Print ISSN 1818-9741
Online ISSN 2091-0959
Vol. XVIII, No. 1, Year 2020

SAARC

(South Asian Association for Regional Cooperation)

Journal of Tuberculosis, Lung Diseases and HIV/AIDS

SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS

Vol. XVIII No. 1 Year 2020

Published and distributed by:

SAARC Tuberculosis and HIV/AIDS Centre (STAC)
Thimi, Bhaktapur
G.P.O. Box 9517, Kathmandu, Nepal
Tel.: 00977-01-6632601, 6632477, 6631048
Fax: 00977-1-6634379
E-mail: director@saarctb.org
Website: www.saarctb.org

EDITORIAL

Original Articles

Case Study

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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Print ISSN 1818-9741
Online ISSN 2091-0959

Editorial

The pandemic of Covid-19 has loomed large on every aspect of life for the last one year. Delivery of all basic and essential health services and routine scientific activities have been severely affected in most part of the world, including SAARC member states. It is, of course, imperative that all measures possible are taken to protect people from coronavirus and to treat those who have become sick. However, it need not be at the cost of people having to die of another preventable and treatable disease.

The potential impact on HIV and tuberculosis programs are arising predominantly from disruptions to the usual activities and services due to COVID-19. These disruptions include mitigation strategies undertaken in response to the COVID-19 pandemic, leading to the scaling back of certain activities and care-seeking; reduced capabilities of the health system due to overwhelmingly high demand for the care of patients with COVID-19; and interruptions to the supply of commodities as a result of effects on both domestic and international supply chains.

The long-term impact on the national and regional efforts to control/eliminate these public health issues is yet to be fully measured. However, some preliminary assessments published so far do suggest that significant gains made in past in efforts to control/eliminate these diseases may be reversed and the timelines aimed for control/elimination of these diseases will be pushed back further.

Extended periods of lockdown and prioritization of COVID-19 over other health services have prevented many people from accessing treatments for non-COVID infectious diseases; at the same time, new cases of these illnesses will have gone undetected. Taken together, this is resulting in a surge of cases.

According to WHO, the global HIV epidemic is not over and may be accelerating during the COVID-19 pandemic, with a devastating impact on communities and countries. According to The Global Fund for AIDS, TB and Malaria (GFATM), in 2020 we will likely see increases in deaths and new infections across all three diseases for the first time in many years as health and community systems are overwhelmed, treatment and prevention programs are disrupted, and resources are diverted. In many of the countries most heavily affected by HIV and TB, the knock-on impact of COVID-19 on these diseases in terms of incremental deaths may outweigh the direct impact of the virus.

The coronavirus is still raging in many countries which also have a high TB burden. With the total number of COVID-19 infections approaching 80 million, deaths standing at more than 1.7 million and effective vaccines far from being available throughout the world (at the time of publication), we can't say how bad the long term impact of the pandemic will be. But we can say that, without appropriate and timely interventions, diseases such as TB and AIDS are likely to take more lives.

For tuberculosis, the greatest impact would be from reductions in timely diagnosis and treatment of new cases. The disruption is expected to lead to an increase in tuberculosis deaths for several years because the disruptions leave individuals untreated for longer, leading to more transmission and more cases in later years.

The greatest impact on HIV has been estimated to occur from interruption to antiretroviral therapy. The greatest increase in HIV deaths was predicted to be caused by forced interruptions to antiretroviral therapy (ART) for some individuals. Smaller impacts are expected to occur due to a reduction in new ART initiations and a gradual accumulation of individuals not taking ART.

The impact on HIV and tuberculosis could be minimised by maintaining core services: continued access to antiretrovirals, maintenance of tuberculosis diagnosis and treatment.

The current pandemic also presents some opportunities. The response to the COVID-19 pandemic may bring prospect for synergies including increased levels of TB testing, particularly in high-HIV settings where symptoms of TB and Covid-19 disease are more difficult to differentiate clinically, better implementation of infection control measures and more effective contact tracing investigations.

In conclusion, disruptions to the services for HIV and tuberculosis resulting from the COVID-19 pandemic and its response, could lead to a substantial number of additional morbidity and mortality. In the short term, maintaining the most critical services, specifically treatment for HIV and tuberculosis (new and current patients) is a priority for reducing the overall impact of the COVID-19 pandemic. The main emphasis in the longer term must be on enhancing the resilience of the health system to cope with catastrophic events such as pandemics, and it may very well demand far-reaching changes and additional resources.

Chief Editor
Director, STAC

DOI https://doi.org/10.3126/saarctb.v18i1.34099

DIAGNOSTIC CHALLENGES AND CLINICAL PROFILE OF SPINE TUBERCULOSIS – AN EXPERIENCE FROM MEDIUM SIZED HEALTH CARE CENTER, SOUTH INDIA

Sushma K[1], Kaiwar S[1], Selvarajan C[1], Mascrenhas AA[1], Flynn A[1]

[1] St. Martha's Hospital, Bangalore, India

ABSTRACT

Introduction: Skeletal tuberculosis accounts for 10-35% of Extra-Pulmonary Tuberculosis (EPTB) and 3% of all cases of tuberculosis. Spine is involved in about 50% cases of skeletal tuberculosis. The diagnosis of Spine TB in the developing world until recently has been carried out by clinical presentation and neuroimaging modalities like X-ray/CT/MRI. Until the molecular era, the diagnostic tests at laboratories had mostly remained less contributory with low reliability and accuracy. The objective of the study was to review the spinal cases of TB and present an overview of the different methods of microbiological diagnosis in patients with Spine TB at our center.

Methodology: Retrospective study (April 2016 – April 2019) of all consecutive patients suspected with pyogenic or Spine TB was undertaken with relevant clinical details. With the radiological screen the probable TB patients were sampled (tissue, pus, abscess fluids and exudates) and were processed for ZN stain, Culture (conventional), Xpert RIF/MTB assay (at reference lab) and Histopathology. Anti-Tubercular Therapy (ATT) was administered to all definitive cases with or without surgery.

Results: A total of 26 patients of Definite TB were identified out of 42 suspected. The mean age was 47 years (14-78 range). Fever (n=17) and pain (n=18) were most common symptoms reported by over 80% of the patients. The twenty-six patients characteristically had positive radiological changes in MRI. Lumbar (n=6)and thoracic (n==6) vertebrae were equally involvedand over 50% (n=14) had two or more vertebral involvement. All 26 spine samples were negative for Acid Fast Bacilli (AFB) by ZN staining. Individually, the positive detection rate by Xpert MTB/RIF was 88% (n=23), by HPE was 65% (n=17) and by culture was 42% (n= 11) respectively. XpertMTB/RIF was 82.3% sensitive and 64% specific when compared with Histopathological Evidence (HPE) alone and the sensitivity and specificity rose up 81% on comparing with cross HPE and or culture.

Conclusion: Improved case detection of Spine TB was noted by using Xpert MTB/RIF assay at our center. We recommend Xpert MTB/RIF molecular test as the first-line investigation at laboratories for all the suspected cases of Spine TB and for confirmation when the clinical and MRI findings are inconclusive or unavailable. Staining and culture have proved less contributory. Age-old Histopathological evidence may no longer be viewed as a reference standard and needs more evaluation. Small and medium sized hospitals may gradually scale-down the Spine TB processing by AFB stain, and consider establishing on-site molecular infrastructure.

Key words: Spine Tuberculosis, Diagnostic Challange, Clinical Profile.

Correspondence:
Dr. Sushma Krishna
Consultant Microbiologist
Central Laboratory
St. Matha's Hospital, Bangalore
Mobile: 91-9740882970
Email: drsushmakrishna@gmail.com

INTRODUCTION

Skeletal tuberculosis accounts for 10–35% of Extra-Pulmonary Tuberculosis (EPTB) and 3% of all cases of tuberculosis. Spine is involved in about 50% cases of skeletal tuberculosis followed by hip

and knee. Spinal tuberculosis is the destructive form of skeletal TB and is one of the main pathologies seen in spinal and general Orthopaedic units in the developing world. The exact incidence and prevalence of spinal tuberculosis however in many parts of the world are not known as many cases go unreported. In countries with a high burden of pulmonary tuberculosis, the incidence is expected to be proportionately high. Aggravating the problem is raising MDR TB, treatment non-compliance and invasion by HIV. [1-4]

India, with a high burden of global TB, has been steering the Revised National Tuberculosis Control Program (RNTCP)forever three decades with over 14,000 designated microscopy centres and regional, state and national level Reference laboratories providing culture and drug sensitivity test (DST) and molecular diagnostic services. [5,6] While this strategy primarily focuses on Pulmonary TB, the diagnostic care is yet to satisfactorily reach out to EPTB patients. There have been no concrete guidelines for the diagnosis of EPTB or the diagnosis of Spine TB in the developing world. Diagnosis is typically carried out by clinical presentation along with systemic constitutional manifestation, evidence of past exposure to TB or concomitant visceral TB, and neuroimaging modalities like X-ray/CT/MRI. Deep seated infections are likely to be missed out during this diagnosis.

The laboratory diagnosis of Spine TB has for long had remained as supportive with low reliability. Direct smear examination of material by Ziehl–Neelsen (ZN) stain yields a positive result for tubercle bacilli only if the sample contains more than 10,000 bacilli/ml, thus, decreasing the sensitivity. Incidence for conventional (LJ) positive cultures for acid-fast bacilli (AFB) in osteo-articular Tuberculosis lesion has ranged between 40- 88% due to pauci-bacillary load (Masood 1992)[7,8]. However, the newer automated cultures of M. tuberculosis has shown promising results but takes 10-14 days and is carried out only in reference labs under RNTCP and at fewer private laboratories. WHO policy included Xpert MTB/ RIF nucleic acid amplification test for the initial diagnosis of EPTB in 2013. The newer 2016 updated policy conditionally states that Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having EPTB and simultaneously emphasizes the need for microscopy, culture and DST for monitoring treatment. This test has better accuracy than a smear and is performed faster than cultures. At most tertiary care levels, histological evidence such as finding caseating granulomas complements the diagnosis of Spine TB. Despite this advancement in diagnostics, it is not uncommon for the spine specialist to stumble upon negative test, result discrepancies and encounter the diagnostic challenges. The objective of the study was to review the spinal cases of TB and present an overview of the different methods of microbiological diagnosis in patients with Spine TB (with special reference to GeneXpert) at our center.

METHODOLOGY

The study was conducted at St. Martha's Hospital, Bangalore, a hundred-year-old missionary run medium sized tertiary health center with 500 beds, mostly serving below poverty line patients. Retrospective study of the charts of over two years (April 2016-19) of 43 consecutive patients suspected with Spine TB was undertaken and demographic and relevant clinical details were collected. Spine OP and IP clinics at hospital receives about 1000 and 150 patients per year respectively.

Sampling of all 'suspected cases' included spine tissue, pus, abscess fluids and exudates being processed for Acid Fast Smear (ZN stain), culture, Xpert MTB/RIF and HPE. The hospital lodges a RNTCP run DOTS center and AFB diagnostic microscopy is covered as the screen under the Memorandum of Understanding. All the samples were processed with Conventional LJ at our laboratory and positive growth sent to the state reference center for automated cultures (MGIT, Biomeruix) for confirmation. Hospital outsourced GeneXpert molecular proceedings to local accredited laboratory till 2017 and to state reference laboratory from 2017 after the wide spread escalation of XpertMTB/RIF in the country. ATT (Anti Tubercular Therapy) is administered to all definitive cases of Spine TB. The regimen

followed is 2-3 months of HRZE +9-10 months of HR with or without surgery. Treatment extends to 24 months for MDR positive patients. For HIV positive patients, it is ART + 14 months of ATT. Details of surgical intervention (if) carried out were noted. The hospital follows a protocol to follow-up the patients until their cure. The patients were followed up for 6 months after termination of therapy by clinical and radiological evaluation. Cure was defined as no suggestive radiological evidence by the end of 6 months of post ATT. Both the outpatients and inpatients of all age groups were included in the study. Approval of hospital management was obtained with patient's informed consent.

A case of 'Suspect TB' was defined as patient presenting symptomatically with TB or signs suspicious of TB or pyogenic spine on examination at the first encounter. A case of 'probable TB' was defined as patients with clinical and radiologic evidence of inflammation of one or more vertebrae and/or discitis pending microbiologic evidence and/ or histopathological and/or clinical and radiologic response to anti-TB therapy without the laboratory evidence. A case of 'definitive TB' was defined as Microbiologic evidence of least one of the following: -a) isolation of M. tuberculosis in blood/ bone, bone marrow/ deep soft tissues and/or (paravertebral, epidural or psoas) abscess specimens by cultureb) positive microscopy (Ziehl–Nielsen staining) for acid-fast bacilli from bone/ bone marrow/ deep soft tissue and/or (paravertebral, epidural or psoas) abscess or any sterile body tissue; or c) positive PCR for M. tuberculosis complex. D) And/or a Histopathological evidence of caseating granulomas.

As the positive result by PCR was the most recent addition for the microbiological evidence of Spine TB at the hospital, the sensitivity, specificity and predictive values were determined using with the HPE for definite TB as the reference and culture with HPE as composite reference standard. Simple descriptive analysis was carried out to characterise the study population. Categorical data were quoted as proportions with 95% CI.

RESULTS

Of the suspected 42 patients, 26patients of were identified as Definite TB. The mean age was 42 years (14-78 range).The mean duration of symptoms had an average 116 days (1- 6.5 months). Seven patients had pre-existing conditions such as Diabetes, IHD etc. Most patients (over 80%) reported with fever(n=22)and pain (n=17). Neural involvement such as tingling, numbness (n=8), paraplegia (n=4) and kyphosis (n=3) were seen in patients. Nine patients had sputum samples positive by GeneXpert amongst which two were also positive by culture and ZN staining. Only four cases showed pulmonary involvement on chest X-ray. Rest of the results with ESR, CRP and leucocyte counts are tabulated in Table 1.

Table 1: Demographic characteristics, clinical symptoms and laboratory findings of Definite TB patients (n=26) at presentation

Characteristics	**Value**
MeanAge	42(14-78) years
Sex, M/F	13/13
Pulmonary Koch positive*	9
Comorbidities	15
Hypertension/Diabetes/CVD/ IHD/anaemia	12
Chronic smokers/Gutkha chewer	3
Clinical symptoms	
Pain	17
Fever	22
Swelling over the back	3
Neurodeficeits	8
Paraplegia	4
kyphosis	3
Constitutional symptoms	12
Median Laboratory findings (range)	
Leucocyte count ($\times 10^3/\mu l$)	6350 (1450-16430)
Haemoglobin level(g/dl)	12.6 (9-15.1)
ESR(mm/hr)	62 (12-141)
CRP**(mg/dl)	10.3 (0.5-232)

*Pulmonary Koch diagnosed either by ZN stain/ culture or GeneXpertor by combination

**CRP was not done in 5 patients

All the patients were screened for HIV and HBs Ag as per the hospital protocol and were negative. Lumbar and thoracic vertebrae involvement was common (n=6) and 77 % (n=20) had over two vertebral involvement. Eleven patients had disc space involvement (Table 2).

Table 2: Imaging characteristics of Spinal TB (n=26) of definite TB patients	
Location	**n (%)**
Cervical	2
Thoracic	6
Cervico-thoracic	1
Thoracolumbar	3
Lumbar	6
Lumbosacral	3
Cervical, thoracic & Lumbar	3
Sacral	1
Skipped lesion(T, L), SI joint	1
No. of Vertebra involved	
1	4
2	14
3	5
4	1
SI Joint	1
Image findings	
Disc space involvement	11
Disc space involvement with paravertebral/paraspinal abscess	9
Paravertebral/paraspinal abscess only	3
Epidural compression with disc space involvement/abscess/combination	4

All 26 spine samples were negative by ZN staining. Individually, the detection rate by Xpert MTB/RIF was 88.4% (n=22), by HPE was 65.3% (n=17) and by conventional culture was 42% (n=11) respectively. XpertMTB/RIF was 82.3% sensitive and 64% specific when compared with HPE alone and specificity rose up to 81% on comparing with cross HPE and or culture (Table 3).

Table 4: GeneXpert performance at the center for detecting TB				
Reference standard	**Sensitivity % (n)**	**Specificity %(n)**	**PPV % (n)**	**NPV %(n)**
HPE only	82.3 (14/17)	64 (16/25)	61 (14/23)	15.7 (3/19)
HPE and/ or culture	81 (17/21)	81 (17/21)	81 (17/21)	19 (4/21)

Note: Patient negative by all three tests(n=1, by culture, HPE, Xpert TB) is excluded from the analysis. For abscess fluid(n= 3), two patients had undergone curettages/ extractionswhileHPE was taken as negative for analysis purpose for one patient.

Gene Xpert results were available from 72 hours- 7 days, HPE reports by 7 days, while culture results took a median of 30 days. All patients received ATT as per the hospital protocol. Nine patients underwent percutaneous biopsy, while 15patients underwent posterior instrumentation with / without decompression/bone grafting /corpectomy/ cage fixaton/plating with biopsy. Purified protein derivative (PPD) testing and INF-Y assay was not carried out in any patients. Twenty five patients had complete cure with normal MRI and ESR/ CRP levels (previously elevated values) on follow-up after completion of treatment, and implants in situ while one patient expired with multi-organ failure and septic shock. One patient with SI joint involvement grew Multi Drug Resistant (MDR) TB with Rifampicin and low level resistance to INH but achieved complete cure with extended 2nd line ATT with Quinolones and Aminoglycosides for 4 months. The remaining 16 suspected patients were treated with antibiotics for pyogenic spine, one of whom turned out to be a case of 'Probable TB' (negative by smear, culture, molecular diagnosis), but recovered with ATT based on radiological and clinical findings.

Table 3: Samples processed in laboratory by different diagnostic tests						
Total number of patients with suspected Clinical history and/or Radiological changes of TB (Probable TB)	**Pyogenic spinal involvement (Non-TB/ bacterial)**	**MTP positive by any one of the three tests (Definitive TB)**	**MTB detected by ZN stain (microscopy positive)**	**MTB grown in conventional LJ (culture positive)**	**Gen Xpert assay positive (molecular test positive)**	**MTB detected by histopathology (HPE positive)**
42	16	26	0	11	23	17

DISCUSSION

Arriving at the diagnosis of Spine TB poses a challenge to treating clinicians at medium sized health care centers across the country in the absence of a defined protocol. Diagnosis thus gets based on strong clinical and radiological suspicion in TB endemic areas. Until recently, the closest available literature for early detection or decision-making algorithms of spinal tuberculosis was from Association of Physicians of India (API)[9] and from WHO[10].The samples processed at our laboratory showed high smear (zero detection rate) and culture negativity results with poor yield. Result tracing was difficult as samples were initially out sourced for molecular tests at multiple places. In the later days, the results of molecular tests sent to state reference laboratory would take anywhere beyond 72hours to 7 days while the running test time would only take 4-6 hours. There was also a longer time in receiving the automated culture reports from reference center (over a month) sent for confirmation. Peripheral hospitals which submit the samples to the pool of samples at reference laboratories promptly needs to follow up for the results till the end. For chronic diseases such as TB, continuity of care is challenging unless followed up.

The Index TB guidance by the Central Ministry of Health at all levels of health care has been introduced with evidence-informed practices for suspecting, diagnosing and managing various forms of EPTB including Spinal TB making a special mention to molecular tests[11]. Molecular evidence around the use of PCR based tests such as Xpert MTB/RIF in Spinal TB have been used often nowadays despite wide sensitivity and specificity ranges. Literature quotes sensitivity from 61 to 90% and specificity from 80 to 90% for spine TB[12-14]. The observed positive rate of 88% in this study seems satisfactory. Xpert MTB/RIF had its sensitivity and specificity of 81%and the lower-side-value may be attributed to false negatives from culture and HPE- perhaps suggesting that age-old HPE may no longer be viewed as a reference standard. However, Jain AK et al found a PCR positive rate of 98% in osteo-articular samples, smear and culture positivity of 12% but 100% positivity for HPE[15]. This probably indicates that the accuracy of histopathological evidence needs further understanding and more evaluation in the coming years.

Higher sample numbers which would have added weight to the results is noted to be the limitation of the study. Retrospective chart reviews invariably carry some degree of selection bias and we acknowledge the same. Nevertheless, we recommend MTB/RIF assay as the first-line investigation at laboratories for all the Probable TB cases and to gradually scale-down the processing by AFB stain. WHO attests this in Standard for TB care in India and has already set up next generation usage of MTB/RIF ultra assay, it needs to be seen to what extent this will be implemented in EPTB[16, 17].Medium sized laboratories may well start establishing their own molecular infrastructure on site.

Contrary to most literature, Spinal TB was noted to be more in the elderly population in this study(46%were over 50 years) as put forward by the Alavi et al[18].The duration of symptoms (pain and fever predominantly) varied to months as stated by Colmenero JDand colleagues [19]. The non-specific constitutional symptoms were also not predominant as is mostly seen with Spinal TB patients. Multiple vertebral involvements (suggestive haematogenous spread) were seen in over 70% of the patients which again calls for rapid diagnosis and early initiation of therapy. Positive MRI findings in Spine TB are well documented in literature; findings were favorable for diagnosis in this study like other studies [20-23]. As up to 38% (n=10) of the patients in this study had pulmonary involvement, it becomes important for the spine surgeons to screen patients for pulmonary involvement as well to curb the TB transmission rates in the population.

CONCLUSION

Improved and faster case detection was noted by using Xpert MTB/RIF assay than the culture and histopathology tests. We hence recommend the use of the same as the first-line investigation at laboratories for all suspected Spine TB cases and

to gradually scale-down the processing by AFB staining and conventional culture. The results of the study may be used to improve existing Spinal TB diagnostics at medium sized hospitals by assessing the usefulness of the tests in their own set-ups and pickon the most optimal and accurate one. Age-old HPE may no longer be viewed as a reference standard and needs further evaluation.

ACKNOWLEDGEMENT

The authors wish to thank the Good Shepherd Sisters community for their relentless service from decades. The authors also thank the Medical Superintendent Dr. Davy Olakkengil, St. Martha's Hospital for the permission granted for the study.

CONFLICT OF INTEREST

None

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DOI https://doi.org/10.3126/saarctb.v18i1.34128

FACTORS ASSOCIATED WITH TREATMENT ADHERENCE AMONG TUBERCULOSIS PATIENTS IN GANDAKI PROVINCE OF NEPAL

Yadav RK[1,2], Kaphle HP[1], Yadav DK[1], Gurung SC[3], Khatri E[4], Baral S[5,6]

[1] School of Health and Allied Sciences, Pokhara University
[2] M&E Officer (WHP –V), Aasaman, Nepal
[3] Birat Nepal Medical Trust (BNMT Nepal), Liverpool School of Tropical Medicine, Department of Clinical Sciences, UK
[4] School of Public Health, Patan Academy of Health Sciences
[5] Manmohan Memorial Institute of Health Sciences, Tribhuvan University
[6] Health Research Together Initiative (HeaRT: Initiative), Kathmandu

ABSTRACT

Introduction: Poor adherence to the treatment regimen is a major cause of treatment failure and the emergence of drug resistance among TB patients. The emergence of resistance to anti-tuberculosis drugs and particularly of multi-drug resistance (MDR), Pre-extensively drug resistance tuberculosis (Pre-XDR) and extensively drug resistance (XDR) tuberculosis have become a major public health problem in several countries and an obstacle to effective global TB control.

Methodology: This research was health facility based cross-sectional study and carried out among TB patients registered under DOTS and receiving treatment more than or equal to 60 days from health facilities of Gandaki province of Nepal. Structured interview schedule and validated questionnaires were used for data collection. Treatment Adherence was assessed by using Nepali version of Morisky medication adherence scale (MMAS-8) questionnaires. Data were entered in Epi-data software and analysis was performed with the help of the Statistical Package for Social Science (SPSS). The odds ratio with a 95% CI was calculated and a P-value of <0.05 was considered as cut off for statistical significance.

Results: A total 180 TB patients were participated in this study. The overall prevalence of treatment adherence among tuberculosis participants was 79.4%. Participants who haven't living with co-morbidities were more than four times more likely to adhere with medicine compared to participants who had living with co-morbidities. Similarly, who had friendly relationship with health workers were more than forty six and half times likely to adhere to medicine with compared to participants who had unfriendly relationship with health workers.

Conclusion: The supportive factors for treatment adherence among Tuberculosis patients were socio-economic factors (Hilly region, hindu religion, nuclear family, literate), life style related factors (no prior alcohol consumption, not habit smokeless tobacco previously), diseases related factors (delay of confirming TB diagnosis, Not experienced side effects, aware about TB symptoms, no co-infection) and accessibility to health care facilities related factors (confirm TB diagnosis cost, favourable time for DOTS centre, health workers supervision during the medication, friendly relationship with health workers, know about the length of the treatment, TB status disclose).

Key words: Treatment Adherence, Tuberculosis, Nepal

Correspondence:
Mr. Rajesh Kumar Yadav
MPH Scholar
School of Health and Allied Sciences, Pokhara University
Pokhara, Nepal
Mobile No.: 9846421643
Email: rky0013@gmail.com

INTRODUCTION

Tuberculosis is one of the most prevalent infectious diseases and a significant public health problem in Nepal as well as global and continues to pose

a serious threat to the health of the population and development of the country. TB is the largest killer among communicable diseases in the 15 to 49 years age group when humans are the most economically active period of life[1]According to the World Health Organization treatment adherence is defined as "the degree to which the person's behavior corresponds with the agreed recommendations from a health care provider." Adherence to tuberculosis medication is very important for improving the quality of life and preventing complications of the disease [2].

Tuberculosis treatment involves taking medications daily for months to years, depending on the level of TB treatment, and failure to complete therapy as prescribed can lead to poor outcomes, including increased risk of failure, disease relapse, continued transmission, development of drug resistance, and death [3]. Several factors as competing causes of patients' non-adherence to TB treatment are socio-economic factors like poor socio-economic status, Sex, occupation and ethnicity, lack of social support[4–8]eastern People's Republic of China, in order to provide scientific evidence for improving the follow-up rate and treatment completion rate., Methods: A total of 262 PTB patients in six counties (districts. Poor treatment adherence of TB patients threatens the well being of an individual and society, defaulting from treatment may increase the risk of drug resistance, relapse, and death, and may prolong infectiousness.[9,10]

Patient's adherence to their medications is a critical and important factor to prevent serious undesirable complications and to reduce the health care resource utilization. Poor adherence to medications is a major public health challenge. Improving adherence could be an important potential source of health and economic improvement, from the societal, institutional and employer's point of view.

TB patients have difficulty in following a long-term treatment regimen. Efforts to improve treatment outcomes require a better understanding of adherence as a complex behavioral issue and the particular barriers to and facilitators of patient adherence. Direct observation and a regular home visit by health workers appear to reduce the risk of non-adherence [8]

Non adherence to medication almost triples the risk of developing multidrug resistance and drug resistance tuberculosis. Nepal Government has set the goal to eliminate TB as a public health problem (<1 case per million population) by 2050. Multidrug resistance and drug resistance TB, a chronic disease that is increasing globally, is associated with higher risks of Drug resistance TB and adverse TB treatment outcomes. This study was conducted with objective todetermine the factors associated with treatment adherence among tuberculosis patients in Gandaki Province of Nepal.

METHODOLOGY

The study design was health facility based cross-sectional study done among the tuberculosis patients.

Sample Size was calulated as Success rate of tuberculosis was 89% (National Tuberculosis Centre, 2019) [1] along with design effect (1.19). The sample size was determined by using the formula

$$n = \frac{z^2 pq}{d^2}$$

Where:

n = Desired sample size
z = Standard normal deviate, usually set at 1.96 which corresponds to 95% confidence level
p = 0.89
q= 1-p (1-0.89) = 0.11
d = Permitted error (5%, if the confidence level is 95%); 0.05

Therefore no = $\frac{1.96^2 0.89 * 0.11}{0.05^2}$= 150.44≈151

Design effect for cluster sampling ≈ 151*1.19 = 179.69 ≈180

A total required number of participants were 180, which was obtained from twenty two DOTS centre.

The following steps were followed for the selection of DOTS centres and TB patients in selected districts. The sample was selected by cluster sampling method. First stage: Three districts of Gandaki Province were selected for the study which included two districts from hilly region and the remaining districts from Terai region. Kaski and Tanahun were selected among the districts of hilly

region as they had the highest load of tuberculosis patients. Nawalparasi East was selected being the only district in the province representing Terai region. Second stage: Among 160 DOTS Centres in three selected districts, 22 DOTS centres were randomly selected as: Kaski (8), Nawalparasi (5) and Tanahun (9) district based on the TB cases load. Third stage: Required sample size was determined based on Probability Proportional to Size (PPS) of total TB cases from selected DOTS Centres. Fourth stage: TB patients to be interviewed were selected randomly from the sampling frame.

The study population were all the TB Patients who are under medication from DOTS centers of selected Districts of Gandaki Province of Nepal.

All the TB patients registered under DOTS therapy and completed 60 days under DOTS medication in the selected districts of Gandaki province and aged 15 years and above were considered as the study participants. Those TB patients from selected DOTS centre who were not present at the time of data collection, who were voluntarily disagree to participate in study and those with mentally severely ill and deafness were excluded from study.

Study method was quantitative. Semi structured questionnaire was used for collecting primary data through face to face interview with dropout and continuous users.

Data was collected from the TB patients using interview schedule in Nepali version at one point in time for each of the patients. A schedule was divided into three sections. The first section was included the socio-demographic characteristics and disease related information. The second section was focus on treatment adherence using Morisky Scale questionnaire. The third section was focus on the treatment adherence and its associated factors and lifestyle related behavior of participants.

Data was collected by face to face interview method with the help of the interview schedule. Data was gathered in the prescribed format on the socio-demographic characteristics, disease condition behavioral and other factors associated with treatment adherence.

Participants' response was closely recorded into the tool. Data was entered in Epi Data software and analysis was performed with the help of the Statistical Package for Social Science (SPSS). Univariate analysis was computed to describe socio-demographic profile of participants and pattern of TB treatment adherence, while mean, standard deviation, Median and Interquartile Range (IQR) was calculate for continuous variables. Bivariate Logistic regression, chi-square and fisher exact were performed for testing the existing significant association between TB medication (adherence and non adherence) and selected independent variables. Multivariate logistic regression model was carried out to identify the most independent and treatment adherence factors related. The odds ratio and 95% CI was reported while showing the association between outcome treatment adherence and independent variables. This results were considered significant at 5% level i.e. p value (<0.05).

Approval was obtained from School of Health and Allied Sciences and ethical approval was obtained from the Nepal Research Council (NHRC). Administrative permission obtained from the Ministry of social development of Gandaki Province, Province health directorate office, Health office Kaski, Health office Tanahun and Health office Nawalparasi East of Gandaki Province. Participants were fully informed regarding study objectives and written consent was obtained prior to the initiation of the data collection. Informed consent was taken from participants whose age was equal and more than 18 years, but for those less than 18 years of age consent was also taken from their guardian.

RESULTS

A total 180 TB patients were participated in this study. Table 1 shows two -fifth (39.4%) of the participants were from kaski district. More than half of participants were 15-40 years of age. Majority (65.0%) of participants were male. Majority (84.4%) of participants were from urban area and more than half (52.8%) of the participants belong to nuclear family. Higher education was quite low (8.3%). One-fourth (26.7%) of the participants were currently unemployed while majority (73.3%) of them was employed whereas (14.4%) were engaged in agriculture and (1.7%) government job.

Table 1:Socio-demographic Characteristics of the Participants		
Characteristics	**Frequency**	**Percentage**
District		
Kaski	71	39.4
Tanahun	52	28.9
Nawalparasi East	57	31.7
Age		
15-40 Year	94	52.2
41-64 Years	68	37.8
>65 Years	18	10.0
Median= 38.50,Interquartile Range(IQR)=28 Min=16, Max=95		
Sex		
Male	117	65.0
Female	63	35.0
Religion		
Hinduism	149	82.8
Buddhism	25	13.9
Christianity	5	2.8
Islam	1	0.6
Ethnicity		
Dalit	40	22.2
Disadvantaged Non Dalit Terai Caste	3	1.7
Disadvantaged Janjati	48	26.7
Religious Minorities	3	1.7
Upper Caste Groups	45	25.0
Relatively Advantaged Janajati	41	22.8
Marital Status		
Single	39	21.7
Married	129	71.7
Divorced	1	0.6
Widowed	11	6.1
Permanent Residence		
Urban	152	84.4
Rural	28	15.6
Family Type		
Nuclear	95	52.8
Joint	85	47.2
Educational Status		
Illiterate	23	12.8
Non Formal Education	30	16.7
Basic Education (1-8class)	56	31.1
Secondary Education (9-12 class)	56	31.1
Higher Education (Completion of Bachelor or Above)	15	8.3
Occupation		
Unemployed	48	26.7
Agriculture	26	14.4
House Keeper	22	12.2

Business	22	12.2
Labor	21	11.7
Students	18	10.0
Private Employee	10	5.6
Others (Driver, Abroad & Retirement)	10	5.6
Government Job	3	1.7

Table 2 shows that More than three-fourth (86.7%) respondents didn't forget to take the medicine, almost all (94.4%) didn't stop taking the medicine even they feel the symptoms are under control, about third-fifth (59.4%) respondents don't ever hassle on sticking to treatment plan, majority of respondents (76.1%) don't have difficulty in remembering to take all medicines.

Table 2:Frequencies of item Responses to Treatment Adherence Questionnaire

Indicators	Yes, n (%)	No, n (%)
Do you sometimes forget to take your medicine?	24 (13.3)	156 (86.7)
People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine?	10 (5.6)	170 (94.4)
Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	9 (5.0)	171 (95.0)
When you travel or leave home, do you sometimes forget to bring along your medicine?	35 (19.4)	145 (80.6)
Did you take all your medicines yesterday? (Yes=0; No=1)	172 (95.6)	8 (4.4)
When you feel like your symptoms are under control, do you sometimes stop taking your medicine?	30 (16.7)	150 (83.3)
Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	73 (40.6)	107 (59.4)
How often do you have difficulty remembering to take all your medicine?	43 (23.9)	137 (76.1)

Catagorization of Morisky Medication Adherence Scale (MMAS-8)

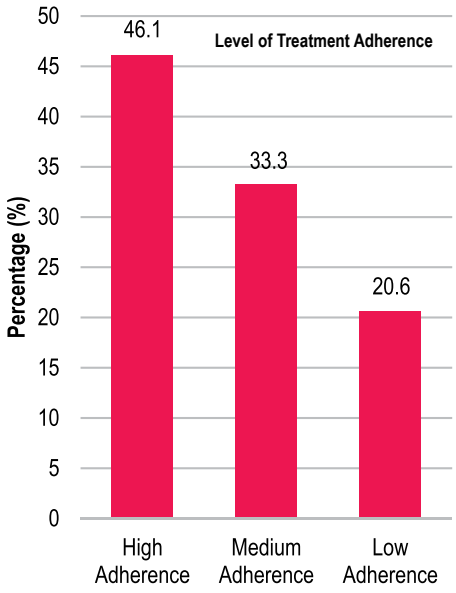

Figure 1 shows the eight item Morisky medication adherence scale (MMAS-8) was used to assess the prevalence of medication adherence among tuberculosis participants. The adherence rate among participants was high adherence 56.1%, Medium adherence 33.3% and 20.6% low adherence. For the bi-variate and mutli-variable analysis, the higher adherence and medium adherence were merged and categorized as adherence 79.4% and non-adherence 20.6%.

Table 3 shows that Hilly region participants were nearly three times (p= 0.005, UOR-2.917, CI=1.386-6.137) more likely to adhere to medicines when compared to Terai region participants. Participants belongs to Hindi religion were more than two and half times (p=0.027, UOR-2.602, CI=1.114-6.080) more likely to adhere with medication than belongs non-hindu religion (Buddhism, Christianity and Islam). Participants living in nuclear family were nearly four times (p<0.001, UOR-3.957, CI=1.780-8.794) likely to adhere with medication than joint family. Literate were more than four and half times (p<0.001, UOR-4.619, CI=1.841-11.589) more likely to adhere to medication with compare to illiterate participants.

Table 3: Association of Socio-demographic Characteristics of Participants with Treatment Adherence					
Characteristics	**Treatment Adherence**		**P-value**	**UOR**	**95%CI**
	No n (%)	**Yes n (%)**			
Ecological Region					
Terai	19 (33.3%)	38 (66.7%)	0.005**	1	Ref
Hilly	18 (14.6%)	105 (85.4%)		2.917	1.386-6.137
Level of Treatment Facilities					
District Hospital	14 (25.0%)	42 (75.0%)	0.089	1	Ref
PHC	7 (33.3%)	14 (66.7%)		0.667	0.224-1.984
HP	12 (25.0%)	36 (75.0%)		1.000	0.411-1.984
UHC	3 (7.9%)	35 (92.1%)		3.889	1.033-14.633
Private Health Institution	1 (5.9%)	16 (94.1%)		5.333	0.647-43.942
Age					
≥65 Years	7 (38.9%)	11 (61.1%)	0.061	1	Ref
15-40 Years	14 914.9%)	80 (85.1%)		3.636	1.205-10.976
40-65 Years	16 (23.5%)	52 (76.5%)		2.068	0.688-6.219
Sex					
Male	28 (23.9%)	89 (76.1%)	0.131	1	Ref
Female	9 (14.3%)	54 (85.7%)		1.888	0.828-4.301
Religion					
Non-Hindu	11 (35.5%)	20 (64.5%)	0.027*	1	Ref
Hindu	26 (17.4%)	123 (82.6%)		2.602	1.114-6.080
Ethnicity					
Others Caste	31 (20.6%)	104 (77.0%)	0.172	1	Ref
Upper Caste	6 (13.3%)	39 (86.7%)		1.937	0.750-5.002
Marital Status					
Married	32 (22.7%)	109 (77.3%)	0.183	1	Ref
Unmarried	5 (12.8%)	34 (87.2%)		1.996	0.721-5.526
Residence					
Rural	9 (32.1%)	19 (67.9%)	0.104	1	Ref
Urban	28 (18.4%)	124 (81.6%)		2.098	0.859-5.123
Family Type					
Joint	27 (31.8%)	58 (68.2%)	<0.001**	1	Ref
Nuclear	10 (10.5%)	85 (89.5%)		3.957	1.780-8.794
Educational Status					
Illiterate	11 (47.8%)	12 (52.2%)	<0.001**	1	Ref
Literate	26 (16.6%)	131 (83.4%)		4.619	1.841-11.589
Occupation					
Unemployment/Students	22 (33.3%)	44 (66.7%)	0.056	1	Ref
Agriculture	5 (19.2%)	21 (80.8%)		2.100	0.698-6.318
Daily wages/Labor	2 (11.1%)	24 (88.9%)		4.000	1.085-14.748
Business	4 (18.2%)	18 (81.8%)		2.250	0.679-7.457
Service (Private/Government)	2 (11.8%)	15 (88.2%)		3.750	0.787-17.875
House Keeper	1 (4.5%)	21 (95.5%)		10.500	1.325-83.239

Table 4 showed that participants who had not consumed alcohol prior were more than three and half times (p=0.003, UOR-3.529, CI=1.555-8.010) more likely to adhere to medicines with compared to participants who had consumed prior of alcohol. Participants who had not habit of smokeless tobacco previously were more than two and half times (p=0.007, UOR-2.833, CI=1.332-6.02) more likely to adhere to medicine with compared to participants who had consumed smokeless tobacco previously. Participants who had not currently consumed smokeless tobacco were more than four and half times (p=0.004, UOR-4.655, CI=1.615-13.422) more likely to adhere to medicine with compare to participants who had currently consumed smokeless tobacco. Participants who had not family history of TB were more than two times (p=0.0237, UOR-2.327, CI=1.052-5.150) more likely to adhere to medicine with compared to participants who had family history of TB.

Table 4: Association of Life Style Related Factors of Participants with Treatment Adherence

Characteristics	Treatment Adherence		P-value	UOR	95%CI
	No n (%)	Yes n (%)			
History of Alcohol Consumption					
Yes	28 (29.5%)	67 (70.5%)	0.003**	1	Ref
No	9 (10.6%)	76 (89.4%)		3.529	1.555-8.010
Current of Alcohol					
Yes	3 (37.5%)	5 (62.5%)	0.238	1	Ref
No	34 (19.8%)	138 (80.2%)		0.411	0.093-1.803
History of Smoking					
Yes	17 (21.8%)	61 (78.2%)	0.719	1	Ref
No	20 (19.6%)	82 (80.4%)		1.143	0.553-2.363
Current of Smoking					
Yes	2 (18.2%)	9 (81.8%)	0.841	1	Ref
No	35 (20.7%)	134 (79.3%)		0.851	0.176-4.117
History of Smokeless Tobacco					
Yes	17 (34.0%)	33 (66.0%)	0.007**	1	Ref
No	20 (15.4%)	110 (84.6%)		2.833	1.332-6.026
Current of Smokeless Tobacco					
Yes	8 (50.0%)	8 (50.0%)	0.004**	1	Ref
No	29 (17.7%)	135 (82.3%)		4.655	1.615-13.422
History of Alcohol and Smoking					
Yes	27 (27.6%)	71 (72.4%)	0.013*	1	Ref
No	10 (12.2%)	72 (87.8%)		2.738	1.235-6.070
Family History of TB					
Yes	13 (32.5%)	27 (67.5%)	0.037*	1	Ref
No	24 (17.1%)	116 (82.9%)		2.327	1.052-5.150

Table 5 showed that participants in whom time taken to confirm TB diagnosis was more than one month, were more than three times (p=0.004, UOR-3.218, CI=1.467-7.059) more likely to adhere with medicine compared to participants who had taken less than one month duration to confirm TB diagnosis. Participants who were in continuous phase of treatment were more than four times (p=U0.050, OR-4.212, CI=1.001-17.724) more likely to adhere with medicine compared to participants who had intensive phase of treatment. Participants who had not experience of side effects of the TB medicine were more than five times (p<0.001, UOR-5.010, CI=2.304-10.893)

Table 5: Association of Diseases Related Factors of Participants with Treatment Adherence					
Characteristics	**Treatment Adherence**		**P-value**	**UOR**	**95%CI**
	No n (%)	**Yes n (%)**			
Type of TB					
Pulmonary	30 (23.1%)	100 (76.9%)	0.182	1	Ref
Extra Pulmonary	7 (14.0%)	43 (86.0%)		1.843	0.752-4.519
Duration of Confirm TB Diagnosis					
<1Months, Early Diagnosis	15 (37.5%)	25 (62.5%)	0.004**	1	Ref
>1 Months, Delay Diagnosis	22 (15.7%)	118 (84.3%)		3.218	1.467-7.059
Phase of Treatment					
Intensive Phase	4 (50.0%)	4 (50.0%)	0.050*	1	Ref
Continuous Phase	33 (19.2%)	139 (80.8%)		4.212	1.001-17.724
Experience of Side Effects					
Yes	25 (37.3%)	42 (62.7%)	<0.001**	1	Ref
No	12 (20.6%)	101 (89.4%)		5.010	2.304-10.893
Know about the Symptoms of TB					
No	17 (34.0%)	33 (66.0%)	0.007**	1	Ref
Yes	20 (15.4%)	110 (84.6%)		2.833	1.332-6.026
Taking drugs other than TB medication					
Yes	18 (40.0%)	27 (60.0%)	<0.001**	1	Ref
No	19 (14.1%)	116 (85.9%)		4.070	1.887-8.780
Contact with any TB patients					
No Contact	28 (20.1%)	111 (79.9%)	0.801	1	Ref
TB Patients	9 (22.0%)	32 (78.0%)		1.115	0.478-2.603
Ever Received TB Treatment					
Yes	5 (20.8%)	19 (79.2%)	0.971	1	Ref
No	32 (20.6%)	124 (79.5%)		0.981	0.340-2.828

more likely to adhere with medicine compared to participants who had experienced of side effects of the TB medicine. Participants who had aware about symptoms of TB were more than two and half times (p=0.007, UOR-2.833, CI=1.332-6.026) more likely to adhere with medicine compared to participants who had not aware about the symptoms of TB. Participants who haven't living with co-morbidities were more than four times (p<0.001, UOR-4.070, CI=1.887-8.780) more likely to adhere with medicine compared to participants who had living with co-morbidities.

Table 6 showed that participants who had spend money for diagnosis of TB NRs 5001 and NRs 15000 where more than five times (p=0.017, UOR-2.630, CI=1.096-6.315) more likely to adhere to medicine with compared to participants who had spend money for diagnosis of TB less than NRs5000. Participants who had time favourable with the preferable time of medication were more than thirteen and half times (p<0.001, UOR-13.732, CI=5.908-31.917) more likely to adhere with medicine compared to participants who had not time favourable with the preferable time of medication. Participants who had waiting time at health facility less than 10 minutes were more than two and half times (p=0.027, UOR-2.602, CI=1.114-6.080) more likely to adhere to medicine when compared to participants who had waiting time at health facility more than 10 minutes. Participants who had supervised by health workers at time of medication were more than two and half times (p=0.009, UOR-2.708, CI=1.285-5.706)

more likely to adhere to medicine with compared to participants who had not supervised by health workers at time of medicine. Participants who had friendly relationship with health workers were more than forty six and half times (p<0.001, UOR-46.667, CI=10.712-203.311) times likely to adhere to medicine with compared to participants who had unfriendly relationship with health workers. Participants who had not fear of stigma and discrimination were more than eight times (p<0.001, UOR-8.190, CI=3.680-18.226) more likely to adhere to medicine with compared to participants who had fear stigma and discrimination.

Table 6: Association of Accessibility to Health Care Facilities of participants with Treatment Adherence

Characteristics	Treatment Adherence		P-value	UOR	95%CI
	No n (%)	Yes n (%)			
Traveling Time (Minute)					
≥30	33 (21.0%)	124 (79.0%)	0.688	1	Ref
<30	4 (17.4%)	19 (82.6%)		1.264	0.402-3.971
Use of Transportation					
No	16 (21.1%)	60 (78.9%)	0.888	1	Ref
Yes	21 (20.2%)	83 (79.8%)		1.054	0.508-2.188
Pay for Transportation					
Yes	20 (20.6%)	77 (79.4%)	0.982	1	Ref
No	17 (20.5%)	66 (79.5%)		1.008	0.480-2.048
Money Spend for Diagnosis of TB					
Yes	33 (22.1%)	116 (77.9%)	0.253	1	Ref
No	4 (12.9%)	27 (87.1%)		1.920	0.627-5.879
Confirm Diagnosis Cost (NRs)					
<5000	14 (38.9%)	22 (61.1%)	0.017*	1	Ref
5001-15000	4 (11.1%)	32 (88.9%)		5.091	1.487-17.534
≥15000	15 (19.5%)	62 (80.5%)		2.630	1.096-6.315
Preferable time for DOTS Centre					
1:00-5:00 PM	6 (26.1%)	17 (73.9%)	0.181	1	Ref
10:00-12:00 AM	30 (22.4%)	104 (77.6%)		1.224	0.852-3.378
Time Favourable	1 (4.3%)	22 (95.7%)		7.765	0.852-70.752
Is that time Favourable					
No	26 (55.3%)	21 (44.7%)	<0.001**	1	Ref
Yes	11 (8.3%)	122 (91.7%)		13.732	5.908-31.917
Waiting time at health facility (Minute)					
≥10	11 (35.5%)	20 (54.5%)	0.027*	1	Ref
<10	26 (17.4%)	123 (82.6%)		2.602	1.114-6.080
Supervision during the time of medication					
Self					
Yes	19 (50.0%)	19 (50.0%)	<0.001**	1	Ref
No	18 (12.7%)	124 (87.3%)		6.889	3.079-15.415
Family Members					

Yes	16 (23.9%)	51 (76.1%)	0.396	1	Ref
No	21 (18.6%)	92 (81.4%)		0.728	0.349-1.517
Health Worker					
No	23 (29.9%)	54 (70.1%)	0.009**	1	Ref
Yes	14 (13.6%)	89 (86.4%)		2.708	1.285-5.706
FCHV					
Yes	3 (37.5%)	5 (62.5%)	0.396	1	Ref
No	34 (19.8%)	138 (80.2%)		0.728	0.349-1.517
Relationship with health workers					
Unfriendly	35 (47.3%)	39 (52.7%)	<0.001**	1	Ref
Friendly	1 (1.9%)	104 (98.1%)		46.667	10.712-203.311
Knowledge about the length of the treatment					
Don't Know	10 (62.5%)	6 (37.5%)	0.002**	1	Ref
When Feeling Better	2 (18.2%)	9 (81.8%)		7.500	1.196-47.049
6 Months	21 (15.9%)	111 (84.1%)		8.810	2.890-26.850
>6 Months	4 (19.0%)	17 (81.0%)		7.083	1.601-31.331
TB Status Disclosure					
No	25 (46.3%)	29 (53.7%)	<0.001**	1	Ref
Yes	12 (9.5%)	114 (90.5%)		8.190	3.680-18.226

Table 7 shows adjusted odds of having medication adherence TB patients was showed that participants who haven't living with co-morbidities more than thirty eight times (p 0.024, AOR-38.176, CI=2.077-308.571) more likely to adhere with medicine compared to participants who had living with co-morbidities. Participants who had time fevorable with the preferable time of medication were more than fifty four and half times (p0.023, AOR-54.454, CI=2.483-2477.147) more likely to adhere with medicine compared to participants who had not time fevorable with the preferable time of medication. Participants who had friendly relationship with health workers were nearly sixty two times (p0.030, AOR-61.873, CI=1.479-2588.423) times likely to adhere to medicine with compared to participants who had unfriendly relationship with health workers.

Table 7: Adjusted relationship of explanatory variables with Treatment Adherence

Characteristics	Treatment Adherence		P-value	AOR	95%CI
	No n (%)	Yes n (%)			
Co-Infection (Taking drugs other than TB)					
Yes	18 (40.0%)	27 (60.0%)	0.024*	1	Ref
No	19 (14.1%)	116 (85.9%)		38.176	2.077-308.571
Time Favourable for DOTS					
No	26 (55.3%)	21 (44.7%)	0.023*	1	Ref
Yes	11 (8.3%)	122 (91.7%)		54.454	2.483-2477.147
Relationship with health workers					
Unfriendly	35 (47.3%)	39 (52.7%)	0.030*	1	Ref
Friendly	1 (1.9%)	104 (98.1%)		61.873	1.479-2588.423

DISCUSSION

The eight item Morisky medication adherence scale (MMAS-8) was used to assess the prevalence of treatment adherence among tuberculosis participants. More than third-fourth (79.4%) of participants adhered to medication whereas one-fifth (20.6%) of participants were not adhere to medication.

Effective treatment adherence is the main intervention to prevent the spread of drug-resistant tuberculosis, other co-infection and improved quality of life. The present study revealed that the overall prevalence of treatment adherence among tuberculosis patients was 79.4% which is similar to a national TB prevalence survey, Nepal, and others similar study conducted in Ethiopia Lady of apostle hospital from Ethiopia [11–14]. Some individual characteristics such as a good relationship with DOTS focal persons, favourable time for TB medicine taken at the DOTS centre and without any co-infection TB patients were factors influencing adherence to medication.

The present study revealed that participants who were literate, unmarried and living in urban population were more likely to adhere with medication which contrasts with the study conducted in china which shows that patients who had higher education, married and permanent residents were more likely to be adherence to medication[8]. The reason behind it may be that unmarried participants were free from family responsibility so they have easy access to medication and in context of resident, participants living in urban areas can easily reached to DOTS centre for their medication.

In this research age, sex, marital status and occupational weren't significantly associated with treatment adherence. Very similar results were highlighted in the study done in Nigeria, Zambia, Ehrabor and Metropolitan area of Buenos Aires, Argentina which shows age, sex, marital status and occupation weren't significantly associated with treatment adherence[14–16] .This study showed statistical significant relationship of religion with treatment adherence but not with ethnicity which is in contrast with the findings from study done in Zambia, Nigeria and Ehrabor which showed both ethnicity and religion as related factors. The possible reason that separate ethnic group has separate medical practices in Nepalese society. They do have different religious belief[14].

A cross sectional study done in Palpa district of Nepal indicated that age and family income were significantly associated with compliance with tuberculosis medicine[17]. However, finding of this research shows that both weren't statistically associated. The possible reason for this might be due to the differences in the tool used in the study.

Very low adherence was shown by study participants having alcohol habit, tobacco consumption with treatment adherence. This was similarly observed in other studies where lifestyles behaviour such as alcohol and tobacco consumption were well-known risk factors for non-adherence[14,18,19]. Those TB patients who don't consume alcohol have good communication with health services providers and also found to be effectively adhered to their treatment regimen.

Another important finding of this study suggests that experience of drug side effects, knowledge of TB symptoms and co-infection were factors affecting the adherence to treatment rate. The possible reason was experience of drugs side effect made some of them believe that the treatment was worsening their condition and so few TB patients stop taking their medication when they encounter adverse drugs side effects such as urine discolorations, vomiting and nausea, etc., which is dependable with several previous studies[4,6,20–22]. Systematic review research had also reported the relationship between treatment cost and adherence rate of medication of TB patients[23].

The present study found that TB patients had stopped the medication for the few days due to drug side effects which had decrease the adherence rate. The participants who didn't experience any drug side effects were five times highly adhere to medication than the participants who had experience drugs side effects.

This study revealed that those who had known about TB symptoms were nearly 3 times highly adhered to medication than those who were not aware of TB symptoms. Study done by Das et al. reported that participants who had correct knowledge of the TB symptoms were 13.31 times more likely to adhered to TB treatment[24]. In the

adjusted analysis, those TB patients who did not take additional drugs other than TB treatment were significantly associated with adherence to medication than those who had taken additional drugs other than TB treatment. However, a study conducted in Northwest, Ethiopia reported that those TB patients who had taken additional drugs other than anti-TB were 2.67 times more likely to non-adhere to TB treatment[25].

According to the research conducted in Kathmandu, Nepal; National tuberculosis program Nepal 2011 report and Ethiopia which shows that majority of respondents were male and suffered from Extra Pulmonary Tuberculosis whereas the present research also shows that majority of respondents were also male but the majority of respondents were suffered from pulmonary tuberculosis. It might be due to the correctional health facilities and present at a time of data collection[26,27].

Xu et al study reported that 16% of non-adherence patients interrupted treatment because of the high medical cost of the treatment[8] whereas the present study revealed that low TB investigation charge was one of the key factor to be associated with adherence to medication than patients having high TB investigation cost. Free TB service policy was formulated with the aim to decrease the financial burden on patients and promote to TB treatment adherence which isn't properly implemented[8,23].

In this study no statistical significance was observed between distance and mode of transportation. However, waiting time at DOTS centre was found statistically significant. The TB patients waiting for less than 10 minutes were 2.602 times more likely to adhere to medication than those who had waited greater or equal to 10 minutes. This finding is supported by the study done in southern Ethiopia, where the patients who waited in health facility less than or equal to 30 min before getting service were 2.53 times more likely to adhere to tuberculosis medicine [21,28].

In the adjusted analysis, patients relationship with health care provider is significantly associated with adherence. This indicates a good relationship with health provider had a positive outcome on adherence to medication. This is similar to the finding of the study done in different places of Ethiopia and eastern Nepal, where good patients service providers relationship was on important reasons for adherence to medication [12,27–30]. A good patient -provider relationship might help TB patients to share the adverse effect of medicine, course of medications etc to the DOTS services provider, but if health professionals do not express good behaviour, the patients might think that their health condition is getting worsen and feel hopeless and interrupt the TB medications[12].

Gebreweld FH et al, 2018, reported that stigma was an evident factor and main obstacle for adherence to TB medication[20]. This study shows that those TB patients who had shared the TB status to other members such as family members and friends had 8.190 times more adhered to medicine than those TB patients who had not disclosed to another person.

The present study revealed that TB patients who had good knowledge of the duration of TB medication were 8.810 times higher chances to adhere to medication than those who don't have proper knowledge about the duration of treatment. A similar study conducted in India shows correct knowledge on the duration of treatment was significantly associated with adherence to TB medication [22,31].

CONCLUSION

The adherence rate among participants was high adherence 56.1%, Medium adherence 33.3% and 20.6% low adherence. The associated factors with adherence was socio-economic factors (Hilly region, hindu religion, nuclear family, literate), life style related factors (not prior of alcohol consumption, not habit smokeless tobacco previously), diseases related factors (delay confirm TB diagnosis, Not experienced of side effects, aware about TB symptoms, haven't co-infection) and accessibility to health care facilities related factors (confirm TB diagnosis cost, favourable time for DOTS centre, health workers supervision during the medication, friendly relationship with health workers, know about the length of the treatment, TB status disclose). This concludes that socio-economic, diseases related factors and health service related factors play more influence rather than other factors that determine TB medication. This study shows that non adherence rate of the participants was three in ten in selected districts of Gandaki province.

Especial emphasis should be given to TB patients with co-infection. Adequate counselling should be provided in order to maintain the treatment adherence and quality of life. Health care provider should behave friendly with TB patients to ensure the treatment adherence. Also health care providers should provide complete information about duration of treatment and side effect of medicine to TB patients so that they can decide towards treatment adherence and ensure their quality of life.

ACKNOWLEDGEMENT

We are greatly thankful to School of Health and Allied Sciences, Pokhara University for providing me opportunity to carry out this research, we are express special thanks Nepal Health Research Council (NHRC) for providing us with the research grant and gratefully acknowledges Ethical Review Board, Nepal Health Research Council for the ethical clearance. We are indebted Ministry of Social Development, Provincial Health Directorate Office, Gandaki Province. Health Office Kaski, Health Office Tanahun and Health Office East-Nawalparasi, and all the DOTS centers that were given the permission to initiate this study and collect necessary data from participants. We are thankful to the participants who participated in the study without which the study would not have been possible.

CONFLICT OF INTEREST

None

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DOI https://doi.org/10.3126/saarctb.v18i1.34132

INTERVENTION STRATEGIES TO MITIGATE PSYCHOSOCIAL CHALLENGES AND IMPROVE THE QUALITY OF LIFE OF MDR-TB PATIENTS – AN EVALUATION STUDY

Thiruvalluvan E[1], Sellappan S[1], Watson B[2], Muniyandi M[3]

[1] DSBR, ICMR-National Institute for Research in Tuberculosis (NIRT), Govt Rajaji Hospital, Madurai, India
[2] Department of Statistics (Epid), ICMR-National Institute for Research in Tuberculosis (NIRT), Chennai, India
[3] Department of Health Economics, ICMR-National Institute for Research in Tuberculosis (NIRT), Chennai, India

ABSTRACT

Introduction: The psychosocial well-being and treatment outcome in MDR-TB is far undesirable as the treatment is characterized by a rigorous treatment regimen for a long duration, adverse side effects, lower cure rate, and high treatment costs. This study aimed to devise an intervention strategy and test its feasibility and effectiveness to ensure the patients' quality of life (QOL) and to promote adherence.

Methodology: The study population included all MDR-TB patients, of age 18 years and above registered in 16 tuberculosis units (TUs) under Chennai Corporation for treatment during the year 2014. Researchers have devised an intervention strategy package that included motivational interview (MI) module, counseling support as well as nutritional support. Participants were included in the study after getting informed consent. Motivational interviewing was offered at five times during the study period. Each participant received minimum 15 individual counselling sessions. All participants but two received nutritional flour packet weighing half kilogram every month.

Results: Of 35 participants enrolled in the study, one third was women. Poor QOL was experienced by 19 participants out of 35 at the start of treatment that came down to 2 after the study. QoL scores in all four domains were significantly high and depression level score was significantly lowered at the end of the treatment. At the start of the treatment twenty, four out of thirty-five participants were dissatisfied with their health that came down to five at the end of treatment.

Conclusion: Intervention strategy not only had a great impact on the QOL of study participants but also contributed to better treatment adherence and desirable treatment outcome. Therefore, researchers emphasize the need to adopt this Intervention Strategy through the provision of trained, professional MDR-TB counsellors. Further, larger studies of multi-state/ multi-site may be taken up to standardize the intervention strategies adopted in this study.

Key words: MDR-TB patients, intervention strategy, Quality of life, treatment adherence

INTRODUCTION

Tuberculosis (TB) remains one of the world's biggest threats despite the advances made in the management of the disease and nearly all TB cases can be cured [(1)]. India has the highest burden of both TB and MDR-TB based on estimates reported [(1)] in Global TB Report 2016. Globally in 2016, about 490,000 people were estimated to become ill with MDR-TB [(2)]. In the same year, the estimated number of MDR/RR -TB cases among notified pulmonary TB cases (2.79 million cases of TB in India in 2016 by WHO) was 84,000 (72,000–95,000) with an incidence (MDR/RR-TB) 147 (95–199) per 100000 11 (7.2–15). While host genetic factors may probably contribute, MDR-TB has clinical as well as programmatic factors that include inadequate or poorly administered

Correspondence:
Dr. Thiruvalluvan Elango
Senior Technical Officer - 3
Department of Socio-Behavioral Research (DSBR)
ICMR-National Institute for Research in Tuberculosis (NIRT)
62, Govt Rajaji Hospital, Madurai-625020
Mobile: +91 9442700551
E-mail:e.thiru@gmail.com

treatment regimen/treatment failure[3,4] or non-adherence[5] to the prescribed regimen leading to the development of MDR-TB.

The community-based treatment program for MDR-TB (DOTS-Plus), specialized treatment using the popular Directly Observed Therapy Short Course (DOTS) initiative, has shown considerable success [6, 7, 8, 9] in the management and treatment of MDR-TB in some parts of the world. However, management of MDR-TB is challenging due to its complex treatment that includes an elevated treatment cost [10], the use of highly toxic anti TB drugs with potential adverse effects [11], longer treatment regimen [12, 13] which often requires 24 months or longer, and it burdens an increased treatment failure and mortality [14, 15] rate. As the treatment for MDR-TB is characterized by rigorous treatment regimen for a long duration, higher incidence of adverse side effects, lower cure rate, and high treatment costs, both psycho-social well-being and treatment outcome in MDR-TB is far negative than drug-sensitive TB. The current paper is to understand the psychosocial issues facing MDR-TB patients in terms of depression, stigma and social support; and to gain insight into the factors that influence treatment adherence and quality of life. Also to explore the feasibility and acceptability (effectiveness) of intervention strategies to promote adherence suitable for MDR TB Patients.

METHODOLOGY

This study was conducted in Chennai Corporation, covering 16 TUs. The study population includes all MDR-TB patients, 18 years of age and above registered for MDR-TB treatment from September 2014 to September 2016.

This was an intervention study conducted to understand the patients' experiences related to MDR-TB diagnosis and treatment and devise an effective and acceptable strategy to promote drug adherence. The study consisted of four individual assessments at 0, 6th, 12th and 18th and 24th month. During the assessment, investigators have identified patients' concerns that include awareness on MDR-TB, the disclosure of MDR-TB to family and their reactions, social stigma (perceived and enacted stigma), economic problem, psychological problems, and drug-related problems. Besides, the patients' lifestyle characteristics such as alcohol consumption and tobacco smoking were also assessed. Based on this assessment, we introduced the need-based intervention on 0, 6th, 12th, 18th and 24th month. Each assessment and intervention sessions were conducted for 30 to 45 minutes.

The interventionists were conducted by trained professional Medical Social Workers. Based on the phase-I findings an intervention strategy was devised that consist of motivational interviewing module, counselling module and nutritional support. The motivational interviewing intervention focused four main topics viz., Session-1: MDR–TB Management, challenges, nutrition; Session-2: Psycho-social issues intervention, Session-3: Alcohol, smoking, suicide thought; and Session-4: Rehabilitation. Study participants were met on five-time during the study period i.e., 0, 6th, 12th, 18th and 24th month over the study period (Table-1). Individual counseling sessions were organized based on the participants' psychosocial need.

Nutritional support in the form of nutritional supplement pockets was provided to the participants as a part of the intervention program. This support addressed the indirect costs incurred by the study participants or in accessing the health

Table 1. Motivational interviewing intervention schedule

Activity /Time point	0 month			6th month			12th month			18th month			24th month		
Assessment/ Motivational/interviewing	√			√			√			√			√		
Counseling	1	2	3	4	7	8	9	10	13	14	15	16	19	20	21
Management/ challenges/ nutrition	√			√			√			√			√		
Psychological issues intervention		√			√			√			√			√	
Alcohol/smoking/suicide thought		√			√			√			√			√	
Rehabilitation			√			√			√			√			√

Motivational interviews were held as per the module developed before the intervention. Motivational interviews focused on 6 different issues mentioned in the table .

facility, or possibly, to mitigate the consequences of income loss related to the disease. Nutritional supplements including a variety of millets and legumes that have high nutritional value were provided to all the participants. Financial support in the form of financial incentives or transportation costs that would help the patients in undergoing preventive care, such as screenings or test, and for their periodical visits to the treatment facility was provided to the participants who needed financial assistance or too low-income participants.

The interview schedule was used to collect information on socio-demographic characteristics of patients. In addition Center for Epidemiological Studies Depression (CES-D) scale was used to measure anxiety; WHO QOL BREF scale was used to measure the quality of life; AUDIT scale was used to measure alcohol and drug abuse and Fagerstrom scale was used to measure smoking. Individual counselling sessions numbering 15 were held. During the study period, various psychosocial issues were addressed. Nutritional support was offered to all participants, but two participants who declined to accept nutritional support. Nutritional flour packet weighing half a kilogram was offered to participants every month.

Descriptive statistics like mean±standard deviation, median with Inter-Quartile Range and frequency with percentage were used, depending on the variable type. Comparison of the proportion who was depressed at baseline with those at 24th month follow up was done using the McNemar test. Paired t-test was used to compare the domain-wise score of the WHO-QOL scale. Statistical significance was determined at 5%. Statistical analysis was performed using SPSS Version 16.0.

This study was approved by the Scientific Advisory Committee and Ethics Committee of National Institute for Research in Tuberculosis, Indian Council of Medical Research (ICMR) Chennai. Written informed consent was obtained from the patients who were willing to participate in the study. Privacy and confidentiality were maintained over the study period.

RESULTS

Overall 35 participants were enrolled in the study. One-third of the participants were women (Table-2). One participant lost to follow-up and the other one died, remaining 33 participants were included for analysis. Mean age of participants was 38 (SD+13). One-third of participants were educated up to 10th standard. More than half of the participants were married. Before the diagnosis of MDR–TB, only 4 participants were unemployed and after the diagnosis 23 participants become unemployed. Sixty-three per cent of the participants were tenants, living in line houses.

Table 2. The demographic profile of the study population (N=33)

Socio-demographic characteristics		n (%)
Age	Mean ± SD	38 ± 13
Gender	Male	22 (66.7)
	Female	11 (33.3)
Education	Illiterate/no schooling	4 (12.1)
	Primary school	3 (9.1)
	Middle school	8 (24.2)
	High school	10 (30.3)
	College	4 (12.1)
	Professional education	4 (12.1)
Marital status	Single	10 (23.3)
	Married	20 (60.6)
	Separated	1 (03.0)
	Widowed	2 (06.1)
Family type	Nuclear	25 (75.8)
	Joint	8 (24.2)
Family size	Median (range)	3 (1,4)
Occupation	Before diagnosis	
	Salaried government sector	7 (21.2)
	Salaried private sector	10 (30.3)
	Daily wages earner	12 (36.4)
	Unemployed	4 (12.1)
	After Diagnosis	
	Salaried government sector	2 (05.9)
	Salaried private sector	5 (15.2)
	Daily wages earner	3 (09.1)
	Unemployed	23 (69.7)
Residence locality	Urban	28 (84.8)
	Semi-urban	3 (09.1)
	Slum	1 (03.0)
	Rural	1 (03.0)

Note: Removed one patient who was "lost" and the other one who died

Findings revealed that the majority of participants were unaware of 'MDR-TB'. Most of the TB patients have not disclosed their TB status (Table-3), even to their family members. Ninety per cent of participants found a government health facility as the primary source for treatment and an equal percentage of participants were aware of two years of the treatment period. As for depending on tobacco and alcohol, 9 participants had the habit of smoking and

12 participants had a history of drinking. However, the AUDIT scale suggested one participant with the drinking problem and Fagerstrom smoking scale suggested 6 participants as very low dependence and 3 participants with medium dependence.

Table 3: Status of disclosure and experience of stigma

Reaction and experiences	n (%)
Informed of diagnosis	28 (84.8)
Reaction to diagnosis	
Shock	8 (24.2)
Worry	16 (48.5)
Disbelief	
Cried	2 (06.1)
Others	2 (06.1)
	5 (15.2)
The reaction of family members	
Rejection	3 (09.1)
Support	23 (69.7)
Agree	5 (15.2)
Not co-operative	
Other challenges faced	
Looked down by neighbours	5 (15.2)
Relatives refused to visit home	2 (06.1)
Loss of job	10 (30.3)
Neighbours do not interact	1 (03.0)
Others	10 (30.3)

The motivational interviewing intervention was offered to all 33 participants at 5 different time points and administered depression assessment scale and quality of life scale. At the initiation of treatment 27 MDR-TB participants had experienced depression. At the end of the treatment, only 7 participants had experienced depression.

Individual counseling sessions were held during the study period and various psychosocial issues were addressed. Psychosocial counselling sessions were conducted to help the participants in understanding MDR-TB and managing the impact caused by the disease in their psychosocial life. The counsellors educated the patients about MDR-TB prevention and transmission, and also about the course of the disease. These sessions not only helped the patients in preparing themselves to face any adverse outcome of the diagnosis but also helped them in alleviating their anxiety and depression level caused due to the illness. The counsellors also encouraged the participants to give importance on or value self-worth, combat fear, on strengthening the patients' sense of responsibility and enabling them to adopt the changes that have occurred in their socio-economic life after diagnosing MDR-TB.

During the counselling sessions, the counsellors reiterated the pros and cons of the medications prescribed to the patient by treating physician. The patients were also counselled on the importance and need to adhere to the treatment and the effects of irregular treatment. The majority of the participants reported difficulties in adhering to the MDR-TB medications due to the severe side effects caused by the drugs or have a time conflict due to their daily schedule. For such cases, the counsellors suggested some feasible plan for drug adherence based on the patients' need and other related events. Such strategies include setting an accurate drug taking the time or forming the habit of stock-taking of drugs, or rescheduling drugs taking time depending on the participants' suitable time. Counselling was provided to those patients who reported substance use (alcohol and smoking) to deal with the issues underlying with substance abuse depending on then usage severity. The counsellors motivated them to keep them adhering to the MDR-TB treatment. Also, the counsellors helped the participants to set different possible ways of dealing with specific problem situations that prompt them to drink or smoke and taught them concrete techniques that would help them to quit or reduce intake. Besides, the counsellors also educated the family members of these participants in understanding about the ill effects of alcohol and smoking and provided them with some techniques during their visit to the treatment facility on how to better help them overcome their addiction.

Nutritional counselling was also given to the participants to assess their usual food intake and identify the areas where change was needed to help them develop a healthier lifestyle and strengthened their immune system. Nutritional awareness using visual aids (such as pictorial menus) and follow-up of their diet quality were done to help the patients make and maintain the needed dietary changes considering to each patient's situation and socio-economic background. For those patients who were having difficulties in maintaining the dietary changes, the counsellors helped them to set achievable health goals by developing a daily plan that promotes healthy eating while also

strengthening their motivation and taught them various ways of maintaining these goals.

Likewise, 19 participants had experienced poor quality of life at the start of treatment and at the end of treatment, only 2 participants had experienced poor quality of life (Table-4). Dissatisfaction with one's health condition was felt by 24 participants at the start of treatment which came down to 5 participants at the end of treatment. Quality of life scores in all four domains and depression level scores had significantly reduced from baseline to 24th month.

Table 4: Quality of life and depression in baseline and at the end of treatment

Depression and QOL at baseline	Baseline	24th month	p-value
CESD depression scale			0.006*
No depression	6 (18.2)	14 (42.4)	
Depressed	27 (81.8)	7 (21.2)	
WHO-QOL scale			
Dissatisfied with his/her health	24 (72.7)	5 (15.2)	0.008*
Physical health (Mean ± SD)	11± 4	16 ± 3	<0.001&
Psychological (Mean ± SD)	12± 3	17± 3	<0.001&
Social relationships (Mean ± SD)	11 ± 4	15 ± 2	0.022&
Environment (Mean ± SD)	13 ± 3	15 ± 3	0.002&
Poor QOL	19 (57.6)	2 (6.1)	<0.001*

*McNemar Test & Paired t-test

DISCUSSION

This study highlights the positive impact of an intervention package that includes MI module, counselling module and nutritional support. One of the most common concerns raised by the study participants was rejection or exclusion from their loved ones that led them to deliberately separate or isolate themselves from their families and social activities. Feeling of guilt and shame, fear of transmitting the infection to their loved ones [16,17,18,19,20] were also expressed as one of the common causes for self-isolation. Social stigma or discriminatory behaviour unleashed by health providers [18, 20, 21] and family members had a far negative impact on the patients' treatment adherence. Study participants had expressed a dislike in making visits to the facility for the reason that they have been reprimanded or being humiliated by the health providers which they found it very disheartening. This may be triggered by many forces including lack of understanding and knowledge of the disease, and myths and misconceptions that are deeply rooted in the society. Because of the stigma attached to this disease, patients experienced a lack of social and emotional support from their family members that undermined their ability to protect themselves or confidence to seek help and care. Research carried out in India that assessed Quality of Life (QOL) of MDR-TB patients found out that the social areas such as personal relationships, social support and sexual activity of MDR-TB patients were low compared to other areas (physical, psychological and environmental) that had an impact in their QOL[22].

Low level of psychosocial support, especially from family, during the treatment also underscored in several other studies which were found to be a factor affecting treatment adherence among MDR-TB patients [18, 23, 24]. Fears of death due to the disease or about their future and family have been yet another concern raised by most of the study participants. Moreover, one of the significant challenges raised consistently by the participants was issues related to MDR-TB therapy. Dealing with severe side effects of MDR-TB drugs like many other studies proved to be very challenging for most of our study participants,[18, 25, 26, 27, 28, 29] which they considered as an additional issue to cope with along with the symptoms of the disease itself. Adding to the adverse effects of MDR-TB drugs is the long MDR-TB treatment course that not only brought changes in the physical ability of the patients to perform their individual routine life but also resulted in the inability to go for work that eventually cost them their job. Our finding is corroborated with the study conducted in India, which reported that five out of ten MDR-TB patients could not resume work even after one year of treatment and had to force reductions in salary due to absenteeism from work [30].

Study participants consistently cited financial burden as a barrier as documented in a study conducted in Indonesia, which reported that the financial impact was higher among MDR-TB patients than that of TB (77% vs 50%)[31]. Similarly, financial issues were reported as the most prevalent issue to care or default among MDR-TB patients in several studies conducted in

China, India, Dominican Republic, Kazakhstan and Nepal[25,32,33,34,35] Some participants managed this issue by borrowing money from family members, which often strained relationships. Many of our study participants reported losing their individuality and self-esteem since they lost their job and became financially dependent on their family members or relatives. Loss of job coupled with the financial crisis led to a more psychological impact on the patients as well as their families during the treatment course.

The psychosocial intervention not only supported treatment adherence for the patients but has also determined the need for a holistic approach to strengthening MDR-TB care and management of the TB control program. The outcome of our intervention was encouraging with improved treatment adherence observed among the participants and in pacifying their unpleasant emotions caused by MDR-TB. Psychosocial support programs have been considered as a successful component to help patients in enduring the long and unpleasant treatment, and thereby resulting in better treatment outcomes and reductions in default among MDR-TB patients. However, the benefits of psychosocial support in MDR-TB should not be limited only to increased adherence to treatment.

Even with the significant medical advances in patient management, psychosocial intervention remains an integral part of the holistic management and care for MDR-TB patients and their family. Our intervention that included psychological counselling, motivational interviewing and nutritional supplementation has shown the conducive result to both emotional and social rehabilitation of MDR-TB patients as well as treatment adherence. Most of our study participants were very positive about the counselling sessions and considered it very helpful during the long treatment journey. An intervention study in Nepal[36] showed improvements in cure rates with 76% among MDR-TB patients who received counselling with financial support. The present study also comprehends the vital and effective role of trained counsellors in enhancing the quality of life of MDR-TB patients through counselling. The impact of psychosocial interventions has also been underscored in some studies which showed significant reductions in depression and default rates and improved adherence to MDR-TB medications. [19, 25, 35, 37, 38]

While (MDR) TB patients have an ethical duty to complete treatment, health providers' obligations to the patients and their caregivers also becomes a moral duty to support patients' ability to adhere to treatment. The current effort in psychosocial intervention for MDR-TB management is understood crucial; however, innovative patient-centred support mechanisms that are accessible and stigma reduction activities are scarce. There is a need not only to standardize an intervention module but also ensure the adoption of the same in the program becomes essential. Therefore, the researchers suggest an intervention package that consists of motivational interviewing, counselling and material support to aide MDR-TB Patients to complete treatment and to stop spreading the disease.

CONCLUSION

The important outcomes of this intervention study were improved Quality of life (QOL), a substantial increase in satisfaction with the health condition, reduction in the experience of depression and treatment adherence. Psychosocial support is a crucial component of MDR-TB treatment to ensure completion of treatment regimens and in enabling psychosocial rehabilitation after treatment. This kind of support will also help the patients endure the long and unpleasant treatment, thereby improved treatment compliance resulting in better treatment outcomes. This study emphasized the need to strengthen the psychological wellbeing and social relationship of MDR-TB patients using proper and consistent psychosocial support interventions and counselling in the TB control program. Furthermore, there is a need to include peer support groups for patients undergoing treatment and transitioning back into the community after treatment. Further, multi-state/ multi-site larger studies may be taken up to standardize the intervention strategies adopted in this study.

CONFLICT OF INTEREST

None

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DOI https://doi.org/10.3126/saarctb.v%vi%i.34136

STRENGTHENING CHILDHOOD TB MANAGEMENT IN NEPAL: CHALLENGES, PROGRESS AND LESSON LEARNED

Shrestha SK[1], Bhattrai R[1], Chettry T[1], Basnet, R[2], Bhattarai R[2], Thapa A[2], Tinkari BS[2], Sharma SK[2], Rajbhandari SK[2], Bhattachan, A[2]

[1] Save the Children, G.P.O. Box 3394, Kathmandu, Nepal
[2] National Tuberculosis Centre, Thimi, Nepal

ABSTRACT

Introduction: Childhood tuberculosis has always been in shadows as Nepal's Tuberculosis Program focused mainly on adults TB resulting in under diagnose with less than 10% of total TB cases notified. Lack of political commitment; absence of guideline and working group, qualified health personnel and diagnostics tool were major implementation challenges.

Methodology: Assessment of childhood TB program was done and critical gap were identified. Childhood TB was prioritized in National TB strategic plan (2016-21). Collaborate with both international and national child experts, public and private organizations to develop guideline, building capacity of health care providers and establishing national working group. Childhood TB focused interventions were implemented in 40 high burden districts since March,2017 focusing on contact tracing, diagnosis, Prevention Therapy, malnourished children in the community and major hospitals.

Results : Political commitment and multi-sectoral involvement, to manage childhood TB was achieved. A total of 93 doctors were trained in the Childhood TB management training and were identified as focal persons to manage childhood TB in their respective regions. Child focused intervention from March 2018-19 resulted in the diagnosis of 521 TB cases among 38,987 malnourished children and 1,764 children were enrolled under TPT after contact tracing of 59,742 family members. With political commitment, prioritization of childhood TB, collaboration of both government and non-government sectors and interventions focusing childhood TB, a significant achievement can be attained in childhood TB management.

Conclusion: Nepal has shown childhood TB management program can be strengthen if NTP prioritizes it, child focused interventions are implemented and collaborate with Child health division, pediatrics association, other government and non-government organizations to increase and strengthen the program.

Keywords: Childhood Tuberculosis, National Tuberculosis Program, Malnourished, Tuberculosis preventive therapy

Correspondence:
Dr. Suvesh Kumar Shrestha
Save the Children, Nepal Country Office,
G.P.O Box 3399, Airport Gate, Shambu Marga,
Kathmandu, Nepal
Mobile: +977-9801047879
Email:suvesh.shrestha@gmail.com

INTRODUCTION

Tuberculosis (TB) remains as a major public health problem in Nepal, as it is responsible for ill health among thousands of people each year. TB also ranks as the sixth leading cause of death in the

country. It is estimated that 44,000 new TB cases occur and 5000-7000 deaths each year due to TB.[1] Despite the efforts there is unacceptable low rate of decline in incidence rate of TB.

Childhood tuberculosis has been neglected as Nepal's Tuberculosis Program focused on adult TB, resulting in under diagnose, with less than 10% of total TB cases notified being children (Figure 1). The major gap observed was lack of political commitment, absence of childhood focused NTP.

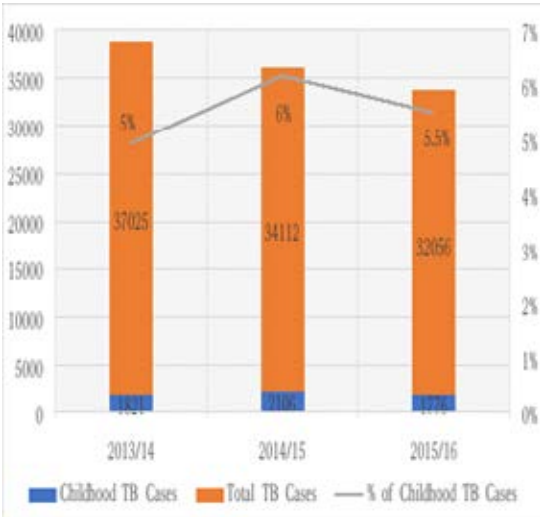

Figure 1: Situation of childhood TB in Nepal [2]

METHODOLOGY

Action taken by National Tuberculosis Program to prioritize Childhood TB management in Nepal are:

2.1 Political commitment and National Priority: The National Strategic Plan for Tuberculosis Prevention and Care (2016-21) has prioritized childhood TB with an objective to increase case notifications among children to at least 10% by 2020.

2.2 Assessment of Childhood TB program: Overall assessment of Childhood TB was done using KNCV Benchmarking Tool for Childhood TB Policies, Practices and Planning. This benchmarking tool is based on the WHO 'Framework for conducting reviews of tuberculosis programmes – Assessing activities to address childhood TB' and the Second Edition of the WHO Guidance for National Tuberculosis Programmes on the management of tuberculosis in children (2014).

The overall findings of the assessment are summarized in the Table below. This assessment was help for nation to prioritize the area and allocate the resource accordingly.

The major gaps identified by the mission were following:

- Evidence of political commitment for childhood TB was partially met
- No active national working group on childhood TB
- No national guidance for childhood TB
- No effective technical assistance for childhood TB
- The childhood TB strategy is not implemented
- National policies does not provides guidance for all providers of Paediatric care are involved in diagnosis, prevention and treatment of childhood TB
- Providers of Paediatric care are not involved in diagnosis, prevention and treatment of childhood TB
- Investigation of child contacts of infectious TB patients is not implemented
- Eligible children does not have access to preventive treatment
- There is not special approaches for diagnosis of DR TB in children are included in the national guidance on TB
- The national treatment guidelines for TB and MDR TB does not have appropriate and specific adjustments for children
- The national treatment strategy of children is not universally accessible for children
- Data on childhood TB are not fully available and used at the NTP
- There is no plan for human resource capacity building for childhood TB

2.3 Development of National first Childhood TB guideline and manual involving NEPAS:

With help of one International Childhood TB expert Nepal developed its first Childhood TB Guideline and Training manual which was in line with WHO recommendation. Both of these documents were finalized with the help of Nepal Pediatrics Associations (NEPAS). This collaboration between NEPAS and NTP is also first time and have brought NEPAS along with their 200 Pediatricians under NTP umbrella.

2.4 Establishing Childhood TB focal person at central level and have NEPAS in National Technical working group for TB management

2.5 Capacity building of health care providers on management of Childhood TB:

There was a clear gap identified among the health care providers to diagnose and treat childhood TB. To address this gap training on childhood TB was panned and based on that training manual and training plan specifically for Childhood TB was developed. The training manual was developed in line with WHO recommendation and in close coordination of NEPAS.

2.6 Training of Health care providers

2.6.1 Masters Training of Trainer for management of TB: As there was a clear capacity gap among health care providers to identify, diagnose, treat and prevent childhood TB so series of training was planned. Initially a group of master trainer was developed by conducting Masters Training of Trainer (mTOT). Twenty one pediatricians from all over the Nepal covering all seven provinces were identified in collaboration with NEPAS and trained. This training have developed group of trainer which will be involved in training other health care providers as well as manager childhood TB.

2.6.2 Regional Level Training: Using the master trainers series of Childhood TB management trainings were conducted at Provincial level. The training was conducted among Pediatricians, General Practitioners (GPs), and Medical officer of referral hospital for management of Childhood TB.

2.7 Childhood TB focused intervention in High TB burden districts:

2.7.1 Contact tracing: Previously National TB program was focused on passive case finding where presumptive TB cases identified in health care setting was further screened for TB. There was no active case finding activities among the contact of bacteriologically confirmed cases. Realizing this gap NTP implemented contact tracing of all household members of PBC (full form??) cases in 38 of the high TB burden districts of Nepal which carries 75% of total TB cases notified (Fig. 2). This intervention was initiated from early 2017. During contact tracing all household members of PBC cases were screened based on symptoms. This also included all the children in those households. Anyone who was found to be symptomatic on screening was then referred for further diagnosis and for those children under 5 years of age who did not have any symptoms was referred for initiation of TB Preventive Therapy (TPT).

Figure 2: Contact tracing districts

2.7.2 Screening among malnourished child:

Wasting (measured by low weight for height compared to the WHO reference population) has remained nearly unchanged over the last decade in Nepal; 11 per cent in 2001, 13 per cent in 2006; and 11 per cent in 2011. As per the WHO decision making criteria, wasting prevalence is at a critical level in Nepal, affecting an estimated 430,000 children under five years of age at any point in time. Nearly, 2.6 per cent or 91,000 under-five year

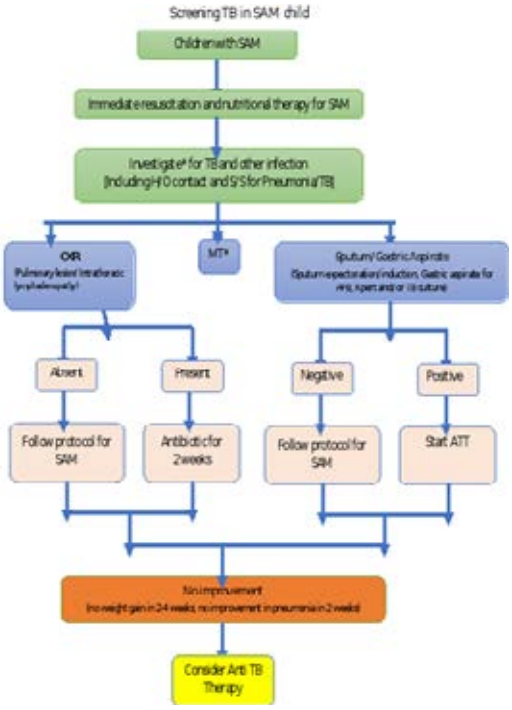

Figure 3: TB screening among SAM children

old children in Nepal are suffering from severe acute malnutrition (SAM). Most of these children are not likely to survive unless they are identified and treated in a timely and effective manner. A further 8.3 per cent, or 290,000 under-five year old children in Nepal, are suffering from moderate acute malnutrition (MAM)[3]. As malnourished child are on high risk of developing TB, as well as one of the sign of TB screening among malnourished children (SAM and MAM) was initiated from early 2017 in 29 high burden districts of both TB and PEM cases. Malnourished children were never screened for TB before. Figure 3 show algorithm to screen TB among SAM children.

2.7.3 Referral cost and diagnostic cost for diagnosis of childhood TB:

Since childhood TB cannot be diagnosed in peripheral health facility where there is no capable human resource as well as instrument, the presumptive TB children cases needs to be referred at hospital where there is a trained health staff. So, NTP have provided referral cost as well as diagnostic cost for all the presumptive childhood TB cases.

2.7.4 Tuberculosis Preventive Therapy:

TPT was also initiated among children under 5 who are contact of PBC cases in districts with contact tracing who are ruled out of having active TB. Figure 4 shows steps to initiate TPT.

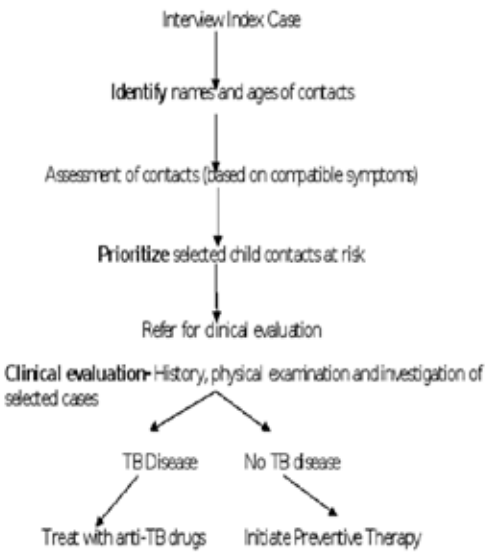

Figure 4. Step to initiate TPT

2.7.5 Procurement of Childhood friendly TB regimen:

New fixed-dose combinations for the treatment of TB in children have been procured. This is an important step in improving treatment and child survival from TB, and slowing the spread of drug resistant TB. Child-friendly medicines improve the daily lives of children and their families struggling with TB. Six months is a long time to take medicine. But the availability of treatment that tastes good and is simple to provide will ease the daily struggles of children, parents, and caregivers alike.

RESULTS

3.1 Status of Gap identified during assessment of Childhood TB program:

Most if the major gaps identified are either fully met or partially met and the current status is shown in the table no1. It is seen that the three gaps which was not met previously have met which include national guidance for childhood TB, investigation of childhood contacts of infectious TB patients is part of the national strategy

Investigation of child contacts of infectious TB patients is fully implemented and special approaches for diagnosis of TB in children are included in the national guidance on TB. Three gaps those are partially met was met fully which are effective technical assistance for childhood TB, national treatment guidelines for TB and MDR TB have appropriate and specific adjustments for children and child friendly formulations are available.

3.2 Development of childhood TB experts:

A total of 93 doctors were trained in childhood TB management training and they became focal persons to manage childhood TB in their respective regions.

3.3 Total achievement of childhood TB focused intervention

Childhood TB focused interventions were introduces in 40 high burden districts of Nepal from

Table 1: Status of Gaps identified during assessment of Childhood TB Program		
Standard	**Gap Identified in Feb 2017**	**Current Status in Feb 2019**
There is evidence of political commitment for childhood TB	Partially Met	Partially Met
There is an active national working group on childhood TB	Not Met	Partially Met
There is national guidance for childhood TB	Not Met	Met
There is effective technical assistance for childhood TB	Partially Met	Met
The childhood TB strategy is fully implemented	Not Met	Partially Met
National policies provide guidance for all providers of Paediatric care are involved in diagnosis, prevention and treatment of childhood TB	Not Met	Partially Met
All providers of Paediatric care are involved in diagnosis, prevention and treatment of childhood TB	Not Met	Partially Met
Investigation of childhood contacts of infectious TB patients is part of the national strategy	Not Met	Met
Investigation of child contacts of infectious TB patients is fully implemented	Not Met	Partially met
The national strategy provides for preventive treatment of eligible children	Partially Met	Partially Met
All eligible children have access to preventive treatment	Not Met	Partially Met
Special approaches for diagnosis of TB in children are included in the national guidance on TB	Not Met	Met
Special diagnostic approaches for TB in children are applied	Not Met	Partially Met
The national treatment guidelines for TB and MDR TB have appropriate and specific adjustments for children	Partially Met	Met
Child friendly formulations are available	Partially Met	Met
The national treatment strategy of children is universally accessible for children	Partially Met	Partially Met
Data on childhood TB are available and used at the NTP	Partially Met	Partially Met
There is a plan for human resource capacity building for childhood TB	Partially Met	Partially Met
The NTP and partners deploy specific initiatives to promote a patient and family centered approach in childhood TB care	Partially Met	Partially Met

Child focused interventions from March 2018-19 resulted in TB diagnosis of 521 TB cases among 38,987 malnourished children, 1,764 children were started on IPT after contact tracing of 59,742 family members. In the year 2018 the childhood TB diagnosed was 5.5% of total case notified.

CONCLUSION

Nepal has shown that childhood TB management can be strengthened when it becomes a priority. Intervention that pay attention on child TB can be implemented in collaboration with the ministry's Child health division, pediatrics association, other government and non-government organizations to increase and strengthen the program. Contact tracing needs to focus on children. Malnourished child needs to be targeted in country like Nepal where there is high burden of malnutrition. Program needs to focus on capacity building of health care providers as diagnosis of childhood TB is challenge

ACKNOWLEDGEMENT

I would like to acknowledge Nepal Pediatrics Society for all the support to strengthen childhood TB in Nepal. I will also like to declare that I have no conflict of interest.

CONFLICT OF INTEREST

None

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DOI https://doi.org/10.3126/saarctb.v18i1.34140

TUBERCULOSIS AND STIGMA IN INDIA: EVIDENCE FROM A NATIONALLY REPRESENTATIVE SURVEY

Barman P[1]

[1]Assistant Professor in Economic, Faculty of Commerce and Management, St. Xavier's University, Kolkata, India

ABSTRACT

Introduction: Infectious nature of pulmonary tuberculosis (TB) is one of the major reasons behind the prevailing stigma and negative attitude towards the disease. These factors stand in the way of seeking an early diagnosis or continuing treatment following a positive diagnosis. This study aims at exploring the shares of adult men and women conforming to TB related stigma in India, a high TB burden nation, and the causal factors behind the same.

Methodology: The study uses unit level data on adult men and women from the nationally representative survey NFHS-3 (2005-06). Simple tools for descriptive statistics and logistic regression analysis have been employed.

Results: Factors affecting TB related stigma among Indian men are age, religion, economic class, education level, family structure and marital status. In case of women age plays no role. However, place of residence, social group and employment status emerge as significant factors impacting stigma among Indian women. Further, stigma levels vary across Indian states for both genders.

Conclusion: Socio-economic and demographic factors that have a role to play in shaping people's attitude towards disease and related health seeing behaviour need to be acknowledged and incorporated in policies targeted towards elimination of TB.

Key words: Tuberculosis, Stigma, Negative attitude, Socio-economic factors

INTRODUCTION

Tuberculosis (TB) continues to plague the world as one of the top ten causes of death globally and the leading infectious cause of mortality. The 30 High Burden Countries including India, identified by WHO, account for around 86 per cent of the annual global TB incidence. India alone contributes towards17 per cent of the global gap between estimated incidence of TB and notification. Further, the COVID-19 pandemic in 2020 threatens to stall the progress in arresting the global TB disease burden[1]. In 2018, India had 2.69 million new cases and 4.4 lakh deaths due to TB[2]. Although the Revised National Tuberculosis Control Programme (renamed recently as National Tuberculosis Elimination Programme) is running in India for two decades now, the burden of TB continues to be appalling. India's contribution to the 'missing millions' suggests that a large number of chestsymptomatics either go completely undiagnosed or are not notified to the national programme even if diagnosed. Stigma potentially has a significant role to play in determining the care seeking discourse of TB suspects and poses a major challenge to TB control[3]. Negative attitudes that societies and communities attach to this disease often act as deterrents to timely care seeking by patients due to fear of social isolation as well as compel a patient to abandon treatment midway.

Correspondence:
Ms. Paramita Barman
Assistant Professor in Economics
Faculty of Commerce and Management
St. Xavier's University
Action Area IIIB, Plot IIIB/1
New Town, Kolkata 7000160, India
Email:paramitabarman11@gmail.com

Most authors have identified the contagiousness of pulmonary TB as a leading cause of stigma. Even among people with relatively good knowledge of TB transmissibility, the perceived risk of transmission can lead to social isolation of individuals with TB. Among other factors fuelling stigma are the perceived associations of TB with malnutrition, poverty, low socioeconomic class, HIV and TB co-infection, etc. Several authors have also tried to capture the prevalence of perceived, internalized and actually experienced TB related stigma and compare its extent in different geographic regions. Concern about suffering the consequences of stigma prevent at-risk individuals from undergoing TB screening and seeking medical assistance after surfacing of symptoms. Even after start of treatment, fear of revelation of positive TB status may result in treatment drop-outs[4]. Studies exploring the attitude, behaviour and understanding of TB by communities in a district in the western region of Ghana, Africa, finds through in-depth interviews with respondents that primarily fear of infection gave rise to negative attitudes towards TB leading to imposition of socio-physical distance and participatory restrictions on patients. Stigma in fact led individuals with obvious symptoms of TB to attribute it to other non-stigmatising conditions or conceal diagnosis from others as well as default on treatment. The study indicated that TB related stigma, ingrained in most societies was a major setback to the success of the national programs to combat TB, in particular with regards to case finding and adherence to treatment.[5,6] Qualitative studies in India find that the manifestations of TB stigma were through social isolation, gossip, uncertain prospects of marriage, verbal abuse, etc. Concealment of TB status was the response to fear of job loss, marital problems and discrimination.[7,8] Often it is through health professionals themselves that TB patients are exposed to stigma.[9] Research has highlighted the inadequacy of an entirely disease-specific focus on TB control without simultaneously understanding the broader family, community and social context in which the illness occurs.[10]Since qualitative studies on TB stigma are quite a few, the present study would contribute to existing literature by exploring the proportions of Indian adults (male and female) who conform to TB related stigma and trying to look into its potential drivers.

METHODOLOGY

The study uses unit level data on adult men and women from the nationally representative *National Family Health Survey* 3 (2005-06).It covers adult men in the 15-54 years age group and adult women in the age group 15-49 years.

Simple tools for descriptive statistics and multivariate logistic regression analysis have been employed in the study. Logistic regression analysis is used to study how the likelihood of an event occurring varies in the presence of confounding factors. It presents an appropriate method of regression analysis when the discrete dependent variable Y is dichotomous in nature, taking only two values 0 (failure) and 1 (success) and involves estimation of the log odds of success. Mathematically, logistic regression estimates a multiple linear regression function of the following form:

$$\log [P(Y=1)/1-P(Y=1)] = \beta 0 + \beta 1Xi1 + \beta 2Xi2 + \beta 3Xi3 + \ldots\ldots + \beta nXi \text{ for } i=1,2,3,\ldots, n$$

Data has been analysed with the help of the Stata 14 software.

Question regarding TB related stigma were asked to only those respondents who conformed to ever having heard of TB. 8 per cent of male and 12 per cent of female respondents who said that they had never heard of TB have been eliminated from the final dataset for analysis in the study.The specific stigma related question asked was whether the respondent would keep it a secret if any member of his or her family had TB. To locate the causal factors, 'Stigma' (0=No Stigma, 1=Stigma) was framed as the binary dependent variable. The explanatory variables considered were residence, religion, reservation, age, level of education, income class, marital status, occupational status and family structure. Except age, all other predictors are categorical. Statistical significance has been considered at $p<0.05$.

RESULTS

In India, 18.60 per cent males wanted to keep TB infection in the family a secret. The corresponding share for females was 19.37 per cent as indicated in Table 1.

Table 1: Percentage shares of adult men and women with TB related stigma in India

TB related stigma	Men	Women
No	50,932 (81.40)*	77,854 (80.63)
Yes	11,638 (18.60)	18,702 (19.37)
Total	62,570 (100)	96,556 (100)

Source : Author's calulation from NFHS 3 data

Figure 1 depicts the percentage shares of men with TB stigma across Indian states. It is revealed that the states of Tamil Nadu, Andhra Pradesh, Meghalaya, Rajasthan, Goa and Karnataka have higher than all-India share of adult men with TB related stigma. States like Bihar, Uttar Pradesh, Madhya Pradesh, Gujarat and Kerala have lower levels of stigma among men compared to the national level. Some of the lowest percentages of stigma are found in West Bengal, Maharashtra, Manipur, Orissa and Assam.

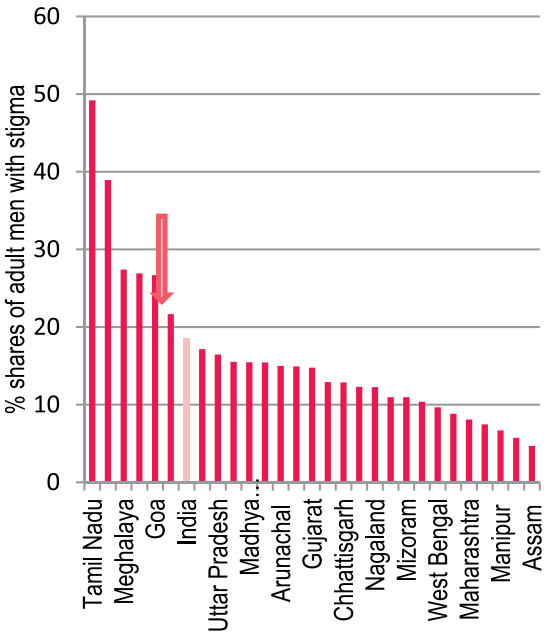

Figure 1: States with higher and lower shares of males with TB stigma compared to all India level

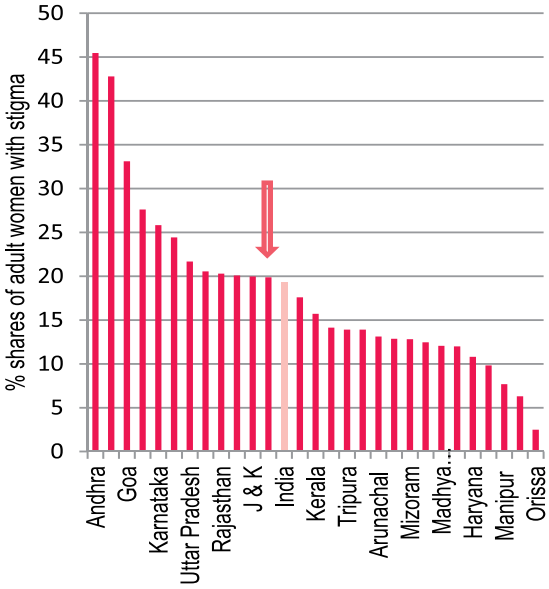

Figure 2: States with higher and lower shares of females with TB stigma compared to all India level

Figure 2 depicts the percentage shares of women with TB stigma across Indian states. Some of the major states like Andhra Pradesh,Tamil Nadu,Karnataka, Gujarat,Uttar Pradesh, Rajasthan,Punjab and Bihar have higher than the all-India percentage of adult women nurturing TB related stigma. In Maharashtra, Kerala, states in the Northeast, Jharkhand and Madhya Pradesh, stigma burden is lower than the national level. Some of the lowest stigma percentages among women hail from West Bengal, Manipur, Assam and Orissa.

Table 2 reports the results of logistic regression analysis to determine the causal factors behind TB related stigma among adult men and women in India. In case of males, the likelihood of TB stigma increases with age (OR 1.15, p=0.038). It falls with non-Hindu religion (OR 0.85, p=0.000), rich income class (OR 0.88, p=0.000), both primary (OR 0.93, P=0.049) and 'secondary and higher' (OR 0.70, p=0.000) education levels, non-nuclear family background (OR 0.91, p=0.000) and married males (OR 0.81, p=0.000). Females from rural areas (OR 0.95, p=0.007) and reserved category (OR 0.88, p=0.000) are less likely to suffer from TB related stigma. It also falls with secondary and higher levels of education (OR 0.82, p=0.000) and married women (OR 0.91, p=0.000). The likelihood is higher among women both from the middle (OR 1.10, p=0.000) and rich (OR 1.05, p=0.028) income classes and those who are employed (OR 1.03, p=0.046).

Table 2: (Annex 4). Logistic regression results for stigma among adult men and women in India						
Explanatory Variables	**Men**			**Women**		
	OR	**P value**	**95% CI**	**OR**	**P value**	**95% CI**
Residence Urban *(Ref)*						
Rural	1.00	0.909	0.95 – 1.05	0.95	0.007***	0.91 – 0.98
Religion Hindu *(Ref)*						
Non-Hindu	0.85	0.000***	0.81 – 0.90	1.02	0.348	0.98 – 1.06
Reservation Unreserved *(Ref)*						
Reserved	0.97	0.244	0.93 – 1.02	0.88	0.000***	0.85 – 0.91
Wealth index Poor *(Ref)*						
Middle income	1.05	0.128	0.99 – 1.12	1.10	0.000***	1.04 – 1.16
Rich	0.88	0.000***	0.82 – 0.93	1.05	0.028**	0.99 – 1.10
Education level No education/Preschool *(Ref)*						
Primary	0.93	0.049**	0.86 – 1.00	0.97	0.296	0.92 – 1.02
Secondary & Higher	0.70	0.000***	0.65 – 0.74	0.82	0.000***	0.79 – 0.86
Age	1.15	0.038**	0.96 – 1.27	0.99	0.214	0.92 – 1.05
Household structure Nuclear *(Ref)*						
Non-nuclear	0.91	0.000***	0.87 – 0.95	0.98	0.288	0.95 – 1.01
Marital status Single (*Ref)*						
Married	0.81	0.000***	0.77 – 0.84	0.91	0.000***	0.88 – 0.95
Employment status Unemployed *(Ref)*						
Employed	0.98	0.653	0.93 – 1.05	1.03	0.046**	1.00 – 1.07
Total Sample	62,570			96,556		
LR Chi2 (11)	420.75			168.34		
Pseudo R2	0.007			0.002		
p>chi2	0.000			0.000		
Log likelihood	-29846.389			-47376.047		
*Source: Analysis of NFHS 3 unit level data; ***significant at 1 per cent **significant at 5 per cent*						

DISCUSSION

The above results hint at a difference in the TB related stigma scenario between adult men and women with respect to quite a few Indian states as well as the national level. At an all-India level, share of women nurturing TB stigma is marginally more compared to men. The state of Meghalaya appears to be a high stigma burdened state in case of men (in comparison to the all India share) but has lower stigma among women. Major states like Gujarat, Himachal, Uttar Pradesh, Punjab and Bihar where stigma from TB among women are on the higher side, are found to have lower stigma among men. An exploration of the possible causal factors behind TB stigma reveals that being married and having secondary and higher level of education significantly decrease the chances of stigma for both sexes. Similar results on the impact of education on TB related stigma have been arrived at by a study conducted in Lagos, Nigeria[11]. Residence and ethnicity are strong determinants of stigma in case of women but not men. Economic class impacts the genders differently with respect to stigma. Men from the rich income class are significantly less likely while women from the same class are more likely to carry TB stigma. The middle income class also increases the chances of stigma

among women while it has no impact in case of men. Studies conducted on TB patients in Addis Ababa, Ethiopia and Lagos, Nigeria, reveal that lower economic status is significantly associated with stigma[11,12]. Primary education and non-nuclear family structure are found to reduce stigma among men while having no influence on stigma among women. Men of higher age are more likely to nurture stigma from TB. Employed women have significantly higher chances of having TB stigma while in case of men employment status seems to have no role to play.

Stigma, which is moulded and disseminated by institutional and community norms and interpersonal attitudes, is a social determinant of health. Being a communicable disease, TB remains shrouded in severe social stigma in some communities which is even more aggravated by incomplete and often incorrect information particularly in relation to the path of spread of infection. Fear of isolation from friends and family may compel individual with symptoms to conceal their health condition and avoid diagnosis. Stigma is also believed to be one of the prime reasons for treatment non-compliance among patients. Defaulting on treatment can have serious consequences for community health including the emergence of more resistant strains of the bacterium.

As studies reveal, the association of negative attitudes like embarrassment, isolation, self-identification as a disease transmitter, etc. with TB discourage timely health-seeking and treatment adherence[6]. Hence providing correct information relating to TB and removing baseless fears can improve the stigma situation and motivate patients to seek health care on time. This is extremely crucial for arresting the spread of infection and effective TB control by the national program. Unidirectional focus on medical treatment of reported cases leaves out many who completely slip out of the program due to lack of a diagnosis, often demotivated by reasons including TB related knowledge deficiency and/or stigma issues. Further, on diagnosis becoming public, most of them suffered shunning and hostile behaviour from friends and family, to which they reacted by isolating themselves, becoming secretive about their illness and even abandoning treatment midway[10]. Since incomplete TB treatment has serious implications for community health, a modification in the outlook and behaviour of community is needed. Paramedical health service providers could play an effective role by counselling patients and their family members on their visits to health facilities about the curable nature of TB and length of treatment necessary to render it non-infectious, thereby providing social support.

CONCLUSION

Due to excessive focus on achieving 'detection and cure rate' targets, the national program dedicated to the control of TB in India often tends to lose sight of the deeper socio-economic issues that shape and mould people's perception of TB including the severe stigma that leads to under-diagnosis, under-reporting and treatment default. Although steps have been taken by the Ministry of Health to improve knowledge and awareness about the disease among the general public, more conscious efforts need to be directed to the spread of correct information about TB taking particular care to reach out to the socio-economically vulnerable strata like the poor, illiterates and socially backward communities who also happen to be the most susceptible groups for contracting the TB disease. Gender sensitive interventions incorporating inter-state variations in TB related stigma burden are also crucial for the program's success in meeting international targets.

ACKNOWLEDGEMENT

The author wish to acknowledge National Family Health survey 3 for giving permission to use the national data.

CONFLICT OF INTEREST

None

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DOI https://doi.org/10.3126/saarctb.v18i1.34142

Case Study

ADULT ONSET STILL'S DISEASE PRESENTING WITH TUBERCULOUS BRONCHOPNEUMONIA: A CASE STUDY

Manmathan R[1], Rathnapala A[1], Siribaddana A[1],

[1] Department of Respiratory Medicine, National Hospital Kandy, Sri Lanka

ABSTRACT

Introduction: The occurrence of Post primary Tuberculosis [TB] can be due to reactivation of previous infection or reinfection. Reactivation of TB could occur due to many conditions including immunosuppressive drug therapy and immunosuppressive diseases. In countries where latent TB is common a good vigilance is needed for early detection of TB when such conditions are managed.

Adult onset Still's disease (AOSD) is a rare systemic disorder of unknown etiology where fever, rash, lymphadenopathy and multi organ involvement occur. ASOD is a challenging condition to diagnose as there are no pathognomonic physical signs or markers. Early diagnosis and initiation of treatment is important as diagnostic delays could lead to serious consequences [(1)].

Occurrence of tuberculosis in a patient with AOSD has not been documented in literature to-date. Here we describe a 46-year-old male who presented with low grade fever and arthralgia for more than one month with organomegaly and pericardial effusion managed as AOSD, later developed Tuberculous bronchopneumonia.

Keywords: Tuberculosis, pericardial effusion, adult onset of still disease

INTRODUCTION

Tuberculosis (TB) contributes to high mortality and morbidity world-wide. Around one third of the world population carry the infection. Latent TB infection may reactivate causing active disease. [(2)] Diagnostic delays play a major role in poor outcome.

Bacteriological confirmation of TB requires sputum examination for AFB or Catridge Based Nucleic Acid Amplification Test (CBNAAT) for TB, and culture. Chest radiography (CXR) and High Resolution Computed Tomography (HRCT) of chest are useful imaging tests [(3)].

Correspondence:
Dr. Rasaiah Manmathan,
Senior Registar in Respiratory Medicine
National Hospital Kandy
Sri Lanka
Ph: 0771348161
E-mail:rmanmathan5@gmail.com

Adult onset of still disease (AOSD) is a systemic disorder of unknown etiology which is characterized by fever, rash, lymphadenopathy and multiorgan involvement. It is a rare disease with a prevalence of 1 in 100,000.(1) ASOD is common in young adults with a bimodal distribution at 15-25 and 36-46 years of age[(4)]. Diagnosis of ASOD is difficult in the absence of specific clinical features or tests. It is important to exclude infection and multisystem disorders with similar presentation. Several criteria have been proposed to diagnose ASOD, Yamaguchi's and Fautrel's criteria being the mostly used [(5,6)].

The Yamaguchi's criteria require five or more criteria where two or more must be major criteria which are Fever >39 °C lasting 1 week or longer, Arthralgia or arthritis lasting 2 weeks or longer, typical rash and Leukocytosis >10,000/mm3 with >80% polymorphonuclear cells. The minor criteria are sore throat, recent development of lymphadenopathy, hepatomegaly or splenomegaly and abnormal liver function tests. Tests for

antinuclear antibody, and rheumatoid factor (IgM) should be negative [5].

Fautrel's criteria requires four or more major criteria or 3 major and 2 minor criteria. The Major criteria are Spiking fever ≥39 °C, Arthralgia, transient erythema, Pharyngitis, Polymorphonuclear cells ≥80% and glycosylated ferritin ≤20%. The minor criteria are maculopapular rash and leukocytosis ≥10,000/mm3. Both criteria do not include pericardial disease. (6) With extensive literature review we could not find occurrence of tuberculosis with AOSD.

Case presentation

A 46-year-old male presented with high grade, intermittent daily fever for 1-month duration which responded to paracetamol. He also complained of arthralgia of small joints of both hands and feet with morning stiffness. He didn't have skin rash or sore throat. He denied history of cough, hemoptysis or contact history of TB. He did not have any remarkable past medical history and was not on any medication.

On examination he was febrile. He did not have lymphadenopathy, joint swelling or rash. There was hepatosplenomegaly of 1cm each. The rest of examination was normal.His lab investigations revealed a neutrophil leukocytosis(white cell count 14 000, N-82%), normal red cell and platelet parameters and normal renal function. Blood, urine and sputum cultures were sterile. His Erythrocyte Sedimentation Rate was 90mm/hour, C-Reactive Protein was 70mg/dL, Gamma GT was 180U/L, Alkaline phosphatase was 220U/L, Aspartate Transaminase was 65U/L, Alanine Transaminase was 70U/L. Sputum for Acid Fast Bacilli (AFB) 3 samples and PCR for TB [gene X pert] were negative, CXR at the disease onset was normal (figure-1).

Mantoux was 12mm. Serum ferritin was elevated at 2550ng/ml. Serology for HIV was negative. Ultrasound scan showed mild hepatosplenomegaly. His autoimmune profile such as Anti-nuclear antibody (ANA), Extracted nuclear antigen panel (ENA), Rheumatoid factor(RF), Anti-CCP antibody, Anti double stranded DNA were negative.

Transthoracic echocardiogram showed thin pericardial effusion with normal left ventricular

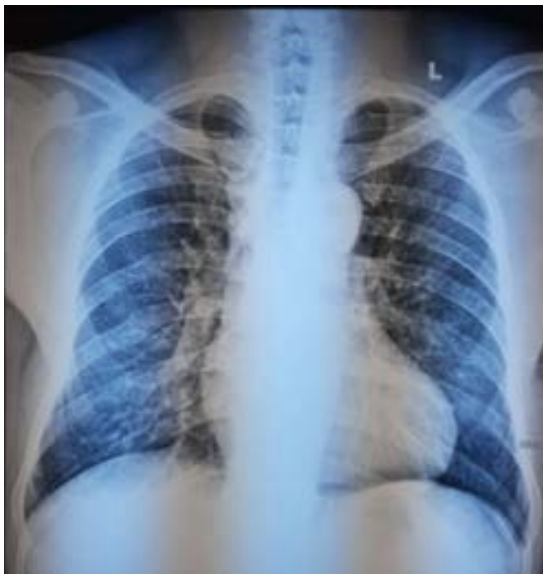

Figure -1 : CXR at the disease onset

function. The patient developed breathlessness after two days and repeat echocardiography revealed a moderate pericardial effusion. Pericardiostomy and pericardial biopsy was done. The pericardial fluid was negative for pyogenic culture, TB culture, and gene Xpert. Histopathology of pericardial tissue revealed no granuloma or evidence of malignancy but showed evidence of an inflammatory response. As the currently used criteria were fulfilled, we made a diagnosis of ASOD and the patient was commenced on Non-Steroidal Anti Inflammatory Drugs and subsequently high dose steroids (50mg). Fever subsided and the pericardial effusion completely resolved within one week. After two weeks of symptom free interval he presented again with fever, cough, and worsening breathlessness. Repeat CXR revealed bilateral patchy consolidation (figure-2).

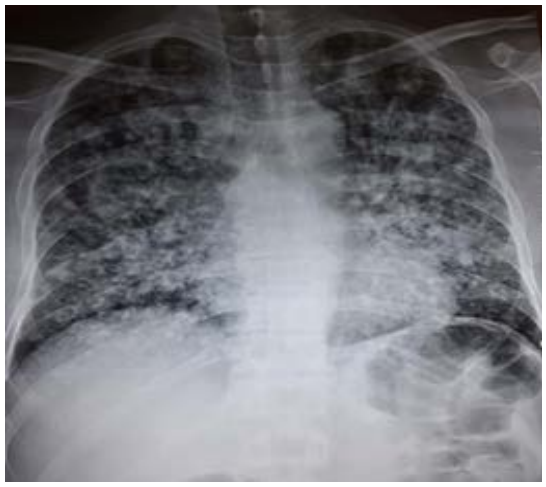

Figure-2 : The CXR following the treatment of AOSD

Sputum AFB was negative but gene X pert gave a positive result on the first sample. The HRCT chest revealed centrilobular nodules and tree in bud appearance suggestive of endobronchial spread of infection (figure-3).

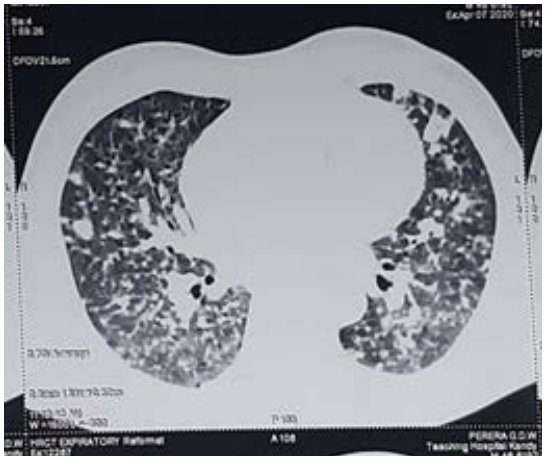

Figure-3 : The HRCT chest following the treatment of AOSD

We reconsidered the diagnosis and tailed off steroids, stopping NSAID. Anti TB drugs were commenced after obtaining sputum for mycobacterial culture. Following initial good response of five days the fever recurred with arthralgia. This was settled following recommencement of steroids and NSAID. We concluded that this patient has ASOD which was followed by rapid development of Tuberculous bronchopneumonia.

DISCUSSION AND CONCLUSION

The initial clinical presentation of our patient had a wide differential diagnosis including infections, connective tissue disorders and vasculitis. As the diagnostic criteria of AOSD highlights, we did a thorough work up to exclude infections and Connective tissue diseases. Although the Yamaguchi's and Fautrel's criteria do not include pericardial disease, it has been reported to occur with AOSD [7]. The patient in this report fulfilled 3 major and 2 minor Yamaguchi's criteria. The ferritin level was elevated but glycosylated fraction could not be used due to non availability.

With ongoing fever and pericardial effusion with a positive Mantoux test of 12mm TB pericarditis was also considered a high possibility at the initial presentation. It was excluded as bacteriology and histology was negative for TB. When high dose steroids were commenced isoniazid prophylaxis was not initiated due to the elevated liver enzymes. Whether isoniazid would have prevented occurrence of TB or the possibility of induction of isoniazid resistance when used as monotherapy in this situation as the severe bronchopneumonia occurred just two weeks of steroid therapy remains to be answered. But the close follow-up and the high sensitivity, specificity and rapidity of gene Xpert of sputum[8] enabled us to arrive at a quick diagnosis. This was important as many other pathogens could cause severe bronco- pneumonia in patients on high dose steroid therapy.

Chest imaging is useful to assess the extent of pulmonary TB. It showed an extensive bronco-pneumonia in our patient. The HRCT identified micronodules which were mainly centrilobular with the typical tree in bud appearance suggestive of TB.

High dose steroid therapy is known to cause reactivation in latent TB leading to active disease. Whether ASOD per se causes reactivation of TB needs to be investigated.

ASOD is a rare disease, with diagnostic difficulties. We suggest to include pericardial disease in the diagnostic criteria. In latent TB close observation for occurrence active disease is important when using immunosuppressants.

CONFLICT OF INTEREST

None

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I. Instruction to Authors

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The SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS is devoted to dissemination of knowledge concerning various aspects of tuberculosis, lung diseases and HIV/AIDS. All articles relevant to the practice of this Journal and quality research are published. The Journal is an appropriate 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/minireview, case report, short communications, and letters to editors within the scope of the journal.

I.2. Editorial Policy

The SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS will evaluate all the manuscript submitted for publications. The manuscript that might raise issues contrary to human welfare will be thoroughly evaluated. The manuscript submitted must contain sufficient detail, and material/information must be made available, to permit the work to be repeated by others. The editorial decision is final decision to accept or reject such manuscripts. The editor-in-chief has full authority over the editorials content of this Journal and the timing of publication of the content. He is responsible for evaluation, selection and editing of individual articles.

I.2.1. Ethical Guidelines

The SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS requirements for submitted manuscripts are consistent with the Uniform Requirements for Manuscripts Submitted to

Biomedical Journals, as updated by international Committee of Medical Journal Editors in April 2010 (http://www.icmje.org).

All authors wishing to submit manuscripts in this Journal are expected to adhere to the highest ethical standards. The following sections include detail information about SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS ethical standards. Failure to comply with the policies may result in a suspension of publishing privileges in this Journal. The editorial board decides to clarify the following issues;

Plagiarism: Misappropriating another person's intellectual property constitutes plagiarism. This includes copying sentences or paragraphs verbatim (or almost verbatim) from someone else's work, even if the original work is cited in the references. The NIH ORI publication "Avoiding Plagiarism, Self-Plagiarism, ad other Questionable Writing Practices: a Guide to Ethical Writing" can be referred to help authors identify questionable writing practices (http://ori.dhhs.gov/edu/education/product/plagiarism).

Primary publication: By submission of a manuscript is a representation that the manuscript or one with substantially the same content, was not published previously and is not in consideration for publication. It is author's responsibility to acknowledge any prior publication with data contained in a submitted manuscript, including his/her own article. In such cases, a copy of the relevant work should be submitted with the manuscript as a supplemental material. Editorial decision is a final decision to accept or reject the manuscript. The original articles submitted to the Journal must represent reports of original research and the original data must be available for review by the editor if necessary.

The manuscript is not acceptable for submission if it, or its data has been published in conference report, symposium, or any proceedings, a technical bulletin, book or any other retrievable sources. However, the following do not preclude submission; publication of limited amount of original data on a website, publication of method/protocol on a non personal website, dissemination of research findings as posters and publication of data in theses and dissertation on a university hosted website.

I.2.2. Permission

The corresponding author is responsible for obtaining permission from the original author and the publishers if he/she wishes to reproduce or modify any table or figures or to reproduce text in part or as a whole from previous publication. In addition to a signed permission (s) a statement indicating that the material has been reprinted with permission must be mentioned as legend of figure or table footnotes. The reprinted text must be quoted within the quotation mark.

I.2.3. Authorship

An author is the one who has substantially contributed to the concept, overall design, execution of the study/ experiments, acquisition of data, writing the manuscript and critically revising the intellectual content. The individuals who provide assistance like, providing strains, reagents, acquisition of funding and collection of data need not to be listed as authors but may be recognized in acknowledgements. All authors must take full responsibility for the initial submission and subsequent revision, including appropriate citation and acknowledgement. They must have agreed upon that corresponding author will have authority to act on all matters related to publication. He/she must communicate all the information related to submission, review and publication to the authors and co-authors. Submitting a manuscript before all co-authors have read it is considered an ethical violation. All authors must agree to the order in which their names are listed in the byline. Statement regarding equal contribution by two or more than two authors should be written as statement below the byline and must be agreed by all authors. The **authorship form** should be submitted along with the manuscript. The change in order of the authors is acceptable only after receiving the signed statement by all authors.

The assistance like, technical help, writing assistance, or a department chairperson who provided general support should be in acknowledgement. Groups of person who have contributed materially to the paper but their contribution do not justify authorship may be listed under headings as, "served as a scientific advisor", "critically reviewed the study proposal", "collected data", provided and cared for study patients" in the acknowledgement.

I.2.4. Conflict of Interest

All authors submitting a manuscript are expected to **declare their conflict** of interest. Conflict of interest in terms of any commercial affiliations as well as consultancies, equity interest, patent- licensing should be expressed. It is the responsibility of authors to provide, in the acknowledgments section, a general statement disclosing financial or other relationships that are relevant to the study. In case if a manuscript uses any commercial products, the name of manufacturer's name should be mentioned in Methodology.

I.2.5. Copyright

On acceptance of the manuscript for publication the corresponding author on behalf of all authors needs to sign the copyright transfer agreement. The article will only be published after signing this agreement. The copyright grants to the author to republish the discrete portion of the article in any other forms like, CD Rom, electronic format, print in the condition that appropriate credit is given to the SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS. Significant portion of the article can not be hosted in the internet without the written permission of the Journal. However, given appropriate credit to the Journal, the article can be published in the University hosted websites.

I.2.6. Use of Human or Animal subjects in research

The use of human subjects or other animals for research purposes is regulated by the SAARC member states and individual institutions within these member states. Manuscripts containing information related to human or animal use should clearly mention that the research has complied with all relevant human subjects and animal right guidelines and institutional policies. If necessary, copies of these guidelines and policy documents should be provided to the editor.

I.2.7. Published statement of informed consent

The SAARC Tuberculosis, Lung Diseases and HIV/AIDS adhere to the Uniform Requirements for Manuscripts for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication. Patient identifiers will not be published, unless written informed consent is given. Photographs of subjects must be accompanied by their signed release authorizing publication. Failure to obtain informed consent of patient prior to submission would result in manuscript rejection.

I.2.8. Submission, Review and Publication Process

I.2.8.1. Submission: Manuscripts can be submitted online (www.saarctb.org) or through an email (saarctb@mos.com.np) to the chief editor, SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS.

I.2.8.2. Review: All manuscripts submitted to the Journal online or through email are unbiased, confidential and undergoes a critical review. The author will be sent an email acknowledging the receipt of the article. The manuscript will be assigned a number (eg. 01/11; first paper received in the year 2011). Each manuscript is reviewed by the editors, editorial board, and ad hoc reviewers.

All submissions first go through an internal review process. The internal review involves the selection of articles based on some criteria like, articles within the aims and scope of the Journal, subject content, originality/flaws in the scientific validity, ethical issues, conflict of interest, little new information, an unprofessional presentation, sufficient quality of English and the compliance of Instruction to Authors. Once the submitted articles meet the eligibility criteria then the article is sent to a Statistician for statistical review.

The statistical review is provided by Statisticians in a form of a written report containing clear and straightforward suggestions and comments for both Journal editors and authors. A statistical reviewer reads a paper throughout, from the title and abstract, to the body text, to tables, figures, and references and makes notes on anything that requires clarification or explanation, or wherever a question may be raised in the text or data. If study is considered statistically acceptable, the statistical reviewer may suggest acceptance of the manuscript on the statistical grounds. If there are statistical errors in data and wrong use of statistical tools, statistical reviewer provides specific suggestions for the author on how to improve the manuscript. However, if errors are made in the study design, the manuscript is not accepted.

The manuscript is then reviewed by the co-editors (researcher/epidemiologist) in SAARC TB and HIV/

AIDS Centre and then by the editor. When all the criteria are met by the manuscript then the editorial board identifies the external reviewer having expertise in the same field. In case some minor changes are needed to be made by the author the manuscript will be returned back to the corresponding author to do so. Corresponding author should be responsible to communicate to other authors.

The manuscript will be uploaded in the website for the review process. The database contains information on reviewing history, including number of current assignments, reviews completed in the past year and length of time taken, date of most recent review, and editor's evaluation of submitted reviews. In case, if articles received in which the regular reviewers are not experienced, we identify reviewers based on their scientific papers published in PUBMED and request to review them.

Inquiries to reviewers are sent via E-mail messages, which include the manuscript and the assignment deadline. When prospective reviewers agree to serve, they are permitted access to the manuscript and reviewing instructions. The time allocated for initial review is 2 weeks and if reviewer fails to do so, three reminders each of one week are allocated. Failure to review manuscript within this time frame will be retracted and sent to another reviewer. Reviewers send their critique back to the office. After receiving the comments from the reviewer it is again analyzed internally. Minimal changes are handled by the editorial team. If there are major changes to be made in the article, the manuscript is send back to the author to make those changes.

Generally, it takes 4-6 weeks from submission to review process and corresponding author will receive the information whether the manuscript has been accepted, rejected or needs minor modification. For the manuscripts rejected by the reviewer the author is informed with the comments of the reviewer. If modification is requested, the corresponding author should

resubmit within a week or withdraw the article. Withdrawn articles can be resubmitted with all the issues addressed and the cover letter should clearly mention that it is the resubmission.

I.2.8.3. Acceptance: When the article has been accepted for publication on the scientific merit, the author will be notified of the acceptance of the manuscript. The volume and the year of publication in which the article will be published will also be mentioned. The duration from the submission to the manuscript acceptance will take 4-6 weeks.

I.2.9. Page proof: The manuscript in a PDF file will be send back to the corresponding author for page proof. The PDF page proofs must be printed out and correction should be made in hard copy. The correction needs to listed and sent back to the Journal. Failure to do so will delay the publication.

1.3. Organization and Format

1.3.1. Principles

All types of articles should be written in English (UK), New Times Roman, font size 12 and in double sized space. The manuscript should be submitted in Microsoft office document .doc or. docx. The text of observational and experimental articles is divided into Introduction, Methodology, Results and Discussion, i.e. IMRAD format. When submitting an article, the first page should contain title of

manuscript, author's list, affiliations, and name, affiliation and address of corresponding author. The second page should

include abstract with key words. The third page should include the body of article (introduction, methodology, results, discussion, conclusion and acknowledgement). The reference should be in different page. The headings like, ABSTRACT, INTRODUCTION, METHODOLOGY, RESULTS, DISCUSSION, CONCLUSION, ACKNOWLEDGEMENTS, and REFERENCES should be written in upper case and bold faced letters. The tables and figures should be in different page.

Table: Type table in separate page. Table should be numbered consequently. Table should be self explanatory with adequate headings and footnotes. The position of the table in the text should be indicated. The heading should be written as, **Table 1 (Annex I).** Title of the table. the table number is in bold faced letters followed by full stop. The table should be cited in the text as (Table 1). The number of tables should be minimized as much as possible with maximum information.

Illustrations (Figure and Photographs): Figure should be numbered consequently in the order of their first citation in the text. They can be inserted as a word document or uploaded as a separate image files. Images (photographs or drawings) should be sharp and usually 5 X 7 inches, in jpeg or tiff format and resolution of 300 dpi. Letters,

numbers and symbols should be clear and of sufficient size so that it is visible when reduced. Legend should be provided at the bottom of the figure. The legend of the figure and photograph should be written as, **Figure 1 (Annex II).** Legend of the figure, the figure number should be written in bold faced letters followed by full stop and then the legend for the figure. The images (figure and photographs) should be cited in the text as (Figure 1). Photograph of a person should not be identifiable unless it is accompanied by the written permission of the subject. Permission to reproduce illustrations as a whole or in part or with modification should be obtained from the original publishers and authors and submitted with the manuscript.

Original Article

- Title page
- Author's Name and Affiliations
- Name and contacts of Corresponding Authors
- Abstract
- Key words
- Introduction
- Methodology
- Results
- Discussion
- Conclusion
- Acknowledgement
- References

All units of measurements should be expressed in SI units.

The drug names should be provided in generic names, the use of generic name is not permitted. Manuscript should avoid contractions like, can't, don't, haven't etc.

The chemical nomenclature should follow the recommendations made by the recognized authority for the names of chemical compounds in Chemical Abstracts (CAS; **http://www.cas.org/**) and its indexes. The biochemical nomenclature should be in accordance with Biochemical Nomenclature Related Documents available at **http://www.chem.qmul.ac.uk/iupac/bibliog/white.html**.

The enzymes name should be used as recommended by the Nomenclature Committee of the International Union of Biochemistry (IUB) as described in Enzyme Nomenclature available at http://www.chem.qmul.ac.uk/iubmb/enzyme.

Binary names, consisting of generic name and a specific epithet (e.g. *Mycobacterium tuberculosis*) must be used for all organisms. A specific epithet must be preceded by a generic name, written out in full in its first appearance (eg. *Mycobacterium tuberculosis*) and can be abbreviated on subsequent uses (e.g. *M. tuberculosis*).

References: The referencing style followed by the Journal is Vancouver Style. Follow the link for the reference, http:/www.library.uq.edu.au/training/citation/vacouver.pdf

Any queries related to organization and format should be addressed to editor SAARC Tuberculosis, Lung Diseases and HIV/AIDS at **saarcjournal@saarctb.org**

The organization and format for submission of different kinds of manuscript are as follows.

1.3.2. Editorial

Editorial is written by the editorial team and is not open to the external authors.

1.3.3. Original article (3000 words)

Title page: This page should contain 1) a concise and informative title not more than 125 characters (including spaces) in bold faced upper case letters and without abbreviations 2) Names and affiliations of all contributing authors in bold faced letters, place an asterisks as a superscript for a corresponding author 3) The full name of corresponding author, designation, affiliation, address, single e-mail should be provided. This will be published in the article to facilitate communication 4) word count of text (not more than 3000 words) excluding titles, references, tables and figures.

Abstract (250 words): Should be written in structured format (Introduction, Methodology, Results and Conclusion) and should not be more than 250 words excluding the titles. Objectives should be the last sentence of the introduction. Do not write the experimental details. The abstract must be understandable without referring the text. Avoid abbreviations and references. Do not include tables and figures.

Key words: Below the abstract identify 3-5 key words to assist indexers in cross-indexing the article. Non-standard abbreviations should be avoided. First letter of each key word should be written in upper case. All the key words should be italicized.

Introduction: The introduction should be sufficient to provide the background information to allow reader to understand the hypothesis and rationale for the study without referring to other publications in the topic. Most appropriate references should be selected to provide most salient introduction rather than explicit review of the topic. Explain the abbreviation at its first appearance

Methodology: This should include sufficient information including study design, setting, study period, study population, selection of subjects (inclusion and exclusion criteria), scientific basis of selection of sample size, method of sampling, data collection procedures in detail, ethical consideration, data analysis and statistical tools used. The information on source of materials (name and location of manufacturer) must be provided. If numerous methodologies already exist, brief explanation of the procedure and the reference is sufficient. If the procedure is new, all technical details of the procedures should be written. This is to allow the study to be repeated by others. Statistical analysis if any should be mentioned in this section.

Results: The result should be presented in a sequential manner in text, tables and figures as concise as possible. Avoid using extensive graphs, tables and figures which can be written in text. Make sure they are all numbered in the order they appear in the text. Whatever has been presented in the table and figure need not to be written in text.

Discussion: This section must not extensively repeat the results instead should provide an interpretation of the results in relation to previously published work. The implications of the findings, their limitation and recommendations should be presented. Avoid unqualified statements and conclusions which are not completely supported by data. Avoid claiming priority. New hypothesis may be labeled as recommendations.

Conclusion (s): Summarize your findings and highlight the importance of the study. Simply do not repeat what has already been mentioned in previous sections of the manuscript. Based on the findings a recommendation should be made.

Acknowledgement (s): The source of any financial support for the work being published must be indicated in this section. Recognition to any personal assistance should also be mentioned in this section. The authors also need to declare financial or competing interest if any.

References: The referencing style followed by the Journal is Vancouver Style. Follow the link for the reference http:/www.library.uq.edu.au/training/citation/vacouver.pdf

1.3.4. Review/Minireview

Reviews should not merely be the collection of previous findings in quotes from journals, reports and text books. It should be up to date, accurate and should contribute significantly to the scientific community. The review should be in depth analysis of the problem, background to this problem, science behind the problem, methodology, discussion, recommendation, conclusion, future perspectives, acknowledgement and references. Abstract should be unformatted and not more than 300 words and the text should not be more than 4500 words. The tables and figures (combined) should not be more than 7. The references should not be more than 40.

The Minireviews should be focused discussions of defined topics relevant to the scope of the SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS. They are not expected to be comprehensive reviews of the literature but rather focused discussions of specific topics. The minireview should include analysis of the problem, background to this problem, science behind the problem, methodology, discussion, recommendation, conclusion, future perspectives, acknowledgement and references. A standard title page should be provided. This is followed by an unformatted abstract which should be not more than 250 words and then the text of the minireview should not be more than 3500. Up to 5 tables, figures, or photographs (combined) may be included. Less than 30 references should be used. Minireviews will be reviewed by the SAARC Tuberculosis, Lung Diseases and HIB/AIDS editors and will be peer reviewed.

1.3.5. Case reports (1000 words)

A Case Report should include five sections; abstract, introduction, case report, discussion and conclusion. The title page must include title, authors list and their affiliations and corresponding author's name, affiliation and address. The abstract should be no more than 150 words. The abstract should be non structured and should include introduction, patient, result and conclusion. The abstract should follow by key words, 3-5 key words. The body of case report should not be more than 1000 words and should include introduction, case report, discussion and conclusion. This should be followed by acknowledgement and references (not more than 10). The total number of tables and figures (combined) must not exceed 2.

1.3.6. Letters to editors (500 words)

Letters to editor should not be more than 500 words and must cite references (not more than 7) to support the writer's argument. For Letters commenting on published articles, the cover letter should state the volume and issue in which the article was published, the title of the article, and the last name of the first author. Letters to the Editor do not have abstracts.

1.3.7. Short communication (1000 words)

The short communications that are within the scope and are of particular interest to the readers of the SAARC Tuberculosis, Lung Diseases and HIV/AIDS are published. Abstract should be no more than 150 words. Manuscripts are limited to 1000 words, one figure, one table and not more than 10 references.

1.3.8. Errata

This section provides an opportunity of correcting errors that occurred during the writing, typing, editing, or publication. These errors could be a misspelling, a dropped word or line, or mislabeling in a figure in a published article. Authors can submit errata using the online manuscript submission or via the email (See below).

1.4. Submitting manuscript

Manuscripts can be submitted online (www.saarctb.org) or through an email (journal@saarctb.org) to the chief editor, SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS. Authors should ensure following documents to be sent if he/she wishes to send manuscript via email or online system. 1) Cover letter 2) Authorship form 3) Declaration form 4) Manuscript (Title page, Abstract, Body of article, References) and 5) Letter of Ethical Approval or A statement of clearance of the study protocol and the study by the Ethical Committee/Board mentioned in Methodology.

1.5. Publication charge

The SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS is available in printable and online open access electronic versions and is free of charge.

Article Submission Guidelines

Guidelines for submission of article to the SAARC Journal of TB, Lung Diseases and HIV/AIDS through Online

We have revised our online article submission option on our website with the aim of streamlining the process for submission of articles and providing better, quicker information to all.

We would like to invite all authors who want to submit a paper to the SAARC Journal of TB, Lung Diseases and HIV/AIDS to do so online via our website: **http://www.saarctb.org**, to use the system, you must first register – to do this, please follow the instructions given below:

- Please go to **http://www.saarctb.org** and click on "**Journal**" you will see sub menus, **"Online Submission of Articles"**
- After click on "Online Submission of Article" you will be prompted to **Login Form** for **Sign up** for new user and **User Name** and **Password** for registered users, if an account already exists for you.
- Similarly, if you are a new user of this site, please "Sign Up" by clicking sign up, and go through the process by completing the format for register you see on the screen and register yourself on the website. Click on **Register**, then information will appear to open your e-mail.
- After successful completion of registration format, go to your e-mail, which is given by you during registration and to click on the link given by e-mail, then "**Article Submission Form**" will open from where you can submit your article. Later, you can directly "Sign In" on the Login Form by giving your User Name and Password.
- Please read the information given on **Article Submission Form** before submitting the article.
- After submitting article, you will see "**Your article has been submitted"** along with the acknowledgement "**Thank you for submission of article, you will be intimated regarding its suitability for publication within 4 months".**

Cover letter for SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS

Date:.....(Date of an email)

To,
The Chief Editor
SAARC journal of Tuberculosis, Lung Diseases and HIV/AIDS SAARC TB and HIV/IADS Centre
Thimi, Nepal

Dear Sir,

Subject: Submission of manuscript of titled, "……(Title of manuscript)"

On behalf of my co-authors, I would like to submit a/an……..(type of manuscript: original article, review, short communication etc.) titled "……(Title of manuscript)" to be published in your esteemed journal. This article is important to be publish in this journal ……..(Mention few sentences why your article is unique and needs to be published in this journal).

The manuscript comprises of; Number of words:…… Number of tables:…….
Number of figure:…… Documents attached herewith (✓):

O Authorship

O Declaration form

O Manuscript

O Ethical approval letter/A statement indicating clearance of the study protocol and the study by the Ethical Committee/Board.

Please, acknowledge the receipt of this article to my email or contact address. Hoping for your kind co-operation in this regards.

Sincerely,

----------(Initial)

Name : ……(Full name)
Affiliation : ……(Organization and post) Postal Address:…….
Phone No : ……(Mobile no.) Email : ……

Authorship form for SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS

Date:……..

To

The Chief Editor

SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS

SAARC Tuberculosis and HIV/AIDS Centre

Thimi, Nepal

Subject: Authorship for article titled "……..(Title of article)"

Dear Sir,

This authorship letter lists the name of authors in order as it appears in the manuscript. The contribution of each author in the work is as follows (✓).

Nature of work	Contribution of each authors						
	1	2	3	4	5	6	Add if any
Concepts							
Design							
Literature search							
Clinical studies							
Experimental studies							
Data acquisition							
Data compilation							
Statistical analysis							
Manuscript preparation							
Manuscript editing							
Manuscript review							
Signature of all authors							

On behalf of all my authors, I hereby declare that above mentioned authors, the order of author in the manuscript and their contribution is correct and I will be responsible for any claim of authorship beside listed in the above list.

Sincerely,

……(Initial) Corresponding author

Name : ……..(Full name)

Affiliation: ……..(Organization and post) Postal Address: ……

Phone No : ……..(Mobile no.) Email : ……

Declaration form for SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS

Manuscript title:……

Manuscript type:……

Corresponding author:

Name (First/Middle/Last):……Degree:……

Affiliation:…… Address:……

Contact number:……Contact e-mail:……

Authors (list authors in the order as appears in the manuscript):

SN.	Name (First/Middle/Last)	Affiliations/Address	Signature
1.			
2.			
3.			
4.			

(Add authors as required)

On behalf of authors, I am submitting the manuscript and I declare that;

1. The manuscript represents original work not published elsewhere nor is being considered for publication.
2. The original data will be provided to the editor if requested.
3. The order of author (s) name provided above is the correct order.
4. All authors have contributed at least a part in this work.
5. I will be responsible for submitting the manuscript and to communicate with editor and my authors. I will also be responsible to review the page proof.
6. We have no competing interest, financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.
7. I certify that financial support or any kind of support like, reagents/supplies/equipments for research, strains of bacteria etc are mentioned in acknowledgement section of the manuscript.
8. I hereby transfer and assign all copyright ownership exclusively to the SAARC Journal of Tuberculosis, Lung Diseases and HIV.AIDS. I shall take permission from chief editor to reproduce this article in any form.
9. I do understand that the decision of chief editor will be final regarding the acceptance of manuscript and publication.
10. I have a right to withdraw my manuscript with prior notice to the chief editor.
11. The clearance of the study protocol and the study by the Ethical Committee/Board.

……..(Initial) Corresponding Author

Date:

SAARC Tuberculosis and HIV/AIDS Centre (STAC)
Thimi, Bhaktapur
G.P.O. Box 9517, Kathmandu, Nepal
Tel.: 00977-01-6632601, 6632477, 6631048
Fax: 00977-1-6634379
E-mail: director@saarctb.org
Website: www.saarctb.org