscultation, she had bilateral basal crepitation. On abdominal examination, fundal height was term size, fetal heart sound was not heard, and on per vagina examination cervix was fully dilated. Other systemic examinations were within normal limits.

Blood investigation reports were within normal limits except uric acid was 9.9 mg%, urea- 83 mg%, creatinine- 2 mg%, lactate dehydrogenase- 1392 U/L and urine analysis revealed 2+ proteinuria. A provisional diagnosis of primigravidae with term pregnancy in the second stage of labour with eclampsia with intrauterine foetal death (IUFD) with hypoxic brain injury was made and she was immediately transferred to the operation theatre for an emergency instrumental delivery under general anaesthesia.

In the operation theatre, preoxygenation was done and premedicated with metoclopramide 10 mg, ranitidine 50 mg and pethidine 30 mg IV. Rapid sequence induction with cricoid pressure was done with ketamine 50 mg, propofol 50 mg and suxamethonium 100 mg and intubated with 7.0 mm internal diameter endotracheal cuffed tube and maintained with oxygen, isoflurane, and vecuronium. Patient was kept on intermittent positive pressure ventilation. After forceps delivery, oxytocin 3 international units, hydrocortisone 100 mg and tranexamic acid 1 gm were given intravenously. The baby was 2800 gm male with Apgar scores 0/10 and 0/10 at 1 and 5 minutes respectively. Intraoperative period was uneventful. Although patient's spontaneous respiration was noticed, she did not gain her consciousness. So, we transferred her to the maternal intensive care unit (MICU) with endotracheal tube *in situ* and maintained on mechanical ventilation on synchronized intermittent mechanical ventilation mode. In MICU, midazolam 1 mg and morphine 1 mg were given via syringe pump every hour. Amlodipine 5 mg twice daily and enalapril 2.5 mg once daily via nasogastric tube were started and continued along with antibiotics and heparin 5000 units subcutaneously twice daily. On the first day, endotracheal tube was changed due to partial blockage. As she regained consciousness gradually and improved spontaneous breathing, she was extubated on the third day. On the second postpartum day, CT scan of the head was done and the report showed low attenuated area in right basal ganglia, frontal and posterior parietal lobes and subtle high-density area was noted in gyral part of both frontal lobes. With supporting CT scan report and clinical presentation, the patient was diagnosed as posterior reversible encephalopathy syndrome due to eclampsia. She was discharged on the fifteenth postpartum day without any residual neurological deficits.

COMMENT

The onset and intensity of PRES varies and are often nonspecific. It is characterised by variable associations of seizure activity, consciousness impairment, headaches, cortical visual abnormalities/blindness, nausea/vomiting and focal neurological signs. Headaches are typically constant, dull, non localised, and unrelieved by medications but resolve as blood pressure is normalised.[4] Mental status changes may vary from general malaise to confusion, decreased level of consciousness and coma. Generalised tonic clonic seizures are often the presenting symptom. A single seizure is infrequent; multiple seizures are more frequently reported. In our patient, we did not find any visual abnormalities, but had severe headache associated with vomiting and followed by multiple episodes of seizure. Hinchey et al[3] described association between eclampsia and PRES, three out of fifteen patients were associated with eclampsia and other etiologies included hypertensive encephalopathy and immunosuppressive medications. Preeclampsia/eclampsia is one of the common causes of PRES and most cases are managed without neuroimaging and the incidence remains unknown. However, it is uncertain whether a cause and effect relationship truly exists between the two or if these represent independent processes with some element of clinical overlap.[5] Fujiwara et al[6] and Mackinney et al[7] have reported that the cause of PRES was eclampsia in 5.5% of patients.

The lesions are seen mainly in the posterior regions of the cerebral hemispheres.[8] These abnormalities partially or completely resolve on follow up scanning, thereby suggesting subcortical oedema without infarction. Our patient had low attenuated area in right basal ganglia and bilaterally low attenuated area in frontal and posterior parietal lobes on CT scan. It

is important to note that neuroimaging usually reveals sparing of the calcarine and paramedian occipital lobe structures, a fact that distinguishes PRES from bilateral infarction of the posterior cerebral artery territory. Although MRI yields higher resolution and may show small, focal abnormalities beyond resolution of CT, it is not mandatory for diagnosis of PRES. [3]

Differential diagnosis of PRES like demyelinating diseases, basilar artery embolism and venous sinus thrombosis should be ruled out. In our patient, etiology was eclampsia because of altered blood pressure autoregulation. Her condition was improved after seizures stopped and blood pressure was normalised with delivery of the foetus.

Recurrent attacks of PRES are mainly related with eclampsia, and their incidence is proportional to recurrent eclampsia.[9,10] With early diagnosis and treatment, patients can recover clinically in a few weeks without any neurological deficit. If not treated on time, the condition can get worse, resulting in cerebral ischaemia, infarcts and even death. As there are no clinically specific signs for the syndrome, it can often be confused with other clinical conditions, leading to mismanagement.[11]

Magnesium sulphate should be initiated as soon as eclampsia is suspected to control seizures. However, during general anaesthesia, in patients receiving standard doses of magnesium sulphate, the effect of neuromuscular blocking agents can be more potential, and their duration can be prolonged.[12,13] Drugs with low biotransformation rates like isoflurane, low renal clearance, short half-life, and low active metabolites like atracurium should be chosen for general anaesthesia. Nitroglycerin and magnesium sulphate are suggested to prevent hypertensive attacks that can occur during the induction of anaesthesia.[14,15] For induction we gave ketamine and propofol combination because her blood pressure was low and she was critically ill. Cohen et al[16] concluded that the use of ketamine did not have any sustained changes in intracranial pressure or cerebral perfusion pressure, which adversely affect patient outcomes, including mortality and neurologic outcome. For maintenance of anaesthesia, isoflurane and vecuronium as a neuromuscular blocking agent were used.

Limitation of our study is that we could not provide her CT scan film as well as could not do follow-up scan. However, we examined her on first follow up after two weeks of discharge. She had no neurological deficits and for that we regularly contacted her through phone calls. She can do everything by her own and other daily activities.

CONCLUSIONS

In emergency room, this patient was diagnosed as primigravidae at term pregnancy in second stage of labour with eclampsia with intrauterine foetal death with hypoxic brain injury and supportive management was done accordingly. However, postoperative CT helped us to diagnose posterior reversible encephalopathy syndrome. Thus, this case report emphasises the need for early diagnosis and prompt treatment of it to decrease long term neurological sequelae.

DISCLOSURE

The authors report no conflicts of interest in this work.

No violation of human rights and safety.

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A Miracle Obstetrical Result: Iso-immunized Baby with HighTiter with Good Foetal Outcome

RC LK
Department of Obstetrics and Gynaecology, Patan Academy of Health Sciences, Lalitpur, Nepal.

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We present a case of 26 years multigravid women ($G_2P_oL_oA_1$) with iso-immunized foetus with high titre 1:512, delivered at 36^{+6} weeks of pregnancy. She visited the hospital in the second trimester of pregnancy for routine antenatal check up. There was a past history of spontaneous abortion at 12 weeks where no immunoglobulin (rhogam) injection was taken. At 22^{+} weeks of gestation, she was admitted in the hospital with titre 1:128 and 1:512. Counseling was done for outcome of foetus and advised for termination, but parents wanted to continue the pregnancy. Dexamethasone injection was given for foetal lung maturity and then discharged. Baby was kept in the nursery and double phototherapy was given and discharged at the seventh day of life.

Keywords: abo- incompatibility; rhesus incompatibility; rhesus isoimmunization, rhesus negative.

INTRODUCTION

Isoimmunization has been defined as the process whereby antibodies are produced in an individual in response to the injection of antigen from another individual of the same species, which the recipient lacks.[1]

Rh incompatibility can occur by two main mechanisms. The most common type occurs when an Rh-negative pregnant mother is exposed to Rh-positive foetal red blood cells secondary to foetomaternal haemorrhage during the course of pregnancy from spontaneous or induced abortion and trauma.[2]

A recent review of the 2001 birth certificates in the US by the Centers for Disease Control and Prevention indicates that Rh sensitization still affects 6.7 out of every 1,000 live births.[3]

Before the introduction of anti-D immune globulin (formerly referred to as Rho[D] immune globulin), haemolytic disease of the foetus and newborn affected 9-10% of the pregnancies and was a major cause of perinatal morbidity and mortality. Most women who become isoimmunized do so as a result of foetomaternal haemorrhage of less than 0.1 mL. Several first- and second-trimester clinical events may cause Rh D isoimmunization. Therapeutic and spontaneous abortions are associated respectively with a 4-5% and a 1.5-2% risk of isoimmunization in susceptible (non-isoimmunized) women. Ectopic pregnancy also is associated with isoimmunization in susceptible women. Threatened abortion infrequently causes isoimmunization, clinical procedures, which may breach the integrity of choriodecidual space, also may cause Rh D isoimmunization. Chorionic villus sampling is associated with a 14% risk of foetomaternal haemorrhage, even if the placenta is not traversed. Likewise, cordocentesis and other percutaneous foetal procedures pose a risk for foetomaternal haemorrhage. External cephalic version, whether or not it is successful, results in foetomaternal haemorrhage in 2-6% of the cases.[4]

The Rhesus blood type was first discovered in 1937 by Karl Landsteiner and Alexander S. Wiener.[5]

Haemolytic disease of the newborn, secondary to rhesus isoimmunisation was once a major contributor to perinatal morbidity and mortality. Today, rhesus immune globulin has markedly decreased the prevalence of this disease so much that less than three cases occur in every 1000 live births.[6]

CORRESPONDENCE

Dr Laxmi RC
Department of Obstetrics and Gynaecology, Patan Academy of Health Sciences, Lalitpur, Nepal.
Email:dr_lax50@hotmail.com
Phone:+977-9851085326

The rarity of this condition warrants referral to a maternal-foetal medicine specialist. Once sensitization occurs, rhesus immune globulin is no longer effective. Maternal antibody titres cannot be used for screening foetal anaemia. Conventionally, serial amniocenteses were performed for spectrophotometric studies to detect foetal bilirubin for estimating foetal anaemia, based on the Liley's reference chart. Serial peak middle cerebral artery velocities using doppler ultrasound have now become the mainstay of screening for foetal anaemia.[7]

It is possible to encounter women with titers as high as 512 with foetuses that are negative for the antigen to which the antibody is directed.[8]

CASE

A 26 years multigravid patient ($G_2P_oL_oA_1$) first visited in outpatient department for antenatal checkup at 18 weeks of pregnancy (by scan) with blood group B-ve and husband O+ve with past history of one miscarriage where no immunoglobulin was taken. She had irregular cycle. Routine investigation was sent where indirect coomb's test was 1:128. Other investigation was within normal limit. With high titre, the husband and wife was couselled about foetal prognosis and for termination but both partners refused admission and termination. They wanted to continue the pregnancy. At 22 weeks of pregnancy, she came with indirect coomb's titre 1:512. In this stage, she was admitted and given two doses (six milligram 12 hourly four doses) of dexamethasone injection, counselling to the couple was contineus for prognosis of the baby but they wanted continuation of pregnancy. At 34 weeks of pregnancy, she was advised for delivery but refused. Ultrasonography was done every two weeks which showed normal foetus till this stage. At 36 weeks of pregnancy, she was presented at labour room with labour pain and delivered vaginally a male baby with apgar score 7/10-9/10 and weighing 2,650 gram.

Baby was transferred to the nursery. Baby's blood group was O+ve, direct coomb's test was negative with high level of bilirubin, received multiple episodes of double and single photo therapy and discharged on the seventh days of life. Table 1 shows the result of indirect coomb's test at different weeks of gestation.

Table 1. Weeks of pregnancy and result of indirect coomb's test.

Weeks of gestation	Result of indirect coomb's test
18	1:128
22	1:128
26	1:512
30	1:512
32	1:512
34	1:512

Baby was admitted twice in the pediatric department with diagnosis of pneumonia and diarrhoea at the age of four months and six months of life. Later three episodes at four moths ans six months of life for follow up visited in outpatient department for upper respiratory tract infection and treated with anibiotics. Now baby is two years old and he is healthy.

COMMENT

Isoimmunised pregnancies are at an increased risk of developing foetal anaemia, hydrops and stillbirth. Pregnancies at risk for haemolytic disease conventionally underwent serial amniocentesis for spectrophotometric measurement of bilirubin as an evidence of foetal haemolysis and anaemia.[9] But our baby was normal in serial ultasonography and direct coomb's test was also negative with high titre (1:512) for indirect coomb's.

To minimise invasive procedures and determine the optimal timing of intervention, a number of studies were performed to evaluate reliability and usefulness of noninvasive parameters.[10]

Our baby also had high level of bilirubin but there was no exchange transfusion but he received multiple episode of phototheraphy.

In summary, the aim of this article is to inform obstetricians and gynaecologists through this evidential case report that isoimmunised baby with high titre (1:512) could have good foetal outcome and not necessarily need termination every time.

DISCLOSURE

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Comparison of Oral Misoprostol with Intramuscular Oxytocin in the Active Management of Third Stage of Labour

Kaudel S[1], Rana A[2], Ojha N[2]
[1]Department of Obstetrics and Gynaecology, Chitwan Medical College, Chitwan, Nepal, [2]Department of Obstetrics and Gynaecology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

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Aims: This study aimed at comparing the efficacy of oral misoprostol 600 mcg with intramuscular oxytocin 10 IU in the active management of third stage of labour.

Methods: This prospective comparative study was performed in Tribhuvan University Teaching Hospital to compare the efficacy of oral misoprostol with intramuscular oxytocin in the third stage of labour for the prevention of postpartum hemorrhage. One hundred and twenty women without risk of PPH were randomly allocated to receive either 600 mcg misoprostol orally (Group A) or 10 unit of oxytocin intramuscularly (Group B) within 1 minute of delivery. The efficacy and the safety of these two drugs were analyzed on the basis of percentages fall in hemoglobin (Hb) and hematocrit (Hct) level from before delivery to 8 completed hours after delivery, need for additional uterotonic agents, need for exploration and uterine evacuation, need for blood transfusion, duration of third stage of labour and the numbers of retained placenta and need for MRP.

Results: Oral misoprostol was observed to be equally effective as intramuscular oxytocin in prevention of post-partum hemorrhage (PPH). There was no statistical difference in the duration of third stage of labour, need for additional uterotonics, need for uterine exploration/evacuation and need for blood transfusion in the two groups.

Conclusions: Routine use of oral misoprostol 600 mcg appears to be as effective as 10 IU intramuscular oxytocin in minimizing blood loss during the third stage of labour.

Keywords: active management of third stage of labour; misoprostol; oxytocin.

INTRODUCTION

Globally, misoprostol which first came into use for prevention of peptic ulcer disease was found useful for termination of pregnancy and then as a miracle drug in the prevention of PPH. But the drug which is being used for this purpose universally is oxytocin for almost half a decade after being introduced in 1963 at the National Maternity Hospital in Dublin, Ireland.[1] Active management of third stage of labour (AMTSL) means expediting the process by early cord clamping, administration of a uterotonic, delivery of placenta by controlled cord traction following uterine contraction and finally uterine massage after delivery of the complete placenta.[2] Through this, shortening of third stage of labour by 50% and reduction of blood loss by 20% have been evidenced, hence AMTSL has been now adopted worldwide as a strategy to reduce excessive blood loss during childbirth.[3]

The use of oxytocin in the AMTSL is fraught with problems of storage, fake and substandard drugs, and the need for trained staff in order to administer it. Misoprostol on the other hand offers several advantages over oxytocin including a shelf life of several years, stability at high temperature, oral administration, minimal side effects, and that it can be administered to hypertensive patients.[4] Based on this framework the present study is aimed at comparing the efficacy and safety of oral misoprostol with intramuscular oxytocin in the active management of third stage of labour.

CORRESPONDENCE

Dr Sudeep Kaudel
Department of Obstetrics and Gynaecology,
Chitwan Medical College, Chitwan, Nepal.
Email: sudeepkaudel@gmail.com
Phone: +977-9855063888

METHODS

This was a prospective study conducted at the labour room and maternity unit in the Department of Obstetrics and Gynaecology, Tribhuvan University Teaching Hospital from 13th April 2012 to 13th April

2013. During the one year study period, 4304 women delivered at TUTH, out of them 2579 (59.9 %) had normal vaginal delivery. Among them 120 women (4.6%) were enrolled in the study. Later 12 of them were excluded because of instrumental delivery (10) and caesarean section (2). Finally 108 women, 54 in each group Group A (600 mcg oral misoprostol) and Group B (10 U intramuscular oxytocin) were studied.

All women with parity of <5, having singleton live pregnancy at or above 37 weeks of gestation, in cephalic presentation, undergoing spontaneous onset of labour and spontaneous vaginal delivery without any complicating factors were included in the study. Informed consent was taken for collection of blood sample for initial hemoglobin (Hb) and hematocrit (Hct) estimation. Then the women were allotted randomly into two groups at the second stage of labour when delivery was imminent by picking an envelope from a capped plastic container with 108 equal sized folded paper envelopes. Deliveries were conducted in the lithotomy or dorsal position and allocated drug was administered immediately after the delivery of the baby. Early clamping of the umbilical cord and controlled cord traction was done immediately after the delivery of the baby without waiting for the signs of placental separation by Brandt and Andrew's method in all the groups.

If the placenta was not delivered within 30 minutes of the delivery of the baby, a diagnosis of retained placenta was made and it was removed manually. Uterine massage was done for about 10 - 15 minutes after expulsion of placenta until the uterus became well contracted in all the women and then the women were taught to massage their uterus every 15 minutes for 2 hours after delivery. All placentas were examined to rule out retained bits of placenta and membranes. Episiotomy wounds, tears and lacerations if present were immediately repaired. The amount of blood loss was visually estimated at the end of the delivery and any additional loss was added up before transferring the patient to the ward after 1 hour of observation in the labour room. Once the hemostasis was ensured and the uterus sufficiently contracted, the women were shifted from the labour table and monitored in the labour room for one hour following delivery. At the end of 1 hour the women were asked about the side effects attributable to the drug and this was recorded if present. When the women were hemodynamically stable, the uterus well contracted and no significant vaginal bleeding, they were transferred to the maternity ward. The level of hematocrit and hemoglobin was measured 8 hours postpartum from the maternity ward. The women were followed up till discharge. Comparison of difference in hematocrit levels in both the groups was maintained. Delayed hemorrhage in the ward requiring exploration, need for additional uterotonics and need for blood transfusion were recorded in the postnatal ward.

After the primary data collection, daily entries of these data were put in the master chart. Analysis was done with the help of a computer using Chi-square (x^2) test and student's T-test. A P value of <0.05 was regarded as statistically significant. The computer programme used was SPSS version 19.

RESULTS

The two groups were balanced at randomization for potential confounding factors like age, parity, booking status and gestational age at delivery. The two groups were also comparable with regard to baseline prognostic labour characteristics like duration of labour, mode of delivery, mean birth weight of the baby and the mean placental weight. The duration of third stage of labour in misoprostol group was also not statistically different to that of oxytocin group.

The visually estimated third stage blood loss ranged from 50 to 300 ml (Table 1).

Table 1. Visually estimated blood loss in third stage of labour (n=108).

Blood loss (ml)	Misoprostol	Oxytocin	P value
0-100	38	37	0.324
101-200	12	16	
201-300	4	1	

The average blood loss observed was 115.5 ml in misoprostol group and 118 ml in oxytocin group and this observation was statistically not significant (p-0.324) (Table 2).

Table 2. Average blood loss in third stage of labour (n=108).

Group	Misoprostol	Oxytocin
Average blood loss (ml)	115.5	118

Mean change in Hb level in misoprostol group was 0.56 ± 0.35 gm/dl as compared to 0.46 ± 0.29 gm/dl in oxytocin group, which was statistically insignificant (p-0.222). Similarly, mean change in Hct level in the misoprostol and oxytocin group was 0.68 ± 0.30 % and 0.75 ± 0.27 % respectively, which was comparable (p-0.257). There was no incidence of PPH (peripartum fall in Hb of 10%) in both the groups (Table 3).

Table 3. Change in hemoglobin and hematocrit levels (n=108).

Variables	Study group		P-value
	Misoprostol	Oxytocin	
Hematocrit (%)			
Pre-delivery	36.52 ± 3.09	36.39 ± 2.79	
Post-delivery	35.85 ± 3.10	35.63 ± 2.74	
Change	0.68 ± 0.30	0.75 ± 0.27	0.257
Hemoglobin (g/dL)			
Pre-delivery	12.33 ± 1.16	12.45 ± 1.07	
Post-delivery	11.83 ± 1.28	12.01 ± 1.04	
Change	0.56 ± 0.35	0.46 ± 0.29	0.222

Four women each in the misoprostol and oxytocin group required additional uterotonics and this was comparable. Those women needing extra uterotonics in misoprostol group responded to additional oxytocin infusion, one requiring 10 unit infusion and other required double the concentration. Two women in oxytocin group required extra oxytocin infusion whereas two women needed rectal misoprostol and injection methergin on the top of oxytocin infusion but were statistically insignificant (Table 4). No woman in either group required uterine exploration or evacuation and there was no need of blood transfusion in both groups.

Table 4. Additional uterotonics used (n=108).

Additional uterotonics used	Misoprostol	Oxytocin	P value
10 U Oxytocin infusion	3	1	0.324
20 U Oxytocin infusion	1	1	
20 U Oxytocin infusion + 800 mcg misoprostol P/R	0	1	
20 U Oxytocin infusion + 800 mcg misoprostol P/R + 1 amp methergin	0	1	

Nine women in misoprostol group had side effects whereas none in oxytocin group experienced side-effects and it was statistically significant (p-0.002). Out of these nine women, six women (11.1%) developed shivering within 1 hour postpartum. One woman (1.8%) developed only fever as a side effect whereas two women (3.7%) had shivering and fever (max. temp 100'F) (Table 5).

Table 5. Side effects of misoprostol and oxytocin (n=108).

Variable	Misoprostol	Oxytocin	P value
Shivering	6	0	0.002
Shivering + fever	2	0	
Fever	1	0	

DISCUSSION

Misoprostol in AMTSL has been reported to effectively reduce the incidence of primary PPH from 18% to 5%. In addition, the time for administration of therapeutic drugs is reduced from 15 minutes to five minutes.[5,6] This practice has become a standard of obstetric care, and misoprostol has emerged as a promising treatment alternative.[7-9] In this study, 600 mcg oral misoprostol was compared with 10 unit IM oxytocin for AMTSL and this dose of misoprostol is recommended by WHO for AMTSL when standard oxytocin is not available. This study found that there was no statistical significance between the effectiveness of these drugs in AMTSL and same result was shown by Oboro et al.[10] in Nigeria which concluded that oral misoprostol 600 mcg can replace 10 unit intramuscular oxytocin in reducing postpartum

hemorrhage in low-risk women, in developing countries. Several other routes of misoprostol like sublingual, vaginal, rectal and buccal have been compared and different doses ranging from 400 to 1000 mcg have been tried in AMTSL.[11-13]

In the misoprostol group, mean duration of third stage of labour was 4.76 ± 1.69 min whereas it was 4.39± 1.37 min in the oxytocin group without any statistical significance (p-0.935) and similar result was obtained in three other comparative studies.[12,14,15] The present study supports that the duration of third stage of labor is reduced by using uterotonics hence reducing the amount of blood loss.

The amount of blood loss was statistically similar in both groups. The mean blood loss in the misoprostol group was 115.5 ± 39.5 ml and in oxytocin group, it was 118 ± 48.6 ml, which was less than the blood loss in other studies.[16-18]

This might be due to visual estimation of blood loss in the index study whereas other studies have used objective measurement of blood loss by placing drape under the buttocks before delivery and removing it after 1 hour postpartum. Most of the studies were unable to find the statistical significance in the blood loss while comparing these drugs in AMTSL.[11,15,19]

Numerically, the amount of blood loss was higher in the oxytocin group in comparison to misoprostol group in this study but this was statistically insignificant (p- 0.324). One patient on each group had blood loss of 300 ml which was the maximum blood loss estimated visually but visual estimation generally underestimates blood loss by 30%, which is clinically inadequate and has presented practical problem.

Several other studies[8,20] have also observed that peripartum fall in hematocrit level by at least 10% from before delivery to 24 hours after delivery, is a better definition than the volume criteria of PPH. In this study the efficacy of the two regimes in the active management of the third stage of labour was mainly based on assessment of the degree of fall in hematocrit following delivery in the two groups. There was no statistical difference in the average fall of hematocrit in between misoprostol and oxytocin group (0.68 ± 0.3 % versus 0.75 ± 0.27 %) such that there was no incidence of PPH in these two groups by hematocrit criteria (p value- 0.257). These observations show that oral misoprostol and intramuscular oxytocin are equally efficacious for AMTSL and this finding is consistent with data from another similar comparative study.[11]

Additional uterotonics were administered in eight women, four in each group. Those women needing extra uterotonics in misoprostol group responded to additional oxytocin infusion only; whereas women in oxytocin group required either oxytocin infusion, or rectal misoprostol and injection methergin on the top of oxytocin infusion but this was statistically insignificant.

A similar comparative study done in Ghana in 2002 has shown less use of additional uterotonics in the misoprostol group as compared in the oxytocin group (7.1% vs 9.3%) , probably because of use of higher dose of misoprostol (800 mcg) in that study as compared to the index study but the result was insignificant.[18]

Next additional parameter in assessment of efficacy of the two regimes was the need for blood transfusion following delivery and the need for exploration and uterine evacuation following delivery in the two groups. Fortunately no women required blood transfusion or uterine exploration/evacuation in these groups as they were well booked and had high hemoglobin and hematocrit before delivery. A similar comparative study done in India in 2011 showed that 1.9% of women in misoprostol and 1.1% of women in oxytocin required blood transfusion whereas MRP was needed in less than 1% in both the cases without bearing any significance.[16] As lesser number of women had participated in the index study, this might be the cause for no requirement of blood transfusion and MRP.

Regarding the side effects of oral misoprostol and intramuscular oxytocin, there were no serious side effects in this study. All the adverse effects were mild and they subsided spontaneously and none of the women required any medications for these effects.

In this study, the analysis of side effects of the two uterotonics revealed the presence of side-effects only in misoprostol group.

Nine women in misoprostol group had side effects and it was statistically significant (p-0.002). Out of these nine women, six women (11.11%) developed shivering within 1 hour postpartum and one woman (1.8%) developed only fever as a side effect whereas two women (3.7%) had shivering and fever (max temp 100'F).

CONCLUSIONS

Misoprostol (oral 600 mcg) and oxytocin (IM 10 unit) were equally effective in AMTSL in this comparative study as there was no PPH in both the groups. Misoprostol had lesser blood loss than oxytocin but this was not statistically significant. Oxytocin had the additional advantage of nil side effects bearing statistical significance. Hence, misoprostol which is as effective as oxytocin can be adopted for the active management of third stage of labour, with minimal self-limiting side effects.

DISCLOSURE

The authors report no conflicts of interest in this work.

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Obstetric Outcome in Teenage Pregnancy in a Free Antenatal Care Setting in Southwest Nigeria

Akadiri O[1], Bakare B[1], Ajenifuja KO[2]
[1]Department of Obstetrics and Gynaecology, State Specialist Hospital Ondo, [2]Department of Obstetrics, Gynaecology and Perinatology, Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife.Osun state, Nigeria

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Aims: The study was done to compare the obstetric outcome in teenage pregnancies with that of non-teenage pregnancies in a setting where antenatal care and delivery is free.

Methods: A retrospective case control study was conducted at the state specialist hospital Ondo southwest Nigeria between January 1st 2011 to December 31st 2011. The data regarding outcome of all teenagers (13-19) delivering in the hospital was compared with that of selected non-teenagers (20 -35 years) taken as control. Chi-square and student t- test was used with 0.05 as level of significance.

Results: There were a total of 3054 deliveries during the study period. Incidence of teenage pregnancy was 4.0% (n=122) with a mean age of 18years. Teenagers were more likely to have anaemia and malaria in pregnancy but less likely to have antepartum haemorrhage and preeclampsia. Teenagers are more likely to have spontaneous vagina delivery compared to non-teenagers. The perinatal outcome did not differ significantly**.**

Conclusions: The majority of the teenagers were nulliparous and most delivered spontaneously by the vaginal route. They are more likely to have instrumental delivery and less likely to have preeclampsia compared to older patients though this was not statistically significant.

Keywords: preeclampsia; teenage pregnancy; obstetric outcome.

INTRODUCTION

Globally about 16 million women aged 15-19 years old give birth each year, this is responsible for about 11% of all births worldwide. Half of all the adolescents births occur in just seven countries; Bangladesh, Brazil, Democratic Republic of Congo, Ethiopia, India, Nigeria and United states.[1] Evidences on the outcome of teenage pregnancy are conflicting; several studies have found an increased incidence of anaemia, pre-term labour and prematurity and an increased incidence of operative deliveries among teenagers, [2- 4].In contrast, some of the authors have stated that there is no increased risk in teenage pregnancies after controlling for confounding variables.[5]

In our centre, all pregnant women have access to free antenatal care and delivery services hence there is no difference in the extent of care. This study aims to determine the problems associated with teenage pregnancy with emphasis on outcome of labor.

CORRESPONDENCE

Dr Olumide Akadiri
Department of Obstetrics and Gynaecology
State Specialist Hospital, Ondo, Nigeria
Email: akadiripatrick@gmail.com
Phone: +2348033816209

METHODS

This was a retrospective case control study. All pregnant women aged 13 -19 years who carried pregnancy to 34 completed weeks and above and delivered between January 1, 2011 to December 31, 2011 at the State Specialist Hospital Ondo had their case notes retrieved and analyzed with respect to their age, booking status, pregnancy, labour and delivery complications. The findings were compared to women aged 20-35 years who delivered immediately after the teenager and meets the inclusion criteria. This served as the control. Women with previous caesarean section, greater than 35 years of age and prior medical complications were excluded. Patients whose first presentation was during labor were regarded as unbooked. Delivery before 37weeks is classified as pre-term and more than 40 weeks is classified as postdate. Patients were classified as having anaemia if the Hamoglobin was < 10.0 g/dl or packed cell volume of 30%. Babies weighing <2,500

g were labeled as low birth weight babies. Data collected was analyzed using SPSS 20. Chi-square was applied with 0.05 as level of significance.

RESULTS

The total number of deliveries during the study period was 3054 out of which 122 were teenagers giving an overall frequency of 4.0%. The mean age of teenage mothers in the study was 18.0±1.08. Majority 44.3% (n= 54) were 18 years while 1.6% (n=2) of them were 14 years, the lowest age in the study. Majority of the teenage mothers 84% (n=103) were unmarried compared to 4% (n=5) in the control. Most of the teenage mothers 82.8% (n=101) were having their first baby compared to 41.8% (n=51) in the control. Less than one-fifth 17.2% (n=21) were having their second babies.

There was a statistical significant difference in the booking status of the cases compared to the control as 75.4% of the teenage mothers in the study were booked compared to 86.8% for non-teenage mothers (P= 0.047) (Table 1).

Table 1. The booking status of teenage mothers compared to non-teenage mothers.

	Cases (n=122)		Control (n=122)	
	Percent	Frequency	Percent	Frequency
Booked	75.4%	92	86.8%	106
Unbooked	24.6%	30	13.2	16
Total	100	122	100	122

P= 0.047

Teenage mothers were significantly more likely to have anemia 22.1% (n=27) versus 9.8% (n=12) p=0.009, and were significantly more likely to deliver past their date 27% (n=33) versus 16.4% (n= 20) P= 0.044. Teenage mothers were also more likely to have malaria in pregnancy though the difference is not statistically significant. (25% versus 19% P= 0.318). There were no significant differences in the incidences of preeclampsia, antepartum haemorrhage (Table 2).

Table 2. The major complications seen during the antenatal period (n=244).

	Cases (n=122)		Control (n=122)		
Antenatal complications	N	%	N	%	P
Anaemia	27	22.1	12	9.8	0.009
Malaria	25	20.5	19	15.6	0.318
Past date	33	27	20	16.4	0.044
Antepartum haemorrhage	1	0.8	2	1.6	0.50
Pre-eclampsia	2	1.6	3	2.5	0.50

The caesarean section rate among the non-teenage mothers (control) was twice the rate for the teenage group (cases) 14.8% (n= 18) versus 7.4% (n = 9). The spontaneous vaginal delivery and assisted breech delivery rate were comparable. The incidence of instrumental delivery was higher among the teenage mothers 9 (7.4%) versus 4 (3.3%) p = 0.154 (Table 3).

Table 3. The mode of delivery of cases and control compared (n=244).

	Cases (n=122)		Control (n=122)		P value
	%	Frequency	%	Frequency	
Svd	102	83.6	97	79.5	0.409
Cs	9	7.4	18	14.8	0.66
Abd	2	1.6	3	2.5	0.651
Inst	9	7.4	4	3.3	0.154
Total	122	100.0	122	100.0	

(svd = spontaneous vagina delivery, cs = caesarean section , abd = assisted breech delivery, inst = instrumental delivery).

The Apgar score at one minute was comparable between the two groups. The frequency of low birth weight was comparable 15.6% (n= 19) for cases compared to 13.1% (n=16) for the control. In the control group 4.9% (n=6) of babies had birth weight greater than 4.0 kg compared to none among the cases. Perinatal mortality was 49.2/1000 live births and 65.8/1000 births in the control. There was no maternal mortality in either group.

Table 4. The perinatal outcome in two groups (n=244).

Perinatal outcome	Cases (n=122)		Control (n=122)	
apgar score at 1 min	%	Frequency	%	Frequency
<7	33	27	34	27.9
>7	89	73	88	72.1
Birth weight				
<2.5 kg	19	15.6	16	13.1
2.5- 4.0 kg	103	84.4	100	82
>4.0 kg	-	-	6	4.9

DISCUSSION

The incidence of teenage pregnancy in this study was 4.0%. This is less than the National demographic heath survey national rate of 23% and the southwest Nigeria regional rate of 9%.[6] It is also lower than the 13.1% reported from a study in Ilorin North central Nigeria[7] but higher than 1.67% from a study in Enugu southeast Nigeria.[8] This regional variation may be due to cultural and religious practices such as child

marriage, which is still prevalent in northern Nigeria. There is aversion to having a child outside wedlock hence this may be responsible for the low incidence in southeast Nigeria.

It is worrisome that 8.2% of the teenage mothers in this study are between 14-16 years old. The age of menarche in various studies within Nigeria is between 13.66 – 15.26 years.[9,10] It implies that the teenagers became pregnant within a year of attaining menarche; this reflects commencement of sexual intercourse at an early age with its consequences of teenage pregnancy, sexually transmitted infections, and cervical cancer amongst others.

The proportion of booked mothers was high in both the cases and the controls; this might be due to the free antenatal and delivery services. However, despite this there was a statistically significant difference in the booking status between teenage mothers and the control. (P=0.047).

Poor clinic attendance has been reported in other studies,[2,11] and some of the reasons adduced for this include poverty, which limits access in terms of affordability. This however was not applicable in our study population as antenatal care and delivery was free.

The incidence of anemia in our study was significantly higher among teenage mothers; this is similar to some other studies.[12,13] This could be because of suboptimal nutritional status at the onset of pregnancy. A higher incidence of clinical malaria in pregnancy was also seen among the teenager mothers and this might also contribute to the anaemia. Teenagers were significantly more likely to deliver beyond their dates, which is similar to the findings from some other studies.[14] This can be due to being unsure of their last menstrual period and also that the pregnancies were unplanned in most cases. Similar to some other studies there was fewer incidences of antepartum haemorrhage and preeclampsia.[13]

It is a common belief that teenagers are less mature physically and the size of the pelvis is small hence, a higher rate of caesarean section is expected. The lower caesarean section rate in this study may be due to reluctance of obstetricians to resort to caesarean section in teenagers especially those who are unmarried so as not to jeopardize their future relationships. The lower caesarean section rate was probably achieved at the expense of a higher instrumental delivery rate. A similar finding of higher instrumental delivery and lower caesarean section rate is found in some other studies.[16]

Low birth weight is closely associated with fetal and perinatal mortality and morbidity, inhibited growth and cognitive development and development of chronic diseases later in life. This study revealed a higher incidence of low birth weight babies amongst teenage mothers similar to findings in some other studies.[13,15] This can be attributed to the higher rate of anaemia and clinical malaria among the cases. There was no maternal mortality in both groups.

The major limitation of the study was the small number available for study.

CONCLUSIONS

This study showed that with equal access to antenatal care services there is little or no difference in the obstetric complication faced by teenagers compared to non-teenagers. Preeclampsia, antepartum haemorrhage and caesarean section rate were less while instrumental delivery rate, anaemia and malaria in pregnancy was more adolescent reproductive health services should be made freely available to reduce the incidence of teenage pregnancies.

DISCLOSURE

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Sex Ratio at Birth: A Retrospective Audit of the Birth Records of a Nigerian Hospital

Onyiriuka AN[1], Ikeanyi EM[2]

[1]Endocrine and Metabolic Unit, Department of Child Health, University of Benin Teaching Hospital, Benin City, Edo State, Nigeria, [2]Department of Obstetrics and Gynaecology, College of Health Sciences, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria.

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Aims: The aim was to determine the sex ratio at birth in St Philomena Catholic Hospital (SPCH), Benin City, south-south, Nigeria and to assess its relationship with birth order and maternal age.

Methods: In this retrospective cohort study, the records of all deliveries at St Philomena Catholic Hospital (SPCH), Benin City, Nigeria between 1st January, 2005 and 31st December, 2014 (10 years) were retrieved and analyzed. Stillbirths and infants with ambiguous genitalia were excluded in the analysis.

Results: The total number of live-births during the 10-year period under review was 13,702 and these consisted of 7,007 males and 6,695 females, resulting in a sex ratio of 104.7:100 (approximately 1.05) at birth. The yearly sex ratios varied from 1.01 to 1.14. The maternal age and the birth order significantly influenced offspring sex ratio at birth ($p < 0.001$). The highest sex ratio was found among third-birth-order offspring and the lowest was found among offspring of fifth-birth order and above. Offspring of mothers aged 25-29 years had the highest sex ratio and those of mothers aged 40 years and above had the lowest sex ratio.

Conclusions: The sex ratio at birth in south-south Nigeria is comparable to values obtained from south-west Nigeria but lower than that obtained from north-west Nigeria. The birth order and maternal age influenced the offspring sex ratio at birth.

Keywords: birth order; maternal age; sex ratio.

INTRODUCTION

The phrase 'sex ratio at birth' (SRB) refers to the number of male live-births for every 100 female births.[1] The SRB affects several critical demographic measures, such as the 'doubling time' of a population as well as the sex composition of a population.[2] Data related to SRB are necessary to understanding trends in infant morbidity and mortality, such as low birth weight, prematurity and sudden infant death syndrome.[3,4] Some researchers have used SRB to assess the impact of environmental factors on the endocrine system and reproductive health of humans.[5-9] Thus, SRB represents a simple, cheap and noninvasive method studying and monitoring the reproductive status of a population.

Sex ratio at birth varies not only from one country to another but also, within the same country and it may be skewed by factors such as age of the mother, birth order and sex-selective abortions.[10] Environmental exposure to endocrine-disrupting compounds may lower sex ratio at birth.[11,12] Thus, SRB has been regarded as a marker of paternal endocrine disruption.[11] Worldwide, estimates indicate that SRB is 105 -107 male births for every 100 female births with a median of 105.9.[1] This median figure is usually used as the baseline for measuring deviations in the sex ratio. Previous studies in Nigeria found a sex ratio of 1.12, 1.04 and 1.05 in the north-west,[13] the south-east,[14] and the south-west,[15] respectively. To the best of our knowledge, there is no report of SRB from south-south, Nigeria. Secular trends in SRB have been reported from different regions and countries of the world. [5,8,11] The above considerations prompted the present study.

The purpose of the present study is to determine the sex ratio at birth in Benin City, south-south Nigeria and assess its relationship with birth order and maternal age.

CORRESPONDENCE

Dr Alphonsus N. Onyiriuka
Department of Child Health,
University of Benin Teaching Hospital,
PMB 1111, Benin City, Nigeria.
E-mail: alpndiony@yahoo.com

METHODS

A retrospective assessment of the birth records of all the deliveries at St Philomena Catholic Hospital

(SPCH), Benin City, Nigeria between 1st January, 2005 and 31st December, 2014 (10 years) was carried out. Stillbirths were excluded in the analysis in conformity with the definition of sex ratio at birth.[1] Infants with ambiguous genitalia were also excluded from the analysis. The deliveries were recorded according to the month and year of delivery. The study design was approved by the hospital authority. The sex ratio at birth was computed, using the formula B/G x 100 (where 'B' is number of male births and 'G' is number of female births). In this study, a birth order refers to the proband's position within his/her sibship.

Statistical analysis was performed using the statistical package for social sciences (SPSS, version 16.0). Descriptive statistics such as frequencies, means, standard deviations (SDs), confidence intervals (CIs) and percentages were used to describe all the variables. Students' t test was used in ascertaining the significance of differences between two means with p-value set at < 0.05.

RESULTS

During the 10 years covered by this review, a total of 13,702 live-births were recorded at SPCH and this consisted of 7,007 males and 6,695 females. Males accounted for 51.1% of the total live- births. A quarter (24.9%) of the total births were recorded in the years 2013 and 2014. The overall sex ratio for the 10 years pooled together was 1.046 (approximately 1.05).

Table 1. Annual live-births according to gender and sex ratio (2005-2014).

Year of Study	Total	Number of males	Number of females	Sex ratio
2005	1128	569	559	1.02
2006	1487	764	723	1.06
2007	1304	659	645	1.02
2008	1230	647	583	1.11
2009	1304	660	644	1.02
2010	1332	690	642	1.07
2011	1105	588	517	1.14
2012	1398	714	684	1.04
2013	1653	829	824	1.01
2014	1761	887	874	1.01
2005-14	13,702	7007	6695	1.05

As shown in Table 1, the highest sex ratio of 1.14 was recorded in the year 2011. The lowest sex ratio was 1.01 and this was recorded in two successive years (2013 and 2014). We evaluated whether the SRB has changed overtime and observed that the percentage of male births increased from 50.4% (95% CI = 49.2-51.6) in 2005 to 52.6% (95% CI=51.4-53.8) in 2008 and then dropped to 50.6% (95% CI= 49.4-51.8) in 2009. Subsequently, the proportion of male births rose to a peak of 53.2% (95% CI=52.0-54.4) in 2011. From 2012 to 2014 the percentage of male births remained relatively low, varying from 50.1% in 2012 to 50.4% 2014 (Table 1). However, no clear trend was apparent in these comparisons except that the proportion of male births have been low in the past three years (2012 to 2014).

Table 2. Sex ratio at birth according to birth order (2005-2014).

Year of study	Yearly total	Sex ratio by birth order				
		1st	2nd	3rd	4th	≥ 5th
2005	1128	1.04	1.03	1.07	1.02	1.01
2006	1487	1.04	1.04	1.06	1.03	1.02
2007	1304	1.03	1.05	1.05	1.04	1.03
2008	1230	1.04	1.06	1.09	1.05	1.04
2009	1304	1.03	1.03	1.05	1.04	1.03
2010	1332	1.02	1.03	1.04	1.04	1.01
2011	1105	1.04	1.06	1.14	1.08	1.05
2012	1398	1.02	1.03	1.05	1.03	1.01
2013	1653	1.01	1.02	1.03	1.02	1.00
2014	1761	1.01	1.01	1.03	1.02	1.01
2005-14	13702	1.03	1.04	1.05	1.03	1.02

As depicted in Table 2, the highest sex ratio was found in the third-birth-order offspring and lowest sex ratio was found among offspring of fifth rank order and above.

Table 3. Sex ratio of offspring at birth according to maternal age groups.

Maternal age in years	Total	Number of males	Number of females	Sex ratio
<20	397	202	195	1.04
20-24	2378	1216	1162	1.05
25-29	5148	2657	2491	1.07
30-34	3688	1893	1795	1.05
35-39	1570	798	772	1.03
≥40	245	124	121	1.02
Unknown	276	140	136	1.03
Total	13,702	7007	6695	1.05

Table 3 showed that the offspring sex ratio was highest among mothers aged 25-29 years and lowest among offspring of mothers aged 40 years and above.

The overall average maternal age was 27.3±4.1 years (95% CI = 27.2-27.4).

Table 4. Offspring gender distribution by maternal age and birth order.

Parameter	Male births (n=7007)	Female births (n=6695)	t-statistic (p-value)
Mean maternal age (years)*	27.2±3.1	28.0±3.6	9.716 (< 0.001)
Mean birth order	2.6±1.2	3.1±1.1	17.777 (< 0.001)

Number of unknown maternal age = 276. *Mean maternal age: Number of male births = 6,866; number of female births = 6,560; Sex ratio = 1.046 (approximately 1.05).

Table 4 showed that the maternal age and the birth order significantly influenced offspring sex ratio at birth.

DISCUSSION

Our data indicate that the offspring sex ratio at birth in the total sample studied was 1.05. This is in complete agreement with 1.05 previously reported from south-west, Nigeria[15] but slightly higher than 1.04 found in south-east, Nigeria.[14] Thus, suggesting that over the years, there has been no significant change in sex ratio at birth in southern Nigeria. In contrast, the sex ratio found in the present study was significantly lower than 1.12 reported from northern Nigeria about a decade ago.[13] Garenne in a review of 56 surveys, totaling 1.130 million births in African countries found that the average sex ratio was 1.033 (approximately 1.03).[16] The reason for the lower sex ratio found in our study compared with that found in northern Nigeria is not clear. One obvious difference between northern and southern Nigeria is climatic, with the north being generally hotter and with less rainfall compared with the south. It is, therefore, possible that more males are born in the relatively hotter north compared with the south of Nigeria. This view is supported by reports of some studies from Finland which indicated that more males are born in years with higher mean annual temperatures.[17-19] The result of another study also suggests that more males are born during warmer periods.[20] In contrast, Dixson et al,[21] in a study in New Zealand, found that the ambient temperature did not influence the proportion of males at birth. However, they noted that temperature may influence human sex ratio at birth but that such effects of temperature are not universal. The reason for the conflicting results is not clear but suggests that other unidentified environmental factors may play a role. The SRB (1.05) found in the present study is slightly less than the worldwide median of 105.9 (approximately 1.06).[1] There is no readily available explanation for this difference.

Data from the present study indicate that the birth of a male offspring was significantly more frequent among lower-birth-order offspring compared with higher-birth-order offspring. Births of fifth rank order and above had the lowest sex ratio. Our finding is in consonance with the report of previous studies[22,23] and suggests that births of lower rank order have higher proportions of males than those of higher ranks. In contrast, other researchers reported that there was no association between birth order and sex ratio.[24] In that study, the study population was 6,689 which was significantly lower than 13,702 used in the present study. A large sample size is known to be more ideal for a sex ratio study. Indeed, in a review of the literature, James stated that in general, results of small-sample studies have been inconclusive and contradictory.[25] Novitski and Kimball, using a large sample size (3,645,750), found a significant association between birth order and sex ratio.[26] On the other hand, the conflicting reports may suggest that unidentified environmental factors may influence the sex ratio rather than demographic factors alone. We do not have any readily available explanation for the higher male births at the third birth-order offspring. It might mean that the female reproductive system is physiologically at its best for survival of male embryos during the third-birth-order pregnancy.

In the present study, male births were significantly more frequent in younger mothers compared with older mothers. We found the highest sex ratio was among mothers aged 24-29 years. Thus, suggesting that younger women tend to have a higher frequency of male births. This view is supported by the report of Rueness et al.[27] They proposed that a higher maternal age serves as a stressor to the female reproductive system during pregnancies due to physical aging. There is some evidence that male embryos are more vulnerable to such stressors in early developmental stages, putting them at a relatively higher risk of early intrauterine death compared with female embryos.[27] Indeed, Hassold et al.[28] found that fetal death rate was higher for male than female fetuses and it is estimated that the increase is about 30% in chromosomally normal spontaneous abortions. In

contrast, Maconochie et al did not find any evidence that maternal age influenced sex ratio at birth.[29]

Large study population which is ideal for studies on sex ratio at birth was the strength of the study. One limitation is that the recorded maternal ages may be inaccurate and this may affect assessment of the association between maternal age and offspring sex ratio. We also did not explore the possibility that male births may be heritable in families.

CONCLUSIONS

The sex ratio at birth in south-south Nigeria is comparable to values obtained from south-west Nigeria but lower than that obtained from north-west Nigeria. The birth order and maternal age influenced the offspring sex ratio at birth.

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DISCLOSURE

The authors report no conflicts of interest in this work.

No violation of human rights and safety.

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Perinatal Outcome of the Second Twin

Joshi R, Baral G

Department of Obstetrics and Gynaecology, Paropakar Maternity and Women's Hospital, Kathmandu

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Aims: The purpose of this study was to determine the perinatal outcome of the second twin compared to the first one.

Methods: This is a hospital based comparative study of 60 pregnant women with twin pregnancy at Paropakar Maternity and Women's Hospital, Kathmandu from 14 January 2013 to13 April 2013. Apgar score and admission to neonatal intensive care unit of the first and the second twins were studied in relation to the gestational age, chorionicity, mode of delivery, inter-delivery interval and birth weight. Mc Nemars test was used with 0.05 as the level of significance.

Results: Among 60 sets of twins, Apgar score of the second twin was found to be lower than the first one (p=0.02) in general and in preterm gestation (p=0.049), dichorionic diamniotic chorionicity (p=0.012), vaginal delivery (p<0.001), inter-delivery interval of <30 minutes (p=0.007) and birth weight discordance of <30 % (p=0.014). Admission to neonatal intensive care unit was not significant (p=0.5).

Conclusions: Second twin had low Apgar score and the neonatal admission rate was similar for both twins.

Keywords: Apgar score; chorionicity; twin pregnancy.

INTRODUCTION

Twin pregnancies have been found to vary in different parts of the world. The highest incidence is in Nigeria (49/1000) and the lowest in China and Japan (2/1000) while Europe and USA have the intermediate incidence (5.9-8.9/1000).[1] The incidence of twin pregnancy has been on the rising trend, 65% since 1980.[2,3] There were 194 (1%) twin pregnancies out of 19,247 total deliveries a year prior to the study at Paropakar Maternity and Women's Hospital in Kathmandu.[4]

This study was warranted due to the increased incidence of foetal malpresentation, preterm labour, birth weight discordance, placental abnormalities and operative deliveries in twin pregnancy.[1] This study was an attempt to find out the outcome of the second twin in terms of the Apgar score at 5 minutes and the need for neonatal intensive care unit admission of the second twin in relation to the gestational age, chorionicity, mode of delivery, delivery interval between the first and the second twin and the birth weight.

CORRESPONDENCE

Dr Rijuta Joshi Jha
Department of Obstetrics and Gynaecology,
Paropakar Maternity and Women's Hospital, Kathmandu
Email: dr.rijutajoshijha@yahoo.com
Phone: +977-9851151830

METHODS

A comparative study of 60 twin pregnancies with non-probability sampling technique was done at Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu, for three months from 14 January 2013 to 13 April 2013. All pregnant women with twin pregnancy of more than 28 weeks of gestation were included in the study. Intrauterine death of one foetus and gross congenital anomalies were excluded. Approval was taken from the institutional review committee of the hospital and written informed consent from the patient was taken. The data were entered in SPSS spread sheet (version 16). Mc Nemars test was used and p-value was considered significant at <0.05.

RESULTS

Total 60 sets of twin deliveries were analyzed. Most of the mothers (88.3%, n=53) were in between the age of 20-34 years and 41.6% (n=25) of them were nullipara followed by 35% (n=21) being primipara. Almost equal frequency of the mothers (51.7% and 48.3% respectively) had the delivery at the gestational age of < 37 weeks and ≥ 37 weeks. Majority of the pregnancy (58.3%, n=35) were dichorionic diamniotic (DCDA). Almost equal frequencies of the deliveries of both twins (45% and 50% respectively) were done vaginally and by caesarean section. Majority (91.7%, n=55) of the cases had inter-delivery interval of < 30 minutes.

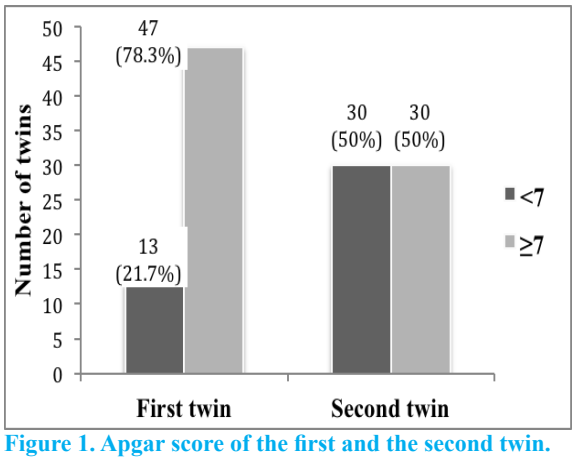

Figure 1. Apgar score of the first and the second twin.

Fifty percent (n=30) of the second twins had Apgar score of < 7 and only 21.7% (n=13) of the first twin had low Apgar score which was statistically significant (p=0.006) as shown in Figure 1, but only 30% (n=18) of the second twins and 25% (n=15) of the first twins required admission to neonatal intensive care unit, and was not statistically significant (p=0.508).

Twenty-five percent (n=15) preterm and 25% (n=15) term second twins, and 10% (n= 6) preterm and 11.7% (n=7) term first twins had Apgar score less than 7.

Vaginal delivery shows significant effect (p <0.001) for low Apgar score (Figure 2A and 2B), but the neonatal intensive care unit admission rate was not different (p=0.68).

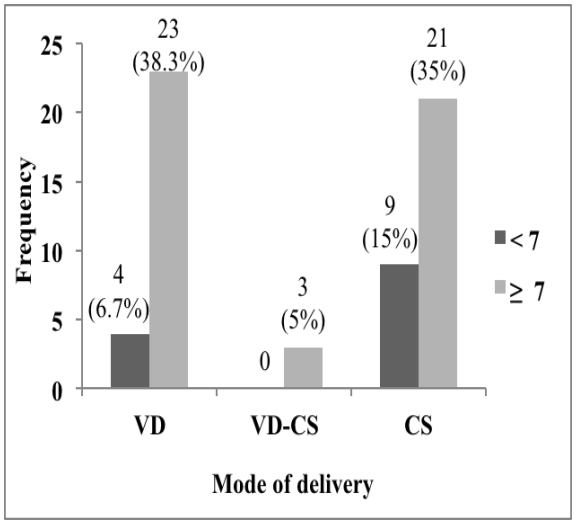

Figure 2A. Apgar score of the first twin in relation to the mode of delivery.

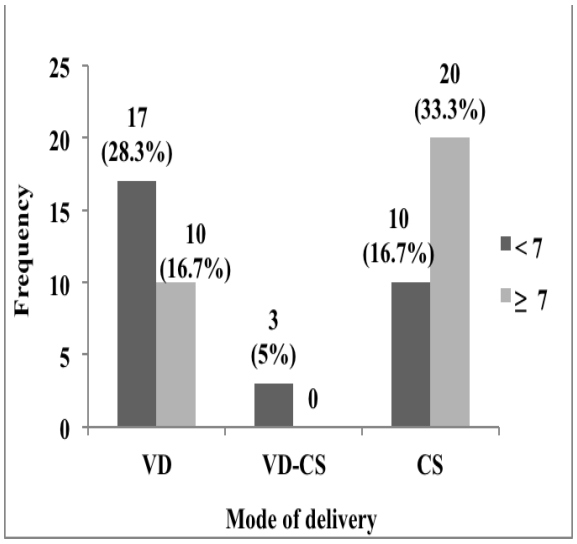

Figure 2B. Apgar score of the second twin in relation to the mode of delivery.

Most of the second twins (91.7%, n=55) were delivered within 30 minutes. Apgar score of <7 in the second twin was found to be statistically significant (p=0.007) with respect to the inter-delivery interval of < 30 minutes but there was no difference in the neonatal admission rate (p=0.219).

There were 75% (n=90) low birth weight babies and only 34.4% (n=31) of them required admissions for neonatal care but, out of 25% (n=30) average weight babies, only two (one first twin and one second twin) were admitted. There was no difference in low Apgar score in either group (p=0.50).

Among the twins with birth weight discordance of <30%, equal number of babies were seen in two Apgar score group in the second twins and 71.7% (43 vs. 13) of the first twins had good Apgar score of ≥ 7 (p = 0.014) compared to the second twins. There was no statistical difference in neonatal intensive care unit admission rate (p=1).

Perinatal mortality was 28.3% (n=17) with 5% (n=3) stillbirths (second twins only) and 23.3% (n=14) early neonatal deaths (10 second twins and four first twins). Perinatal mortality was more on the second twins (21.7%, n=13). The causes of early neonatal death for the first twins were sepsis (n=2), prematurity (n=1) and respiratory distress syndrome (n=1). In the second twins, the causes were sepsis (n=4), perinatal asphyxia (n=4), prematurity (n=1) and respiratory distress syndrome (n=1).

DISCUSSION

Since the past three decades there has been tremendous increase in multiple gestation, which has not only created a public health concern but also a medical dilemma.[2,3] Compared to the singleton pregnancies, in twin pregnancy there is much higher occurrence of almost all obstetric complications with much worse perinatal outcomes due to increasing morbidity and mortality. Even among the first born and the second born twin, the second born twin is in much disadvantage. This study was conducted to evaluate the difference in the perinatal outcome between them.

In this study, low Apgar score in the second twins was comparable to the similar study done by Hartley and Hitti,[5] Prins,[6] and Chang et al.[7] This could be due to reduced placental circulation after the delivery of the first twin, breech deliveries, and potentially greater susceptibility of second twin to hypoxia. Higher rate perinatal mortality rate in second twin (16.7% vs. 6.7%) could be due to higher susceptibility of the second born twin to hypoxia, sepsis and respiratory distress. Similar higher perinatal mortality in second born twin was seen in other studies.[8-11]

There was only slight increase in neonatal admission for the second twins (30% vs. 25%). The major cause for admission in neonatal unit was prematurity for both the first twins (n=13) and the second twins (n=12). This was followed by birth asphyxia (four second twins and one first twin). Similar finding was observed in the study done by Hanumaiah et al[8] in India where very low birth weight was the leading cause for neonatal admission followed by respiratory distress and birth asphyxia.

The preterm second twins had lower Apgar scores (p=0.049), which could be due to the reason that preterm babies are more easily affected by asphyxia than their term counterparts. Similar to this study, Dera et al[12] and Armson et al[13] also observed lower Apgar scores in premature neonates which they have attributed to the lower gestational age and low birth weight.

The second twin babies born preterm encountered higher rates of neonatal morbidities and mortalities compared to the twins born at term. Similar findings were seen in a study done by Crowther, [11] Smith et al[14] and Hack et al.[15]

Dizygocity was more common in this study than monozygosity which was similar to the observations made by Lewi and Deprest,[16] and Katz et al.[17] In cases of monochorionicity, more of the second twins had Apgar score <7 than the first twin (MCDA: 6 vs. 4; MCMA: 6 vs. 3) similar to the study done by Shrim et al.[18]

Perinatal mortality rate in this study was similar to the study done by Hack et al,[15] Wieczorek and Krasomski,[19] Victoria et al,[20] Sperling et al,[21] and Oldenburg et al.[22]

Vaginal delivery puts more stress on foetus resulting in lower Apgar score for the second twin (p <0.001). This could be explained by the fact that during the vaginal delivery, the second born twin is under stress of labour for a longer time than the first-born twin. Armson et al[13] and Yang et al [23] also observed low Apgar score for second twin who delivered vaginally.

Similar to the study by Ginsberg et al,[24] the Apgar score of the second twin was lower than the first twin in all the three cases of vaginal delivery of first twin and caesarean section for the second twin (one had zero score and two had 4-6). There was comparable low-Apgar score at 5 minutes in the twins who were delivered by caesarean section (23.3% of the second twins and 20% of the first twins). Similar to this study, Bisschop et al[25] did not observe any difference in the neonatal outcome of either twin at caesarean section.

Even when the second twin was delivered within half an hour of the birth of the first twin, the second twin had more chance of having Apgar score < 7 than the first twin (p=0.007). This can be explained by the fact that long inter-delivery interval in between the twins can lead to the foetal hypoxia due to diminished placental perfusion.[26] There were less number of cases (n=5) with ≥30 minutes of inter-delivery interval to compare the Apgar scores.

Three first twins and two second twins with ≥30 minutes inter delivery interval had early neonatal deaths. With regard to stillbirths two second twins and one first twin had inter-delivery interval of <30 minutes. Similar to this finding, in study done by Ezechi et al,[27] neonatal death were higher than still birth rates in retained second twin (47.3 % vs. 41.9%).

There was no correlation between neonatal admission and inter-delivery interval. In a study done by Healy and Gaddipati,[28] there was not increased neonatal intensive admission even when the inter-delivery interval increased to >30 minutes.

Birth weight discordance between the twin pairs

was calculated (in percentage) using the formula "birth weight of larger twin minus birth weight of the smaller twin and divided by the birth weight of the larger twin and finally multiplied by hundred". When the birth weight discordance was considered, in <30% sub group, the second twins had more chance of having Apgar score of <7 (p=0.014). There was less number of cases (n=8) with ≥30% birth weight discordance to compare the Apgar scores. Sujuki et al[29] found that the smaller twin (usually the second twin[1,3]) among the discordant twin pair had higher risk of lesser Apgar score at birth and umbilical artery pH of <7.1.

All stillbirths and 71% of early neonatal deaths had birth weight discordance of <30 % among perinatal deaths and similar result was reported by Garite et al.[30] It can be explained by the fact that the birth weight discordance is not an independent factor leading to the adverse perinatal outcome in twin pregnancy.[29] Some studies have shown birth weight discordance to be associated with increased mortality in the smaller second twin because of the twin to twin transfusion, which was not seen in this study.[31,32]

In those women who had twins with birth weight discordance of < 30%, there was not increased chance of the second twin being admitted to neonatal intensive care unit. In the study done by Mazhar and Kanwal,[33] higher percentage (16 % and 12.5%) of twins needed admission only to the intermediate care baby unit in birth weight discordant pair than concordant pair (7.8% and 7%).

Overall in this study, major differences between the first twin and the second twin could not be proven statistically. The much favorable outcome for both the first and the second born twin in this study may be due to the small group of patients, appropriate and timely antenatal diagnosis of twins, careful intra-partum monitoring of both foetuses; and majority of the women included in the study had uncomplicated ante-partum as well as intra-partum period and half of them had undergone caesarean section.

Although the second twin is more prone to birth asphyxia as a result of the prolong inter-delivery interval, umbilical cord prolapse, early placental separation, impaired placental perfusion, abnormal presentation and increased operative vaginal delivery which leads to much higher perinatal mortality in the second twin, many of these factors were not seen in this study which may be due to the increased operative mode of delivery.

CONCLUSIONS

The Apgar score of the second twins were lower than the first ones but the perinatal mortality among them were only slightly different. Neonatal intensive care unit admission rates were similar. The second born twins were likely to have lesser Apgar score (<7) in preterm, dichorionic-diamniotic placentation, vaginal delivery, inter-delivery interval of <30 minutes and birth weight discordance of <30%. Further study with a bigger sample is required to describe more on the foeto-maternal parameters of twins.

DISCLOSURE

The authors report no conflicts of interest in this work.

No violation of human rights and safety.

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Tuberculosis of the Cervix – Mimicking Cervical Cancer

Chaurasia A, Tyagi K, Dhingra V
Department of Obstetrics & Gynecology, Motilal Nehru Medical College, Allahabad,Uttar Pradesh, India.

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DEAR EDITOR,

Tuberculosis is a major socioeconomic and public health burden in India, afflicting approximately 14 million people. Though the actual incidence may be underreported due to its asymptomatic presentation and paucity of investigations, the prevalence of genital tuberculosis in infertile women ranges between 2-16%.[1] It frequently affects the upper genital tract, amongst which fallopian tubes are involved most frequently in 90%, endometrium in 60% and cervix least commonly, in about 5 - 24%[1] of the cases. Tuberculosis of cervix accounts for 0.1- 0.65% of all the cases of tuberculosis.[2] We present such a case due to the rarity of this condition and its clinical resemblance to a dreadful disease, "carcinoma of cervix."

A 20 years married, nulliparous lady of low socioeconomic status was referred to us as a suspected case of cervical carcinoma. She was having amenorrhoea for four months, discharge from vagina, postcoital bleeding for two months and a growth on cervix. Accompanying symptoms were lower abdominal pain, malaise, anorexia, weakness and significant loss of weight. There was no past history or family history of tuberculosis or history of any addiction but being married, she was sexually active. On general examination, she was thin built (BMI- 17 kg/m^2), had moderate pallor, pulse rate 88/minute, blood pressure 110/80 mm of Hg and no palpable lymphadenopathy. Systemic and abdominal examinations were normal. On genital examination, vulva was normal, speculum examination showed copious, non-foul smelling, blood tinged discharge and a friable papillary growth, almost covering the whole of the ectocervix.

Contact bleeding was present. Wet and KOH mounts were made as well as Pap smear was taken for cervical cytology. Mounts were negative for Trichomonas vaginalis, Candida albicans and Gardenerella vaginalis (bacterial vaginosis). On bimanual pelvic examination, the growth was firm to hard having irregular surface. Uterus was anteverted, normal sized, firm, mobile and the fornices were free and nontender. Per rectal examination did not reveal any induration or nodularity of parametrium and rectal mucosa was smooth and freely mobile. After ascertaining negative urine pregnancy test, she was advised routine blood and urine investigations along with HIV testing. Tests revealed 8 gm/dl haemoglobin, lymphocytic leucocytosis and raised ESR. HIV test was negative. Pap smear showed few epitheloid cells, chronic inflammatory cells but no dyskaryotic cells. Cervical biopsy was taken from the growth for further histological evaluation. The most striking feature in cervical biopsy specimen was the presence of numerous granulomas with Langhans giant cells, epitheloid cells and marked lymphocytic infiltration but without caseation (Figure 1).

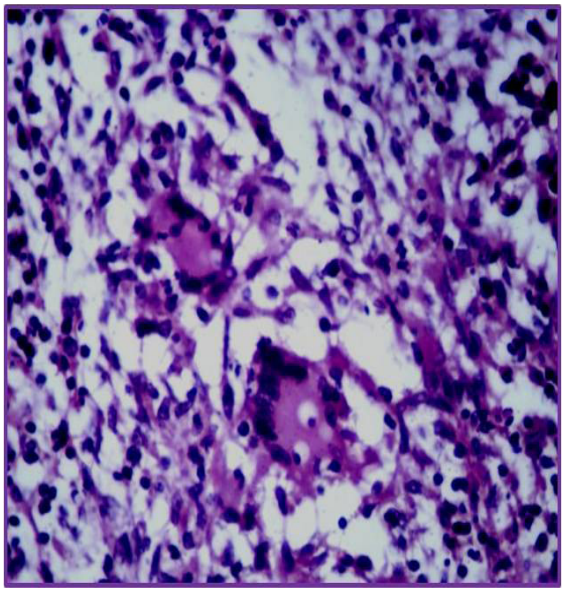

Figure 1. Microscopic view of cervical biopsy specimen (H & E stain and 40X magnification) showing Langhane's giant cells, Epitheloid cells (Slipper shaped) and Lymphocytic infilterates.

CORRESPONDENCE

Dr Amrita Chaurasia
Department of Obstetrics and Gynecology, Motilal Nehru Medical College, Allahabad, UP, India.
E mail: dr.amrita.chaurasia@gmail.com
Phone : +91-9235750677

After two days of cervical biopsy patient had an episode of sub acute intestinal obstruction for which she was managed conservatively. The reports of PAP smear and cervical biopsy excluded the presence of carcinoma rather predominant epitheliod and Langhans giant cell raised the suspicion of tubercular infection. So, we got her Mantoux test and chest X-ray done. Morning sputum was sent for AFB (acid fast bacilli) staining on three consecutive days and vaginal discharge was sent for mycobacterium tuberculosis culture. CT abdomen was advised to know associated presence of pelvic or abdominal tuberculosis but due to financial constraints, patient did not get it done. Mantoux test showed 18 mm induration but chest X-ray, sputum tests were normal. Mycobacterium culture of the discharge was also negative. Though CT of the abdomen could not be done, there was a strong clinical suspicion of associated abdominal tuberculosis as she had an episode of subacute intestinal obstruction. Though she neither had a positive AFB stain of sputum nor a positive mycobacterium culture, considering her positive Mantoux test , preponderance of graunulomas, epitheloid cells and chronic inflammatory cells in cervical biopsy report as well as seeing the burden of disease in India , especially Uttar Pradesh, we started antitubercular treatment with four drugs : Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. The doses were adjusted according to her weight. She was also given progesterone challenge for withdrawal menstrual bleed following which menstruation occured. Response to the antitubercular drugs was dramatic with resolution of the constitutional symptoms first and gradual resumption of normal appearance of cervix later on . Initially on first visit after a month, we noticed shrinked growth but it took total of approximately four months to disappear. After two months of intensive treatment, maintenance therapy was begun with three drugs (isoniazid, rifampicin, and ethambutol) for another 7 months.

In developing countries, genital tuberculosis is common in the age group ranging from 20 -40 years. Genital organs most frequently affected are fallopian tubes, uterus and ovaries.[2] Tuberculosis of cervix accounts only for 0.1-0.65% of all the cases of tuberculosis.[2] .Mycobacterium tuberculosis and mycobacterium bovis are primarily responsible for pelvic tuberculosis. Infection reaches there either by haematogenous or lymphatic route from a primary focus in chest or lymph nodes. Primary affection of cervix is rather uncommon, but may be introduced by a partner with tubercular epididymitis. Rarely, infected sputum, if used as a sexual lubricant,may also be a route of transmission.[2] Tuberculosis of cervix may manifest as vaginal discharge, postcoital bleeding with macroscopic papillary growth or ulceration on the cervix.[3] At a glance it may be misinterpreted as cancerous growth of cervix. A case similar to the present case which was confused with cervical malignancy had been reported by Agarwal et al in 2009.[3] Microscopically, caseating granulomas are suggestive of tuberculosis but also found in amoebiasis, schistosomiasis, brucellosis, tularemia, sarcoidosis, and foreign body reaction.[4] Although staining for acid fast bacilli and mycobacterium culture are confirmatory, many a times may not be very useful in making a diagnosis due to their high false negativity. Isolation of mycobacterium in tissue specimen is the gold standard for diagnosis, but one third of cases are culture negative, therefore presence of typical granulomata in histopathology may be sufficient for diagnosis, if other causes of granulomatous cervicitis have been excluded. Retrospective diagnosis can also be made if patient improves clinically after starting treatment with antitubercular drugs.[5] Similarly this patient also had negative AFB staining and mycobacterial culture, but presence of granulomas motivated us to start antituberculer therapy that improved her illness. The incidence of tuberculosis has increased recently due to HIV pandemic requiring more careful attention of the health providers towards the suspicion and diagnosis of the disease. Though not for the first time in literature, this case report is noteworthy as it reemphasises the spectrum of symptomatology of cervical tuberculosis and its management as well as it also reinforces the inclusion of cervical tuberculosis in the differential diagnosis of growth on cervix especially in the patients, residing in areas having high prevalence of the disease.

CONCLUSIONS

In young woman, presenting in a tuberculosis endemic area with suspicious growth on cervix, the two most probable differential diagnoses will be carcinoma or tubercular infection. Confirmation of the diagnoses can always be done by doing biopsy of the lesion. But

to ensure that the diagnosis is not mistaken, biopsy should preferably be taken including both the normal and abnormal areas of the cervix with meticulously avoiding the necrotic areas.

DISCLOSURE

The authors report no conflicst of interest in this work.

No violation of Human rights and safety.

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It should be accompanied usually by upto 30 references within the framework of 4000 words. Generally, only up to six, either figures/tables/charts/illustrations are allowed.

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No 'Tabs' should be given in the text. Findings should be analysed by statistical methods and be well interpreted showing level of significance as far as possible.

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