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EDITORIAL

Original Articles

AIMS AND SCOPE:

The SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS is the official journal of the SAARC TB and HIV/AIDS Centre (STAC). The Journal's main aim is to continuing education of personnel and the dissemination of the most up-to-date information in the field of tuberculosis, lung diseases and HIV/AIDS. It is devoted to dissemination of knowledge concerning various aspects of tuberculosis, lung diseases and HIV/AIDS. All articles and health research relevant to the practice of this Journal are published. This Journal is a forum for the publication of articles concerning the social, economic, public health, epidemiology, diagnostics, genetics etc. in the area of tuberculosis, lung diseases and HIV/AIDS. The scientific manuscripts presenting the results of public health importance are encouraged. The novel case reports which adds to the existing knowledge and consistent with the scope of Journal will be considered for publication. The Journal accepts review/mini-review, case report, short communications, and letters to editors within the scope.

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Editorial

In this issue qualitative study which was conducted by SAARC TB and HIV/AIDS Centre (STAC) on **'BARRIERS TO DIRECTLY OBSERVED TREATMENT FOR MDR-TB PATIENTS IN NEPAL**- revealed many important findings.

As revealed in the study that some patients need to sell their properties to take medicine and some have to borrow loans, which are frequently offered at exorbitant rates. Also in that study all participants of MDR-TB patients acknowledged difficulties, regarding transport costs to obtain treatment, although men were more concerned with the economic burden of treatment. Similarly, studies from Vietnam and Pakistan cite structural barriers such as financial constraints (direct and indirect cost) e.g. loss of income, cost of travel and lodging as the causes of non –adherence to TB treatment.

TB causes catastrophic economic effects on both the individual suffering the disease and their households. National economies are also affected with estimates suggesting significant impact that will hamper national development.

Majority of people in SAARC member states are under the poverty line and the urban poor are increasing. Most of the TB patients come from the lower socio-economic group. People cannot afford the travel cost and other expenses from their earnings. It has been observed consistently that poverty is associated with much higher risk of TB infection, prevalence of TB disease, and of adverse outcomes of treatment including mortality. Tuberculosis also worsens poverty, as the poor spend much higher proportion of their income on the direct and indirect costs associated with TB care.

Even though National TB Programmes provide free drugs and baseline diagnostic tests to the patients, many patients experience other associated health care costs, e.g. payment for ancillary drugs and extra diagnostic tests, as well as considerable non-medical costs, including expenditures for day to day transport and accommodation. Furthermore, patients and other household members who care for them may suffer reduced earnings due to loss of employment opportunities, and may experience the intangible costs related to social stigma associated with their illness.

Incentives are a valuable way to help a person to overcome the barriers to complete a long duration treatment like MDR-TB. Many studies conducted in other SAARC countries shows that modest incentives in a structured programme can produce an effective public health intervention in a typically poor and urban population. There are also other projects where cash and non-cash incentives have improved adherence.

Hence, member states of SAARC should identify these issues seriously and should provide solutions to these poor patients. Some member countries already have address those by providing nutritional support to TB patients and families, financial incentives to patients and providers, health system strengthening, and linking patients with existing social and financial support systems of the government.

Addressing poverty, requires inter departmental/ ministerial coordinated activities and the National TB Programme will proactively facilitate this coordination. National Programme will make active efforts to establish linkage with such services. These interventions at population level are expected to have additional impact on accelerating decline in incidence and mortality of TB.

Prof. Dr. R. P. Bichha
Director, STAC

ASSOCIATION OF SOCIO-DEMOGRAPHIC PROFILE WITH PREVALENCE OF MULTI DRUG RESISTANT TUBERCULOSIS AMONG RETREATED PULMONARY TUBERCULOSIS PATIENTS IN NORTH INDIA

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ABSTRACT

Methods: An observational cross sectional study, which includes 116 patients of sputum smear positive pulmonary TB of age 18 or above. Further, detailed history taking regarding different demographic profile was done. Also, they were subjected to CB-NAAT and rifampicin resistant cases were considered as MDR-TB.

Results: Proportion of MDR-TB was 31.89% among retreatment TB cases. 56.75 % (n=21) of MDR-TB cases were between the age group of 21-40 years. Proportion of MDR-TB was higher among males (75.67%), married (59.45%) and rural dwellers 59.45%. Proportion was 61.76% among patients with BMI <16; 31.57% with BMI 16-16.99, 28.57% with BMI 17-18.49 and 5.7% with BMI 18.50-24.99. MDR-TB proportion was less 29.72% (n=11) in patients with history of TB contact in family. Pulmonary TB including MDR-TB was more common among illiterates (37.83% among MDR).

Conclusion: Proportion of MDR-TB was high among retreatment cases in north India. Among them low BMI and education status are modifiable factor and this study signifies that MDR-TB burden can be reduced by improving health and education status of patient.

Key words: Pulmonary TB, Retreatment case, Socio-demographic profile, MDR-TB

INTRODUCTION

Tuberculosis (TB) is leading cause of death due to a single infectious agent. Worldwide 4.1% of new TB cases and 19% of retreatment TB cases have multi-drug resistant TB (MDR-TB).[1] Tuberculosis (TB) is as old as mankind.[2-4] Globally TB is leading cause of mortality due to a single infectious agent.[5] India has the highest TB burden in the world and accounts 25% of global burden.[1]

In 2016, 6.3 million new cases of TB were reported worldwide and an estimated 1.3 million TB deaths in HIV negative people.[1] An important cause of TB epidemic is emergence of multi drug resistant (MDR) strains of Mycobacterium tuberculosis. Globally, an estimated 4.1% of new TB cases and 19% of previously treated cases have MDR-TB.[1] In 2016, an estimated 600000 people were eligible for MDR-TB treatment and 47% of these cases were in India, China and Russian Federation.[1] Despite the availability of good quality treatment that can cure most cases of TB, levels of MDR-TB remain worryingly high in India. MDR-TB is consider as a man-made phenomenon and occur as a result of inappropriate treatment of drug sensitive TB.[6] Prevalence of MDR-TB mirrors the functional state and efficacy of TB control program in the country. The present study is aimed to find out association of various socio-demographic profiles with prevalence of MDR-TB to reveal modifiable risk factor so that we can modify them to prevent development of MDR.

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MATERIALS AND METHODS

Study Design- An observational, cross sectional study.

Study Period- From August, 2016 to August, 2017.

Study Settings- All patients aged >18 years of either sex with pulmonary TB were enrolled in this study as per inclusion and exclusion criteria.

Inclusion Criteria:

1. Patients with pulmonary TB confirmed by sputum smear examination
2. Patient who are about to start DOTS retreatment regimen

Exclusion Criteria:

1. Patients not giving consent for participation in the study
2. Pregnant women
3. Patients with co-morbid illness like Diabetes, AIDS, Kidney disease, Liver disease and Psychiatric illness

After obtaining informed consent, patients qualifying inclusion criteria will be assessed as follows:-

- Recording of demographic data
- Investigations: Routine haematological, Bacteriological examination (sputum smear examination for M. TB and CB-NAAT(Cartridge based nucleic acid amplification test). Standard chest X-ray postero-anterior view

Patients of retreatment pulmonary TB cases were selected from Department of pulmonary medicine, M.L.N. Medical College, Allahabad. The sputum was collected as the clinical specimen for further examination and investigation. Sputum sample consists of fresh discharged material from the bronchial tree, with minimum amounts of oral or nasopharyngeal material. Specimens were transported to the laboratory as soon as possible after collection. The sputum samples were sent for sputum-smear microscopy for tubercular bacilli at the time of enrolment, further they were subjected to CB-NAAT examination.

Statistical analysis- All patients detail was recorded and analyzed in Microsoft excel sheet.

Ethical approval- The study was started after getting Ethical Clearance Certificate from Institutional Ethics Committee. As per protocol informed consent was taken from the patient/ guardian.

RESULTS

Table 1. Proportion of MDR-TB among patients at start of retreatment ATT regime

	MDR-TB	Non-MDR TB
Patients at start of retreatment regimen (n=116)	37(31.89%)	79(68.11%)

A total 116 sputum positive pulmonary TB patients were included in the study. This study shows that 31.89% (37 out of 116) patients of retreatment pulmonary TB was found to be MDR-TB.

Table 2: Proportion of MDR-TB in different gender among patients at start of retreatment regimen

	MDR-TB	Non-MDR TB
Male	28(75.67%)	55(69.62%)
Female	9(24.32%)	24(30.37%)

The proportion of MDR-TB in retreatment category has been found to be higher in males 75.67% (n=28) than females 24.32% (n=9). Mean age of MDR-TB patients was 34.71±14.72 years in males and 34.22 ± 21.18 years in females. (p value=0.5).

Table 3: Proportion of MDR-TB in different age group among patients at start of retreatment regimen

Age group (in years)	MDR-TB	Non-MDR TB
11-20 (n=13)	6(16.21%)	7(8.86%)
21-30 (n=33)	13(35.13%)	20(25.31%)
31-40 (n=26)	8(21.62%)	18(22.78%)
41-50 (n=20)	4(10.81%)	16(20.25%)
51-60 (n=16)	3(8.10%)	13(16.45%)
>60 (n=8)	3(8.10%)	5(6.32%)

(χ2 yate's corrected=2.57, p value=0.73)

The mean age in patients with MDR-TB was 34.37±15.09 and in Non-MDR TB was 39.29± 15.09 years. About 50.8% (n=59) of retreatment TB patients and 56.75% (n=21) of MDR-TB cases were in the age group of 21 to 40 years, which is known to be the most economically productive period of life. (p value=0.73).

Table 4: Proportion of MDR-TB in population with different BMI groups (according To WHO) among patients at start of retreatment regimen

BMI group (kg/m^2) (acc. To WHO)	<16 (n=34)	16-16.99 (n=19)	17-18.49 (n=28)	18.5-24.99 (n=35)
MDR-TB	21 (61.76%)	6 (31.57%)	8 (28.57%)	2 (5.71%)
Non-MDR TB	13 (38.23%)	13 (68.42%)	20 (71.42)	33 (94.28%)

(**$\chi 2=25.15$, p value=0.000014**)

Among retreatment cases proportion of MDR-TB was 61.76% among patients with BMI <16; 31.57% among patients with BMI 16-16.99; 28.57% among patients with BMI 17-18.49 and 5.7% among patients with BMI 18.50-24.99. As BMI is decreasing below 24.99, proportion of MDR-TB was increasing. (p value=0.000014).

Table 5: Proportion of MDR-TB in population with different Marital Status (among patients at start of retreatment regimen)

	Married	Unmarried
MDR-TB (37)	22(59.45%)	15(40.54%)
Non-MDR TB (79)	64(81.01%)	15(18.98%)

(**$\chi 2=6.10$, p value=0.013**)

Among retreatment TB cases, majority were married 74.13% (n=86), only 25.87% (n=30) were unmarried. Proportion of MDR-TB is higher among married (59.45%) than unmarried (40.54%). (p value=0.013).

Table 6: Distribution of MDR-TB cases in rural and urban dwellers

Residence	Rural	Urban
MDR-TB (37)	22(59.45%)	15(40.54%)
Non-MDR TB (79)	36(45.56%)	43(54.43%)

(**$\chi 2=1.94$, p value=0.16**)

In retreatment cases proportion of MDR-TB was more among rural patients 59.45% (n=22) than urban patients 40.54% (n=15). Among Non-MDR mostly patients belong to urban 54.43% (n=43) area than rural 40.54% (n=15). (p value=0.16).

Table 7: Relation of MDR-TB with Literacy among patients at start of retreatment

Education Status	MDR-TB (n=37)	Non-MDR TB(n=79)
Illiterate	14(37.83%)	36(45.56%)
Primary(1^{st} -5^{th})	11(29.72%)	13(16.45%)
Secondary(6^{th} -12^{th})	9(24.32%)	25(31.64%)
Graduate & above	3(8.10%)	5(6.3%)

(**$\chi 2=3.07$, p value=0.38**)

Out of 116 patients of retreatment cases, 43.10% (n=50) were illiterate. Among literates 20.68% (n=24) studied up to Primary, 29.31% (n=34) up to secondary and 6.8% (n=8) were graduate and above. Pulmonary TB including MDR-TB is more common in illiterates 37.83% (n=14). In this study as the education status is increasing, proportion of MDR-TB is decreasing. But there is no significant relation of literacy with proportion of MDR-TB. (p value=0.38).

Table 8: Family history of TB contact and proportion of MDR among retreatment TB patients

Family history of TB contact	MDR-TB (n=37)	Non-MDR TB (79)
Present (n=37)	11(29.72%)	26(32.91%)
Absent (n=79)	26(70.27%)	53(67.08%)

(**$\chi 2=0.11$, p value=0.7**)

Among retreatment cases, proportion of MDR-TB was less 29.72% (n=11) in patients with history of TB contact in the family than the patients with no history of TB contact 70.27% (n=26). So the family history does not appear to be associated with MDR-TB. (p value=0.7).

Among retreatment cases, proportion of MDR-TB was less 29.72% (n=11) in patients with history of TB contact in the family than the patients with no history of TB contact 70.27% (n=26). So the family history does not appear to be associated with MDR-TB. (p value=0.7).

DISCUSSION

This study shows that about one third of retreatment cases having MDR-TB, while Global TB report reported 20% of retreatment cases and 3.5% of new cases having MDR-TB.

This study shows that proportion of MDR-TB is higher among males (75.67%). This finding was in commensuration with Sharma et al[7],Qiao Liu et al[8],in which they reported higher prevalence among males, while N Lomtadzeet al[9] et al reported higher prevalence in females.

According to study 56.7% of total MDR-TB patients were in the age group 21-40 years. This finding was in commensuration with Kai man Kam et al[10], Omar Salad Elmi et al[11], Gneyaa Bahtt et al[12] in which they reported higher proportion of MDR-TB in age group of 15-45 years.

This study shows that there is an inverse relationship between BMI (below 24.99) and occurrence of MDR-TB among retreatment cases. This finding was supported by Kumar A et al[13], Poulomi Mukherjee et al[14], Xin-Xu Li et al[15] reported that most MDR-TB patients were malnourished and low BMI is one of the risk factor significantly associated with MDR-TB.

In this study among MDR-TB patients was 59.45% were married. This finding was in commensuration with Girma Mulisa et al[16], Meghan D. Morris et al[17], Feleke Mekonnen et al[18] reported that in their study 75%, 75%, 50% were married respectively.

Out of total MDR-TB patients among retreatment category 59.45% resides in rural area. Almeida D et al[19], HE Jenkins et al[20] however reported higher percentage of MDR-TB patients were found in urban area.

In this study proportion of MDR-TB was more among illiterates (37.83%), 29.72% were educated up to 5th standard. This finding was in commensuration with Wei-Bin Li et al[21], Mahfuza Rifat et al[22] reported that MDR-TB patients have education status <primary school.

In this study only 29.72 % of MDR-TB patients have history of TB contact. Elizabeth Clara Barroso et al[23], Wahab F et al[24], TN Dhole et al[25] reported that family history of TB contact was not significantly associated with MDR-TB.

CONCLUSION

The present study shows that proportion of MDR-TB was high among-retreatment cases of pulmonary TB, males, married, low education status, rural dwellers. MDR-TB was more common among severe malnourished patients. Low BMI and education status are modifiable factor and this study signifies that MDR-TB burden can be reduced by improving health and education status of patient. So the nature of TB bacilli becoming drug resistance by could be prevented by taking care of simple preventive measures and certain attributes.

CONFLICT OF INTEREST

None

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BARRIERS TO DIRECTLY OBSERVED TREATMENT FOR MULTI DRUG RESISTANT TUBERCULOSIS PATIENTS IN NEPAL - QUALITATIVE STUDY

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ABSTRACT

Introduction: To prevent the multi drug resistant tuberculosis (MDR-TB) is important to adhere long duration of drug regimen. There are many factors or barriers that are likely to affect adherence to the long treatment regimen.

Objectives: To find out the barriers for adherence to MDR –TB treatment.

Methods: The study was conducted as an institutional based qualitative study, using a convenient sampling technique. Data was collected from 50 current MDR-TB patients by trained field health workers using semi structured interviewer administered questionnaire in all regions in Nepal. Twenty five focus group discussions (FGD) were also conducted with MDR-TB patients, cured MDR-TB patients, DOTS Committee Members, health workers and close relatives of MDR-TB patients to supplement the findings.

Results: Out of 50 respondents 19 were females and 31 were males. Their age varied from 22 years to 61 years. Majority of patients had a previous history of irregular TB treatment. Forty out of fifty patients (80%) were living in either rented houses or hostels (in Mid Western Region). Knowledge about TB and MDR-TB was satisfactory in majority of participants in both studies. Majority of participants were satisfied with facilities and services provided by MDR-TB clinics. There is a very little stigma associated with MDR-TB in Nepal. FGD revealed the onset of MDR-TB was attributed to causes such as smoking, alcohol abuse, poor nutrition, and contact with TB patients. Lack of money to go to health facility daily for treatment was reported as major barriers to adhere to MDR-TB treatment.

Conclusion: Financial constraints were the major barrier for these patients. To sustain proper MDR-TB programme, Government of Nepal and other organization should provide social support to these patients.

Key words: MDR-TB, Barriers, Nepal

INTRODUCTION

Anti –TB drug resistance largely arises when patients with the disease are prescribed sub-optimal regimen not conforming to international recommendations in terms of the combination, dosage and duration for which the drugs are prescribed, or when patients for a number of reasons do not take their medicines as prescribed. Drug resistance that arises through genetic mutation contributes to a much lesser extent.

Multidrug –Resistant TB or MDR-TB refers to *Mycobacterium tuberculosis* isolates that are resistant to at least both isoniazid and rifampacin, the two most effective first line anti TB drugs. MDR-TB can only be treated with second –line drug regimen comprising reserve or second-line drugs, which are much more expensive, have to be used for a longer duration, entail significantly higher side – effects and result in much poorer outcomes as compared to first –line regimen.

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Along with HIV/AIDS, MDR TB is the most important threat to TB control. Countries with a high MDR –TB prevalence generally have a history of poor TB control. The major barrier to MDR-TB treatment is the high cost of second –line drugs which are at least 300 times more expensive than first- line drugs based on Green Light Committee (GLC) prices and between 1000 – 3000 times more expensive when market prices are used**.** In Nepal these second line drugs are given to the patients free of charge. Additional barriers include extensive laboratory requirements to conduct culture and drug susceptibility testing (DST), severe adverse events associated with second–line drugs and fear of non response or development of resistance to second –line drugs. In addition, private practitioners and public providers not linked to the NTP diagnose and treat MDR-TB patients in many countries including China and India which account for 35% of the global TB case- load, and treatment practices often fail to meet acceptable standards. The misuse of second- line drugs could lead to the creation of TB strains resistant to all known anti-TB drugs.

MDR-TB problem in Nepal:

In Nepal MDR-TB management services are available from all five Regions of the country.

In Nepal previous work has shown that MDR –TB is a public health problem. Since 1996, surveillance of anti- tuberculosis drug resistance has been conducted with the co-operation of the World Health Organization, the National TB centre and GENETUP. The proportion of MDR-TB among new cases in Nepal, has fluctuated from a little over 1% to 3.6% in the surveys that have been conducted since 1996 making the trend difficult to interpret. In 2015 WHO estimates that there were 1500 (CI: 950-2100) MDR-TB cases in Nepal. The proportion of new cases with multidrug-resistant TB (MDR-TB) was 2.2% among new cases and 15.4% among retreatment cases based on survey carried out in 2011/12, and new surveillance on MDR-TB has not been done in recent years. In 2014/15, total of 379 MDR-TB and 71 XDR TB were enrolled for treatment. Treatment Success Rate (TSR) of MDR patients was 71%, however the TSR of XDR is low at 33%. Total of 22 deaths among MDR Cases and 3 deaths in XDR were reported in 2014/15. The drug resistant pattern in Nepal showed much higher levels of resistance to fluoroquinolones (36%). Among the MDR patients, 8% further develop XDR.[(1)]

Constraints and challenges in MDR-TB case management in Nepal:

Lack of socio-economic support for patients and infection are key challenges for optimal performance of MDR-TB management in Nepal. Lack of focal staff at central level is another key constraint. Also MDR –TB management programme is managed through existing staff within PHC who received no extra remuneration or incentives for the additional responsibility [(1)].

Magnitude of adherence and non-adherence:

The gap between the medication prescribed by the health care provider and that taken by the patient is wide. Based on a number of rigorous reviews from the studies done in developed countries, it has been found that the adherence among patient suffering from chronic diseases only 50% on an average. The magnitude and impact of poor adherence in developing countries is assumed to be even higher. Hence, the impact of poor adherence grows as the burden of chronic diseases grows worldwide. Poor adherence is the primary reason for suboptimal clinical benefit[(2)]. It causes medical and psychosocial complications of diseases reduce patients' quality of life, and wastes health care resources. Taken together, these direct consequences impair the ability of health care systems around the world to achieve population health goals. Adherence problems are observed in all situations where the self- administration of treatment is required, regardless of type of diseases, disease severity, and accessibility to health resources. Medication adherence can be surprisingly low even among inpatients when they are on self- administration programmes [(3)].

With regard to treatment non-adherence, several qualitative studies reported different factors associated to it; they are related to poor socio-economic position of patients [(4)]., inadequate and poor health care delivery system [(5)(6)], treatment related problems like dissatisfaction with the treatment due to medication side effects[(7)] and patients related factors like lack of understanding of adherence[(8)], equating well being with cure[(9)],etc.

These all above mentioned studies amply indicate that the perceptions, beliefs, experiences and knowledge of individual about chronic diseases like TB have important bearing in interpretation of symptoms, give those meanings, decide with whom

to consult, and how long remain in the treatment. We are not aware of any study from SAARC region dealing with all these aspects related to MDR-TB and its treatment. Hence the aim of this study was to achieve the following objectives.

Objectives:

General Objectives:

To find out factors, conditions and barriers relating to adherence to MDR-TB treatment in Nepal and to find out knowledge, perceptions, attitudes, practices, beliefs, and experiences of service users and service providers about MDR TB and its management**.**

Specific Objectives:

1. To find out factors affecting patients' adherence to MDR –TB
2. To find out service users and service providers knowledge, perceptions, attitudes, practices, and beliefs, about MDR TB and its management.

METHODOLOGY

Study settings:

Selected institutions in Nepal where MDR-TB treatment were carried out was the focal point for the study.

Study design:

This study used qualitative research methods to address the research objectives. Qualitative research is defined as any kind of research that produces findings not arrived at by means of statistical procedure or other means of quantification. The application of qualitative methods allows the researcher to study selected issues in depth and detail [(10)]. Following qualitative methods were use for this study.

1. Focus Group Discussion
2. Semi structured interviews

Sample size and sampling:

Qualitative studies generally focus in depth on a relatively small number of cases selected purposefully. There are no hard and fast rules for sample size in qualitative research. As Hudelson points out (1994)" The sample size will depend on the purpose of the research., the specific research questions to be addressed, what will be useful, what will have credibility, and what can be done with available time and resources[(11)]."

In qualitative sampling, the selection of respondents continues until the point of redundancy (saturation). When new interviews no longer yield new information and all potential sources of variation have been adequately explored, sampling may stop [(12)]. Considering all these factors, for semi structured interviews, fifty (50) MDR TB patients were enrolled from the five MDR-TB treatment centres in Nepal.

(1) Focus group discussions (FGD)s: Series of five FGDs were carried out in each region of Nepal with the following groups.

1. MDR patients
2. Close relatives /Friends of MDR patients
3. Health workers who are working in MDR-TB treatment clinics
4. Cured TB patients
5. Members of DOTS committee.

On an average seven to 10 individuals participated in the one to one and half hour sessions .A trained health worker conducted these FGDs using a set questionnaire. The FGD with the participants were held during the day in an open space, where the participants and moderator of the FGD sat together in a circle. During the FGD with MDR-TB patients, others were kept out of the vicinity. Staff of the National TB programme was asked not to be present so that participants would feel free to voice their honest perception about barriers faced by MDR-TB patients.

Semi structured interviews:

Semi- structured qualitative interviews were conducted with 50 MDR-TB patients, who were taking the second line Anti TB drugs. Interviews were conducted, with the help of an interview guide in Nepali language as it is the vernacular language of the informants**.** During interview every effort was taken to maintain privacy of the patient. Children (age below 15 years) were excluded from the study

Ethical Issues:

Permission from relevant authorities Director NTC, Regional Directors, District TB and Leprosy Control Officers etc) was taken before commencement of the study.

Verbal informed consent was obtained from patients before starting interviews. Confidentiality of the status of patients was maintained at all times.

Analysis of data:

Focus Group Discussion: Analysis of data was done using following steps

(a) Data immersion – reading and rereading each set of notes or transcripts until familiar with the content.

(b) Data coding

(c) Data display

(d) Data reduction

(e) Interpretation and conclusion drawing

Semi structured questionnaire was analysed using SPSS software.

Results:

Table 1: Distribution of MDR-TB cases by sex

Male (%)	Female (%)	Total
31 (62%)	19(38%)	50(100%)

Table 2: Distribution of MDR-TB cases by Age

Age group (years)	No	%
15-24	03	06%
25-34	21	42%
35-44	15	30%
45-54	07	14%
55-64	04	08%
Total	50	100%

Minimum age = 22 years Maximum age = 61 years

Table 3: Distribution of MDR-TB cases by marital status

Marital status	No	%
Married	24	48%
Unmarried	21	44%
Widower	02	04%
Divorce	01	02%
Separated	01	02%
Total	50	100%

Table 4: Distribution of MDR-TB cases by literacy status

Literate (%)	Illiterate (%)	Total
38 (76%)	12(24%)	50(100%)

Table 4(a): Distribution of literate MDR-TB cases by educational status (n=38)

Educational status	No	%
Primary	25	65.8%
Secondary	11	28.9%
Higher	02	5.3%
Total	38	100.0%

Table 5: Distribution of MDR-TB cases by current place of living

Place of living	No	%
Own house	07	14%
Rented house/ leased	32	64%
Hostel	08	16%
Others	03	06%
Total	50	100%

In the literate group educational status was divided into 3 groups as primary, secondary and higher education.

Table 6: Distribution of MDR-TB cases by current employment status

Employed (%)	Unemployed (%)	Total
06(12%)	44 (88%)	50(100%)

All current employed patients (6) worked as farmers.

Table 7: Distribution of MDR-TB cases by monthly family income

Monthly family income(NRs)	**No**	**%**
Less than 3000	36	72%
3001 - 5000	10	20%
More than 5001	04	08%
Total	50	100%

Knowledge of TB and MDR-TB

There were five questions concerning about knowledge in terms of causes of tuberculosis, duration of treatment for both TB and MDR-TB, impact of irregular or defaulter treatment, curability and spread from one patients to another.

Table 8: Distribution of MDR-TB cases by Knowledge of TB and MDR-TB			
Variables to know about Knowledge	**Know (%)**	**Don't know (%)**	**Total**
Causes of TB	**20(40%)**	**30(60%)**	**50**
Treatment duration	**45(90%)**	**05(10%)**	**50**
Impact of irregular treatment	**41(82%)**	**09(18%)**	**50**
Curability	**50(100%)**	**00(0%)**	**50**
Mode of spread	**22(44%)**	**28(56%0**	**50**

Quality of services:

Quality of services was assessed in terms of waiting time per visit, information given to the patients about TB and MDR-TB and its treatment and side effects, relationship between patients and health care providers to get high compliance of patients with treatment and facilities available at clinics.

Waiting time:

Table 9: Distribution of MDR-TB patients by waiting time in the clinic		
Waiting time	**No**	**%**
One to 2 hours	**46**	**92%**
More than 2 hours	**04**	**08%**
Total	**50**	**100%**

Table 10: Given information by health workers about disease, treatment and side effects to the patients		
Given information by health workers	**No**	**%**
Information given was sufficient	**47**	**94%**
Information given was not sufficient	**03**	**6%**
No information was given	**00**	**00**
Total	**50**	**100%**

Table 11: Relationship between patients and health service providers		
Relationship between patients and health service providers:	**No**	**%**
Good relationship	**48**	**96%**
Poor relationship	**02**	**04%**
Total	**50**	**100%**

Table 12 :Service provided and Facilities available at clinic					
Facilities available at the clinic	**CR**	**ER**	**WR**	**MWR**	**FWR**
Sitting facilities	Yes	Yes	Yes	Yes	Yes
Toilet facilities	Yes	Yes	Yes	Yes	Yes
Drinking water	**No**	Yes	Yes	Yes	Yes
Maintained confidentiality	Yes	Yes	Yes	Yes	Yes
Availability of drugs	Yes	Yes	Yes	Yes	Yes
Clinic arrangements	Good	Good	Good	Good	Good
Courtesy of health worker	Good	Good	Good	Good	Good
Cleanliness of the clinic	**Not good**	Good	**Not good**	Good	Good
Competence of the Health Worker	Good	Good	**Not good**	Good	Good

CR-Central Region
ER-Eastern Region
ER- Western Region
MWR-Mid Western Region
FWR-Far Western Region

Accessibility of services:

Accessibility of service was assessed by using 4 questions.

(a) Travelling time
(b) Travelling and other costs
(c) Mode of transportation
(d) Availability of services during public holidays and "Bandha" days

Table 13: Distribution of MDR-TB patients by travelling time to reach the clinic		
Travelling time	No	%
Less than one hour	43	86%
More than one hour	07	14%
Total	50	100%

Table 14: Distribution of MDR-TB patients by travelling and other cost per day to attend to the centre		
Travelling cost/per day	No	%
Less than 100 NRs	37	74%
More than 100 NRs	13	26%
Total	50	100%

Table 15: Distribution of MDR-TB patients by mode of transport to attend the centre		
Mode of transport	**No**	**%**
By foot	24	48%
Bus	11	22%
Rickshow	07	14%
Tampo	04	8%
Bicycle	04	8%
Total	50	100%

Majority (92%) stated clinic was open during public holidays and Bandha days. Four patients stated clinic was closed on Saturdays but open on Bandha days.

Drug side effects experienced by patients (n=50)

Table 16:Distribution of MDR-TB patients by side effects of drugs		
Side effects of drugs	**No**	**%**
Gastritis	3/50	6%
Loss of appetite	6/50	12%
Itching	7/50	14%
Jaundice	1/50	2%
Joint pain	10/50	20%
Hearing disturbances	1/50	2%

Table 17: Barriers to attend the Clinic daily					
Barriers	**CR**	**ER**	**WR**	**MWR**	**FWR**
Environmental obstacles	2/10	3/10	-	-	-
Financial problems	-	3/10	-	1/10	5/10
Family problems	1/10	-	-	2/10	-
Other health related problems	1/10	4/10	-	1/10	-

Out of 10 patients in the Far Western region, five (50%) stated that they were not attend the clinic regularly due to the financial problem. This percentage in the Eastern and Mid Western region was 30% and 10% respectively. Two patients in the Central and 3 patients in the Eastern region had not attended clinic regularly due environmental obstacles. Four patients in the Eastern and one each in the Central and Mid Western region did not attend clinic regularly due to other health related problems.

Major Finding of FGD:

The participants (MDR-TB patients and their relatives) demonstrated a basic knowledge of the symptoms of TB, causes and spread of TB. Whereas Health workers, DOTS Committee members and cured TB patients had more in-depth knowledge. Most said they knew it was an infectious disease that caused coughing up blood sometimes along with weight loss and fever. Majority of the health workers and DOTS committee members in every FGD stated that do not have any fear to treat and care for TB patients. They know TB is a treatable disease.

Many participants agreed that men and economically poor people are more prone to be infected by TB.. The reasons for this might be that men moves more outside and habituated to smoke more than females. Most of the participants including health workers group mentioned that there is a strong relation between TB/ MDR-TB and poor nutrition. They further stated poor people cannot afford enough nutrition; hence they are more vulnerable to develop TB and MDR-TB.

Many participants in the MDR-TB group stated that they trust the government health workers more as compared to the traditional healers and private sector medical personnel. In answer to the question -why patients would feel more comfortable going to the government doctor?, the answer came up as they feel comfortable with the services given by them and they are assured about the medicine quality which is given by government health workers. Many MDR-TB patients and cured TB patients stated health workers are co operative and helpful. They feel health workers are part of their family and understand their problems. They are easy to communicate with and most of all, they feel confident that they will keep their health problem a secret.

Most people received their information about TB from, Television, Radio and print media. Some participants in the relatives of MDR-TB group learned about the disease from the patents and from the treatment centre. About half of the MDR-TB patients group had seen posters visual aids demonstrating symptoms or some kind of information about TB especially in and around treatment centre.

Majority of the MDR-TB patients and relatives of the MDR-TB patient pointed out that MDR-TB is a ‘dangerous’ illness. This result in loss of weight and weakness associated with inability to work. In

consequence the patient leaves the job or reduces the routine activity.

Based on the FGDs with health workers, following areas were identified as those within which the health workers played key roles.

1. Patient focused activities such as evaluating patients prior to starting treatment, giving treatment, monitoring patients during treatment.
2. Health education activities
3. Coordination activities such as documenting important clinical and programmatic information, attend meetings workshops conducted by NTP etc.

The first response of HCWs in Nepal, when asked about how to address the problems of non adherence, they often stated that a tracing system needs to be initiated**.** The health workers spent most of the time in patient care activities and this was the most important part of their work. This attitude of health workers is encouraging as health workers are the primary persons responsible for educating patients and their family members about MDR-TB and its management. But majority of health workers stated that they need self protection equipments like face marks for protection against the disease.

During FGD, majority of participants agree that patients prefer to attend Central Region clinics, because they think clinics in the Central Region have more facilities than other regions. Majority of DOTS Committee members, cured TB patients suggested that health care workers should intensively supervise patients because they may discontinue treatment.

Cured TB patients, DOTS Committee members and health workers acknowledged that the use of unqualified private practitioners before government medical services was wide spread and this is the main reason for spread of MDR-TB in Nepal. Few MDR-TB patients stated that they had used traditional healers previously. Motivation for using traditional medicine varied but many patients claimed to have done so because of easy access, confidentiality, local availability and on the advice of others. All participants in the FGDs thought most MDR-TB patients could not afford the fares to attend treatment clinic, and felt women experience more problems due to lower income. Nearly half of the female MDR-TB patients interviewed stated that they would prefer a female health worker to deliver their treatment.

Barriers to DOT for MDR-TB patients in the Central Region:

(a) **Financial Barriers:**

Majority of participants in all FGDs agreed financial problems were most common barrier for patient's to adhere to long duration of treatment. Majority of MDR-TB patients were either staying in rented home or relative's home which is in close proximity to the clinic. Usually they spend 3000-5000 NRs per month for accommodation and other expenses. One patient said that, he has sold one of his parents land to get the money to pay the expenses. The general consensus was that a very small percentage of patients from study population had access to their own source of income. Many depend on the family members for their expenses. Some patients arranged this money from loans with high interest rates. Many patients, Health Workers/ DOTS Committee members/ relatives of patients indicated that financial aid would improve the system.

(b) Stigma and discrimination in the society:

The majority of MDR-TB patients said that in general they would inform their family members if they found they are having MDR-TB but they might be afraid to tell outsiders especially land lord. Some patients feared that they will not get accommodation if land lord know about their disease status. Hence, they have a tendency to hide the disease. In addition, most felt that, if unmarried female patients were exposed that they have the disease, they might experience difficulty to get married

Major barriers to get DOT in Western Region:

- Less cooperation from family, mostly for the female
- Long distance to treatment Centre from the house. Since there is no provision of lodging nearby the Centre.
- Financial constraints. Loss of employment and earning.

Barriers to DOT for MDR-TB patients in the Far Western Region

- Lack of financial support for the treatment. Though the medicine is free of cost, most of the participants revealed that the patients loose their job because of the disease.

- Lack of adequate family and social support.
- Side effects of the anti TB drugs (weakness, psychological stress, depression, irritation, anxiety, gastritis, headache, loss of memory power, joint pain, itching and numbness of feet).

Barriers to DOT for MDR-TB patients in the Eastern Region

- Long distance to travel
- Side effects of the drugs
- Financial problems
- Stigma and discrimination from the community

Barriers to DOT for MDR-TB patients in the Mid Region

- Long distance to travel
- Side effects of the drugs
- Financial problems
- Stigma and discrimination from the community

DISCUSSION

Although the aetiology of tuberculosis can be traced to Mycobacterium, it has frequently been observed that there is a predisposition for the disease among populations with low socio –economic status. Relevant observations can be made on a global scale, where the highest burden from the disease is observed in developing countries, as well as within countries, where the disease is largely confined to sub populations within various characteristics of socio-economic deprivation such as homelessness or absolute poverty [13][14][15]. Insufficient patients compliance to anti TB drugs has repeatedly been proposed as one of the main causes of the ineffectiveness of many tuberculosis control programs, and a variety of contributing socio-economic factors have been described [16][17][18]. Non adherence to treatment often results from inadequate knowledge or understanding of the disease and its treatment, psycho-social and economic factors, complexity of treatment, occurrence of side effect, and insufficient patient/ caregiver communication [19][20].

Socio-economic factors:

In the present study the youngest age of MDR-TB patients was 22 years and oldest was 61 years. Forty eight %of respondents belonged to the young age group (15-34 years) and 92 % economically productive age group (15- 54 years).This is in line with national level statistics in Nepal where largest number and proportion of MDR-TB belongs to 15-54 age group with almost half of the registered patients in age group 15-34 years. It has direct impact on the family, society and national economy. This study showed that the 88% of MDR-TB patients were unemployed and 92% respondents had average monthly income less than 5000 NRs (US $50). Concerning the sex, 62% of MDR-TB patients were male and 38% were females. This trend corresponds with ratio of male to female registered under DOTS programme in Nepal. Statistics show that globally when males and females are provided with equal access to health care services, there are more female TB patients, and in developing countries like Nepal that most of the TB patients are male. According to one study conducted by Smith in Nepal, women and daughters are the last to seek medical help in Nepal's male dominated society. Women do not open up with problems. Study also stated that, even in Kathmandu there are still many families who take sick sons for medical treatment, while keeping their sick daughters behind home. Usually women with their nurturing roles, give less priority to their own health problems. The first indicator of pulmonary TB, the cough is not seen as a problem by rural women in hilly Nepal. According to the Smith [21] " the women sit by the fire every day , as many women smoke, so they expect to cough and even they do go to the health clinic they may not report their cough as a symptom ". The study showed that the 44 out of 50 MDR-TB patients were currently unemployed. Most of the patients were in employment had stopped working due to their ill health. This shows the MDR-TB population is mainly the work force and thus the morbidity and mortality that TB population suffer will affect the economy, as well as the cost to the health services in the country.

In this study 44% were never married. Two percent of the respondents reported separation from their spouse. The divorce rate of study population was very low (2%).This may be due to socio-cultural practices prevailing in the SAARC region especially Nepal where divorce is unacceptable by the society. The majority of MDR-TB patients had received either no or primary education. Few 5.6% made it to higher education. Many studies conducted in the past revealed that low education level was significant predictor for non-adherence [22]. Hence these uneducated patients should be monitored carefully for treatment adherence by the health care workers.

Knowledge, perception belief of TB and MDR-TB:

Patients' perception of the implication of tuberculosis symptoms, their beliefs and attitudes are potential determinants of compliance [23].The sensation of being cured due to resolution of symptoms, even though treatment has not been completed, has been found to be a common reason for discontinuation of treatment [20].

The present study revealed that only 40% of MDR-TB knew causes of tuberculosis was some kind of organism, the rest mentioned causes of tuberculosis was smoking, alcohol, hard work, heredity and didn't know. Similarly poor knowledge was observed in the questions related to mode of spread. This result was found similar with the result of study done in Vietnam [24]. In the study from Kenya [25], Liefgoohe et al (1997) also found that informants believed their TB was caused by life style and eating habits, drinking "traditional alcohol" and smoking cigarettes as well as sharing facilities with TB patients, findings which are in conformity with the present study. This misunderstanding was thought to be linked to the long time history of tuberculosis in developing countries. It was evident that they still seem to keep traditional ideas on tuberculosis, which reflected in their awareness. In comparison to this, knowledge on duration of treatment, impact of irregular treatment, and curability were satisfactory among study population.

Perception is important factor to change behaviour and implement knowledge in daily life. Studies have shown that higher compliance to TB treatment is associated with patients who knew the TB as the cause of some kind of micro –organism compared to those who mentioned other causes like smoking and alcohol. It is true that who believe TB caused by alcohol, smoking and other cause; they used to focus on avoiding these factors to cure their disease rather than treatment. While preparation of health messages to public, these factors should be considered by the concern authorities.

However, the present study shows different findings in relation to belief in the curability of TB and MDR-TB. While many patients in the Kenyan study [25] thought that TB could be cured but not completely, there was general agreement about curability in the present study.

Studies have demonstrated that compliance with anti tuberculosis therapy is enhanced if patients receive an educational programme [26], which is most effective if provided as one to one counselling [27].Hence, adequate counselling and education of patients and close relatives on TB and the necessity for prolonged treatment may play an important role in ensuring completion of treatment.

Quality of Services:

Quality of services was assessed in terms of waiting time per visit, information given to the patients about TB and MDR-TB and its treatment and side effects, and relationship between patients and health service providers to get high compliance of patients with treatment

Poor behaviour by health care providers towards patients and poor quality of communication between them can affect patients' confidence, leading to treatment non adherence, especially when treatment is prolonged as with TB and MDR-TB. In the study from Madagascar [28] , it was reported that lack of opportunity to ask questions, insufficient explanation from health workers about disease and treatment, and no information about disease from a doctor were significantly associated with non adherence to TB treatment .In contrast majority of patients and their relatives in the present study were satisfied with the care given by health care workers. Even during holidays (official and unofficial "Bandh") health workers were available in these centres**.** This is encouraging because earlier studies conducted in Nepal revealed serious breakdowns in the health care worker –patient relationship (Smith 1998)

It is encouraging that more than 90% of MDR-TB patients stated that they have to wait less than 2 hours to get the services from the treatment centre. Study conducted by Russell mentioned that poor compliance was associated with increased waiting time in the clinic [29]. The study revealed that, the Centres in Eastern, Mid and Far Western regions in Nepal had most of the essential resources for the provision of care for MDR-TB patients. In contrast centres in Western and Central regions were lacking certain essential facilities such as drinking water, maintenance of cleanliness and competence of health workers especially giving intra muscular injections.

Infection control is a one of the strategy in preventing TB and MDR-TB. Cleanliness of the clinic is a basic requirement for any health care setting for this purpose. Without adequate and regular supervision, the proper hygienic standard could not be maintained.

During FGDs many health workers stated that they need protective equipment to prevent against TB and MDR-TB. Studies have shown that health care workers caring for TB patients are at risk for TB infection and disease. Risk is greatest in those HCW with the closest and longest duration of contact with the TB patient. The International Union Against Tuberculosis and Lung Disease and the WHO published a joint statement on the control of TB transmission in healthcare settings. It emphasized the following:

- Early identification of infectious TB patients
- Prompt and effective treatment of such patients
- Isolation of infectious TB patients
- Environmental control with proper ventilation
- Protection of healthcare workers and others

Transmission of TB to HCWs in a public hospital in Brazil was approximately four times greater than the rate in the community [30]. In countries like Estonia [31], Turkey [32] Malawi [33],[34] India [35] and Thailand [36] the TB incidences among HCWs were also high, and the quoted risks were 1.5 to 11 fold that in the general population or other comparator groups. Nonexistent or ineffective TB infection control facilitates TB transmission in health care settings. Hence special emphasis should be made by the programme managers in improving these aspects of care in Nepal. This should be accompanied by provision of infrastructure facilities in the clinics such as personal protection equipments, adequate space and ventilation, facilities for hand washing etc.

FINANCIAL BARRIER

Of the MDR-TB group, almost all indicated that they face problems to attend the clinic in a regular basis. Out of 10 patients in the Far Western region, five (50%) stated that they were not attending to the clinic regularly due to financial problems. This percentage in the Eastern and Mid Western region was 30% and 10% respectively. This factor is an important public health risk because adherence to daily treatment is the key to successful outcome of MDR-TB .Also untreated sputum positive person can infect 10 to 14 other in a year. Thus, there are important economic and non-economic barriers to treatment adherence which merit attention for both patient and societal benefit. Even though the second line drugs to the patient are given free of charge, the data demonstrate that non –medical costs pose more sizable economic barriers. Thirteen out of 50 MDR-TB patients in the present study stated that their travelling and other costs to attend the clinic were more than 100 NPR (1US$) per visit. In the context of treating patients with drug sensitive tuberculosis, transportation costs have also been identified in other studies as a significant patient cost [37].

As revealed in Focus Group Discussions it is a disturbing fact that some patients have to sell some of their properties to buy medicine and some have to take out loans, which are frequently offered at exorbitant rates. In Nepal many are under the poverty line. The urban poor are increasing day by day. Most of the TB patients come from the poor society. People cannot afford the travel cost and other expenses from their earnings. In the present study all participants of MDR-TB patients (except mid western region) acknowledged problems, regarding transport costs to obtain treatment, although men were more concerned with the economic burden of treatment. Similarly, studies from Vietnam [4][5][8] and Pakistan [7]) cite structural barriers such as financial constraints (direct and indirect cost) like loss of income, cost of travel and lodging as the causes of non –adherence to TB treatment.

Incentives are a valuable way to help a person overcome barrier to complete a course of treatment of long duration. In FGD, many patients, Health Workers/ DOTS Committee members/ relatives of patients indicated that financial aid would improve the system. .Many studies conducted in other countries show that modest incentives in a structured programme can produce an effective public health intervention in a typically poor, urban population. There are also other projects where cash and non-cash incentives have improved adherence [38].

Majority of participants in the FGDs thought most MDR-TB patients could not afford the fares to attend treatment clinic, and felt women experience more problems due to lower income. Similar findings were reported in study done by Eastwood and Hill in Gambia. Although many studies have addressed the health provider and drug related costs of tuberculosis, there have been few analyses of the patient-related costs .In rural Uganda and Thailand , respectively , Saunderson and Kamolratanakul et al [39][40]demonstrated that patients bear more than 60% of the total burden of tuberculosis costs. The provision of free drug alone is therefore not sufficient. Possible solution to this problem may be to provide accommodation and travel aid for the very poor.

Focus group discussions revealed many MDR-TB patients preferred to attend Central region clinics, because they have more confidence in the Kathmandu health services. Similar findings were reported in the study conducted by Smith 1998 in Nepal. This belief is another factor that leads patients to spend more money for accommodation and other expenses. Even though Nepal government has provided services in all five regions, this message has not reached the public. Like drug sensitive tuberculosis, given the availability of treatment facilities at district clinic, accommodation cost and travel distance may be reduced. These changes are expected to benefit the patient through reduced economic barriers for patients and care givers, including transportation expenditures, accommodation costs, and lost income. A South African study of treatment strategies has also demonstrated the significant economic benefit to patients of using nearby clinics for drug distribution[37].These benefits to patients must, however, be weighed against other risks and benefits of decentralization before a decision can be made regarding the ultimate impact on tuberculosis control.

Cured TB patients and health workers acknowledged that the use of unqualified private practitioners before government medical services was wide spread and this is the main reasons for MDR-TB in Nepal. Few MDR-TB patients stated that they had used traditional healers previously. Motivation for using traditional medicine varied but many patients claimed to have done so because of easy access, confidentiality, local availability and on the advice of others. Quality of care has been found to be an important determinant in patients choice of health facility and can lead to by passing free public health facilities in spite of free paying services in some settings.[41]It is encouraging that, majority of MDR-TB patients in the present study believe that government treatment for MDR-TB is much better than private sector treatment including traditional healers. The importance of staff, community, motivation and a feeling of ownership of the programme in the success of the DOTS strategy in Nepal has recently been highlighted [42].

During FGDs majority of DOTS Committee members, cured TB patients suggested that health care workers should intensively supervise patients because they may be discontinuing treatment. The first response of HCW s in Nepal, when asked about how to address the problems of non adherence, they often stated that a tracing system needs to be initiated. This is important because non adherence of MDR-TB patients can spread their disease to normal population.

SOCIAL STIGMA AND DICREIMINATION

Findings of FGDs revealed very little stigma and discrimination associated with TB and MDR-TB patients among health workers, family members and friends of the patients. But few TB patients mentioned cases of landlords evicting these patients and several patients were hiding their diagnosis from their landlords and outsiders. The stigma associated with TB might well be another reason why many Nepalese travel so extensively when they seek medical care. Many important points that came up in the FGD concerned treatment seeking behaviours of women. Female patients were more bothered than male patients about the lack of privacy in the clinic. Nearly half of the female MDR-TB patients interviewed stated that they would prefer a female health worker to deliver their treatment.

LIMITATION

Care should be taken before generalizing these findings, due to the small number of cases interviewed in the study and qualitative nature of the study. Non randomized sampling method may also have introduced hidden biases even though it is common in all qualitative studies. Finally, the reasons stated for barriers by the study participants have been taken as a statement of fact. This, however, cannot be validated and must be accepted as a limitation of the study finding. Despite the above considerations, the present study highlights areas for concern that require action to further improvement in MDR-TB treatment in Nepal.

CONFLICT OF INTEREST

None

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A STUDY OF HIV/AIDS CO-INFECTIONS AND COPING STRATEGIES OF KEY POPULATION OF NEPAL

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ABSTRACT

Introduction: Nepal is considered as a concentrated HIV epidemic among key population like Migrant Labour Worker (MLW), Sex Worker (SW), Injecting Drug User (IDU) and Spouse of Migrant Labour Worker (SMLW). Hence, the HIV infection has significantly contributed to be HIV/TB co-infected among key population. Intervention of Anti Retroviral Therapy (ART) and Direct Observed Short Course (DOTS) have significantly reduced HIV associated morbidity and mortality in Nepal. The objective of this study was to analyze coping strategies to access the HIV/TB services in relation to socio-economic status of key study population.

Methods: The study was conducted in five districts Jhapa, Morang, Sunsari, Kavre and Parsa of Nepal. The HIV/TB respondents were selected from previous background of key population: MLW, SW, IDU, and SMLW. 343 respondents were selected through snowballing and convenient sampling technique. The data were collected through face to face interview using pretested questionnaire. Descriptive statistics, Chi-square, and ANOVA test were applied to analyze the collected data.

Results: Among 343 HIV/TB co-infected respondents, more than two fifth (44.3%) were belonged to MLW, followed by one third (34.1%) of respondents were SMLW. Therefore, the HIV/TB co-infection was significant association (p=0.001) with employment status and key study population. In addition to this, the study showed that there was significant difference between facing stigma/discrimination and study districts (F=11.03, p=0.001) of respondents. Similarly, there was significant difference between used of previous saving and occupation of family (F=10.461, p=0.001) as coping strategies to access HIV/TB services.

Conclusion: Despite the existing stigma and discrimination, the key study population had used various coping strategies to access the health care services in relation to their socio-economic status.

Key words: Key study population, HIV/TB co-infection, stigma /discrimination.

INTRODUCTION

HIV and TB both are leading causes of death worldwide, particularly in developing countries[1]. Since the emergence of HIV, the TB is the most opportunistic infection among People Living with HIV (PLHIV) and it is responsible to kill one third (33%) of PLHIV[2]. Moreover, the HIV infection impairs human immune system and cause rapid progression of active TB disease. It is estimated that, around 40% of AIDS related death occurs due to HIV/TB co-infection in Asia[3]. The HIV/TB co-infection is common who have below (<200/mm^3) Cluster of Differentiation 4 (CD4) and WHO clinical stage II[4]. To control the global challenges of HIV/TB co-epidemic, WHO launched HIV/TB collaborative activities in 2004. However, Direct Observed Treatment Short course (DOTS) is less effective due to HIV/TB co-infection in Asia[5].

In 2009, UNAIDS stated that around 72% of low and middle income countries have low-level or concentrated HIV/AIDS epidemic[6]. In fact, the concentrated epidemic nurtures HIV infection rapidly among key population[7]. As other developing

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countries, Nepal has also experienced concentrated epidemic among key population: Injecting Drugs User (IDUs), Men Who Have Sex with Male (MSM), Sex Worker (SW) and their clients, Transgender (TG) and Migrant Labour Workers (MLM) and their spouse[8].The most of HIV new infections are largely driven by sexually transmitted. The male labour migrants are predominantly to transmit new HIV infection accounting for 19% in total[9].

As of July 2015, in Nepal, out of 39,249 PLHIV, estimated 2,576 people died due to AIDS. [10]. However, the number of estimated death is decreasing after the intervention of ART service and its use[11]. Government of Nepal has also introduced ART service through different hospitals network and the ART coverage reached at 26.5% by the end of 2014. As a result, the HIV/TB mortality has been decreasing as increasing use of ART coverage in Nepal[10]. However, widespread existing stigma and discrimination against HIV and TB, PLHIV may hide their status and delay on accessing in counseling and treatment service. Hence, HIV/TB co-infection is becoming one of the major public health problems[12]. Considering the fact, this study was conducted to find out distribution of HIV/TB and coping pattern to access the services among the key population.

METHODS

A cross-sectional and descriptive study was conducted in five districts such as Jhapa, Morang, Sunsari, Parsa and Kavre of Nepal. This study is carried out duration of one year from May 2015 to April 2016. The objective of the study was to identify the coping strategies of key population to access the HIV/TB services with their socio-economic status variables.

343 sample size was obtained by using estimation of proportions of less than 10,000:

nf=n/1+n/N,
where
nf means the desired sample size.

N is total number of population for the study (3,230 reported HIV cases which were obtained from District AIDS Coordination Committee 2016); n is obtained through using following formula,

$n=Z^2pq/d^2$

After the confirmation of sample size, researcher has prepared 500 cumulative lists of HIV/TB co-infected individuals with help of NGOs and Community Care Centers (CCCs). The research team set guideline to select the respondents. The eligible respondents were enrolled who were age of 18 or older and who had diagnosis report of HIV/TB. The respondents were also ensured that they had rights to reject or discontinue from the study at any time.

Ethical approval was obtained from Nepal Health Research Council (NHRC) before data collection. Written informed consent was also taken from each respondent before conducting the study. To maintain confidentiality of respondents a separate code was given for each respondent. The content validity, face validity, internal and external validity of tools was maintained with help of expert and panel discussion. Translation back translation and piloting of study were done to maintain high reliability of data before the study.

The study adopted snowballing and convenient sampling techniques to approach the respondents. The face to face interviewed were taken in separate room of NGOs and CCCs using pretested questionnaire. Researcher also made home visit to collect data until to meet required sample size with the help of peer educators and CHBC workers. The collected data were cleaned, coded, edited, checked, and reviewed before entry in the computer. The entered data were analyzed by SPSS version 20.0. Cross tab, Pearson Chi-square and ANOVA test were applied for statistical analysis. Statistical significance level was set at p=0.05 with 95% confidence interval.

RESULTS

Table 1. HIV/TB co-infection among in key study population

Variables	Gender %		
	Female	Male	Total
Injecting drug user	0.6	8.5	9.0
Sex worker	10.2	2.3	12.5
Spouse of migrant labour worker	14.0	20.1	34.1
Total	48.1	51.9	100.0

Source: Filed survey 2016

Table 2. Employment status among key study population					
Variables	Employment status%				Chi-square test
	Employed				
	Migrant Labour Worker (MLW)	Self-employed	Un-employed		
Key study population	Injecting Drug user	3.5	26.5	14.3	Asymp. Sig. (2-sided) =0.001
	Sex worker	1.2	0.3	7.6	
	Spouse of MLW	0.3	2.0	10.2	
	Spouse of MLW	4.4	1.5	28.3	
*.Significant at the 0.05 level					

Source: Filed survey 2016

Table 2 compares the employment status after being HIV/TB co-infection of key study population. The study found that the HIV/TB co-infection was significant association (p=0.001) with employment status and key study population. However, the participants were asked about effect of HIV/TB on their employment status. Looking at unemployed status due to HIV/TB co-infection, it was seen that the spouse of MLW was much higher (28.3%) rate of unemployed than other study population. Despite the differences of unemployed status among key study population, the migrant labour worker had higher (26.5%) self-employed status than other key study population. Similarly, both spouse of MLM and Migrant Labour Worker had higher employed status than other key study population as shown table 2.

Table 3 shows that there was significant difference between disclosed HIV/TB status and study districts (F=5.004, p=0.001), followed by family reaction to HIV/TB status and study districts (F=6.241, p=0.001) and facing stigma/discrimination and study districts (F=11.03, p=0.001) of respondents. Similarly, there was significant difference between disclosed HIV/TB status and key study population (F=5.658, p=0.001), followed by family reaction to HIV/TB status and key study population (F=5.812, p=0.001), facing stigma/discrimination and key study population (F=6.940, p= 0.001).

On the other hand, there was no significant difference between disclosed HIV/TB status and gender (F=2.662, p=0.104), family reaction to HIV/TB status and gender (F=0.206, p=0.650) of respondents. Similarly there was no significant difference that facing stigma/discrimination and gender (F=0.235, p=0.628) of respondents.

Table 3. Prevalence of stigma/discrimination				
Variables	Description	F values	p values	Remarks
Gender	Disclosed HIV/TB status	2.662	0.104	Insignificant
	Family reaction to HIV/TB status	0.206	0.650	Insignificant
	Facing stigma/discrimination	0.235	0.628	Insignificant
Key study population	Disclosed HIV/TB status	5.658	0.001*	Significant
	Family reaction to HIV/TB status	5.812	0.001*	Significant
	Facing stigma/discrimination	6.940	0.001*	Significant
Study districts	Disclosed HIV/TB status	5.004	0.001*	Significant
	Family reaction to HIV/TB status	6.241	0.001*	Significant
	Facing stigma/discrimination	11.03	0.001*	Significant
***.Significant at the 0.05 level**				

Source: Field Survey 2016

Table 4. Socio-economic status variables and coping strategies to access services				
Variables	Description	F values	p values	Remarks
Education	Used of previous saving	4.349	0.014*	Significant
	Selling asset	1.109	0.331	Insignificant
	Borrowing loan	0.022	0.979	Insignificant
Family income	Used of previous saving	1.532	0.218	Insignificant
	Selling asset	6.824	0.001*	Significant
	Borrowing loan	0.255	0.775	Insignificant
Occupation of family	Used of previous saving	10.461	0.001*	Significant
	Selling asset	1.073	0.361	Insignificant
	Borrowing loan	3.616	0.014*	Significant
*.Significant at the 0.05 level				

Source: Field Survey 2016

Table 4 presents the data of ANOVA which includes F and p values to measure the significance difference between coping strategies and three socio-economic status variables of study. The study found that there was significant difference between used of previous saving and education (F=4.349, p=0.014) as coping strategies to access HIV/TB services. Similarly, there was significant difference between selling asset and family income (F=6.824, p=0.001) as a coping strategies to access HIV/TB services. Likewise, there was significant difference between used of previous saving and occupation of family (F=10.461, p=0.001), borrowing loan and occupation of family (F=3.616, p= 0.014) as coping strategies to access HIV/TB services.

On the other hand, there was no significant difference between selling asset and education (F=1.109, p= 0.331) and borrowing loan and education (F=0.022, p= 0.979) as coping strategies to access the HIV/TB services. Similarly, there was no significant difference between borrowing loan and family income (F=0.255, p=0.775) as coping strategies to access the HIV/TB services. Likewise, there was no significant difference selling asset and occupation of family (F=1.073, p=0.361) as coping strategies to access HIV/TB services.

DISCUSSION

The current study provides the information about distribution of HIV/TB prevalence among key population of five districts of Nepal. Majority (74.4%) of HIV/TB co-infection was found among two key population- MLW and their spouse. It is obvious that the MLW are responsible to transmit HIV to their spouse through the sexual contact. This finding is similar to the finding of national report of NCASC 2013, which stated that the most of HIV infections were transmitted by sexually, where male migrant workers were responsible to transmit HIV infection to the general population[9]. Likewise, Carvalho stated that HIV infection cause to the prevalence of TB among PLHIV as advancement of AIDS[13].

HIV/AIDS substantially increased in morbidity and mortality due to loss of immune system of individuals. Therefore, the infected individuals may face considerable variation the effect of HIV/AIDS on their employment status. The current study found that more than 42% of migrant labour workers and their spouses become unemployed due to effect of HIV/TB co-infection. A study done in Bostwana and found that the HIV prevalence had direct relationship with unemployment. In case of female, the unemployment rate was higher than male in the same age group[14]. The current study is also consistent with findings of previous study done by Henry et.al. in France where they concluded that the incidence of unemployment was high among HIV infected than general population. The main cause of unemployment among PLHIV was psychological rather than physical symptoms[15].

Although, HIV and TB are biologically difference but stigma of either disease is more or less same. Both diseases can lead to isolation, exclusion and devaluation from their friends and family as advancement of illness[16]. Moreover, female patients have to face high stigma with their older age and low education. However, the prevalence of stigma found high in TB disease than HIV[17]. In some setting, it is found that TB is an incurable and

inherited disease therefore infected people would show undesirable habits and hesitate to go in timely diagnosis and treatment[18]. This current study also corroborates with previous study done by Pradhan et.al. in India where, the family reaction is the influencing factors for development of stigma and discrimination in the community and most of PLHIV hide their status even in their family[19]. Our study also found same situation that there was significant difference facing stigma/discrimination and key study population. This means the PLHIV are very sensitive regarding the issue of HIV/TB co-infection and they hesitate to disclose their status in all condition.

TB and HIV treatment services are available for free of cost for all people. However; people with HIV/TB co-infection have facing higher levels of post-diagnosis catastrophic cost than those with HIV or TB only[20]. Therefore, the current research had tried to find out coping strategies of key study population to access the HIV/TB services in relation to their socio-economic status. The study found that there was significant difference between used of previous saving and education as coping strategies to access HIV/TB services. Similarly, there was significant difference between selling asset and family income to access HIV/TB services. Likewise, there was significant difference between used of previous saving and occupation of family, followed by borrowing loan and occupation of family to access HIV/TB services. It may be cause of perceived severity of HIV/TB co-infection and to have good quality of life. A study conducted in India stated that the improved understanding of HIV/AIDS, affiliation to PLHIV support group have created positive coping behaviour with HIV/TB co-infection service[21]. On the contrary, both male and female HIV infected has been facing gender related barriers while accessing HIV/TB services[17]. This current study also corroborates with previous findings of the study in relation to existing practice of stigma and discrimination in the society.

CONCLUSION

Overall the study results suggested that the HIV/TB co-infection was found among key population. The HIV/TB co-infection was relative higher among Migrant Labour Worker and their spouses. The existing stigma/discrimination was also contributing factor to be HIV/TB prevalence. The HIV/TB controls programme and policies should be comprehensively reviewed to protect general population. However, coping strategies to access HIV/TB services were significantly difference for use of previous saving and education and family occupation of respondents.

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CONFLICT OF INTEREST

None

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A MEASURE OF TRANSMISSION OF TUBERCULOSIS INFECTION AMONG CHILDREN IN HOUSEHOLD CONTACT

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ABSTRACT

Introduction: Tuberculosis (TB) is transmitted through droplets from patients having pulmonary TB, Young children living in the same household are at higher risk Tuberculosis, with great potential to benefit from screening and preventive treatment. This study was conducted with the objectives to estimate the prevalence of TB infection among under five years old children in household contact with pulmonary tuberculosis patients, and assess the factors associated with transmission of TB.

Methods: Pulmonary TB patients receiving treatment from the DOTS Centres in Sunsari District (Index Case-IC) were visited in their household to identify and assess contacts below five years of age. Transverse induration greater than10 mm was defined as a positive Mantoux test suggestive of tubercular infection.

Results: Among 190 household contacts, Mantoux was positive in 13.7% (95%CI: 11.2-16.2). Higher sputum bacillary load (adjusted OR=3.03; 95% CI 1.01-9.1) and spitting habits of Index Cases (aOR=3.1; 95% CI 1.2-7.7),first-degree relationship (aOR=3.5; 95%CI 1.4-8.7) and longer duration of contact (aOR-6.7; 95% CI 1.4-32.2), were factors significantly associated with positive Mantoux test in the under-five years old household contact.

Conclusion: The prevalence of tuberculosis infection among under-five children in contact with pulmonary tuberculosis patients was 13.7%, which is nearly double than the results of first national tuberculin survey (7%), conducted by National Tuberculosis Centre. This highlights the need for a competent & functioning contact tracing mechanism to halt the chain of transmission of infection. Social and behavioral factors existing in the household were significantly associated with the transmission of Tuberculosis infection.

Key words: Tuberculosis, Contact Tracing, Under Five Children.

INTRODUCTION

An estimated one million children fell ill with Tuberculosis (TB) and 170 000 children died in 2015[1]. Children constitute 10% of the Global TB cases.[2,3] Those infected with TB bacteria have a 10% lifetime risk of developing the disease.[1]

Ignorance and stigma among the community, insufficient contact investigation, limited access to diagnostic tests, and a host of other barriers to childhood TB diagnosis was identified by a study in Peru.[4]While intense scientific and clinical research efforts into novel diagnostic, therapeutic and preventative interventions have focused on TB in adults, childhood TB has been relatively neglected.

However, children are particularly vulnerable to severe disease and death following infection, and those with latent infection become the reservoir of

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infection with reactivation in adulthood, fuelling the future epidemics.[5] Epidemiology of childhood TB follows that of adult cases, and children constitute nearly 40% of the caseload in high incidence communities.[6]

Transmission of TB to young children usually results from household contact with an infectious case.[7,8,9] Risk factors for transmission of TB in the household include a wide variety of environmental and host characteristics existing within the household. Intimacy of contact, sleeping arrangements and sputum status of the TB patient have been implicated as risk factors in the transmission of TB, or even Acute Respiratory Infection to Household Contacts, especially under-five year old children who are generally confined to the house.[10, 11, 12] Limited social contact of very young children reduces their likelihood of becoming infected, unless the caregiver is the source case. However, additional caregivers like grandparents or extended family members taking care of the children during the day are also important.[13]

OBJECTIVES

To study the prevalence of Tuberculosis (TB) infection and factors associated with transmission of infection among children less than five years of age living in the same household with pulmonary TB patients of Sunsari District.

METHODS

A community-based cross-sectional study was carried out in 3 municipalities and 49 Village Development Committees (VDC) of Sunsari District, situated in south-west of Koshi zone in the eastern development region of Nepal. This district has 1, 62, 407 households with 4.7 members per household and an under five population of 68052.[14]There are 14 Directly Observed Treatment Short Course (DOTS) centres and 52 sub-centres that registered 568 sputum positive and 362 sputum negative cases in this district in 2015.[15]

All household contacts under five years of age of newly diagnosed patients with Pulmonary TB (both sputum smear positive and negative) registered in the National Tuberculosis Program (NTP), and attending the DOTS clinics in Sunsari District were included in the study. Household contact (HC) was defined as a child less than 5 years of age, living in the same house and sharing the same kitchen as the Pulmonary TB patient. The sample size was calculated by the single proportion formula as 188 based on a similar study done in India.[16]Total of 190 eligible children were enrolled in this study covering more than 95% of the total eligible household contacts of TB patients of Sunsari district.

Stratification was done at two levels- firstly all Pulmonary TB cases from the DOTS register of Sunsari district were identified (Index Case-IC),following which, house to house visits were conducted to identify eligible HC's under five years of age. A pretested semi-structured questionnaire was used to extract information from a single respondent (parents/ caretakers of the child) and a general clinical examination of both IC and HC were performed. Children who were already diagnosed with TB were excluded from the study.

After explaining the risks involved in the procedure, the household contacts were tested intra-dermally with 0.1ml of 5TU PPD with Tween 80 (SPAN Divergent Ltd, Surat, India - calibrated against Batch RT 23 manufactured by Statens Serum Institute, Denmark) and followed up in their homes within 48 to 72 hours, where the width of reaction (indurations) in the horizontal plane was noted by the pen method. Mantoux test was considered positive for indurations of 10 mm or more, which was suggestive of Tubercular Infection.

All children were managed according to the standard National Tuberculosis Program guidelines.[17]Children with positive screening result were referred to BP Koirala Institute of Health Sciences (BPKIHS), a tertiary care hospital and evaluated by the Consultant Paediatrician. They underwent chest x-ray, GeneXpert test and other relevant tests for the diagnosis of TB. Those diagnosed as TB Disease were treated under DOTS regimen, and those under-five children with TB infection were provided with Isoniazid Preventive Therapy (IPT) in the local DOTS centres.

Operational definitions:

Relationship with contact*:* The connection between the HC and the IC, categorized as first degree (father/mother/siblings) or second degree (other than the father/mother/siblings)

Proximity of contact: The closeness or intimacy of contact between the IC and HC; categorized as Solitary (different room sleepers), room sharers (same room/different bed) or same surface co-sleepers (same bed)

Duration of contact:

The infectious period extends from approximate dates start of TB symptoms to the period of effective treatment (demonstrated by negative sputum smears) and diminished symptoms; the duration of contact for HC was determined by the time they spent with the IC during the infectious period. Information from the patient interviews and other documents were assembled to assist in estimating the duration of contact.

Contact ethnicity:

The indigenous nationalities of Nepal classified based on Nepal Demographic and Health Survey 2011.[18]

Sputum bacillary count:

The number of TB bacilli present in sputum identified by microscopy and categorized based on American Thoracic Society guidelines into five categories.[19]Generally speaking, the sputum sample must contain 5,000 to 10,000 Acid Fast Bacilli per millilitre of specimen to be detected on Ziehl-Neelsen staining, whereas 10 to 100 organisms are needed for a positive culture.[19]

Injudicious spitting habits: The presence of a careless habit of spitting in and around the house in the Index case.

Statistical Analysis:

Odds Ratio (OR) with confidence limit was calculated for inferential statistics. Logistic regression analysis was performed for all independent variables with p-value <0.20 in the bivariate analysis, This was done to identify associated factors for transmission of infection from Index Case to Household Contacts with the probability of significance set at 95% of Confidence Interval (CI).

Ethical approval was obtained from the Institutional Review Committee of BPKIHS at the onset of the study and permission was taken from the DOTS centres of Sunsari district to gather information on the Pulmonary TB patients. Informed written consents were obtained from the legal guardian of the children after explaining the objectives, and the methods.

Pretesting was done on 10% of the sample size not included in the final study, following which necessary corrections were incorporated. Quality was assured by calibrating the measuring instruments to check for precision during data collection, double checking for errors before entry. During entry, data was checked for completeness, coded and labelled clearly. All the procedures and observations including interviews, clinical examination and Mantoux test were performed by the Principle Investigator.

RESULTS

The study population consisted of 108 Index Cases (IC) and their 190 eligible under five contacts with Household Contact/Index Case (HC/IC) ratio of 1.76.The mean age of the IC were 44.5 years (SD = 18.05) and 68.5% were males. Similarly, 84(77.8%) of the IC's were sputum positive Pulmonary TB patients and 28(25.9%) had a habit of spitting injudiciously in and around the house (Table 1).

Table 1: Index Case distribution by socio-demographic, sputum status and personal habits

Characteristics	Categories	Frequency (n=108)	Percentage (%)
Age	15-29 years	28	25.9
	30-44 years	30	27.8
	45-59 years	22	20.4
	60 years & above	28	25.9
Gender	Male	74	68.5
	Female	34	31.5
Sputum Status	Positive	84	77.8
	Negative	24	22.2
Education	Illiterate	40	37.0
	Primary	22	20.4
	Secondary	31	28.7
	≥ Intermediate	15	13.9
Injudicious Spitting Habit	Absent	80	74.1
	Present	28	25.9

Mantoux test was positive in 13.7% (95%CI: 11.2-16.2) of the household contacts. Among the HC's, 43(22.6%) shared the same bed with IC, while 133 (70%) slept in different rooms. A Total of 189 (99.5%) children gave a history of BCG vaccination, while BCG scar was visible only in 182 (95.8%). Nutritional status assessed by computing with for age and graded based on Indian Academy of Paediatrics (IAP) grading for malnutrition showed 28 (14.7%) children to be undernourished, while severe malnutrition (grade IV) was no observed (Table 2).

Higher sputum bacillary count (2+/3+)and presence of injudicious spitting habits in and around the house in the IC, closer relation and proximity to IC, more than 60 days duration of contact and household contacts of hill janjati ethnicity were found to be significantly associated with a positive TST on bivariate analysis (Table 3).

Goodness of fit: Chi-square = 13.8, df = 7, p = 0.054 aOR- Adjusted Odds RatioVariable(s) entered on step 1: Sputum bacillary count, smoking & spitting habit of IC, proximity & relation of IC to contact, duration of exposure and ethnicity of contact.

Presence of injudicious spitting habit of IC [adjusted OR = 3.1; 95%CI(1.2-7.7); p-0.016], first degree relationship between IC and contact [aOR = 3.5; 95%CI(1.4-8.7); p-0.009], higher sputum bacillary load(2+/3+) [aOR = 3.03; 95%CI(1.01-9.1); p-0.048] and duration of contact with IC more than 60 days [aOR = 6.7; 95%CI(1.4-32.2); p-0.018] remained significant in the logistic regression analysis after adjusting for other variables (Table 4).

Table 2: Household contact characteristics

Characteristics	Categories	Frequency (n=190)	Percentage (%)
Age Groups	< 3 years	100	52.6
	3 year – 5 years	90	47.4
Gender	Male	101	53.2
	Female	89	46.8
Proximity to IC	Solitary (Different Room Sleepers)	133	70
	Room Sharers (Same Room/ Diff. bed)	14	7.4
	Same Surface Co-sleepers (Same bed)	43	22.6
Overcrowding	Present	146	76.8
	Absent	44	23.2
Socio-Economic Status	Below poverty line (<1.9$/day)	182	95.8
	Above poverty line (≥ 1.9$/day)	8	4.2
BCG Scar	Present	182	95.8
	Absent	8	4.2
IAP classification for Malnutrition	Normal (>80)	162	85.3
	Grade I (71-80)	18	9.5
	Grade II (61-70)	9	4.7
	Grade III (51-60)	1	0.5
Mantoux Test (TST)	Positive (≥10mm)	26	13.7
	Negative (<10mm)	164	86.3

Table 3: Bivariate analysis

Characteristic	Category	Mantoux Test		Total (n=190)	OR	95% CI		Significance (p-value)
		Negative	Positive			Lower	Upper	
Sputum Bacillary Count (n=144)	0/1+	93.7	6.3	79	1.0			
	2+/3+	81.1	18.9	111	**3.45**	1.2	9.6	**0.013**
IC spitting Habit	No	91.8	8.2	134	1.0			
	Yes	73.2	26.8	56	**4.09**	1.74	9.6	**0.001**
Proximity to IC	Diff. Room	90.2	9.8	133	1.0			
	Same Room	77.2	22.8	57	**2.7**	1.17	6.3	**0.017**
Duration of Contact	≤ 60 days	95.7	4.3	47	1.0			
	> 60 days	83.2	16.8	143	**4.5**	1.03	19.9	**0.03**
Relation with IC	2nd Degree	91.0	9.0	122	1.0			
	1st Degree	77.9	22.1	68	**2.8**	1.22	6.6	**0.012**
Contact Ethnicity	Others	90.9	9.1	110	1.0			
	Hill Janjati	80.0	20.0	80	**2.5**	1.07	5.8	**0.031**

Table 4: Logistic Regression Analysis					
Characteristics	Category	Adjusted OR (aOR)	95% CI		Significance (p-value)
			Lower	Upper	
Relation of Contact to IC	Second Degree	1			
	First Degree	3.5	1.4	8.7	0.009
IC Spitting Habit	Absent	1			
	Present	3.1	1.2	7.7	0.016
Sputum Bacillary Count of IC	Low bacillary count (0/1+)	1			
	High Bacillary Count (2+/3+)	3.03	1.01	9.1	0.048
Duration of Contact	≤ 60 days	1			
	> 60 days	6.7	1.4	32.2	0.018

DISCUSSION

Higher risk of infection among household contacts of Pulmonary TB patients than the general population have been reported earlier.[11,16,21,22,23]This study reports 13.7% (95%CI:11.2-16.2) transmission of Tuberculosis infection to under five year old HC's of Pulmonary TB patients established by a positive Mantoux Test (≥10 mm) and factors associated with it. This is in contrast with the first national survey done in Nepal, which presented a national prevalence of infection of 7.0% (95%CI:4.2–9.7).[24]This warrants for a strong contact tracing mechanism in the National Tuberculosis Program (NTP) to curb the transmission of Infection. Although contact tracing has already been introduced in Nepal in recent years, its implementation in the field remains to be seen.

The intimacy of contact with the IC also has bearings on transmission of infection and more the intimacy, greater the chances of infection. Bed sharing has been shown to transmit respiratory infections in a study from The Gambia.[12] Similarly, the intimacy of contact as judged by sleeping in the same room with the Index case increased the chances of contact having a positive Mantoux Test by 2.7 times in this study. [OR=2.7; 95%CI (1.2-6.3); p=0.017]. Similar results have been demonstrated by another study on older HCs in Dharan.[25]These findings points to the fact that proper care of young children needs to be highlighted in counselling Pulmonary TB patients at DOTS centres.

Social determinants, habits, traditions and customs increase the risk of infection among certain ethnic population as demonstrated by a study in Greenland.[26]Hill Adibasi/Janajati (disadvantaged indigenous nationalities of the hills)are a dominant ethnic group in Nepal comprising 27.3% of the total population.[27] The National Legal Code (Muluki Ain) proclaimed in the period of autocratic Rana rule in 1854 AD categorized them as non-enslavable matwali (liquor drinkers) based on their fondness for alcohol.[28]An extended analysis of Nepal Demographic and Health Survey 2006 revealed that 43% of the women of this ethnicity cited lack of money for treatment as a problem in accessing health care.. Only 80% children of this ethnicity received all basic vaccinations compared to 92% for Hill Brahmins.[28]

According to the findings of this study, Hill Janjati contacts under five years were 2.5 times more likely to have a positive TST [OR=2.5; 95%CI (1.07-5.8): p=0.031] than other ethnicities of Sunsari district. Higher rate of transmission of TB bacilli could be explained on the basis of their social customs and consistently lesser access to and use of a range of health services. Further, little is known about the genetic susceptibility to tuberculosis, but studies have reported that polymorphisms in the genes for the interferon gamma receptor are associated with susceptibility.[29] This association of ethnicity of the Household Contacts with a positive Mantoux test could be explained by these findings of genetic and socio-cultural differences. However more research is required to explore this finding.

Grading of sputum smear, a quantitative measure of TB bacilli in the sputum samples, has been suggested as a parameter that can represent the severity and the infectiousness of the disease. Dissemination of increasing number of tubercle bacilli from an infectious case results in higher risk of infection in under-five contacts. Presence of TB bacilli in the sputum of the Index case and the bacillary load in the sputum have been implicated in the transmission of tuberculosis infection in

various studies.[11,16, 21, 22, 30] This study similarly demonstrated this fact, where higher the load of sputum bacilli (2+/3+) of the IC, more likely the transmission to household contacts. [aOR=3.03; 95%CI (1.01-9.1): p=0.048]

The presence of injudicious spitting habits in and around the house by IC showed a 3.1 times greater chance of the HC acquiring the infection [aOR=3.1; 95%CI (1.2-7.7): p=0.016]This calls for stringent legal and regulatory measures to outlaw spitting at public places to prevent the spread of Tuberculosis and other air borne pathogens. Notices declaring spitting as illegal and the cause for spread of Tuberculosis were publicized as early as 1900 AD.[31]Many experts at that time believed that spitting was the sole cause for spread of disease among mankind and New York Department of Health began to conduct anti-spitting campaigns to transform this traditional habit from annoyance into a public health threat.[32] Recent study from India has shown quite a large proportion(49.2%) of the study population practicing injudicious spitting.[33]This plays a role in the spread of TB, as the organism can survive for prolonged periods outside the human body. Patients with correct knowledge regarding hazards of indiscriminate sputum disposal had significantly better practice of appropriate sputum disposal as compared to patients with incorrect knowledge (p=0.0001) in a study from India.[34]This calls for Behavior Change Communication activities to curb this practice common in Nepal.

The closeness of relation of contact to the Index case has been implicated in transmission of infection in some studies.[10,11,22, 30] First degree relationships (spouse/son/daughter of the Index case) provide closer contact between IC and HC, increasing the chances of transmission of infection. First degree relations also tend to live together within the same household in closed spaces, resulting in higher chances of infection. Closer relationship of the contact to IC (first degree) [aOR=3.5; 95%CI(1.4-8.7): p=0.009] was found to be associated with transmission of TB infection to HC's. Similar results have been observed in studies conducted in Indonesia[30] and Nepal.[25]

Greater duration of contact (>60 days) between the IC and HC was found to be 6.18 times more likely to result in a positive TST in this study [aOR=6.7; 95%CI (1.4-32.2); p=0.018]. This follows the fact that longer duration of exposure results in more chances of transmission due to prolonged exposure. This fact has also been highlighted by some studies.[35, 36]

CONCLUSION

The findings of this study emphasize the importance of integrating behaviour change communication activities during counselling of Pulmonary TB patients at DOTS centres on infection prevention measures (proper sputum disposal) and good care of young children in the household. This will serve as a cost-effective means to curb the transmission of TB infection to young children in those households.

LIMITATION OF THE STUDY

The sampling frame included only TB patients registered in national DOTS Registers, which could have excluded pulmonary TB patients and their contacts managed solely in private sectors. Although a negative history of HIV was obtained in all subjects, HIV testing was not feasible due to time and resource constraints. Toddlers(<3 years) are usually confined to the household, however, older children (4-5 years) could have been exposed to TB case while playing outside of the house, although a negative history of exposure outside the household was obtained in all subjects.

CONFLICT OF INTEREST

None

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None

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CLINICAL PROFILE AND MANAGEMENT OF EMPYEMEYA THORACIS: EXPERIENCE FROM EASTERN NEPAL

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ABSTRACT

Introduction: The management of Empyema Thoracis is challenging. It requires specialist medical and surgical care at the same time. There are of lack of data regarding the clinical profile and the steps of day to day management, hence this study aims to identify these parameters and focus on the gaps in management that is commonplace in our setting and that are representative of other resource limited settings as well.

Methods: Clinical profile, etiological agents, hospital course and outcome of 30 patients with empyema thoracis treated from 2012 to 2014 in B.P. Kiorala Institute of Health Sciences was analyzed. All patients were diagnosed on the basis of aspiration of frank pus from pleural cavity.

Results: 28 cases (93.3%) were Male and the mean age was 42.07±18.28 years. 73.3% of the empyema was Right sided and 60% were classified as medium sized and 40% as small sized. 60% of the patients were smokers. 80% of the case were diagnosed as bacterial infection whereas 20% were presumed tubercular on clinical basis and responded to treatment. Fever was the commonest presentation in 80% of the cases followed by shortness of breath (66.7%), cough (60%), chest pain (53.3%) and sputum production (20%). On investigation, pH was not measured in the fear of clogging the ABG machine. Pleural fluid glucose was below 40 mg/dl in all the cases. The median ADA value was 54.30 (15-350) and ADA was higher than 40 U/l in 10 cases with non-tubercular empyema. All cases were managed with Chest tube insertion and antibiotics. Four patients had to be referred for BPF closure whereas five for decortications. In all cases requiring decortications, a "pleural peel" could be identified in Chest Xrays. Since the patients were being managed in different units the outcome of referred patients could not be ascertained.

Conclusion The gaps in the management of empyema in resource limited setting starts from inappropriate early treatment, inadequate diagnostic facilities, delayed referral and lack of early and appropriate surgical intervention. All these factors combine to the increased morbidity and mortality associated with the management of Empyema thoracis.

Key words: Empyema thoracis, Clinical Profile, Referral

INTRODUCTION

Empyema refers to the presence of pus in the pleural cavity. Though different cut off levels of WBC and protein have been used in literature in an attempt to define Empyema[1,2], the simplest approach is to reserve the term for patients presenting with pleural effusion who have thick, purulent appearing pleural fluid[3].

The management of Empyema involves antibiotics, tube thoracostomy and often, surgical intervention. It requires specialist Medical and Surgical Care at the same time. As early drainage of pus is essential for the treatment of empyema, surgical procedures besides tube thoracostomy need to be employed early to prevent significant morbidity and mortality. Video Assisted Thoracoscopy Surgery (VATS) is

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the procedure of choice for surgical intervention due to its safety and tolerability[4]. Where VATS is not available, procedures such as rib resection and "window" creation for open drainage are still being employed.

In a resource limited setting without VATS, thoracoscopy or dedicated thoracic surgeon, the only modalities of management remain medical and tube thoracostomy supplemented by intrapleural fibrinolytics. Thus, the morbidity in such setting is expected to be higher and also representative of the prevalent situation in other resource constrained settings.

MATERIALS AND METHODS

We conducted a retrospective study of the medical records and chest radiographs of consecutive cases diagnosed as Empyema and admitted to the Respiratory and Internal Medicine services of the B P Koirala Institute of Health Sciences, Nepal during a 2 year period from Jan 2012 to Jan 2014.

The hospital serves as a referral hospital for the whole of Eastern Nepal.

In the cases with Empyema, the relevant data were scanned and included in the study only if the patient chart was viewed as Complete. Complete chart was defined as having detailed epidemiological data, a complete medical history and clinical examination, investigations including Pleural fluid analysis for sugar/protein/light's criteria, Adenosine Deaminase and malignant cytology if diagnosis was inconclusive by routine analysis, other special tests of pleural fluid as required, like, Amylase etc. Only the initial fluid examination was recorded. Once the above parameters were present, the Digital Radiographic Library was explored. The X-Ray was reviewed by a Pulmonology trainee. The size of the effusion was estimated on the initial upright inspiratory posteroanterior chest film. Effusions were classified as; large effusion if effusion covered greater than 50 percent of the hemithorax, medium if 25 to 50 percent was covered, and small effusion if effusion covered less than 25 percent of the hemithorax.

STATISTICAL ANALYSIS

Data with parametric distribution have been expressed in mean ± SD whereas data with non parametric distribution have been expressed as median (25th percentile and 75th percentile). Data was entered in Microsoft Excel, copied to SPSS 17 and descriptive and frequency data were analyzed.

RESULTS

A total of 30 cases diagnosed as Empyema had complete medical chart and were considered. 28 cases (93.3%) were Male and the mean age was 42.07±18.28 years. 73.3% of the Empyema was Right sided and 60% were classified as Medium sized and 40% as Small sized. Smoking was the commonest risk factor in 60% of the cases. 24/30(80%) of the cases were diagnosed as Parapneumonic, whereas 6/30(20%) were diagnosed as Tubercular. Of the cases of Tuberuclar Empyema, AFB staining was positive in two cases whereas the other four cases were diagnosed on clinic-epidemiological background and high ADA levels.

The mean duration of symptoms before presentation to hospital was 23 days. 90% (27/30) of the patients has already received oral antibiotics from pharmacies.

Fever was the commonest presentation in 80% of the cases followed by shortness of breath (66.7%), cough (60%), chest pain (53.3%) and sputum production (20%) (Table 1).

Table 1. Symptoms

Symptoms	Frequency (%)
Shortness of breath	20/30 (67%)
Fever	24/30 (80%)
Cough	18/30 (60%)
Sputum production	6/30 (20%)
Chest pain	16/30 (54%)
Weight loss	2/30 (7%)

Six patients were afebrile during presentation. The mean duration of fever in the Tubercular Empyema group was 50 days.

Pleural fluid glucose was below 40 mg/dl in all the cases. The median ADA value was 54.30(27-141 U/l and ADA was higher than 40 U/l in 10 cases with non-tubercular empyema (Table 2).

Table 2. Pleural fluid features

Parameters	Values
Pleural fluid Neutrophils*	77.33±25.06

Pleural fluid Lymphocytes#	10(10-30)
Pleural fluid Sugar (mg/dl)*	14.40±5.04
Pleural fluid Protein (g/dl)*	4.99±2.06
Pleural fluid ADA (U/l)#	54.30(27-141)

***Mean±Standard Deviation, #Median (Interquartile Range, ADA Adenosine Deaminase**

Microbiological culture was positive in 11/30(37%) of the cases with 14 organisms being cultured. Staphylococcus was the most common organism (Table3). Anaerobic culture was not employed and Mycobacterial culture was unavailable at the time.

Table 3. Isolation of microorganisms (n=30, 14 isolates from 11 patients)

Organism	Frequency (%)
Staphylococcus aureus	8/14 (57%)
Gram negative rods	5/14 (36%)
Pneumococcus	1/14 (7%)
Anaerobes	0/14

All cases were managed with Chest tube insertion and antibiotics. 4 patients had to be referred for BPF closure whereas 5 for Decortication. In all cases requiring decortications, a "pleural peel" could be identified in Chest X-rays (Table 4).

Table 4. Outcomes.

Outcome Variable	Frequency (%)
Improved	19/30 (63%)
Died	1/30 (3%)
Leave Against Medical Advice	1/30 (3%)
Referred for Bronchopleural fistula closure	4/30 (14%)
Referred for Decortication	5/30 (17%)

DISCUSSION

The management of Empyema in resource limited setting is punctuated by a lot of gaps.

The mean duration of symptoms before presentation to hospital was 23 days. 90% of the patients had already received oral antibiotics from pharmacies. The widespread use of antibiotics in the community for even the most trivial of causes leads to decrease in Culture positivity once the patient reaches the hospital. In our study, culture was positive in only 37%[11]. Again due to resource limitation anaerobe culture is not routine and we speculate this is the same for most settings in our part of the world. At the time of the study, even culture facilities for Mycobacterium were not available. Banga et al.[5] reported a culture positivity of 42%[13] while Baranwal et al.[6] reported a culture positivity of 48% in pediatric patients in the same center as ours. Staphylococcus aureus was the commonest organism isolated, a trend found in most other studies as well[5,6].

Empyema was diagnosed to be Tubercular in 20%[6]. The diagnosis was on the basis of pus AFB positivity in two cases whereas in the other four cases the diagnosis was made on the basis of clinic-epidemiological background and radiological features. Tuberculosis as a cause of Empyema has been variably reported with rates varying from 0% to 42%[5]. The varying rates could depend on culture availability, the use of solid or liquid cultures as well as the technique of culture.

The Median pleural fluid ADA value was 54.30U/l (IQR,27-141). ADA was more than 40U/l in 42%[10] of the cases of Non-Tubercular Empyema. This underlines the difficulty in using ADA values to differentiate the etiology of pleural effusion as Tubercular or Non-Tubercular in cases of Empyema[3].

Management of the patients involved use of Antibiotics, tube thoracostomy and intrapleural Streptokinase was used in seven cases. Tube thoracostomy was done with 28 Fr chest tube in 60% cases whereas 14 Fr Pigtail catheters was used in the remaining 12 cases. The distinction was made on appearance and thickness of the pus aspirated. Medical management was successful in 63% patients. One patient died during treatment and one patient left against medical advice.

Bronchopleual fistula was encountered in 14%[4]. These patients were observed for two weeks duration after which they were referred for Surgical management. There was no spontaneous improvement in any of the cases. Bronchopleural fistula (BFP) which is an abnormal connection between the bronchus and the pleural space can be divided into central BFP and the peripheral BPF. In the central type, there is direct communication between a large bronchus and the pleural space, whereas in the peripheral type, the air leak is from a peripheral bronchus or from the lung parenchyma

into the pleural space[7,8]. The common causes of peripheral BPF are necrotising infections such as pulmonary tuberculosis, pneumonia and even empyema[8,9]. The incidence of BPF resulting from these suppurative lung and pleural diseases has not been clearly documented in the literature; however, the incidence following pulmonary or lobar resection ranges between 4-20%[10]. The management of this condition is very challenging as recurrences are common leading to incomplete removal of the pus; failure of closure of the fistula and inability to obliterate the residual pleural cavity[11]. There was a high rate of BPF in our study compared to other studies. The high rate could be attributed to delayed presentation as well as concomitant pulmonary processes. The presence of BPF complicates the management of Empyema and whether early surgical intervention would be able to reduce the frequency of BPF would be a point of interest.17%[5] had to be referred for Decortications and in all these cases pleural peel was evident on radiological examination. In a study involving 179 patients, Decortications was necessary in 55% of patients with anaerobic infections and in 50% with aerobic infections[12]. In another study, decortications was required in 24%[11] cases[13]. Surgical decortications has persistently shown to be highly successful in treating Empyema[13]. Wong and colleagues[14] reported that surgical decortications with VATS significantly reduced hospitalization duration compared with tube drainage treatment in paediatric patients. Thourani and colleagues[15] reported that surgical decortications reduced the hospital stay compared with simple drainage through a catheter or chest tube. They also calculated that early decortications has charges similar to those of primary intervention (image-directed catheter or tube thoracostomy) but is more cost-effective than failed image-directed catheter and thus advocated the use of early surgical intervention as the most optimal and cost-effective initial modality for the treatment of empyema thoraces. Though early surgical intervention has become the treatment of choice, how early is early enough is the big question? Chung and colleagues[16] found that Patients with symptom durations of less than 4 weeks showed better early results than those with symptom durations greater than 4 weeks. Thus, symptom duration can be considered a reliable preoperative factor in deciding the surgical management of empyema or cases involving loculated pleural effusion. The evidence in favor of early surgical management points to a huge resource gap in the management of Empyema in resource limited setting. Not only is the surgical management not done in most centres, referral is also delayed. In our study, the patients were referred after a mean of 43 days from symptom onset.

CONCLUSION

The gaps in the management of Empyema in resource limited setting starts from inappropriate early treatment, inadequate diagnostic facilities, delayed referral and lack of early and appropriate surgical intervention. All these factors lead to the increased morbidity and mortality associated with the management of Empyema thoraces. These gaps need to be fulfilled by awareness at the public level, logistical up gradations at institutional level, trained manpower generation at all levels and an inclination towards early surgical intervention among the physicians.

CONFLICT OF INTEREST

None

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STUDY ON CULTURE POSITIVITY AMONG SPUTUM SMEAR NEGATIVE TUBERCULOSIS SUSPECTS ATTENDING THE NATIONAL TUBERCULOSIS CENTRE, NEPAL

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ABSTRACT

Background: Globally, more than half of all TB cases are not detected. If they are not diagnosed and get treatment infection transmission may continue and patients suffer and may eventually die. Pulmonary TB either smear positive or negative is normally diagnosed by Ziehl- Neelsen stained sputum smear examination microscopy. Since the culture is the gold standard, evaluation of smear negative TB cases by this method is likely to detect more cases.

Objectives: The objective of this study is to find out culture positivity among smear negative patients.

Methods: All the three sputum samples reported negative by Ziehl-Neelsen microscopy from a total of 138 new TB suspected cases more than 15 years of age at NTC Laboratory. Nepal were cultured on Lowenstein-Jensen media. Tubes showing sufficient growth (culture positive) were recorded and all the culture positive results were informed to NTC. The culture positive samples were processed for DST on first line drugs using proportion method.

Results: The culture positivity rate was 5.1% (7 of 138 cases) All the positive cultures were processed for DST on first line anti-TB drugs and none showed resistance of the total 138 suspected Tuberculosis patients, 94 (68.1%) were males and 44 were females (31.9%) with male: female ratio 1:047. The mean age of the total patients were 30.69. Nearly 42% of them belonged to 31-50 years. Mean age of the male patients was significantly higher than total of the female (p<.001).

Conclusions: Seven smear negative cases among the total of 138 suspected TB patients attending NTC were culture positive. Similar study has to be done in other parts of the country.

Key words: new TB suspects, smear negative, culture positive, diagnosis of tuberculosis.

INTRODUCTION

The detection and management of smear positive pulmonary disease is the principal aim of National Tuberculosis Control Programmes. However, smear negative disease is also a common clinical problem.

Several studies[1] have identified the clinical characteristics of persons with the most infectious from of TB those harbouring the largest number of organisms, with acid-fast bacilli (AFB) found by microscopic examination of stained sputum (AFB smear positive). However, patients with active TB who have negative sputum smear results are also capable of transmitting the infection. (McPhredan FM et al/Grzybowski et al)[2,3] The relative transmission rate of smear negative TB patients compared to smear positive TB patients has been calculated at 22% using a molecular epidemiological technique[4] . Although persons with smear negative TB are less infectious than the smear positive patients, the overall contribution to disease transmission is considerable because half of all patients with TB can present with negative sputum smear findings. [5]

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The microscopic examination of sputum smear stained by Ziehl-Neelsen method can detect bacilli when they are of the order of 10^4 per ml of sputum. Sputum smear microscopy has been shown to have a sensitivity of 96.5% specificity of 34.9% with a positive predictive valve of 17.3% and negative predictive value of 99.9% in Gizybowski's series.[6]

It is known that considerable transmission occurs before the level of bacilli reach 10^4/ml in the sputum. During this period of unknown duration the person continues to transmit the infection. It has also been established that sputum smear microscopy is less sensitive in HIV associated TB. Therefore it is important to diagnose from the smear-positive case of the future, not only for individual person but also for public health perspective. .

It has been proved that the probability of finding acid-fast bacilli by sputum smear microscopy is directly related to the concentration of bacilli in the sputum. Thus, when 1 ml of sputum contains fewer than 10,000 but more than 1,000 organisms per ml, the chances decreases rapidly, the result being negative in about 96% of cases.[7]

All sources of error being eliminated, the concentration of bacilli is the sputum is determined largely by the type of tuberculosis lesion from which the bacilli originate. Thus, a cavity about 2 cm in diameter (opening into a bronchus) may contain some 100^8 i.e., one hundred thousand times fewer. Sputum from patients with tuberculosis lung cavities, containing softened necrotic particles with enormous amount of bacilli, will thus usually be found positive by direct smear microscopy. In contrast, sputum from patients with nodular, encapsulate lesion discharging only small amounts of bacilli will almost invariably be negative by smear microscopy. Only by using refined laboratory techniques, such as culture, can small number of bacilli be demonstrated[9].

About 5000-10,000 acid fast bacilli (AFB) per millilitre of sputum must be present for detection by smear, whereas culture required only 10-100 viable organisms.[10] Hence, smear negative culture positive patients generally have minimal disease with low bacillary counts rather than far advanced cavitary TB with heavy bacillary burden. For example, a US study of HIV negative culture positive patients estimated that negative smears are obtained from 60%-80% of patients with minimal disease, from 30%-40% of cases with more extensive disease, but only 5%-10% of patients with extensive cavitary lesions. [11]

Study conducted by the NTI Bangalore revealed that 35% culture positivity among smear negative patients. Smear negative culture positive cases are also associated with mortality. Longitudinal surveys conducted between 1961 and 1963 among untreated TB patients in Bangalore District, South India found that the mortality rate during the first 18 months of follow-up was 34.7% for smear postive patients, 14.1% for smear negative culture- positive cases, and about 5% for smear negative culture negative cases diagnosed radio logically.[12]

The difficulty of demonstrating small number of bacilli regularly has been shown in studies described elsewhere (1970)[13], (1971)[14], (1976)[16]. The burden of sputum smear negative tuberculosis in Nepal is not known. According to our knowledge, culture results among smear negative TB suspects were not studied in Nepal. Hence, the aim of this study was to find out culture postivity among smear negative patients.

MATERIALS AND METHODS

Study Design: Prospective study

Study Population: All the new suspected TB cases attending National TB Centre (NTC) Laboratory, Nepal for diagnosis.

Inclusion criteria: All the new TB suspects more than 15 years of age attending the NTC OPD Clinic/ diagnosed by all three sputum smear & declared smear negative on microscopic examination in NTC Laboratory.

Exclusion criteria: Smear +ve and/or AFB detected after sample processing/inoculation suspected EP and contaminated samples while processing for culture.

Study site: NTC OPD Clinic/NTC Laboratory.

Sampling method: Consecutive or non randomized sampling method was applied. The details of the patients (name, age, sex, type of patient, sputum examination requested for) were collected from the Laboratory register.

Sample size: 138. The sample size was calculated by using the formula recommended by WHO [16] as

$$n = \frac{z^2 (p) (1-p)}{d^2}$$

Where n= sample size

Z= 1.96

p= anticipated prevalence # (10%)

d=absolute precision (5%)

While applying equation/formula; $n = (1.96)^2 * (0.1)1-0.1) / (0.05)^2$

$= 3.84 *(0.1) (0.9) /0.0025$

$=138$

(Anticipated prevalence of 10% for smear negativity was assumed since the smear positivity rate among new case is 10% which is very close to the rate of smear negative or the ratio of smear positive and smear negative 1:1).

Sputum smear negative samples from a total of 138 new TB suspects (3 sputum samples per suspect were pooled and counted as one sample) were processed for this study. The samples showing AFB positive after processing or contamination, were replaced (approximately 10-15%) with new sample from new TB suspects. Record for the same was maintained and intimated to NTC, Nepal whenever required.

Data Collection: A separate laboratory register (an original source of data) was maintained for the details of suspects and smear or culture results.

Ethical issue: As secondary sample was used institutional permission was taken from National Tuberculosis Center (NTC), Nepal.

Laboratory procedures:

- The NTC Laboratory staffs were oriented for keeping all the samples until microscopic examination and to coordinate with SAARC TB Reference Laboratory (STRL) staff.
- All three fresh sputum samples (3-5 ml each) found negative after examination were collected.
- After centrifugation, inoculation was done and observed every week upto eight weeks.
- All the positive cultures were processed for DST on first line anti-TB drugs (SHRE*) using proportion method.
- All the information for culture positive samples was sent to NTC. The DST results were also sent to NTC after completion. The records for culture and DST were maintained.

S= Streptomycin

H= Isoniazid

R= Fifampicin

E= Ethambutol

RESULTS

Age and sex distribution of the study sample

Among the total of 138 suspected tuberculosis patients, 94 (6.1%) were males and 44 were females (31.9%) with male: female ratio 1:0.47. The mean age of the total patient was 30.69 years. Nearly 42% of them belonged to 31-50 years age group. Mean age of the male patients was significantly higher than that of the female (p<001).

Table 1: Distribution of Smear negative and culture positive results (sex & age wise)

Smear negative	Culture positive			
	15-30 yrs	31-50 yrs	>50 yrs	Total (%)
Male	2	2	2	6(4.35%)
Female	-	1	-	1 (0.72%)
Total	2	3	2	7 (5.07%)

One hundred and forty seven (147) sputum samples were received in the STRL. Five samples were discarded due to the contamination. Another four samples were negative in the routine laboratory and positive in STRL were also excluded from the study.

Table 2: Comparison of smear results in reference laboratory and routine laboratory (n=144)

NTC Routine Laboratory	SAARC TB Reference Laboratory			
		Smear +ve	Smear –ve	Total
	Smear +ve	0	0	0
	Smear –ve	4	140	144
	Total	4	140	144

False negative rate at routine laboratory is =4/144=2.8%

Table 3: Culture positivity among smear negative TB suspects (n=138)

Smear results in reference lab	Culture results		
	Culture+ve	Culture–ve	Total
Smear +ve	0	0	0
Smear –ve	7	131	138
Total	7	131	138

Culture positivity rate among smear negative TB suspects =7/138=5.1%

DST pattern of culture positive patients (n=7: No resistance was reported.

DISCUSSION

The most striking shortcoming perhaps of current TB control efforts is the inability of programmes to accurately diagnosed TB in a large proportion of patients, particularly in HIV infected individual and children. Globally, more than half of all TB cases are not detected, the results of health care system weakness and the inadequacy of available technology. If diagnosis is absent, patients are not treated, transmission may continue patients suffer needlessly and many eventually die. Pulmonary TB either smears positive or negative is normally diagnosed by Ziehl-Neelsen stained sputum smear microscopy. Major drawback of this method is, it requires more than 5000 bacilli per ml of sputum to detect on a smear. Since the culture is the gold standard, evaluation of smear negative TB cases by this methods is likely to detected more cases.

Before the HIV epidemic, two well- performed sputum examination were considered as a single culture.[12] With the increasing rate of smear-negative disease and the rising prevalence of drug resistance, culture facilities may need to be more widely available in developing countries, and new convenient TB diagnostics are urgently needed. [17]

During this study, we found that 7 (5.1%) smear negative TB suspects were culture positive. Study conducted by Dhingra et al [18] reported 9.3% of culture positivity among smear negative patients. Similarly, Prasad[19] reported 7% culture positivity among smear negative cases. In our study samples from TB suspects were taken where as in other 2 study compared to other studies may be due to this reason.

In a Romanian and Indian study, 35% of 557 Romanian patients and 28% of 296 Indian patients had positive cultures initially. [20]

The proportion of cases of smear-negative tuberculosis will depend primarily on clinical mix, but can be minimized by: (a) good sampling (b) careful technique (c) technical expertise (d) good microscopic facilities. There will still be a proportion of patients in whom organisms are scanty such patients pose a diagnostic challenge.

The association of AFB-negative smears with lower bacillary burdens and minimal pulmonary lesions would imply that the infectivity and the mortality of smear negative disease should be lower, and that less intensive chemotherapy may adequately treat this condition. Study conducted by Rouillon et al [10] revealed that revealed that the prevalence of infection among children exposed to smear-positive cases varied between 30%-65%, whereas the tuberculin reactivity rate was only 4.7% -26.8% among contacts of smear negative patients, whose TB diagnoses were based on positive culture. In Rouillion's study prevalence of infection was measured by tuberculin reactivity. However, in studies in high incidence environment in India and Africa, the infection rate among young contracts of smear-negative cases was similar to that in the general population or in house-holds without documented TB.[10] To prevent such transmission it necessary to detect culture positive cases.

The sensitivity of the AFB result is known to be poor, varying between 30% and 70% depending on a number of factors relating to how the test is implemented. The sensitivity is improved by concentration of sputum specimens and use of fluorescent microscopy, but reduced in patients with HIV disease.

Truly negative smear results of course, do not preclude TB disease. Culture of clinical specimens will confirm the diagnosis in smear positive cases and usually identify that many cases again of smear negative disease. This is because the culture is more sensitive (80% - 85%), being able to detect as few as 10 bacteria per ml of sputum. It is also very specific (98%) and allows, DST as well as genotyping of the isolate.[21] Until recently, smear negative TB cases were thought not to contribute significantly to secondary transmission. The frequency of coughing, viscosity of the sputum, organism virulence and host factors are likely to play a role. Population based studies have estimated that smear negative patients with

TB may contribute to at least 17% of the disease incidence in a community.

Patients with smear negative PTB are substantially less infectious than those with smear positive PTB. The risk of contracting disease for house hold contract of smear negative, culture positive patients is about one tenth of that for contracts of smear positive patients. Positive culture of M. Tuberculosis with smear negative PTB in sub-Saharan Africa revealed that about one quarter to one third of the smear negative pulmonary patients were confirmed diagnosed by culture as tuberculosis. Most of the smear negative cases found to have tuberculosis by culture were also diagnosed as HIV positive serologically.

In Zimbabwe; 12 smear negative cases among 36 HIV +ve found to be culture positive for tuberculosis. Likewise, Zambia 11 cases of 27 HIV positive Rwanda 17 cases of 92 HIV positive and Malawi 30 cases of total 73; HIV test not done).

Children are more likely to become infected with TB and to be more susceptible to acquiring TB from smear negative sources. In one study done in British Columbia, Canada showed that 10% of children with TB acquired their disease from smear negative sources. During this study, 2.8% of false negative rate in routine laboratory was detected in comparison to reference laboratory. In many laboratories the staffs have to perform a wide range of duties, which reduces the time devoted to sputum smear microscopy.

Many positive AFB sputum specimens become falsely negative if left in a sputum container for over a week. There is often quality control performed, either by the laboratories themselves of by Central Reference Laboratory. The sensitivity of microscopic diagnosis could be improved by liquefying sputum with house hold bleach (sod hypochlorite sol) and concentrating mycobacteria by centrifugation. In Ethiopia, the sensitivity of sputum smears compared with culture was 31% when smear were prepared directly from sputum after sod hypo treatment and centrifugation.[22]

There are three types of laboratory services run by NTC Nepal (routine sputum examination, general laboratory, and culture and DST laboratory. Besides these, being a National TB Reference Laboratory, planning, procurement, training, supply, supervision, EQA of sputum microscopy for central region of the country as well as 5 regional quality control laboratories is done by 8 laboratory staff (2 Med technologists, 5 Lab technicians and one Lab attendant). NTC lab examines averagely 100 samples a day and smears are prepared directly from sputum (may fish up saliva only or miss the stuffy part). In this study, 3 smear negative samples were pooled and taken as one/ suspect, and homogenization or liquefaction of the specimen was done with 4% NaOH followed by centrifugation to concentrate organisms. In such way, the accumulation of the organisms may have increased. But among a total of 4 false negative smears; 3 were scanty to 1+ positive and only one was detected 3+ by SAARC TB Reference Laboratory, for which sputum specimen were not collected on the same day. Nevertheless, each step of the laboratory procedure of sputum collection to recording and reporting should be completed properly, correctly and appropriately.

Till date, no study done for significant data how much is the culture positivity among smear negatives, in Nepal, It is encouraging that out of 7 culture positives none of the culture was resistant to first line Anti TB drugs.

CONCLUSION AND RECOMMENDATION

Seven smear negative cases among the total of 138 suspected TB patients attending NTC, were culture positive. Internal QC should be regulated in NTC laboratory and regular. Refresher training to laboratory staff is important. NTC laboratory should participate in national EQA programme and national EQA system should be strengthened. Similar survey to be done in other parts of the country, where high incidence and prevalence of TB cases occurs and the proportion of smear positive and negative is very close to minimize the chances of disease transmission especially to the children (0-14 yrs).

CONFLICT OF INTEREST

None

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