

# Histological Examination of Tissue Obtained in Early Pregnancy Loss

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## ABSTRACT

### Background

It is a routine practice to send histological sample after surgical evacuation of early pregnancy loss.

### Objective

This study was carried out to see the justification of regular histological study by carrying out the histological study of early pregnancy loss and to find the prevalence of gestational trophoblastic disease in early pregnancy loss.

### Method

It was a descriptive prospective study, conducted in Nepal medical college teaching hospital from February to October 2020 in Obstetrics and Gynaecology department. Clinical data such as age, parity, gestational age and diagnosis were collected of 130 patient of early pregnancy loss. Then histological study were sent after surgical evacuation.

### Result

Among the age group, 21-30 age group was maximum. (64.61%), more than half of the patient was primigravida (53.07%) and most of the cases were between 6 to 9 weeks of gestation. Incomplete abortions were maximum (43.07%), missed abortions 38.46%, blighted abortions 16.15%, inevitable abortions 1.53% and septic abortion was 0.76%. Among histological finding, 72.30% were product of conception, 15.38% of the cases had no product of conception, decidual tissue only in 6.92%, partial mole in one case (0.76%), complete mole in one case (0.76%) and hydrophic changes in one case (0.76%). The total cases of Gestational trophoblastic diseases (GTD) were 3(2.30%).

### Conclusion

In our study we found 2.3% of cases of GTD, which was quite high in compare to Western word. So it is a good practice to do histological study of all cases of EPL in our country to detect GTD, determining cause for recurrent pregnancy loss and detecting unexpected fetal pathology.

## KEY WORDS

*Early pregnancy loss, Histology, Gestational trophoblastic disease*

## INTRODUCTION

Abortion is defined as loss of pregnancy before 20 weeks of gestation or fetus weighing less than 500 gram.<sup>1</sup> Ten to twenty percentage of the clinical pregnancies spontaneously get aborted during first trimester.<sup>2</sup> Early pregnancy loss (EPL) is spontaneous abortion within 12 weeks of gestation. It is a routine practice to send histological sample after surgical evacuation of EPL. In view of the maternal risks associated with ectopic pregnancy and molar pregnancy it is recommended that practitioners should always consider sending tissue obtained at the time of uterine evacuation (medical or surgical) for histological examination.<sup>3</sup> Other reasons to send histological study of all the patient with early pregnancy failure, include detecting incomplete pregnancy failure, determining cause for recurrent pregnancy loss and detecting unexpected fetal pathology.<sup>4</sup> Sometimes sending histological examination of the tissue obtained become mandatory to protect doctor from medicolegal issues.

But there are some schools of thought, who think that histology should only be sent when diagnosis is uncertain before and after evacuation.<sup>5,6</sup> It is waste of money and resource and not justified.

Alsibiani in her article, stated that only in selective cases histological study should be done since the incidence of molar pregnancy is very low in their country, Saudi Arabia.<sup>7</sup> Heath V and his team<sup>4</sup> also had similar opinion. On the other hand, Rhasid in his research supports for routine histological study.<sup>8</sup> The author found 0.2% molar pregnancy and 15% partial mole out of 375 biopsies of EPL, which was quite significant in number. Similar view was found in other articles.<sup>9-11</sup>

We are concerned of not missing gestational trophoblastic (GTD) disease in cases of EPL. Since proper follow up is required in these patient for treatment. This study was conducted to see the incidence of molar pregnancy and other pathology in histological findings of EPL and to see whether routine histological study is justified or not.

## METHODS

It was a descriptive prospective study which was conducted in Nepal Medical College Teaching Hospital. It was conducted from February 2020 to October 2020. The number of the patient was calculated with the formula- $(\text{Early pregnancy loss prevalence} - 10 - 20\%)^2 N = z^2 pq / d^2$  Where, N=required sample size, Z=confidence interval at 95% (standard value of 1.96), P= estimated prevalence, q=100-20=80, d=margin of error at 6% (standard value of 0.1), sample size (n) =  $1.9 \times 1.9 \times 15 \times 85 / 36 = 127.85$ . So the estimated sample size was 130.

Detailed history was taken of the cases of EPL and their clinical data such as age, parity, gestational age and clinical diagnosis were collected. They were admitted and then surgical evacuation was done according to hospital protocol.

The samples obtained were placed in 10% formaldehyde and sent for histology. Before enrolling the patients in the study informed written consent was taken. Ethical approval taken from research and institutional review committee (IRC).

Inclusion criteria: All the cases of EPL such as incomplete abortion, missed abortion, blighted ovum and inevitable abortion who underwent surgical evacuation and gave consent to be involved in the research.

Exclusion criteria: Those cases of medical termination and cases who refused to give consent to be involved in the research.

The data was entered in the computer, statistical analysis was performed using SPSS (VER.16.00) with the formula Chi-square wherever required. Data considered significant if  $p < 0.05$ .

## RESULTS

During the period of study, histological study was done of 130 patients with EPL after surgical evacuation. The age distribution is given in table 1. Among the age group, 21-30 age group was maximum (64.61%). When correlating the age group with the number of abortion, the age group 21-30 had significant relation with the number of abortion, ( $p < 0.001$ ). The parity and gestation of the study group are given in table 2 and 3. More than half of the patient were primigravida (53.07%) (table 2) and most of the cases were between 6 to 9 weeks of gestation (70.77%) (table 3). The type of EPL is showing (table 4) where we found that incomplete abortions were maximum (43.07%). Missed abortions were 38.46%, blighted abortions were 16.15%, inevitable abortions were 1.53% and septic abortion was 0.76% (table 4). Among histological finding, 72.30% were product of conception, 15.38% of the cases had no product of conception, decidual tissue only without chorionic villi in 6.92%, partial mole in one case (0.76%), complete mole in one case (0.76%) and hydropic changes in one case (0.76%) (table 5). Table 6 shows the correlation between diagnosis and the histological study which was not significant ( $p = 0.858$ ). The case with hydrophi change had high B human chorionic gonadotrophin (B hcg) level. Follow up was done for six weeks till the hormone became normal. So the cases of GTD were 3 (2.30%) out of 130 cases. There was a case of suspected ectopic pregnancy who underwent surgical evacuation. With chorionic villi in histological finding and correlating with B hcg report ectopic pregnancy was excluded.

**Table 1. Age range of the patient EPL (n=130)**

Age in years	Number of patients	Percentage
≤ 20	9	6.92
21 – 30	85	65.38
31 – 40	29	22.31
≥ 41	7	5.38

**Table 2. Parity of the patient with EPL (n=130)**

Parity	Number	Percentage
Primigravida	69	53.07
Gravida 2	54	43.07
More than gravida3	7	5.38
≥ 41	7	5.38

**Table 3. Gestation of patient with EPL (n=130)**

Gestation in week	No. of patient	Percentage
<6	20	15.38
6-9	92	70.77
>9	18	13.85

**Table 4. Type of abortion of patient with EPL (n=130)**

Types of abortion	Number	percentage
Incomplete	56	43.07
Missed	50	38.46
Blighted	21	16.15
Inevitable	2	1.53
Septic	1	0.76

**Table 5. Histological findings of patient with EPL**

Histological findings	Number	Percentage
Product of conception	99	76.15
No product of conception	20	15.38
Decidual tissue only	8	6.15
<b>Gestational Trophoblastic Disease</b>		
Partial mole	1	0.76
Complete mole	1	0.76
Hydropic changes	1	0.76

**Table 6. Correlation of histological finding with diagnosis in early pregnancy loss**

Histological finding	Incomplete	Missed	Blighted	Inevitable	Septic	Total
Product of conception	41 (41.41)	41 (41.41)	14 (14.14)	2 (2.02)	1 (1.01)	99
No product of conception	11 (55)	5 (25)	4 (20)	0 (0)	0 (0)	20
Decidual tissue	3 (37.5)	4 (50)	1 (12.5)	0 (0)	0 (0)	8
<b>Gestational trophoblastic disease</b>						
Partial mole	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1
Complete mole	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1
Hydropic change	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	1
Total	55 (42.31)	51 (39.23)	21 (16.15)	2 (1.54)	1 (0.77)	130

## DISCUSSION

Spontaneous abortion is a common health issue, which requires immediate treatment and some cases need long time follow up, such as ectopic pregnancy and GTD. There is controversy regarding the practice of routine histological examination of tissue removed during the miscarriage. Novac his team recommended that all the specimens should be submitted to histological examination to investigate whether the abortion was due to dysmorphic or disruptive causes, to exclude the presence of GTD and sometimes simply to confirm that pregnancy had occurred by showing the presence of fetal or placental tissues.<sup>12</sup> There are many authors, who recommend routine histological study.<sup>13-16</sup> On the other hand, there few authors, who think that regular histological should be done only in special cases.<sup>4,7</sup>

In our study, the age group 21-30 years was maximum 64.61%. When correlating with the number of EPL age group, 21-30 years showed significant value ( $p < 0.001$ ). Which shows that the age group 21-30 years is significant risk factor for EPL. The study done by Makaju and his team also found the majority of women belong to age group 21-30 years (62.20%).<sup>17</sup>

Among the type of EPL, 43% of the cases were incomplete abortion in our study which can be compared to the study done by shetty and Rhasid.<sup>8,18</sup> In their study the majority of EPL were incomplete abortion, 88% and 65% respectively.<sup>8,18</sup> Whereas, in the study done by Alsbiani of EPL the cases of incomplete abortion and missed abortion were both 45.30%.<sup>7</sup>

As regard to the histological finding, product of conception was highest in our study (73%), decidual tissue only 8% and the cases of GTD were 2.3%. Similar result was found in other studies. The study done by Rashid found product of conception 86.6%, decidual tissue 5.6% and GTD 4.4%.<sup>8</sup> Tashi and his team also found product of conception in 69%, partialmole in 2.1%, complete mole in 2.1%, exaggerated placental site and placental trophoblastic nodule was detected in 0.12%.<sup>15</sup> Similarly El-Halaby and his team found 94.5% of product of conception, 3.1% partial mole, 1.2% complete mole and 1.2% ectopic pregnancy.<sup>16</sup> On the other hand, the study done by Fram, there were quite high incidence of GTD (17% partial mole and 1% complete mole).<sup>13</sup> There were some studies where the histological finding with GTD was very less in compare to our study. Alsbiani in her study observed only 0.2% complete mole and 0.2% partial mole and Heath and his team also found only two (0.13%) molar pregnancy among 1576 patients on histological examination.<sup>4,7</sup> This wide ranges of finding of GTD in histological study of all these studies are probably due to different incidence of GTD in different part of the world.

The five year prevalence of GTD at BP Koirala Institute of Health Science in Nepal from 2008-2012 was 4.17 per 1000 live birth during the study period.<sup>19</sup> In Asia, the incidence

of molar pregnancy is very high. It is 1 in 80 pregnancies in Asia whereas in the Western world, it is only 1 in 500-1500 pregnancies.<sup>20-22</sup> The study done to compare GTD among Asian women of North England and North Wales showed that Asian women are at increased risk of having molar pregnancies compared to the western populations.<sup>23</sup> We are in the part of world where the incidence of GTD is high and we need to do histological study of product of conception of even unsuspected cases of EPL, without any feature of GTD in USG, so as not to miss any cases of GTD. In our study there were 2.30% of GTD which we would have missed if we had not sent for histology study.

Specially in cases of recurrent abortion, along with karyotyping histology study has a very important role in detecting causes of abortion. Novak and his team in their prospective study showed the significant presence of villous scalloping with trophoblastic invagination associated with abnormal karyotypes, particularly triploidy.<sup>24</sup> It was found that chorionic intervillitis is associated with recurrent fetal demise.<sup>25</sup> When there is such finding, there may be association of genetic and nongenetic abnormalities

like abnormalities of Tryptophan abnormalities, factor v mutation and Antiphospholipid antibody syndrome.<sup>26</sup>

The study was done in a tertiary level hospital where the sample was taken from limited area of Kathmandu. So histological study should be done of EPL from multicenter location of Nepal including rural and urban communities with larger sample size to guide the revision of practice at a national scale.

## CONCLUSION

In our study we did the histological study of EPL and tried to find the prevalence of GTD. The prevalence of GTD was 2.3% which was high in compare to other studies done in western countries. In view of high incidence of GTD in Nepal, we should make it a regular practice to send all samples of EPL for histology and is cost effective. We should send the sample for histology not to miss GTD, other pathology such as chronic inflammation of the endometrium and rule out ectopic pregnancy.

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