Original article

RISK FACTOR AND/OR PREVALENCE OF TUBERCULOSIS IN NEPAL: A SYSTEMATIC LITERATURE REVIEW

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ABSTRACT

Introduction: This review was to synthesise evidence regarding the risk factor and/or prevalence of Tuberculosis in the Nepalese community.

Methodology: A search strategy was used to identify the English language primary research studies published on or after 2018. Four databases namely, Cochrane, PubMed, ProQuest, and Web of Science were used to search data, and themes were identified to synthesise the data.

Results: A sum of 1097 studies was recognised after the four database searches, excluding duplicates. Just four studies met the inclusion criteria after full article screening and were included for synthesis. All the included studies showed evidence on prevalence of Tuberculosis. Three studies identified male gender as a risk factor for contracting Tuberculosis. Three studies showed the prevalence of Tuberculosis in health disorder context to be around or over 10%, only one study showed about four per cent of prevalence of Tuberculosis in admitted patients

Conclusion: Male genders possess a greater risk of contracting Tuberculosis in health disorder context, with the exception in Rifampicin-resistant Mycobacterium Tuberculosis(RR-MTB) which showed the opposite outcome. In terms of prevalence, majority of the sample exhibited around ten per cent and over prevalence of Tuberculosis in health disorder context , apart from one study which showed around four per cent prevalence of Tuberculosis in admitted patients. Therefore, further research is required to bridge these gaps

Key words: Risk factor; prevalence; Tuberculosis; TB; Nepalese Community

INTRODUCTION

Tuberculosis (TB) is a bacterial infection spread by inhaling tiny droplets produced when an infected person coughs or sneezes. It primarily affects the lungs but can affect any part of the body, including the abdomen (stomach), glands, bones, and nervous system.[1]

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TB can cause symptoms like prolonged cough with or without blood, chest pain, weakness, fatigue, weight loss , fever and night sweats. Even though it is a preventable and curable disease it claimed around 1.6 million lives in the year 2021, and over 80 % of cases and deaths are from low and middle income countries.[2] TB was a major public health problem in Nepal a decade ago, as around 4000-5000 people die from it each year.[3] Unfortunately, it remains a crucial public health threat as annual death rate has been re-estimated at 17,000, which is 3.3 times higher than the previous estimate.[4]

There are many risk factors that make people vulnerable to be infected by TB namely, being HIV positive, and smoking, having diabetics, being a

heavy alcoholic, malnutrition, and air pollution.[5] Therefore, to prevent TB, it is crucial to identify risk factors among contacts.[6] The contacts may be the family, friends or co-workers with latent TB. Prevalence is the measure of the frequency of a disease or health condition in a population at a particular point of time[7] and is essential in exploring the affected population which may inform us about the rate at which the disease is spreading and essential actions to be taken to control the spread. Therefore, various types of Evidence synthesis such as rapid review ,scoping review, meta- analysis and systematic review of literature on the risk factor and / or prevalence of TB in Nepal is critical to develop interventions to control the spread of the disease.

A systematic review can be described as a replicable integration technique to provide information as per responsible, pre-planned criteria and has three distinct features: recognises important sources, assesses research, and combines proof.[8] On the other hand, meta-analysis is a quantitative, formal, epidemiological examination which uses a systematic method to evaluate past research studies to determine decisions about that group of research. To the authors' knowledge this is the first review study to summarise risk factor and/or prevalence of TB in Nepal. The aim of this study is to map and describe the existing evidence base on the risk factor and/or prevalence of TB in various health disorder context in the Nepalese community. Therefore, it is anticipated that the result of this study will reveal reseaarch gaps to guide health experts in decision- making in Nepal, as well as developing policies and interventions tailored towards bridging the gap.

Operationalization & Strategy

Eligibility:

To meet the criteria for a systematic review a comprehensive, a priori inclusion/exclusion criterion was established.[9] Only studies published on or after 2018 were considered for inclusion to reduce the outcome variance due to the out-dated technology. Only studies available in English were considered due to practical limitations. Relevant studies included any primary research, peer reviewed and quantitative studies. There are several recommended strategies and framework that can be utilised such as PCC, PICO, SPIDER,

SPICE and ECLIPSE to develop research question.[10] The Co Co Pop framework can be used for reviews addressing a question relevant to prevalence or incidence,[11] therefore this review has utilised Co Co POP framework(Table 1)

Table 1: Condition, Context , Population (Co Co Pop) FRAMEWORK		
Condition	Context	Population
Tuberculosis any form	Any Health Disorder	Nepalese
Tuberculosis any type	Government Hospitals	Other residing in Nepal
Tuberculosis any stage	Private Hospitals	Any age
	Community clinics	Any Sex
	Nepal	

METHODOLOGY

Search Strategy

This review was conducted to estimate the risk factor and/or prevalence of TB in Nepal. The authors' checked DARE database (www.library.ucsf.edu) and the Cochrane Library to ensure that this review has not been conducted before to avoid duplication. The authors' also checked if there were any similar on-going systematic reviews in the PROSPERO database from (http:www.Crd.york.ac.uk/Prospero). These checks reassured that there had been no similar studies undertaken previously. All relevant and published studies in the databases namely: Cochrane Library, ProQuest, PubMed, Web of science, were searched. In addition, to the studies that were retrieved from the literature search, authors' hand-searched the references of all the relevant articles to ensure that eligible studies are not excluded.

Table 2: Search Strings and Parameter for ProQuest only
Search strings & Parameter (ProQuest)
risk factor OR riskiness OR increasing chances* OR high chance* OR danger* OR dangerous* OR threat* OR threatening* AND prevalence OR occurrence* OR occurring* OR frequency* OR frequent*OR common* OR commonness* AND tb OR tuberculosis AND Nepal

Table 3: Inclusion/ Exclusion Criteria	
Inclusion Criteria	**Exclusion Criteria**
• Study that aims to identify risk factor and/ or prevalence of TB in any health disorder context. • Study that aims to identify risk factor and/or prevalence of TB of any form, any type, and any stage.	• Study that was undertaken outside Nepal.; or published before 2018 • Study that aims to identify risk factor and/ or prevalence of any health disorder in TB context. • Study that aims to identify risk factor and/ or prevalence of TB in environmental context. • Health promotion techniques for improving TB awareness • Study involving non-human research • Reviews, notes, case-reports, commentaries, editorials.

Retrieved articles were exported to the reference management software called RefWorks to remove duplicate studies. All the articles were then initially screened by "Title" and if necessary by abstract to exclude papers that did not align with the inclusion criteria. Full-text articles were obtained for studies that met the inclusion criteria. Any disagreement was handled based on the established inclusion criteria. By applying the inclusion criteria ,four articles have been considered as the main results of the literature review. The screening and selection process can be seen in (Fig 1) prism flow diagram
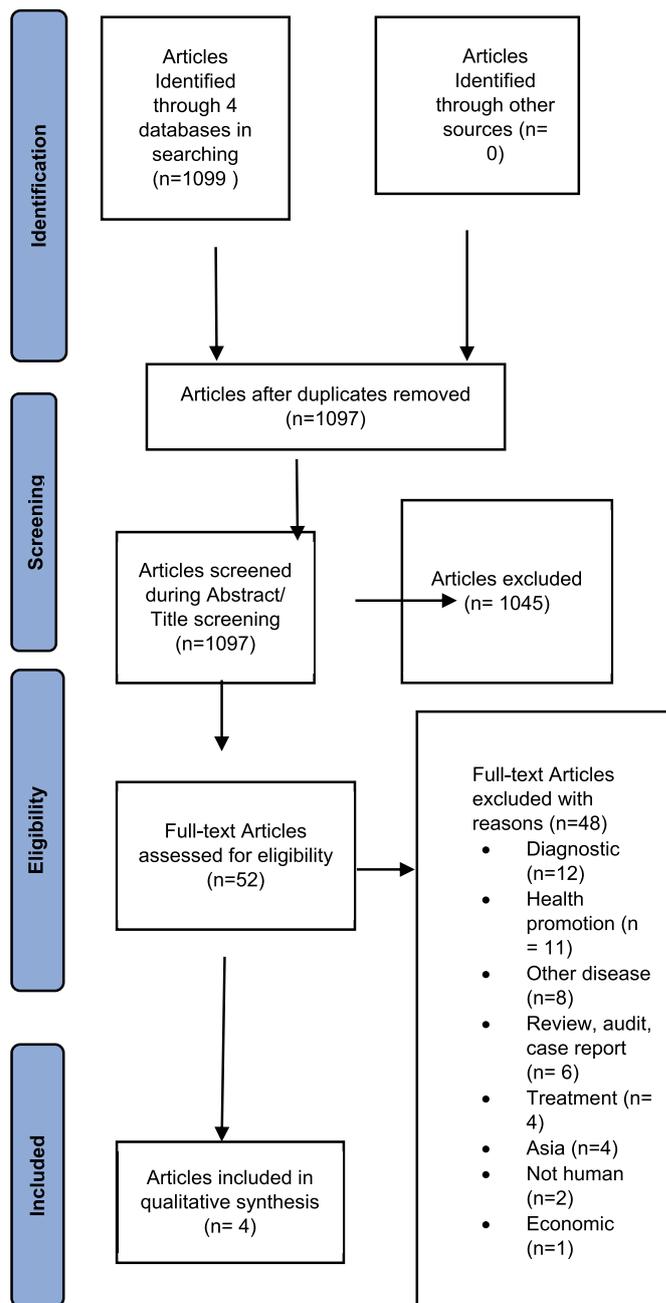

Figure 1: PRISMA Diagram of findings and the inclusion/exclusion process [Source: Adapted from Nwagbara et al.,2021][12]

Table 4: CKD=Chronic Kidney disorder, PLHIV=People living with HIV,MTB=Mycobacterium tuberculosis, RR-MTB=Rifampicin-resistant Mycobacterium tuberculosis						
Authors & Date	**Location**	**Aim**	**Study Design**	**Sample Size**	**Risk factor**	**Prevalence**
Pradhan & Sigdel;2020	Ktm	To identify prevalence, clinical presentations &outcome of TB in CKD patients.	Cross-sectional	401		13.7%
Adhikari et al;2022	Ktm, Pokhara, Bheri, Seti, Dharan	To identify prevalence of TB and associated risk factor in PLHIVs	Cross sectional	403	Male, Dalit HIV stage 3,4,family history	9.9%
Thapa et al;2021	Patan	To identify prevalence of TB in admitted patients.	Des cross-sectional	6829	Male patients	3.06%
Sah et al;2020	Bhaktapur	To assess prevalence rate of MTB &RR-MTB in suspected PTB patients	Retro spective cross-sectional	990	Male, Past ATT Treatment. Female	MTB-13.8% RR-MTB-10.2%

Data extraction

Data were extracted using a standardised data extraction format prepared in Microsoft Excel by two reviewers, independently. The name of the first author, date, location, study aim, study design, sample size, risk factor and prevalence were collected.

Methodological Quality

Guaranteeing that reliable, legitimate and representatives studies are incorporated within the research review is crucial .It is a vital step in ensuring that any future research can benefit from the rigorous and comprehensive synthesis of available evidence.[13] Four studies have thus been examined and assessed for methodological quality. For this purpose, two reviewers independently utilised the JBI Critical Appraisal Checklist for cross- sectional study,[14] to evaluate the quality of each study.

Data Synthesis

There are several themes that appeared in terms of findings, methodology, and study quality indicator

Gender (male v/s female)**:**

Studies revealed similar findings even though they have different sample. In the larger study, by Thapa

TABLE 5: Methodological Assessment of included article. Y=yes, N=no, UC=unclear								
Citation	**Questions**							
	1	2	3	4	5	6	7	8
Adhikari et al;2022	N	Y	Y	Y	UC	Y	Y	Y
Pradhan &Sigdel ; 2020	UC	Y	Y	Y	UC	Y	Y	Y
Sah et al;2020	N	Y	Y	Y	N	N	Y	Y
Thapa et al; 2021	N	Y	Y	Y	N	N	Y	Y
%	0%	100%	100%	100%	0%	50%	100%	100%

and his colleague [15] found that being a male was a risk factor for catching TB in admitted patients. Similarly, in the various centre study Adhikari and his colleagues [16] revealed that being a male People living with HIV (PLHIV) carried higher risk of catching TB than female PLHIV .Similarly , a study by Sah and his colleague [17] also found that men carried a higher risk of catching MTB than female. By contrast, in the same study [17] found that females carried a higher risk of catching RR-MTB than males.

Prevalence (10 % and above v/s below 5%):

In the study[17] it was found that prevalence of MTB was nearly 14% and prevalence for RR-MTB was around 10%. Similarly, in the much smaller study[18] of sample size (401), prevalence of TB in CKD patients was 13.7%.Furthermore; a study[16] found that prevalence of TB in PLHIV was nearly 10%. By contrast, a study[15] showed that prevalence of TB in admitted patients was about 4%.

Pulmonary v/s Extra Pulmonary:

Only two studies assessed prevalence of pulmonary and extra pulmonary TB in health disorder. Pulmonary TB (73.20%) was higher prevalent in admitted patients than extra pulmonary TB (26.79%).[15] However, a study[18] showed extra pulmonary TB (69.1%) was more prevalent in CKD patients than pulmonary TB (21.8%).

Location:

The sample from most studies was single centred and limited to Kathmandu Valley.

Study Design:

All studies had quantitative & cross-sectional approach with sample size varied from 401 to 6829. Out of four studies, one study[17,] had both adult and children as a study sample, however, three studies [15,16,18] had only adult populations.

Study selection:

The inclusion criteria, distinguish the study populace in a consistent, reliable, uniform, and objective manner.[19] Not a single study had a clearly defined inclusion/ exclusion criteria that was established before the recruitment of the sample.

Confounding is frequently alluded to as a "mixing" or "blurring" of effects"[20] where the impacts of the exposure under investigation on a given result are blended in with the impacts of an extra factor or set of variables bringing about a distortion of the genuine relationship. It can be prevented by use of randomisation, restriction, or matching. In contrast to other types of bias, it can also be controlled by adjusting for it after completion of a study using stratification or multivariate analysis.[21] Not a single study has clearly mentioned that they have identified confounding factors.

RESULTS

Risk factor of TB in various Health disorder

Three studied announced proof on risk factor of TB. Males carried nearly 8% higher risk of contracting TB than females in PLHIVs.[16] Similarly, the author also pointed out that being a WHO stage 3 and stage 4 HIV patients and belonging to a marginalised caste also carried a higher risk of catching TB. Similarly, male genders carried around 2% higher risk of catching MTB and being a marginalised cast also increases the chances of MTB and previous history of TB treatment also increases the chance of catching MTB.[17] However, in the same study17, authors found that female genders doubled the risk of catching RR-TB. Furthermore, a study15 showed that male genders (70.33%) nearly doubled the risk of catching TB in admitted patients than female patients(29.67%).Prevalence of TB in various Health disorder studies showed there was a significant prevalence of TB in various health disorders. A study16 found that there was a nearly 10 % prevalence of TB in PLHIV. Similarly, a study18 showed that around 14 % of prevalence of TB in CKD patients. Furthermore, the prevalence of MTB in suspected patients was about 14% and prevalence of RR-MTB in suspected patients was approximately 10 %.[17] However, a study15 showed around 4% prevalence of TB in admitted patients.

All these studies have attempted to answer the problem and used cross-sectional quantitative research. Quantitative research is common with most epidemiologist and infection control professionals.[22] This incorporates estimating the predominance of specific infections or distinguishing connects furthermore with indicators of infections.[23] Albeit these examinations have achieved extraordinary advancement in disease

control and prevention, usually they cannot assist us clarifying why certain elements influence the utilisation of infection control practices and recognise the basic systems through which they do as such.[24] Since all the four studies were quantitative and unable to give explanation was consider as a disadvantage.

Setting up inclusion and exclusion criteria for the study population is a norm, required practice when planning high-quality research protocols .Inclusion measures are characterised as the vital highlights of the target populace the researcher will use to address their examination question.[25] Not a single study had a clear inclusion, exclusion criteria that was established before the sample recruitment, and thus considered as a disadvantage.

A confounding variable is extra factor that can ruin the experiment and give useless result. Ignoring confounding in non-randomised study will often result in "distorted" or incorrect estimate.[26] Therefore, identifying and controlling potential confounding variable is one of the most crucial tasks for the researchers. Included 15,16,17,18 studies fail to identify it, thus considered a drawback influencing the general validity and reliability of studies in this field.

DISCUSSION

The findings of this review reported evidence on the risk factor and prevalence of TB in various health disorders. Included studies15,16 revealed male genders carried higher risk of catching TB. Similarly, a study17 revealed males carried higher risk of MTB ,however, in the same study the author found that females carried higher risk of catching RR-MTB. The possible explanation for this might be, habit like smoking, alcoholism and drug addiction are more common in male than females which are risk factor of catching TB.[27,28]

Similarly, three studies16,17,18 found that the prevalence of TB is around 10% and above in various health disorder context. However, only study 15 revealed that prevalence of TB was below 5% in health disorder context. Rural areas have higher prevalence of bacteriologically positive pulmonary TB than urban areas.[29,30] Nevertheless, the reason for the variation in similar urban location would be interesting to explore in future research. Since this study revealed that male gender have higher risk

of catching TB and have around 10 per cent TB prevalence in various health disorder contexts. It is advisable that all admitted in- patients especially male must be given respiratory hygiene advice and ensure the patient has tissue waste disposal and hand hygiene facilities available.

CONCLUSION

This systematic review showed that male genders possess a greater risk of catching TB in various health disorder contexts, with an exception in RR-MTB, which revealed the opposite outcome. In terms of prevalence, majority of the sample exhibited around ten per cent of prevalence of TB in various health disorder contexts, apart from one study which showed around four per cent of prevalence of TB in admitted patients. Therefore, further research is required to bridge these gaps. Moreover, there is a gap in the literature in terms of study location, population, and study design. Finally, it is deemed important to strengthen health education, information broadcasting, and awareness on risk factor and prevalence of TB in various health disorder contexts. It also requires that country pledge to step up for the provision of accurate and up-to-date information on risk factor and prevalence of TB in various health disorder contexts through the relevant institutions and institute.

RECOMMENDATION

While the published study provides valuable information regarding risk factor and /or prevalence of TB in Nepal, there is a gap in the literature related to the study location, population, and study design. Further research is required in rural areas of Nepal to explore if it would provide similar results. Additionally, it would be interesting to explore the reasons for variation in prevalence, even though all the study samples share similar urban location. Previous research showed males are more prone to catching TB, as they have risk factors like smoking, alcohol consumptions.[31] This systematic review also supports that male are at a greater risk of catching TB than females in various health disorder context, apart from RR-MTB, which revealed the opposite outcome. Henceforth, it would worth research amongst solely male children and female children to know the outcome. Since childhood Tuberculosis is an under prioritised disease in Nepal[32] more TB research is warranted

on risk factor, prevalence, and incidence of TB to control this disease amongst children. Finally, Cohort studies should also be encouraged to find incidence rate of TB in various health disorder context.

FUNDING

ETHICAL ISSUES & LIMITATIONS

As far as limitations, just a few studies were qualified for inclusions. To the authors' knowledge this is the first review to map evidence on risk factor and/or prevalence of TB in Nepal. It very well may contend that a more indulgent cut-off for eligibility for the investigation may have been embraced. The decision to exclude studies, assessing risk factor and /or prevalence of TB in environmental context, may therefore be consider by some to be contentious. However, the aim of the study is to assess risk factor and/or prevalence of TB in health disorder context, thus it is deemed important to exclude those studies to ensure that the outcome is as useful as possible. Finally, the studies included for this investigation were restricted to those recorded on the four databases (Cochrane, PubMed, ProQuest and Web of science).Some studies on this subject may have been barred if it was not recognised during searching phase.

CONFLICT OF INTEREST

There is no conflict of interest to disclose.

DATA AVAILABILITY

Data availability statement

Data derived from public domain resources and databases namely:

1   Cochrane : Search Manager | Cochrane Library

2: PubMed : Advanced Search Results - PubMed (nih.gov)

3: Proquest:https://www.proquest.com/ search/2148995?accountid=15977

4: Web of science : https://www.webofscience. com/wos/woscc/summary/e2e0c060-03e8- 4098-82b5-a2c7909d7107-34d2d882/ relevance/1

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