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EDITORIAL

Original Articles

Case study

AIMS AND SCOPE:

The SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS is the official journal of the STAC. The Journal's main aim is the 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 relevant to the practice of this Journal and quality health 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/mini-review, case report, short communications, and letters to editors within the scope of the journal.

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Editorial

WHO declared tuberculosis as a global public health emergency in 1993. Global target for reducing the epidemiological burden of tuberculosis (TB) - measured as incidence, prevalence and mortality- have been set for 2015 within the context of millennium Development Goal (MDGs) and the Stop TB Partnership. The SAARC region, with an estimated annual incidence of 3.1 million TB cases, carries 37% of the global burden of TB incidence among which only 1.7 million are notified in the health system. Hence the number of missing cases is 1.4 million that accounts for almost half of the global missed cases.

The framework of the post-2015 global tuberculosis strategy is clearly defined and target is set for 2035. (The 75% reduction in tuberculosis deaths (compared with 2015) and 50% reduction in tuberculosis incidence rate by 2025). Reaching these targets in SAARC region will also require revisiting and adjusting the new strategy based on progress.

The region will require innovative, multisectoral, and integrated approaches for achieving the targets. It is also necessary to expand and strengthen partnerships with all care providers, civil society organizations and communities.

Ensuring universal access to early and accurate diagnosis of tuberculosis will require the strengthening and expansion of a network of diagnostic facilities with easy access to new molecular tests; information and education to people with symptoms of tuberculosis to seek care in service delivery.

The STAC, will coordinate with Member States in reviewing, adopting and implementing their post-2015 tuberculosis strategies in the SAARC region.

USING LOW COST INFORMATION TECHNOLOGICAL METHOD FOR COLLECTING CORE HIV/AIDS DATA IN TAMILNADU STATE AIDS CONTROL SOCIETY, INDIA

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ABSTRACT

Introduction: The value of mobile technology incorporated into the health system lies with its ability to make data and information available in a meaningful way to the users. mHealth services started in Tamilnadu AIDS Control Society(TANSACS) in 2010 for monitoring HIV/AIDS activities. The objective of the study was to examine the SMS based reporting system functioning in TANSACS.

Methodology: The reporting system was examined using interviewing and experiencing methods. Mobile phones are used to collect the data from the pre-coded SMS from reporting units; then it is stored in MySQL. Reports are generated daily.

Results: The daily performance of Integrated Counseling Testing Center and Anti-Retro Viral Therapy Center, and the weekly performance of Sexually Transmitted Clinic and ICTC stock positions were collected using this system. The later two were discontinued as the same was collected using other system. This reporting method is low cost and useful for collecting fewer data from facilities. The disadvantages are the reporting percentage was less due to non-reporting and congestion of reporting large number of centers in a short duration of time span, limited updation, offline facility and needed dedicated person.

Conclusion: This reporting method helps to identify the pocket with alarming (high) positivity of HIV and service gap on day to day basis to develop intervention strategy and to bridge the gap. It is recommended to upgrade the present system with SMS gateway system for better performance and compliance at user level.

Keywords: mHealth**,** Mobile phones, SMS, Text message, Data collection, TANSACS, Chennai

INTRODUCTION

eHealth is the use of Information and Communication Technologies (ICT) for health. mHealth(Mobile Health) is a component of eHealth. To date, no standardized definition of mHealth has been established. The Global Observatory for eHealth (GOe) defined mHealth as medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices. It involves the use and capitalization on a mobile phone's core utility of voice and short messaging service (SMS) as well as more complex functionalities and applications including general packet radio service (GPRS), third and fourth generation mobile telecommunications (3G and 4G systems), global positioning system (GPS), and Bluetooth technology.[1]

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According to the International Telecommunication Union there are now close to 5 billion mobile phone subscriptions in the world, over 70% of them reside in low- and middle-income countries and over 85% of the world's population is now covered by a commercial wireless signal.[2] Mobile phones are currently used in connection with a wide range of public health initiatives and examples exist from both developing and developed countries. The advantages of mobile technologies are vast: availability, accessibility, innovation, cost effectiveness, real-time access to information, and portability are just a few.[3] mHealth is being applied in maternal and child health, and programmes reducing the burden of the diseases linked with poverty, including HIV/AIDS, malaria, and tuberculosis (TB).

South-East Asia shows higher than average adoption (around 70%) of mHealth services than other regions. mHealth applications are being tested in such diverse scenarios as improving timely access to emergency and general health services and information, managing patient care, reducing drug shortages at health clinics, enhancing clinical diagnosis and treatment adherence, among others.

Tamilnadu AIDS Control Society (TANSACS) is an implementing agency for HIV/AIDS control program in Tamilnadu. Monitoring and supervision is the important process in program management. Program data have been collected for this purpose from all HIV/AIDS service facilities on monthly basis through Computerized Management Information System (CMIS) since 2006. In the view of getting needed core information from service facilities on day to day basis, SMS (Short Messaging Service) based reporting system has been initiated in TANSACS..

METHODOLOGY

The SMS based reporting system was started in the year 2010 in Tamilnadu AIDS Control Society (TANSACS) adopting an educational institution daily monitoring system of a district. The effectiveness of the reporting system was examined using interviewing and experiencing technique. All the users those sending the reports and officers utilizing the reports were asked for the usage and relevance of this reporting. And the reporting performance was analyzed at state wise data base.

Setting: All the service facilities of 787 Integrated Counseling and Testing Centers (ICTCs), 49 Anti Retro Viral Therapy (ART) centers and 156 Sexually Transmitted Infections (STI) Clinics in Tamilnadu functioning under TANSACS have been sending SMS. This data collection through this system is currently ongoing in the state.

Implementation and pre-testing: All the necessary information regarding this reporting was passed to all centers and Pilot program was conducted in a week period. Pilot testing was successful with only few errors in entering invalid data code which was later corrected before implementation of proper reporting. SMS costs are supported by the program.

SMS application: A simple SMS application was developed with the help of National Informatics Center (NIC) .Front end JAVA and back end Visual basics was used in this application. MySQL Database application has been used for data storage. All the required applications were installed in TANSACS headquarters office at Chennai. A mobile phone and easily memorable SIM number have been chosen for SMS collection. Mobile is connected with computer's SMS application via mobile PC-Suite application.

Data Flow: SMS information sent by reporting units have been transferred from mobile to SMS application through PC-Suite and date stored.

SMS formats: Specific SMS formats developed depending upon the data need from service facilities. The format coding starts with type of facilities district code, center code and subsequent program data fields.

Working Design: The reports which are generated from this reporting (State wise,

district wise and center wise) from this system are shared with Project Director daily.

RESULTS

SMS based reporting has created a sense of remote presence by the head office. Project Director monitors the centers performance on daily basis. Out of the four SMS reporting currently ICTC daily reports and ART daily reports are exist now. The STI clinic performance and ICTC kit weekly SMS systems are withdrawn as other technique of cloud services are introduced for this type of reporting. Alternative reporting method using Google Drive have been introduced for getting STI Clinic and ICTC kit data as it is convenient, user friendly and proper follow up.

Hardware and Software: The hardware for this system is a mobile phone with SIM and Windows installed computer. It needs daily on/off by a person. And the SMS Software is designed to operate manually. Hence, this consumes on average six hours of a staff per day. The software up-gradation or modification can be done by the program developer only.

Date Collection: The SMS data collection protocol is given in Table 1 and model formats are given in Table 2.

The SMS formats are pre-coded. It starts with code of the facility (ICTC-IC, ICTC Kit- KIT, ART-ART and STI Clinic-STI). After that two digit District code are given in all the reports except ART Daily; ART reports are coded with ART Center numbers. Then program indicators are coded sequentially.

Monitoring of the SMS from centers and Reports: A qualified and experienced person is allotted at Monitoring and Evaluation section. Knowledge of computer and mobile application are essential to follow up the system and update the centers facilities. He is managing the data collection, generation of reports and sharing the reports to Project Director.

All the SMS will be stored in real time basis in the system. The SMS receiving status is generated every hour and shared to district facilities for action. The different kinds of reports generated from this system include SMS receiving status, non-reporting status, SMS received in wrong format and program report. These outputs are given in Figure1, 2 & 3.

Table 1. SMS data collection and frequency

Facility	Indicators collected	Frequency	SMS Sending Time
ICTC	Total tested, total positive and Anti-Natal Clinic Attendees(ANC) positive	Daily	4pm – 6 pm
ARTC	Adult Pre ART registration, Child Pre ART registration, ART registration and CD4 testing	Daily	4pm – 6 pm
STI Clinic	Total attendees, TI-NGO referral, RMC and referral to ICTC	Weekly	Monday 9 am – 10 am
ICTC KITS	HIV Testing kits position center wise	Weekly	Friday 9 am – 10 am

TI-NGO - Targeted intervention Non-Governmental Organization, CD - Cluster Differentiation
RMC - Regular Medical Checkup

Table 2. SMS formats of different facilities

Type	Format	Example
ICTC Daily	IC <district code> <ICTC code> <Total HIV test> <Total HIV +VE> <ANC +ve>	IC 01 01 123 12 1
ICTC KIT Weekly	<KIT> <District code> <ICTC centre code> < Current Stock of Kit – I > < Current Stock of Kit –II > < Current Stock of Kit – III> < Current Stock of Kit – IV>	Kit 01 01 9999 9999 9999 9999
ART Daily	ART <ART center code> <Pre ART Adult reg.> <Pre ART Child reg.> <ART reg.> <CD4 tested>	ART 01 50 5 10 100
STI Clinic Weekly	STI <District code> <STI centre code> <Total STI atten.> <Ref. by TI-NGO> <MHC Scrn> <Ref. to ICTC>	STI 01 03 100 25 10 75

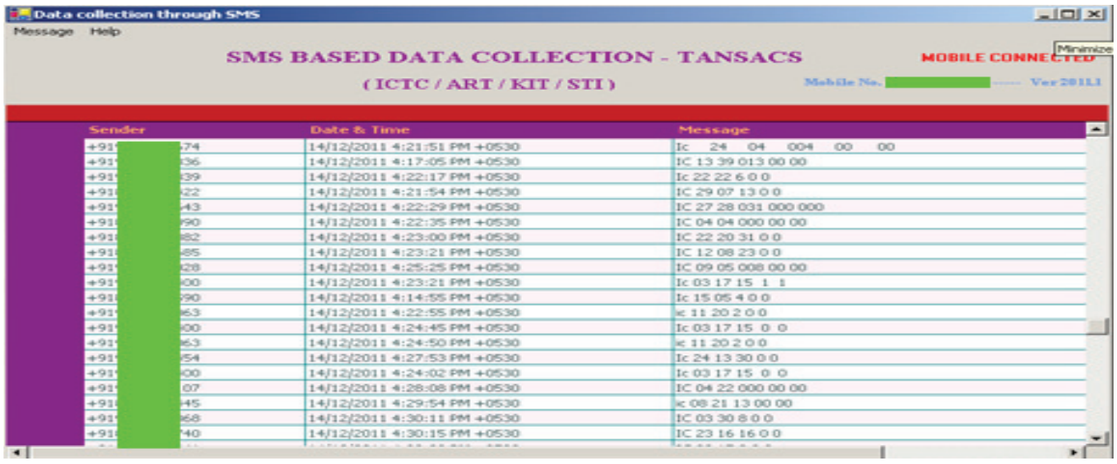

Figure1. SMS Receiving Status

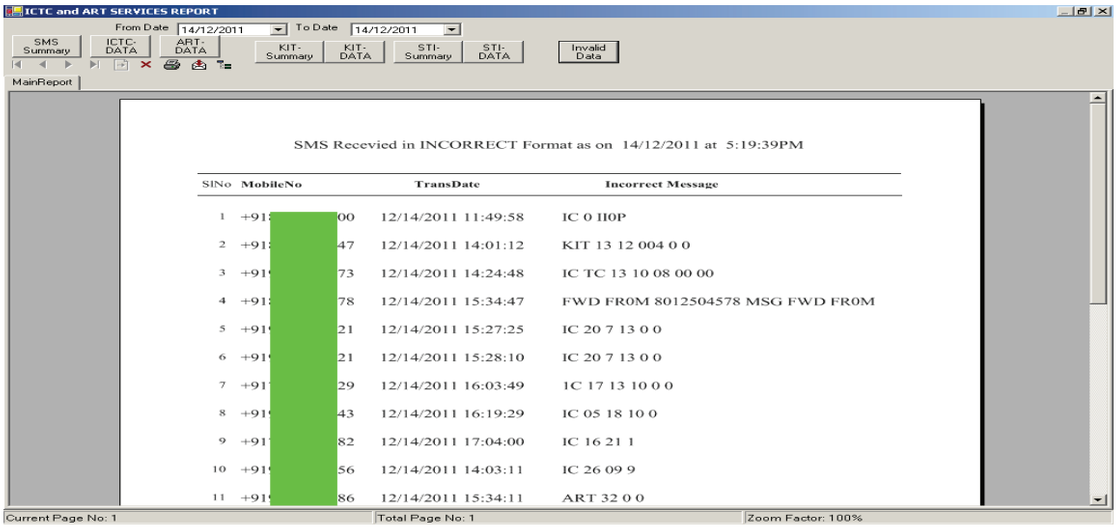

Figure 2. Wrong SMS formats report

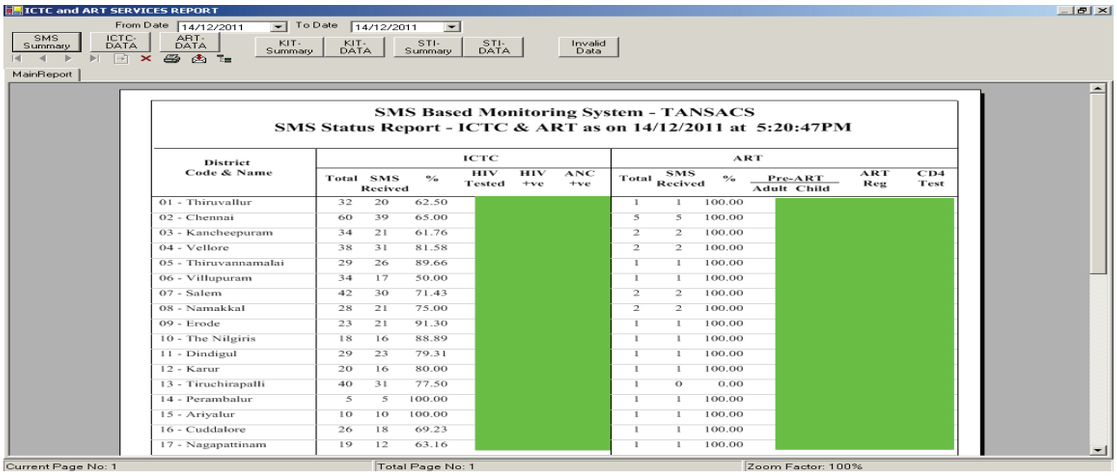

Figure 3.SMS Reporting status report

Compliance in Reporting: The purpose of this intervention is to measure scheme impact on the ground by aggregating and analyzing quantitative data collected according to certain defined parameters. As such, the success of the program is entirely contingent on official compliance to report data through SMS. We observed the average percentage of ICTC reporting is 65% in 2012 (Figure 4) and average ART performance is 96% in the year 2012. Based on these observations, it clear to conclude that compliance remains low.

The lower percentage of reporting is mainly due to SMS congestion because the 950 reporting units have been reporting in span of two hours. Other reasons include negligence from the centers and incapacity of mobile platform to handle huge volume of data at a time. The percentage of ICTC was increased to 90-95% today after giving time slot for SMS sending to districts and close monitoring.

Data Usage and impact: The generated report is actively monitored by Project Director and direction given on daily basis. A positive impact developed for Prevention of Parent to Child Transmission (PPTCT) services and ART program.

SWOT analysis: Determining the strengths and weaknesses of the program in the context of ICT-facilitated access to public information, lays the groundwork for identifying opportunities and threats that should either be exploited or mitigated for positive results.

Strengths:

1. Easy to use and low cost technology
2. Minimal training required
3. Sustainable
4. Mobiles are affordable, readily available at the local level, and can be used for multiple purposes
5. Non-dependent on electricity, infrastructure and connectivity at reporting center level
6. SMS are supported by the System

Weaknesses:

1. Jamming of reports due to which all reports are not delivered.
2. Not able to handle huge volume of data at a time
3. Underutilization of data
4. Need manual assistance always
5. Not able to collect more indicators
6. Errors of reporting are more
7. Less secure - Centers mobile numbers are not registered with the system. Hence any one can send the SMS to our data base.

Opportunities:

1. Motivate concerned authorities to take action on problems that the data suggests

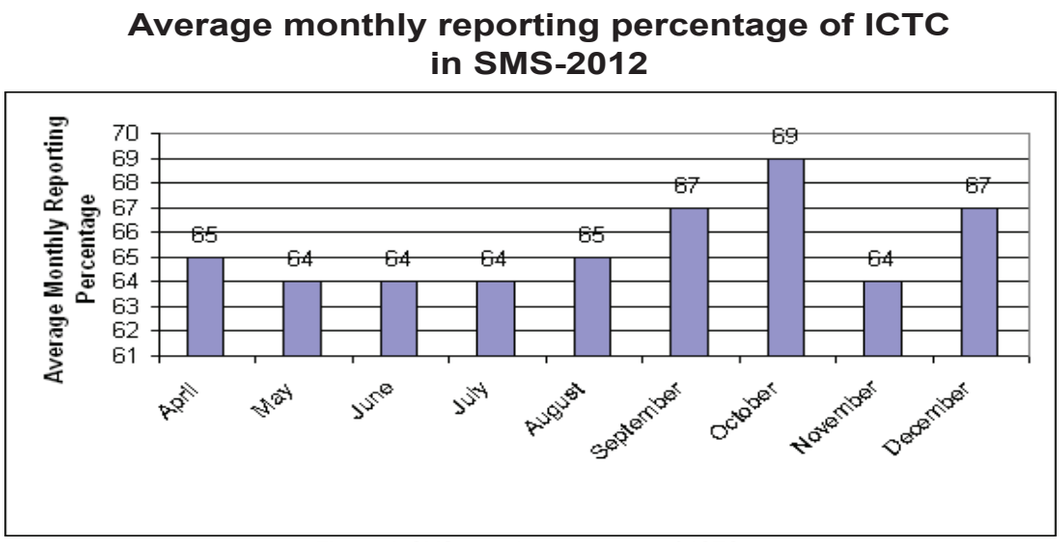

Figure 4. SMS reporting percentage of ICTCs

2. Promote citizen-centric organizations & citizens to access portal data and act as a 'watchdog' through feedback mechanisms
3. Increase compliance & ensure accurate reporting through capacity building and/or positive and negative reinforcement.
4. Utilization of data for improved public service delivery

Threats:

1. Resistance by local level staff to report
2. Fear of transparency leading to an administrative decision to dissolve program at user level based upon their performance; hence wrong reporting may be possible.
3. Collection of meaningless data as per the lack of validating its credibility.
4. As the system can accept the format send from any number, the data received may not be reliable.

DISCUSSION

The SMS-based monitoring system mandates information to flow from local levels of government to the State. As a result, it has contributed to internal efficiencies, altering the approach the government takes to deliver public services. The main advantages of using SMS messages for health campaigns are their low cost and broad reach. By means of technological improvement monitoring has become easy nowadays. But it has its own advantage and limitations. Short Message Service is provided by all mobile service providers. And mobile phones are available with most of the staff. SMS based reporting system is mainly used to rigorously monitor the uptake of the services (ICTC & ART), HIV positivity, Treatment and service utilization. It also helps to validate the data/information quality by cross verifying the Records with MIS reporting (Monthly consolidation) and Registers (during officers' visit to the field). It also helps to indentify the pocket with alarming (high) positivity and service gap on day to day basis to develop intervention strategy and to bridge the gap by further analysing the profile.

The existing SMS reporting system uses only SMS services. A Real-Time Bio-surveillance Program (RTBP) using mHealth Survey application to work on any Java-enabled mobile phone to collect and transmit digitized patient health records through GPRS (General Pocket Radio Service) piloted in Tamilnadu. Though this advanced application can collect the information effectively, the resistance of health workers to use the device, busy work schedule, low knowledge to adopt the technique and provide special equipments to every one were limitations.[4] Many surveys have been conducted using mobile phone as in National Rural Employment Guarantee Scheme.[5] ART medication, Vaccination reminder have been used using mobile technology nowadays. The mHealth Alliance and the Stop TB Partnership have released a report outlining ways that mobile health technology could be used to combat tuberculosis and HIV.[6] Many programs has started using the ICT techniques like HIV Sentinel Surveillance, District Level Household Survey-4.[7]

Government of India, Department of Information Technology, National Informatics Centre is providing SMS Gateway to government Institutions.[8] If TANSACS utilize this facility, it is able to monitor the reporting online and security issues will be minimized.

Mobile health provides benefits for all: patients, non-patients, health care professionals and managers.[9] As mobile health systems move towards scale, existing guidelines and strategies need to be revised to reflect new demands on executive sponsorship; National leadership of eHealth programs; eHealth standards adoption and implementation; Development of eHealth capability and capacity; eHealth financing and performance management; and eHealth planning and architecture maintenance.[10] Regulations regarding standards adoption and interoperability of mHealth and eHealth systems will play a key role in shifting market

dynamics to favour interoperability.

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EFFECT OF STORAGE ON SPUTUM SMEAR POSITIVE SAMPLES IN RELATION TO MICROSCOPY AND CULTURE FOR LABORATORY DIAGNOSIS OF PULMONARY TUBERCULOSIS

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ABSTRACT

Introduction: The cornerstone of the laboratory diagnosis of tuberculosis is direct microscopic examination of stained sputum specimens for tubercle bacilli. Sputum examination by microscopy is quick, easy and inexpensive whereas culture is most sensitive. The objective of the study is determine the storage effect on sputum specimens for smear positivity and culture isolation rates.

Methodology: This experimental study was conducted at B. P. Koirala Institute of Health Sciences, Dharan, Nepal. A total of 150 smear positive sputum samples which were also inoculated on a set of two Lowenstein-Jensen medium were taken for this study. All the samples were stored at room temperature (25°C) and in the refrigerator (4°C) for upto 7 days. On day 7, microscopy and culture were performed from each of these.

Results: On day 0, out of 150 smear positive samples, 39 smears were graded 3+, 46 were 2+ and 65 were 1+. Positive culture results for the 3+, 2+ and 1+ sputum's yielded 35, 46 and 46 samples respectively. Comparison of results after storage at RT and refrigerator for 7 days showed no statistical significance in smear reading while culture yield showed significance difference.

Conclusion: Smear results were not affected after storage but isolation rates were decreased at both temperature.

Key words: Storage, Sputum, Microscopy, Culture, Pulmonary tuberculosis

INTRODUCTION

The cornerstone of the laboratory diagnosis of tuberculosis is direct microscopic examination of appropriately stained sputum specimens for tubercle bacilli.[1] The smears stained by Z-N method can detect bacilli when they are at the order of 10^5/milliliter(ml) of sputum, whereas, a more sensitive staining technique like fluorescent stain detects the bacilli when they are at the order of 10^4/ml of sputum.[2] Culture method is more sensitive than microscopy as it can detect 10-100 mycobacteria per ml of sample. Therefore culture is considered the gold standard for diagnosis of TB.[3] A study done by Paramasivan et.al. (1983) who showed storage at RT in a tropical country for 28 days had no effect on smear results but the culture positivity rates were significantly decreased after storage.[5] Similar findings were shown by Banda et.al. (2000) and Rao et. al. (1966).[6,7] The objectives of the study was to determine the storage effect on sputum specimens for smear positivity and culture isolation rates.

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METHODOLOGY

This was an experimental study conducted from 1st July 2006 to 12th March 2007, B. P. Koirala Institute of Health Sciences, Dharan, Nepal. All the smear positive sputum samples from new cases

were included in this study. Sputum samples were decontaminated by modified Petroff's method. Microscopy and culture on a set of 2 L-J media were done on the same day.[1,4]

A total of 150 were included in this study. All the samples were stored at RT (25°C) and in the refrigerator (4°C) for upto 7 days. On day 7 microscopy and culture were performed from each of these.

Direct Microscopy: Smears were stained by Ziehl-Neelsen staining method and reported according to National Tuberculosis Control (NTC) guidelines.[4]

Culture isolation: With the help of sterile wire loop, 2-4 loopful of the centrifuged sediment were distributed over the surface of L-J media and incubated at 37°C for upto 8 weeks. All cultures were examined after 72 hours for contaminants and weekly thereafter.[1] Any growth was confirmed by Z-N and other biochemical tests Nitrate positive, Niacin positive and catalase negative at 68°C as *Mycobacterium tuberculosis.*

Data were entered in Microsoft Excel sheet and comparisons were done applying the Chi-square test.

RESULTS

The effects of storage on smear grading and culture isolation are shown in tables 1 and 2 respectively. A total of 150 smear positive samples, 127 isolates are Confirmed as *Mycobacterium tuberculosis*. The grading of culture results are shown in table 3.

Table1. Comparison of smear results before and after storage

Initial smear grading	Storage factor	Smear grading on day 7
3+(n=39)	Room temperature	3+(n=39)
	Refrigerator	3+(n=39)
2+(n=46)	Room temperature	2+(n=46)
	Refrigerator	2+(n=46)
1+(n=65)	Room temperature	1+(n=65)
	Refrigerator	1+(n=65)

Table 2. Comparison of culture yield before and after storage of sputum samples

Smear Grading	Comparison	Positive	Negative	Total	P value	
3+	Initial	35(89.74%)	2(5.12%)	37(94.86%)	Between Initial and RT <0.05	Between Initial and Refrigerator >0.50
	Room Temperature	25(64.1%)	8(20.5%)	33(84.6%)		
	Refrigerator	33(84.61%)	2(5.12%)	35(89.73%)		
2+	Initial	46(100%)	0	46(100%)	Between Initial and RT <0.001	Between Initial and Refrigerator <0.01
	Room Temperature	29(63.0%)	13(28.26%)	42(91.26%)		
	Refrigerator	37(80.43%)	6(13.0%)	43(93.43%)		
1+	Initial	46(70.76%)	16(24.61%)	62(95.37%)	Between Initial and RT >0.05	Between Initial and Refrigerator >0.10
	Room Temperature	32(49.23%)	23(35.38%)	55(84.61%)		
	Refrigerator	51(78.46%)	10(15.38%)	61(93.84%)		

Table 3. Shows grading of culture results

Number of mycobacterial isolates	Recording	Report
18	No growth	Negative
5	Contaminant	Contaminant
20	20-100 colonies	Positive(1+)
30	200 colonies	Positive(2+)
32	200-500 colonies	Positive(3+)
45	>500 colonies	Positive(4+)

DISCUSSION

In the present study, we tried to evaluate the effect of storage of sputum samples at two different temperatures viz room temperature (25°C) and refrigerator (4°C) on the sputum smear grading and culture yield. It was seen that storage had no statistically significant difference in the smear grading (table 1).This finding agrees well with

previous studies done by Paramasivan et.al.(1983) who showed storage at RT in a tropical country for 28 days had no effect on smear results.[5]

Similar findings were shown by Banda et.al. (2000) and Rao et.al. (1966).[6,7] However viability of the stained bacilli is not ensured since both the dead and living bacteria are stained. This was reflected by the findings in our study where statistically significant difference was observed when sputum samples were cultured after storing in the two different temperatures (table 2).

Comparison of the culture positivity of different sputum smear grades showed a significant difference at both temperatures for smear grades 2+ only. The samples graded 3+ showed significant difference with storage at room temperature and the samples graded 1+ did not show a statistically significant difference in either of the storage temperatures. However comparisons of the overall culture positivity for the stored samples showed a statistically significant difference in culture yield when stored at RT but not when stored at refrigerator for 7 days.

A study done by Takayama et.al, to look for the effect of temperature on *Mycobacterium tuberculosis* viability had shown that at 20^0C – 25^0C, the mycolic acid synthesis was decreased and thus the viability was lost.[8] Similar study performed by Paramasivan et.al. showed that the viability of *Mycobacterium tuberculosis* started decreasing significantly from the third day when stored at room temperature .The proportion decrease in culture yield after storage at RT for 3,7,14,21,28 days were 83%, 68%, 22%,13% and 0% respectively. While before storing it was 88%.[5]

Besides storage, the type of decontaminants, the duration of contact of the specimens with the decontaminant [9] and the centrifugation speed and time [10] may also affect the viability of tubercle bacilli and thus the culture positivity. Often, the culture positivity is reduced because of the culture contaminants. As seen in the present study where the contamination rate before storage was 3.3% and after 7 days of storage at RT, the contamination rate increased to a high of 20.66%. Similar increase in contamination rate when stored at RT were observed by Rao et.al. (1966) Contaminants in culture may be due to concomitant bacterial flora in the pathological specimens and extraneous bacterial flora appearing at the time of collection or during storage under unfavorable environments. Such extraneous contaminants being predominantly spores and fungi are possibly more resistant to preculture treatment of specimens and more damaging to obtain maximum yield of positive cultures.[7]

The rate of contamination and the subsequent reduction in culture positivity for sputum stored at 4^0C in the refrigerator were lower. This could possibly be because of the reduced chances of extraneous contamination as well as the unfavorable temperature for the normal flora to overgrow the tubercle bacilli.

CONCLUSION

In conclusion, this study shows that smear results were not affected after storage at room temperature and in the refrigerator upto 7 days. But bacterial viability was decreased both at room temperature and in the refrigerator. However, the culture isolation rates were better for specimens kept in the refrigerator than at room temperature. In countries like Nepal where most villages lack an equipped laboratory for culture of *Mycobacterium tuberculosis*, and where skilled personnel are also scarce, sputum microscopy should remain the mainstay for diagnosis of pulmonary tuberculosis as there is no effect on smear reading after storage at room temperature. However, with the rise in the multidrug resistant tuberculosis cases and the adaptation of DOTS-Plus programme in the country, there will be more need for culture confirmation of the cases. In such conditions, the samples collected from the fields and the remote areas should be transported at 4^0C in the culture laboratory as soon as possible as culture isolation rate was shown to decrease with storage. Although this study did not include a systemic analysis of the maximum effective storage time of sputum with cetyl-pyridinium chloride (CPC), which is a satisfactory preservative for mailing sputum for TB diagnostics because it decontaminates specimens collected in remote areas and increase the yield of positive cultures after 20 days or longer.For transport of sputum specimens requiring storage up to 7-8 days, CPC method has advantages over the standard NaOH

method in reducing the contamination, yielding more positive cultures, elimination of pathogenic fungi from sputum specimens and stability of regent at room temperature. However, a large- scale study must be conducted under field conditions to investigate the effect of storage of sputum specimens with CPC.

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SURVEILLANCE OF TUBERCULOSIS AMONG HIV POSITIVES IN NEPAL

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ABSTRACT

Background: According to National Centre for AIDS and STD Control size estimation report, 2012, overall HIV infection in Nepal is estimated at 0.28% in the 15-49 years age group which corresponds to about 48,648 people living with HIV in Nepal. HIV infection is the most potent risk factor for converting latent TB into active TB, while TB bacteria accelerate the progression of HIV. The objectives of the surveillance were to analyze the impact of the HIV epidemic on the TB situation, to explore the trend of HIV prevalence among TB patients and to provide information for collaboration between HIV/AIDS and TB programmes on formulation and implementation of a joint TB/HIV strategy.

Methodology: This is an institutional based prospective survey (sentinel surveillance) for measuring prevalence of TB among people living with HIV/AIDS. This survey was conducted at 6 sites representing all five regions of Nepal from July 2012 to February 2013. The calculated sample size for the surveillance study was 400. The findings were processed/analyzed using SPSS (version16) computer software to measure central tendency and dispersions.

Results: The study reveals that 11.5% prevalence of TB was found in total examined HIV clients. Prevalence of TB among HIV clients was highest (28.8%) in Seti Zonal Hospital followed by 23.1% found in BPKIHS, Dharan, and 15.3 percent in Western Regional Hospital, Pokhara. The prevalence of TB was found higher in age group of 35-65 years and above. The prevalence of TB among enrolled HIV clients was comparatively high in male (14.4%) than in females (8.4%). TB prevalence was also found higher in illiterate clients in comparison to higher educated. Prevalence of TB among migrants was higher (14.6%) followed by spouse of migrants (11.5%) and IDUs (11.1%). The prevalence of TB was found 10.7 percent among HIV clients enrolled for ART/PART. The study reveals that 5.4%, 3.1% and 3.1% were pulmonary positive; pulmonary negative and extra pulmonary TB respectively.

Conclusion: The prevalence of TB was found significantly higher in age group of 35-65 years, high risk and illiterate group of HIV clients. Therefore, special focus should be given for migrants, spouse of migrants and IDUs and illiterate community people to avoid TB co-infection and also for enrolment of HIV clients in Pre ART/ART centres.

Key words: HIV clients, TB/HIV Co-infection, Pulmonary and Extra-pulmonary TB, Pre ART/ART

INTRODUCTION

HIV infection is a major threat in the global resurgence of tuberculosis (TB), especially for tuberculosis control in many developing countries. A person with HIV is up to 30 times more likely to develop TB than a normal person with a healthy immune system. In resource-limited settings, TB is one of the main opportunistic infections and a leading cause of mortality in people living with HIV/AIDS. TB is the biggest killer of people with HIV/AIDS, shortening their lives by 6 to 24 months. Globally, it was estimated that 11% of new adult

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TB cases in the year 2000 were infected with HIV. Rates of smear-negative and extra pulmonary TB have been rising in countries with HIV epidemics. Delayed diagnosis may be an important cause of excess mortality in people living with HIV. Diagnosis of tuberculosis poses particular difficulties among smear negative and extra pulmonary TB cases.

Tuberculosis, although curable, is one of the most common causes of HIV- related illness and death. Eleven million adults living with HIV/AIDS (PLWHA) are estimated to be co-infected with Mycobacterium tuberculosis, with 71% of those co-infected living in Sub-Saharan Africa and 22% living in South-East Asia, while 17% in South Asia. There are about 1175 incident HIV positive TB cases in Nepal (2007). HIV fuels the tuberculosis epidemic in several ways. HIV is the most powerful known risk factor for reactivation of latent tuberculosis infection to active disease. The annual risk of developing TB in a PLWHA who is co-infected with M tuberculosis ranges from 5 to 15 percent. HIV increases the rate of recurrent TB, which may be due to either endogenous reactivation (true relapse) or exogenous re-infection. Increasing tuberculosis cases in PLWHA poses an increased risk of TB transmission to the general community regardless whether they are infected with HIV or not.[1,2] Study conducted by Dhungana et al (2008) in Kathmandu revealed that 23% prevalence of TB was observed in HIV positive subjects in 2005.[3] Studies done in United Mission hospital, Tansen (2005) showed that TB prevalence in HIV cases increased from 10.8% in 2002 to 39.5% in 2004.[4,5] As the HIV/AIDS and TB epidemics have progressed, surveillance has become widely recognized as a critical activity in understanding the trends of epidemics and in enabling sound strategy to be developed for responding to them. Apart from above mentioned local studies. Surveillance of Tuberculosis among HIV positive patients is scarce in Nepal.

METHODOLOGY

This is an institutional based prospective survey (sentinel surveillance) for measuring prevalence of TB among people living with HIV/AIDS (PLWHA). This survey was conducted at 6 sites representing all five regions of Nepal from July 2012 to February 2013. The calculated sample size for the surveillance study was 400. Pre-ART and ART registers were taken as sampling frame to enrol the clients for the study. Only those individual who provide written consent for participation in the survey were included in the study. All consenting PLWHA over 15 years of age, who are registered for ART irrespective of the CD4 count, at the time of initiation of the study, were considered to enrol in the study.

All the enrolled PLWHA were screened for active TB based on presence of signs and symptoms indicative of tuberculosis. All the screened suspects were further subjected to the relevant diagnostic tests X- Ray chest and CD4 count. Standard diagnostic criteria for smear positive; smear negative and Extra Pulmonary Tuberculosis used by National Tuberculosis Program (NTP) Nepal was used to classify tuberculosis disease. All samples (including suitable medium) for culture were sent to National Tuberculosis Centre (NTC) lab for processing of culture, Drug Susceptible Test (DST) and Acid Fast Bacilli (AFB) microscopy was done at microscopy centres. All X-ray films were sent to the NTC for examination. Sputum samples were examined by trained technicians under the supervision of microbiologist or pathologists in National Laboratory, Kathmandu, Nepal. A Team of four experts (Radiologist, Chest physician, Pathologist and Microbiologist) reviewed all relevant reports and laboratory results in order to determine the diagnostic criteria used for each patient. All diagnosed patients were referred to nearest DOTS clinic to start treatment for Tuberculosis.

Prior to the data entry, data were cleaned with the consultation of concerned supervisor in the respective sites. During data processing, there were constant check for relevancy, consistency, and accuracy of the data sets. The findings were processed/analyzed using SPSS (version16) computer software to measure central tendency and dispersions (descriptive statistics): mean, median, standard deviation by age, sex, and geo-location, etc. Some inferential statistical analysis was done considering the sample distribution and policy interest for programming. Final results of the sentinel surveillance were disseminated among key stakeholders (government, civil society organizations and external development partners).

RESULTS

National Tuberculosis Centre conducted the study in six sentinel sites with the objective to ascertain the

prevalence of TB among HIV Clients. Based upon the study conducted among 395 HIV Clients who were examined for TB and analysis is performed accordingly and findings are shown as below:

Table 1. Distribution of Clients by Sentinel Sites and Sex wise

Sentinel Sites	Male %	Female %	Total
BPKIHS Dharan	69.2	30.8	52
Sukraraj Tropical Hospital	49.5	50.5	101
TUTH	39.3	60.7	61
Western Regional Hospital	42.4	57.6	59
Bheri Zonal Hospital	66.7	33.3	60
Seti Zonal Hospital	44.1	55.9	59
Total	**51.3**	**48.7**	**392**

Above table describes the Sentinel Site and Sex wise data of the respondents; out of the total, 392 respondents who are HIV positive and visited the six sentinel sites and examined for Tuberculosis, highest number 101 clients were from Sukaraj Tropical Infectious Disease Control Hospital (SUTH), Teku followed by 61, 60 and 59 were from Tribhuwan University Teaching Hospital (TUTH), Seti Zonal Hospital (SZH), Western Regional Hospital (WRH), Pokhara respectively. The lowest number i.e. 52 respondents visited in BPKIHS, Dharan.

Sex wise, highest i.e 69.2 percent were male clients visited in BPKIHS, Dharan followed by 66.7%, 49.5% and 44.1% clients visited and examined for TB in Bheri Zonal Hospital (BZH), SUTH and SZH respectively. Highest percent of female clients (60.7%) visited in TUTH followed by 57.6%, 55.9% and 50.5% female clients visited and examined in WRH, SZH and SUTH respectively. 51.3 percent of Male Clients examined for TB in comparison of 48.7 percent of female clients.

From table 2, it can be illustrated that prevalence of all forms of TB among HIV clients was 11.5% whereas facilities wise, it is evident that prevalence of TB among HIV clients was highest i.e. 28.8% in Seti Zonal Hospital followed by 23.1% found in BPKIHS, Dharan, and 15.3% in Western Regional Hospital, Pokhara. Only 3.3% of clients were found TB positive in Bheri Zonal Hospital and there was not a single case of TB positive in TUTH. Thus, it is concluded that highest prevalence of all forms of TB among HIV clients was found in Seti Zonal Hospital and BPKIHS. Therefore, specific intervention such as treatment, care and support need to be deployed in those most affected areas. The p value is highly significant among HIV clients who were tested for TB investigations.

Table 2. Sentinel Sites wise Prevalence of all form of TB among HIV Clients

Sentinel Sites	TB prevalence (%)	No TB Prevalence (%)	N=392	Test statistics (Chi – Square)
BPKIHS Dharan	23.1	76.9	52	P Value = 0.0000
Sukraraj Tropical Hospital	5.0	95.0	101	
TUTH	.0	100.0	61	
Western Regional Hospital	15.3	84.7	59	
Bheri Zonal Hospital	3.3	96.7	60	
Seti Zonal Hospital	28.8	71.2	59	
Total	**11.5**	**88.5**	**392**	

Table 3. Age group wise TB Prevalence among HIV Clients

Age Groups	TB prevalence (%)	No TB Prevalence (%)	N=392	Test statistics (Chi – Square)
15-19	0.0	100.0	8	P Value = 0.396
20-24	11.8	88.2	17	
25-29	6.5	93.5	62	
30-34	9.1	90.9	99	
35-39	15.3	84.7	98	
40-44	10.4	89.6	48	
45-49	16.7	83.3	24	
50-54	23.8	76.2	21	
55-59	0.0	100.0	6	
60-64	0.0	100.0	5	
65 and above	25.0	75.0	4	
Total	**11.5**	**88.5**	**392**	

Invalid Chi-square test

Age group wise analysis of TB prevalence among HIV clients showed highest (25%) among age group 65 and above followed by 23.8% among 50-54 age group and 15.3% in 35-39 age groups. The

younger age groups have less prevalence of TB positive among HIV positive clients. From this it can conclude that older the age group, higher chances of getting TB positive, hence specific interventions are required for treatment, care and support in this age groups. Though analysis have shown there is association between age groups and TB prevalence, the p value is not significant.

Table 4. Distribution of Sex wise prevalence of TB among HIV clients

Sex	TB prevalence	No TB Prevalence	N=392	Test statistics (Chi – Square)
Male	14.4	85.6	201	P Value=0.06
Female	8.4	91.6	191	
Total	**11.5**	**88.5**	**392**	

From table 4, it is evident that among enrolled HIV Clients in all sentinel sites, out of the total prevalence of all form of TB; comparatively it is more in males (14.4%) than in females (8.4%). It can be concluded that more community awareness activities should be scaled up to increase access of female clients in sentinel sites for investigations of TB.

Table 5. Occupation wise distribution of prevalence of TB among HIV Clients

Occupation	TB prevalence	No TB Prevalence	N=392
Agriculture/ Farming	18.5	81.5	92
Business	3.2	96.8	31
Housewife	5.2	94.8	58
Service	7.3	92.7	55
Labour/ daily waged	25.0	75.0	24
Students	.0	100.0	6
social worker	.0	100.0	18
Not identified	13.0	87.0	108
Total	**11.5**	**88.5**	**392**

The table 5 showed that among the prevalence of TB in HIV Clients, highest percent (25%) was found in Labor/daily wages followed by Agriculture/Farming (18.5%) and doing Service (7.3%). The prevalence was found comparatively less in housewife (5.2%) and business group clients (3.2%). There was not a single case of TB found in Social Workers and Students. Thus, specific interventions required to improve the nutritional status of HIV Clients for labor and those working in agriculture.

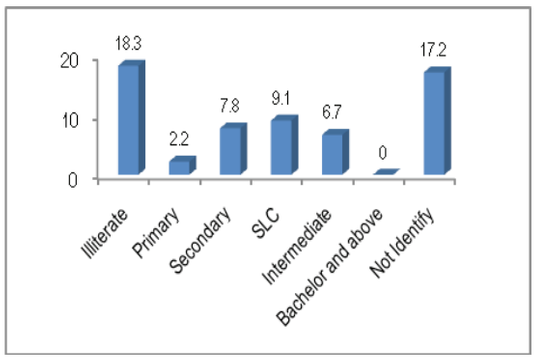

Figure 1. Education wise distribution of prevalence of TB

Form figure 1, it is evident that among the prevalence of TB in HIV clients, 18.3% prevalence of TB was found in illiterate clients followed by 9.1% in SLC graduate and 7.8% in secondary level education clients. The Prevalence of TB was not found in bachelor and above clients which shows that the higher the education lower the TB prevalence. There is need to focus for targeted interventions to improve nutritional status of illiterate HIV clients to prevent TB as co-infection.

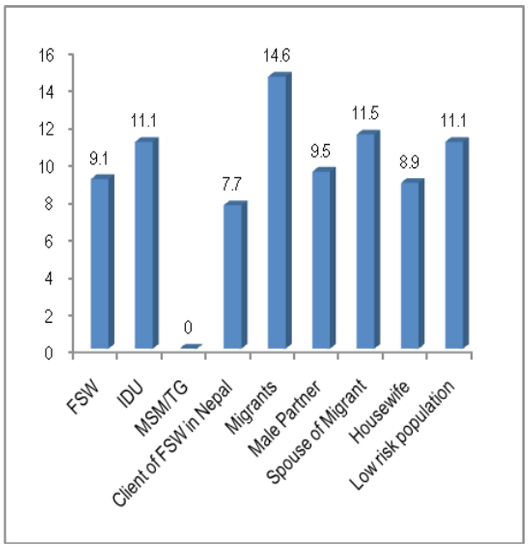

Figure 2. Distribution of TB Prevalence among Risk Groups

The figure 2 revealed that highest (14.6%) of TB prevalence was found in Migrants followed by 11.5% in spouse of migrants and 11.1% in IDUs/ Low risk Population respectively. 9.5% Male partner were found having TB prevalence followed by 9.1%, 8.9% and 7.7% in FSW, Housewife and Clients of FSW in Nepal respectively. Specific interventions required for migrants, spouse of migrants and IDUs to avoid co-infection of TB.

Table 6. Distribution of Status of TB among Pre ART/ART enrolled Clients

Enrolled ART and PART	TB prevalence (%)	N=347	No TB Prevalence	Test statistics (Chi – Square)
Enrolled Pre ART/ ART	10.7	251	89.3	P Value=0.427 which is not significant
Not sure	13.5	96	86.5	
Total	**11.5**	**347**	**88.5**	

From table 6, it is evident that prevalence of TB was found 10.7% among HIV clients enrolled for ART/PART and rest 13.5% were not sure about their enrolment in Pre ART/ART. 45 clients did not answer whether they are enrolled in Pre ART/ART.

Table 7. Distribution of Type of TB among tested HIV Clients

Sentinel Sites	Pul. Positive (%)	Pul. Negative (%)	EP (%)	No TB (%)	N= 392
BPKIHS	9.6	1.9	11.5	77	52
Sukraraj Tropical Hospital	2.0	2.0	1.0	95	101
TUTH	0.0	0.0	0.0	100	61
Western Regional Hospital	15.3	0.0	0.0	84.7	59
Bheri Zonal Hospital	0.0	1.7	1.7	96.6	60
Seti Zonal Hospital	8.5	13.6	6.8	71.1	59
Total	**5.4**	**3.1**	**3.0**	**88.5**	**392**

The table 7 reveals that out of total HIV clients tested, 5.4%, 3.1% and 3.0% were pulmonary positive; pulmonary negative and extra pulmonary TB respectively whereas 88.5 percent of the HIV Clients were diagnosed as not having TB.

Table 8. Distribution of Family History of TB among HIV Clients

Family History of TB	N=392	%
Yes	36	9.2
No	356	90.8
Total	**392**	**100**

The table 8 shows that 9.2% of the HIV clients were found having family history of TB and rest 90.8% stated that they do not have family history of TB.

DISCUSSION

Co-infection with TB among HIV has already been reported as one of the most significant global public health concerns. TB/HIV co-infection remains a major contributor to the disease burden in developing countries.[6,8] However, the same concern applies in developing countries with poor resources. This was evident from the present study where the prevalence of all form of TB among HIV positive clients was as high as 11.5% i.e., 45 HIV-positive subjects were co-infected with TB out of 392 tested. This value is by slightly higher than those obtained from Ukraine (10.1%), Uganda (5%) and the United States of America (1%) and a little bit lower than that of India (16.52%).[9] Other study also showed that the prevalence of M tuberculosis–HIV co-infection in adults is 0.36% and co-infection prevalence rates equaled or exceeded 5% in 8 African countries.[10] Although, the prevalence of TB cases in HIV-positive subjects observed in this study was substantially lower than that reported in other studies; for example 28.12% gotten by Ige et al at Ibadan in 2005.[11] And Noeske et al. reported that 256 out of 799 (32%).[12] This high prevalence may be attributed to the low standard of living, inadequate shelter with attendant overcrowding, low awareness levels of TB/HIV co-infection in Nepal.

However, it ranges with facilities and region wise that prevalence of TB among HIV positive clients was highest i.e. 28.8% in Seti Zonal Hospital followed by 23.1% found in BPKIHS, Dharan, and 15.3% in Western Regional Hospital, Pokhara. The most important demographic risk factor was location. Prevalence of TB infection observed in the study is consistent with the findings of previous investigators in Norman Markowitz, Nellie I. Hansen, Philip C. Hopewell, Jeffrey Glassroth, et al.[13]

Socio-demographic characteristics of those co-infected clearly showed that TB prevalence among HIV clients had highest (25%) among age group 65 and above followed by 23.8% among 50-54 age group and 15.3% in 35-39 age groups. The younger age groups have less prevalence of TB positive among HIV positive clients. From this it can conclude that older the age group, higher chances of getting TB infection. Though analysis had shown there is association between age groups and TB prevalence, the p value is not significant. However,

findings of this study is different from similar kind of other studies for examples: Alex Okoh et al. in a study done in Benin City, Nigeria reported that the age group of 31-40 years had the highest frequency (22.5%) followed by the 21-30 years age group (20.5%).[14]

The prevalence of all form of TB among HIV clients is comparatively more in males (14.4%) than in females (8.4%). Similar study showed that the highest prevalence of co-infection was recorded among males aged 30-39(35.6%) and in females aged 30-39(32.1%).[15]

The study showed that among the prevalence of TB in HIV Clients, highest percent (25%) was found in Labor/daily wages followed by Agriculture/Farming (18.5%). The prevalence was found comparatively less in housewife (5.2%) and business group clients (3.2%). An increasing number of studies maintain that there is a strong link between poverty, economic inequality and TB, HIV and TB-HIV co-infections. On the one hand, poverty and economic inequality lead to people living with TB-related high-risk factors (poor housing, poor sanitation and poor nutrition) as well as indulging in HIV-related high-risk behavior (having multiple sex partners, low levels of condom use and the sharing of needles and other injecting equipment).TB and HIV co-infection further exacerbate poverty, economic inequality, individual as well as social suffering among the members of these vulnerable groups.[16]

This study revealed that highest (14.6%) of TB infection was found in Migrants followed by 11.5% in spouse of migrants and 11.1% in IDUs/Low risk Population respectively. 9.5% Male partner were found having TB infection followed by 9.1%, 8.9% and 7.7% in FSW, Housewife and Clients of FSW in Nepal respectively. The findings of this study is consistent with Latent Tuberculosis among Persons at Risk for Infection with HIV, Tijuana, Mexico.[17]

Out of total HIV clients tested, 5.4%, 3.1% and 3.1% were pulmonary positive; pulmonary negative and extra pulmonary TB respectively. The forms of TB infection among HIV-positive subjects observed in this study are supported by Dhungana JR., Tuberculosis and HIV co-infection in patients attending Tansen Hospital, Palpa, Nepal and other study as well. Mohanty et al. has reported 31.59%[18] while Deivanayagam et al. has reported 15% patients as smear positive[19]. It has been shown that sputum smear is often positive in the early stage of HIV infection.[20]

CONCLUSION

The study reveals that 11.5% prevalence of TB was found in total examined HIV clients. Prevalence of TB among HIV clients was highest (28.8%) in Seti Zonal Hospital followed by 23.1% in BPKIHS, Dharan, and 15.3% in Western Regional Hospital, Pokhara.

Age group wise analysis of TB prevalence among HIV clients showed highest in the age groups of 35-65 and low in younger age groups. It indicates that prevalence of TB was high in older age groups. The prevalence of TB among enrolled HIV clients was comparatively high in male (14.4%) than in females (8.4%). It can be concluded that more community awareness activities should be scaled up to increase access of female patients in sentinel sites for investigations of TB. Occupation wise prevalence of TB showed that highest percent (25%) in Labor/daily wages followed by Agriculture/ Farming (18.5%) and doing Service (7.3%) in comparison to housewife (5.2%) and business group clients (3.2%).

Regarding education wise prevalence of TB; highest found in illiterate clients in comparison to higher educated. Prevalence of TB was found 10.7 percent among HIV clients enrolled for ART/PART and rest 13.5 percent were not sure about their enrolment. The study reveals that 5.4%, 3.1% and 3.1% were pulmonary positive; pulmonary negative and extra pulmonary TB respectively whereas 58.9 percent of the HIV Clients were diagnosed as not having TB. The study also showed that 9.2 percent of the HIV clients were found having family history of TB and rest 90.8 percent stated that they do not have family history of TB.

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DISTRIBUTION OF *MYCOBACTERIUM* SPECIES PRESENT IN SPUTUM OF SUSPECTED PULMONARY TUBERCULOSIS PATIENTS

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ABSTRACT

Introduction: *Mycobacterium tuberculosis* complex organisms are responsible for TB, which led human civilization to suffer since antiquity and still remains one of the leading causes of morbidity and mortality worldwide, even after development of effective chemotherapy and vaccination due to emergence of MDR and XDR strains. Non tuberculous mycobacteria are now considered important pathogens with significant number of infections in immunocompromised as well as immunocompetent individuals. The study was conducted in order to distribute the mycobacterial isolates obtained from sputum samples of suspected new pulmonary TB patients to differentiate the pulmonary disease as pulmonary TB or pulmonary mycobacteriosis, compare ZN and Fluorescence microscopy for detecting acid fast bacilli and to find gender differentiation of mycobacterial infection.

Methodology: A cross-sectional study was conducted during September 2010 to August 2011 at National TB Centre of Nepal. A total of 200 patients' sputum samples were selected for culture after screening sputum samples from 1500 suspected new pulmonary TB patients according to Bartlett pulmonary specimen culture criteria. The mycobacterial species obtained on culture were distributed to *Mycobacterium tuberculosis* complex and various Runyon groups of NTM and identified which were possible on the basis of growth rate, cultural characteristics, pigmentation and available biochemical tests.

Results: Among 200 sputum samples selected for culture, 125(62.50%) were ZN microscopy positive, 128 (64%) were Fluorescence microscopy positive and 129 (64.50%) were culture positive, and 138 patients were positive for *Mycobacterium* either singly or multiply with ZN, Fluorescence microscopy or culture, of which 98(71.01%) were male and 40(28.99%) were female. Among culture positives 113 (87.60%) belonged to *M. tuberculosis* complex all identified as *M. tuberculosis* and 16 (12.40%) were NTM. Among NTM 13(81.25%) were Nonphotochromogens, 2(12.50%) were Scotochromogens and 1(11.11%) was a rapid grower identified as *M. vaccae*.

Conclusion: The study revealed that Fluorescence microscopy is superior to ZN microscopy, mycobacterial infection is more prevalent in male than females and besides *M. tuberculosis* complex, an important proportion of mycobacterial infection is also caused by NTM, so exact speciation and drug susceptibility testing of the isolates is necessary for the commencement of appropriate treatment to the patients.

Key words: TB, NTM

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INTRODUCTION

Mycobacterium is the single genus in Mycobacteriaceae family with more than 100 species and comprises non motile, non sporing, weakly Gram positive, acid-alcohol fast, aerobic or microaerophilic, straight or slightly curved, rod

shaped actinobacteria, 2-10μ in length and 0.2-0.4μ in breadth; with G+C content of DNA 61-71 mol% (except *M. leprae* with 54-57 mol%) and posses mycolic acid in their cell wall.[1] The high G+C content of the DNA of Mycobacteria is similar to other mycolic acid producing bacteria, *Nocardia* (60-69 mol%),*Rhodococcus* (59-69 mol%) and *Corynebacterium* (51-59 mol%),which may support the consolidation of these genera into a single family.[2]

Mycobacterium tuberculosis complex is a group of closely related species, comprising *M. tuberculosis, M. bovis*, *M. africanum, M. microti*, *M. canettii*, *M. caprae* and *M. pinnipedii* which causes Tuberculosis (TB) in human and animals, which led human civilization to suffer since antiquity and still remains one of the leading causes of morbidity and mortality worldwide, even after development of effective chemotherapy and vaccination due to emergence of MDR and XDR strains.[3-4] Other mycobacterial species that do not cause TB and frequently found in environmental habitat which may colonize and occasionally cause infection in human and animals, called mycobacteriosis, are called as Non Tuberculous Mycobacteria (NTM).[5] Some NTM are rarely associated with disease whereas some others can cause significant pulmonary and extrapulmonary disease in immunocompetent and disseminated infection in immunocompromised people.[6] Based on phenotypic characters, especially growth rate and pigmentation; Runyon in 1959 classified NTM into four Runyon groups, viz. photochromogens, scotochromogens, non-photochromogens and rapid growers.[7] Mycobacteria are naturally divisible into slowly growing and relatively rapidly growing species which require more than 7 and upto 7 days respectively to produce visual colonies under ideal culture conditions. Non-chromogenic NTM is separated from *Mycobacterium tuberculosis* complex on the basis of biochemical tests.

Mycobacterial species may be obligate pathogens, facultative pathogens or saprophytic at all, which may be present in the clinical specimens as the causative agent of disease or an environmental contaminant, but for the immunocompromised individuals there may not be any non pathogenic mycobacterial species.[19] The clinical isolates of mycobacterial species should be classified and possibly identified upto species level which may guide the appropriate combinations of antibiotics for effective chemotherapy and effective case management.

METHODOLOGY

Research design

This cross-sectional study was conducted at National Tuberculosis Centre of Nepal since September 2010 to August 2011. 200 suspected new pulmonary Tuberculosis cases were selected for study from 1500 randomly selected suspected new pulmonary Tuberculosis patients with typical clinical symptoms of TB and sputum specimen satisfying Bartlett pulmonary specimen culture criteria.

Data collection

Three sputum samples, viz. on the spot on previous day; and early morning and on the spot specimens on the following day were collected from each patient.[10] The sputum samples were observed with standard Ziehl-Neelsen and Fluorescent microscopy and appropriately reported.[10] The sputum was further processed for culture, within seven days of collection, stored in refrigerator at 4°C if prompt processing not possible and delay anticipated.[1] The sputum was digested and decontaminated with N-Acetyl-L-Cysteine Sodium Hydroxide and cultured on paired Lowenstein Jenson media under ideal culture conditions.[1] One of inoculated tubes was wrapped completely with Aluminium foil before incubation. The rapid growers were separated on subculture after sub culturing the Mc Farland 1 compared test suspension and identified if possible with available biochemical tests Niacin accumulation, Nitrate reduction, 68°C Catalase and growth of PNB containing LJ media. The slow growers were separated as photochromogens, Scotochromogens and non-chromogens after comparing pigmentation on wrapped and unwrapped tubes, and illuminating non-pigmented colonies on wrapped tubes to light source of 100W tungsten bulb placed 20 cm from the culture for 3-5 hours with cap loosened and again incubated for observation of pigmentation of colonies after 48 hours.[3] Each isolate was tested with available biochemical tests, non-chromogens were separated to *M. tuberculosis* complex and non-chromogenic NTM and species identified where possible.

Data analysis

The data were analyzed with Microsoft Office Excel 2007.

Research ethics

The participants were left free whether to take part or not in the research, not related to their mainstream diagnostics and therapeutics consideration. Written consent was taken from each patient to administer questionnaire and processing sputum sample and all findings kept confidential only to investigator and consented patient.

RESULTS

Among 200 selected patients; 125(62.50%) were ZN microscopy positive,128 (64%) were Fluorescence microscopy positive and 129 (64.50%) were culture positive with 4% contamination in culture and 138 were positive by either single or multiple microscopic observations or Culture, of which 98(71.01%) were male and 40(28.99%) were female. Considering culture as gold standard, the sensitivity of ZN and Fluorescence microscopy were 90.84% and 94.57% respectively; and specificity of ZN and Fluorescence microscopy were 91.18% and 91.54% respectively.

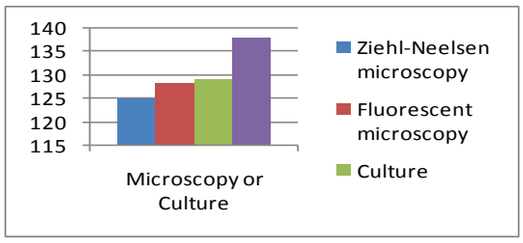

Figure 1. Chart showing the ZN, Fluorescent Microscopy and Culture of Sputum

Among culture positive, 113(87.60%) belonged to *M. tuberculosis* complex, all identified as *M. tuberculosis* strains and 16(12.40%) were NTM.

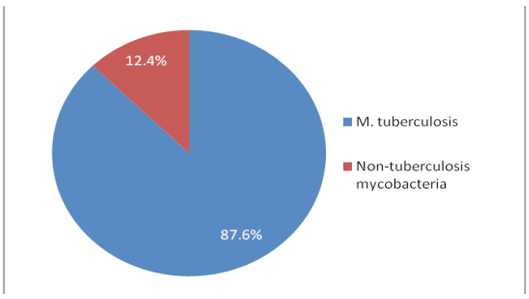

Figure 2. Pie-chart showing percentage of *M. tuberculosis* & NTM

Among 16 NTM, 13(81.25%) were non-photo-chromogenic NTM, 2(12.5%) were scotochromogens, 1(6.25%) was rapid grower identified as *M. vaccae*; photochromogens were not isolated at all.

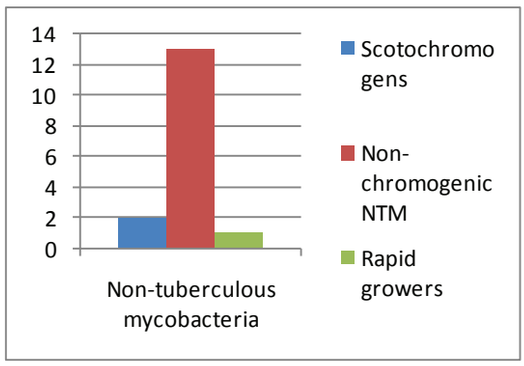

Figure 3. Chart showing scotochromogens, non-chromogenic NTM and rapid growth

DISCUSSION

Sputum is the material coughed up from the lower respiratory tract and expectorated from the mouth, it contains mucous, cellular debris, microorganisms and possibly blood or pus; the amount, colour and constituents of the mucous are important in the diagnosis of many illnesses, including PTB, pneumonia and lung cancer.[8] The criteria developed by Bartlett rejected 17% of specimens for culture but missed fewer potential pathogens so economical for expensive culture of sputum.[9]

In the present study, the number of patient positive for *Mycobacterium* by either culture or ZN microscopy or fluorescent microscopy were 138, among which 71.01% were male and 28.99% were female which is similar to 69% male and 31% female among 15,468 new smear positive cases recorded during July2008-July 2009 affecting mostly 15-45 year age group, i.e. productive age group, so greatly affecting the economic and social status of the country.[10] Male population is slightly less than female population as seen in Census 2011 in Nepal but the gender differentiation in TB may be due to exposure of male to external environment or males visiting health centre independently for disease diagnosis but low detection of female TB cases remains a troubling public health issue demanding urgent focused study.[11]

Considering Culture as the gold standard ZN staining showed the sensitivity 90.84% and specificity

91.18%, and fluorescence staining showed the sensitivity 94.57% and specificity 91.54%. The lower magnification of 200-250□ in Fluorescence microscopy allows examiner to observe lesser number of fields and gives results faster than by ZN microscopy. Fluorescence microscopy is considered superior to ZN microscopy.[12-13] Respiratory specimen yields higher smear positivity rates and if more than one specimen is submitted to the laboratory, up to 96% of patients with PTB may be detected by acid fast stains and smear positivity is correlated with the number of colonies recovered in culture.[14]

Among 129 Culture positive cases, 87.60% person had *M. tuberculosis* complex and 12.40% had NTM infection. Overall 1/3rd of the world's population is currently infected with TB and 5-10% of infected people become actively sick.[15]

In some laboratories NTM are more commonly isolated from respiratory secretions than *M. tuberculosis* and pulmonary mycobacteriosis are probably underdiagnosed.[6] Pulmonary mycobacteriosis caused by MAC predominate and account for 48-70% of all NTM infections.[6] MAC is believed for widespread disseminated infection in AIDS patients.[16-17]However in patients without HIV infection, rapidly growing mycobacteria, *M. kansasii* and *M. marinum* meets criteria for NTM disease than patients with positive *M. avium* culture.[18] Significant geographic variability exists both in the prevalence and species responsible for NTM disease.[6]

CONCLUSION

Among 200 patients, whose sputum specimen was selected for culture, 138 were found positive either singly or multiply by ZN, Fluorescence microscopy and culture. The mycobacterial isolates obtained in culture from sputum of suspected new pulmonary TB patients were distributed, and ZN and Fluorescence microscopy were compared for detection of acid fast bacilli. There is also presence of high number of NTM in culture and their involvement in pulmonary disease should be identified. We recommend *Mycobacterium* species should be identified to the species level and drug susceptibility testing of each new *Mycobacterium* isolates should be performed for the commencement of appropriate treatment of mycobacterial diseases.

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HIV SEROSTATUS AND TREATMENT OUTCOME AMONG PATIENTS REGISTERED UNDER RNTCP

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ABSTRACT

Introduction: High prevalence of HIV and TB leads to increased morbidity in TB patients due to HIV related opportunistic infections and increased death rates leading to low cure rates. Hence, this study was conducted with the objectives to compare the TB treatment outcome in HIV sero-positive and HIV sero-negative patients registered under RNTCP in Vadodara district and to determine the factors affecting same.

Methodology: This is a "Retrospective Cohort" study carried out on All TB patients registered under RNTCP in the whole Vadodara region, i.e. Urban, Rural and Tribal in the year 2009 over duration of 8 months from February to September 2011. A cohort of 274 HIV–ve TB patients and 121 patients in the HIV+ve TB patients cohort were interviewed using a semi-structured pre-tested study instrument to find out the factors affecting the treatment outcomes after taking written and informed consent.

Results: TB treatment success rate was found to be significantly lower in HIV+ve TB (83% in New sputum positive, 54% in New sputum negative, 79% in Extra-pulmonary cases and 49% in retreatment cases) patients as compared to HIV–ve TB patients (96% in New sputum positive, 94% in New sputum negative, 93% in EP cases and 83% in retreatment cases). Death rate was six times more and default rate was four times more common among HIV+ve TB patients as compared to HIV–ve TB patients.

Conclusion: The past history of TB and non-initiation of ART was the predictor variables significantly associated with treatment non success.

Key words: HIV-TB, Co-infection, Cohort, Treatment Outcome, India

INTRODUCTION

Tuberculosis (TB) is one of the leading infectious causes of death, accounting for over 2 million deaths per year worldwide. Globally, 8.8 million new cases of TB occur every year, of which 1.8 million occur in India.[1]

An estimated 3.6 million persons are living with HIV/AIDS(PLHA) in the South-East Asia Region.[2] It is estimated that there are 2.3 million PLHA in India with an estimated adult HIV prevalence of 0.3%.[2]

HIV prevalence among TB patients was estimated to be 4.9%. Among the 1.5 million TB cases reported in the national program in 2008, an estimated 73,720 were HIV-infected.[2] An estimated 11–13% of incident cases were HIV-positive.[3]

TB and HIV tend to fuel each other. HIV infection makes an individual more prone to TB, while the HIV epidemic can worsen the TB scenario as it increases the risk of disease re-activation in people with latent TB infection. This is further substantiated by the fact that an HIV positive person has 50-60% lifetime risk of developing TB disease as compared to 10% risk of developing the TB disease in a lifetime in an HIV negative person. TB is an opportunistic disease that preys on weakened immune systems. If the person harbouring the TB bacilli is also HIV infected, then there is higher risk of developing TB disease.

This increased risk is detectable as early as HIV seroconversion, and the risk of TB almost doubles during the first year after HIV seroconversion. While

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anti-retroviral treatment can substantially decrease the risk of TB, this risk always remains higher in HIV positive individuals. Furthermore, among cured TB survivors with HIV infection, the risk of recurrent TB is also quite high.[4] TB patients who are HIV positive have higher risk of dying during treatment than HIV negative TB patients.[4,5]

Tuberculosis is still the leading cause of mortality among HIV infected patients and this accounts for one third of the deaths due to AIDS worldwide.[6,7] Several studies have reported a striking impact of HIV infection on mortality among TB patients.[8,9] Mortality rate from HIV associated TB in developing countries is high; however, it is not clear whether it is due to failure of anti-TB treatment or complications of HIV.[10]

There is paucity of data from India on the impact of HIV related immune-suppression on response to TB treatment and subsequent mortality.[11]

In India, the TB epidemic in the country is predominantly driven by the non-HIV positive TB cases. It is estimated that nearly 5% of the TB patients are HIV infected.

Treatment with DOTS (Directly Observed Treatment, Short course) is the accepted standard even for HIV positive TB patients. It improves the quality of life and increases the life span of an HIV infected TB patient. Due to high prevalence of HIV and TB, there is increased morbidity in TB patients due to HIV related opportunistic infections and increased death rates leading to low cure rates.

This study was conducted to find out the difference in treatment outcomes among the HIV sero-positive and sero-negative TB patients. The objectives of the study were to compare the TB treatment outcome in HIV sero-positive and HIV sero-negative patients registered under RNTCP in Vadodara district and to determine the factors affecting the outcome of TB treatment among HIV sero-positive patients.

METHODOLOGY

Study area

This is a "Retrospective Cohort" study carried out on patients registered under RNTCP in the 9 Tuberculosis Units (TUs) of Urban, Rural and Tribal areas of Vadodara District registered from January to December 2009. The study was conducted over duration of 8 months from February to September 2011.

Sample size and study population

The sample included two cohorts of TB patients, one with HIV+ve sero-status and the other with HIV–ve serostatus, put on appropriate categories of treatment regimes under RNTCP in the different TUs of Urban, Vadodara district (Rural) and Chhotaudepur (Tribal) region. The first cohort comprised of all TB patients with HIV positive status (126- 91 for Urban Zone, 29 for Rural and 6 for Tribal Zone, of which 5 had migrated, making the final sample of 121) registered during January to December 2009. The comparative cohort constituted of TB patients with HIV negative status registered in the same time period in a proportion of 1:2, matched according to age, gender, DOT provider, TB treatment category and RNTCP quarter of registration in all the three regions, TU wise (187 for Urban Zone, 75 for Rural and 12 for Tribal Zone, thus making a sample total of 274).

Patients who died during the course of treatment (23 in the HIV positive TB patient cohort and 9 in the comparable cohort (HIV negative TB patients) could not be interviewed. But demographic details and other history was noted from the TB treatment cards and relatives.

Eligibility criteria of patients

All TB patients registered under RNTCP in the whole Vadodara region, i.e. Urban, Rural and Tribal in the year 2009 were included in the study.

TB patients who were less than 15 yrs of age, those who did not give their consent to participate in this study and those with unknown HIV status were excluded.

Data collection

Necessary permissions were obtained from concerned authorities and Institutional Ethical committee for Human research (IECHR). A meeting was held with the District Tuberculosis Officers (DTOs) and Senior Treatment Supervisor (STSs) to explain the study and discuss their role in the same.

From each TU, the list of all TB patients registered during January to December 2009 was obtained. A list of all TB patients with HIV+ve status (126) and the list of HIV–ve status TB patients was prepared in proportion of 1:3 ratio by matching them. Considering non availability, migration or non-response, the final ratio of 1:2 was reached.

A semi-structured pretested study instrument in

accordance with the objectives was used for data collection. Interviews of all the selected HIV+ve TB patients were done to determine the factors affecting the outcome of TB treatment, each lasting 15-20 minutes. The patients were approached at the time when they came in for their DOTS treatment. Those who did not come for DOTS (in case of treatment completed/failure/defaulter), were interviewed at their home along with the STS. Interviews were conducted in the vernacular language after explaining objectives of this study and taking written informed consent. Common study instrument was used for both the cohorts to minimize bias. Due importance was given privacy and confidentiality.

Data management and analysis

The forms were checked for errors and data was entered in the excel 2007 worksheet using check files. Analysis was done using SPSS 17 software. Chi-square test and Relative Risk was used to measure strength of association. Multivariate analysis using logistic regression model was used to analyze the association between treatment outcome and potential predictor variables.

RESULTS

A total of 121 patients in the HIV+ve TB patients cohort and 274 HIV–ve TB patients were selected in the comparison cohort who were matched according to Age, Gender, DOTS provider, RNTCP quarter of registration and TB treatment category. Patients who died during the course of treatment (23 (19%) in the HIV positive TB patient cohort and 9 (3.3%) in the comparable cohort (HIV negative TB patients) could not be interviewed. But demographic details and other history was noted from the TB treatment cards and relatives (figure 1).

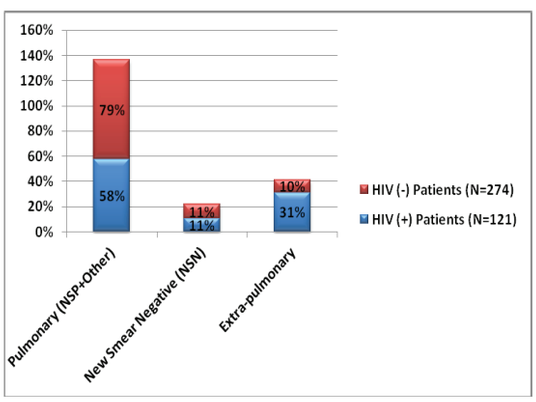

Figure 1. Distribution of Type of Tuberculosis among HIV+ve and HIV–veTB patients

The mean age of males among HIV+ve cohort was 36 years and among comparison cohort was 37 years. The proportion of male TB patients with HIV+ve and HIV-ve status was 83.5% and 82.8% respectively. In terms of educational status, almost 50% patients in both the cohorts were educated up to primary level of education. Almost 55% of patients in the seropositive cohort and 57.7% of patients in the seronegative cohort belonged to unskilled group of occupations. 8.3% patients in the seropositive group and 5.8% in the seronegative group were unemployed.

Almost three fourths of the patients from HIV+ve cohort and HIV–ve cohort were put on TB treatment Category I (68% in both groups), 29% and 3% of HIV+ve TB patient were put on Category II and Category III TB treatment respectively, while 22% and 10% of HIV-ve TB patients were put on Category II and III TB treatment, 31% patients with Extra-pulmonary TB (EPTB) who were HIV+ve while 10% of HIV–ve had EPTB, the difference being statistically significant (table 1).

Table 1. Distribution of Type of Tuberculosis among HIV+ve and HIV–ve TB patients

Koch's Lesion	No. of Patients with TB in		
	HIV (+) Patients (N=121)	HIV (-) Patients (N=274)	
Pulmonary (NSP+Other)	70 (58%)	215 (79%)	X^2=32 P value <0.0001
New Smear Negative (NSN)	13 (11%)	31 (11%)	
Extra-pulmonary	38 (31%)	28 (10%)	

The outcome category TB treatment success used in this study included RNTCP defined outcomes Cured and Treatment Completed. The outcome catregory TB treatment "not success" included Death, Defaulted and Failure. TB treatment Success rate was 68.6 % and 93.4% among HIV+ve cohort and HIV–ve cohort respectively (statistically significant difference). Thus, the Treatment Success was 4.78 times higher among HIV–ve TB patients as compared to HIV+ve TB patients (table 2/ figure 2). The detailed RNTCP defined treatment

outcomes is shown in table 3, the difference being statistically significant.

Table 2. TB Treatment Outcome among HIV+ve and HIV–ve TB patients (N=395)

Treatment Outcome	HIV+ (N=121)	HIV- (N=274)	Relative Risk	95 % CI of Relative Risk
Treatment Success*	83 (68.6%)	256 (93.4%)	4.78	2.87 - 8.03
Treatment Not Success**	38 (31.4%)	18 (6.6%)		
$\chi 2$= 40.5, p value= <0.0001				

*TB Treatment Success = Cured, Treatment Completed,
**TB Treatment Not Success = Died, Defaulted, Failure

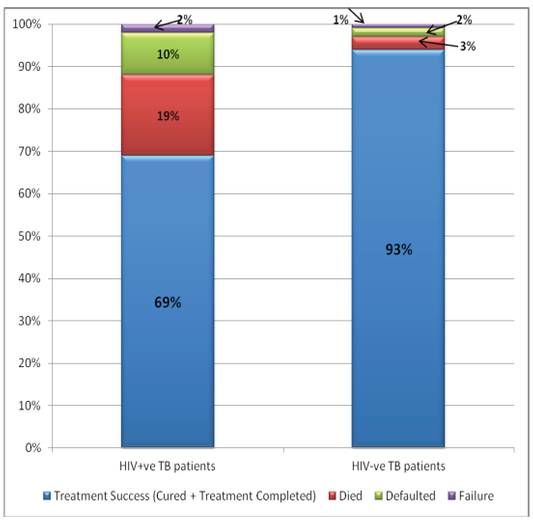

Figure 2. Treatment outcome among HIV+ve and HIV-ve TB patients

Table 3. TB treatment outcome comparison among HIV+ve and HIV–veTB patients

Treatment outcome	HIV+ (N=121)	HIV- (N=274)
Cured*	34+49=83 (69%)	184+72=256 (93%)
Died	23 (19%)	9 (3.3%)
Defaulted	12 (10%)	6 (2.2%)
Failure	3 (2.5%)	3 (1%)
$\chi 2$= 43.7, p< 0.0001		

* Cured category also includes treatment completed as outcomes of pulmonary (new smear negative) + Extra pulmonary

Table 4 shows comparision of TB treatment outcome among HIV+ve & HIV-ve TB patients across RNTCP defined type of patients. TB Treatment success rate among New smear positive category is 83% and 96% in HIV+ve and HIV-ve group respectively. Treatment success rate in new smear negative HIV+ves was 54% while in New smear negative HIV-ve patients it was 94%. EP HIV+ve success rate was 79% as compared to 93% in the EP HIV-ve category. The Re-treatment category patients had very poor treatment success rate (49%) in HIV+ve patients as compared to HIV–ve patients (84%).(Both differences are statistically significant). HIV+ve TB patients showed a higher default rate (2.9% in new smear positives, 15.8% in new smear negatives and 20% in retreatment cases) as compared to HIV–veTB patients (0.7% in new smear positives, 3.2% in new smear negatives, 3.6%EP and 4.9% in retreatment cases). Default rate in HIV-ve EP cases was more (3.6%) as compared to HIV+ve EP cases. (figure 3).

Table 4. Comparison of TB treatment outcome among HIV+ve & HIV-ve TB patients across RNTCP defined type of patients

		HIV+	HIV-	
New smear Positive	Treatment Not Success	06 (17%)	06 (4%)	χ^2=6.405 p value = 0.0114
	Treatment Success	29 (83%)	149 (96%)	
	Total	35	155	
New smear Negative	Treatment Not Success	06 (46%)	02 (6%)	χ^2=7.22 p value = 0.0072
	Treatment Success	07 (54%)	29 (94%)	
	Total	13	31	
Extra pulmonary	Treatment Not Success	08 (21%)	02 (7%)	χ^2=1.465 p value = 0.2262
	Treatment Success	30 (79%)	26 (93%)	
	Total	38	28	
Re Treatment	Treatment Not Success	18 (51%)	10 (17%)	χ^2=11.233 p value = 0.0008
	Treatment Success	17 (49%)	50 (83%)	
	Total	35	60	

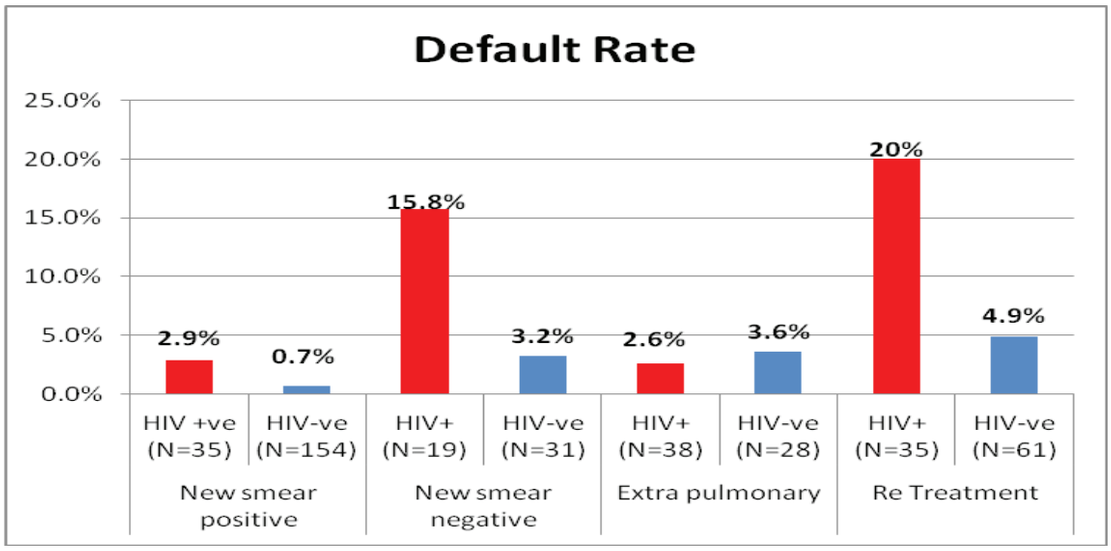

Figure 3. Comparison of default rates among HIV+ve and HIV-ve TB patients
(Numbers under bars indicate no. of patients in each cohort)

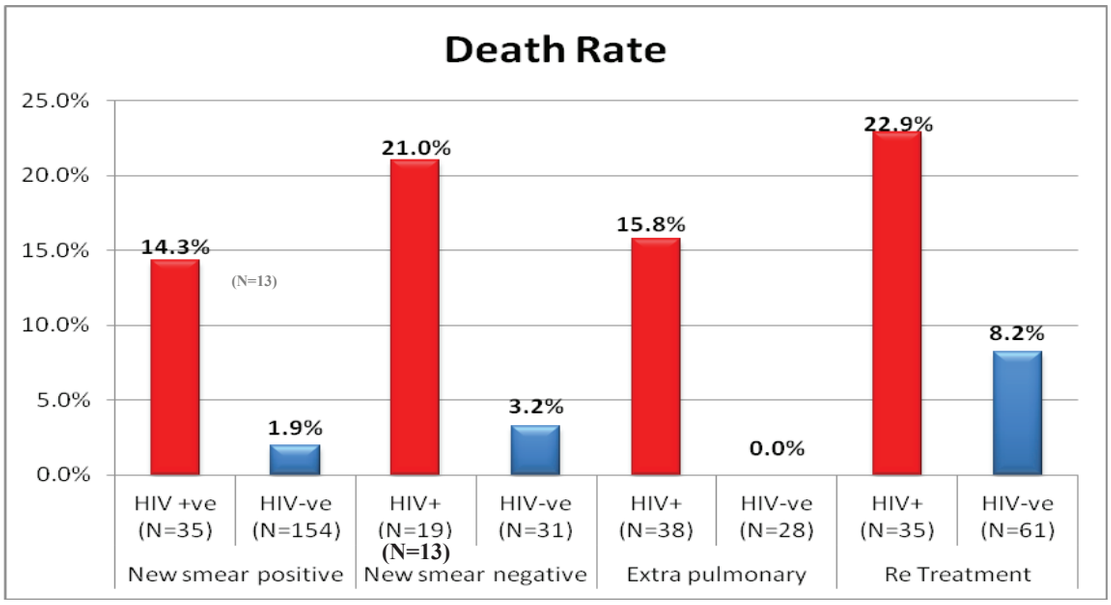

Figure 4. Comparision of Death rates among HIV+ve and HIV–veTB patients
(Numbers under bars indicate no. of patients in each cohort)

Death rates were higher in HIV+ve TB patients than in HIV-ve TB patients (14.3% vs 1.9%, 21% vs 3.2%,15.8% vs nil, 22.9% vs 8.2% in the new smear postive, new smear negative, EP and re-treatment cases respectively)(figure4).

Treatment success rate among HIV+ve TB patients for urban, rural and tribal region was 72%, 62% and 50% respectively whereas treatment success rate among comparison group was 92.5%, 95% & 100%.

In Rural region, proportion of deaths (31%) among HIV+ve patients was significantly high as compared to HIV–ve TB patients. Even Urban region registered 14% of deaths among HIV+ve TB patients. High proportion of defaults among HIV+ve TB patients was seen across all the residential areas (10%, 7% and 16.7% in urban, rural and tribal areas respectively).

Multivariate logistic regression was used to find the factors affecting the treatment outcome (treatment

not success) among HIV+ve TB patients. The odds of having past history of TB was 5 times higher among 'treatment not success' group whereas Non initiation of ART was 4 times higher among 'treatment not success' group as compared to 'treatment success' group (table 5).

Death rate among HIV+ve TB patients in whom delayed or non-initiation of ART was noted was 89% as compared to 11% in whom ART was initiated. χ^2(Yates corrected) = 46.49, p<0.0001)

DISCUSSION

The great burden of tuberculosis incidence and mortality in developing countries is in adults aged 15-60 years which includes the most socio-economically productive members of the society. Due to their age factor and socio-economic dependence of family, they involve themselves in earning and get exposed to other cases in community.[12] Globally, the number of male TB cases exceeds that among women in all age groups except children (WHO 2008). Male preponderance was similar to other studies done by Mukhopadhyaya and Chennaveerrappa et al(67.4% males,32.6% females).[13,14] In the study done by Mukhopadhyay, the supposed reason for greater male preponderance was greater exposure.

As per RNTCP guidelines, Anti-TB treatment under the DOTS strategy remains same for HIV infected and non-infected TB patients. All new

Multivariate logistic regression:

Table 5. Factors affecting Treatment outcome among HIV+ve TB patients

Predicted Independent Variable	Categories	N=121	TB Treatment Not success (Death, Default, Failure)	p Value
			Adjusted OR (95% CI)	
Age	≥ 45 yrs	31	I	
	15 - 29 yrs	28	3.434 (0.804 - 14.67)	0.096
	30 - 44 yrs	62	2.5 (0.646 - 9.665)	0.184
Gender	Male	100	I	
	Female	21	2.461 (0.659 - 9.191)	0.181
Literacy	literate	106	I	
	Illiterate	15	3.122 (0.896 - 10.879)	0.074
Occupation	skilled/semi skilled	45	I	
	unskilled	66	1.029 (0.285 - 3.716)	0.965
	unemployed	10	2.569 (0.427 - 15.455)	0.303
Geographic area	Urban	45	I	
of residence	Urban Slum	41	0.503 (0.107 - 2.358)	0.383
	Rural	29	0.606 (0.109 - 3.364)	0.567
	Tribal	6	0.562 (0.042 - 7.472)	0.662
DOTS Site distance	≤ ½ KM	13	I	
	> ½ KM	108	2.791 (0.394 - 19.788)	0.304
Type of TB	Pulmonary	83	I	
	Extra Pulmonary	38	0.838 (0.232 - 3.034)	0.788
Past History of TB	Absent	85	I	
	Present	36	5.074 (1.771 - 14.532)	**0.002**
H/O TB contact	No	103	I	
	Yes	18	1.605 (0.375 - 6.875)	0.524
ART given	Yes	76	I	
	No	30	3.903 (1.315 - 11.581)	**0.014**
	Status not known	15	94.78 (10.49 - 856.3)	0.000

Considering all the possible predictor independent variables associated with treatment outcome (treatment not success) among HIV+ve TB patients such as age, gender, literacy, occupation, geographic area of residence, distance from the DOTS site, type and past history of TB, history of TB contact, logistic regression analysis was applied. Figures in bold show p values that are statistically significant

TB cases known to be HIV+ve should be treated with Category I regimen since they are more likely to be seriously ill. In our study, most of the new smear negative and extra pulmonary TB patients with HIV+ve serostatus were put on TB treatment category I. This explains lesser number of patients in category III among HIV+ve cohort in this study.

The proportion of EPTB was three times higher among patients having HIV/TB co-infection as compared to HIV seronegative TB patients. Extra-pulmonary TB has been reported in upto 70% of HIV+ve TB cases when the CD4 lymphocyte count is less than 100. The main types of extra-pulmonary TB seen in HIV-infected patients are lymphadenopathy, pleural effusion, pericardial effusion and miliary TB. Study conducted by S. K. Sharma et al showed 53-62% cases of Extra-pulmonary TB among HIV+ve TB patients. The most common extrapulmonary site in HIV-positive individuals was the lymph node. However, neurological, pleural, pericardial, abdominal, and virtually every body site could be involved in HIVpositive patients.[15] In a study conducted in Northern Myanmar by V. Westerbarkey, almost 4 times higher number of Extra-pulmonary cases were noted in HIV+ve TB patients as compared to HIV–ve TB patients. HIV+ patients had a significantly higher rate of extra-pulmonary TB than HIV– patients (50.7% vs. 13.5%; p=<0.01).[16]

In this study, statistically significant difference was noted in the treatment outcomes of HIV+ve and HIV-ve groups, treatment success being more in HIV-ve cohort. TB treatment outcome in HIV infected patients depends on CD4 count and immune status at the time of TB treatment initiation which may further deteriorate even while on TB treatment (without ART). Depending on other opportunistic infections TB treatment outcome without ART may result in High Mortality, Relapses and Re infections.[17] This results in low TB treatment Success rate among HIV+ve TB patients. A study by Westerbarkey et al showed improvement in TB treatment success rate from 58.3% to 93.3%, among patients who were put on ART. Mortality of all cases, however, was significantly higher in HIV+ patients (19.5% vs. 6.0%; p=<0.01).[16]

A study conducted in Tanzania by J van den Broek et. al. showed Treatment success rate of 59% among HIV+ve and 82% among HIV–veTB patients. The overall mortality was 19% and was associated with HIV infection.[18] Another study conducted in Sagamu., Nigeria by O J Daniel and O K Alauska, showed 60.3% treatment success rate among HIV+ve TB patients and 80% among comparison cohort.[5]

On comparing the RNTCP defined treatment outcomes, Cure rate (69%) (includes Treatment completed for EP and new smear negative cases) is highly compromised in HIV+ve cohort, since HIV infection is the major contributing factor for treatment failure. The proportion of EP cases are higher among HIV+ve TB patients. These cases, though being Sputum Smear Negative, are put of RNTCP category I since they are considered seriously ill. The best achievable RNTCP outcome among such patients is 'Treatment Completed' as they cannot be labelled cured. This explains the apparently high proportion of the patients with outcome of Treatment Completed among HIV+ve as compared to HIV–ve cohort. Death rate (19%) and Default rate (10%) are also much higher than comparison cohort. The Death rate is almost 6 times more common and the Default rate is 4.5 times more common among HIV+ve patients as compared to seronegative TB patients. The failure rate is low and acceptable in both the cohorts as per RNTCP norms(figure 2). A study conducted in Nigeria showed similar findings. The cure rate was significantly lower in HIV infected compared with non-HIV infected TB patients (60.3% v 8~.0~:p=0.0001). However, among survivors it was not significant (71.4% v 82. 5%;p=0. 07). Overall mortality was 5.1% which was significantly higher in HIV positive compared to HIV negative TB patients (15.5% v 3. 1%;p=O.00007).

In general the Treatment Success rate is lower among patients on Re-treatment Category as compared to New Smear Positive and New Smear Negative/ Extrapulmonary categories. This rate goes further down among seropositive TB patients on re-treatment category. Hence the HIV+ve patients on re-treatment category stand the highest risk of TB treatment failure (table 4). As per the norms of RNTCP, among New smear Positives Cure rate should be ≥85%.[19]

Comparative analysis of default rates between the two cohorts showed higher default rate among HIV+ve TB than HIV–ve TB patients across all the RNTCP categories. Among the HIV+ve TB patients, those on Re-treatment had the highest default rate. Longer duration of TB treatment for re-

treatment category(8 months) than New treatment category(6 months) poses a risk of compromised patient compliance. Furthermore, the Immune Reconstitution Inflammatory Syndrome(IRIS) among patients on ART forces the patient to leave TB treatment incomplete. A study conducted in Thailand concludes the same. Of 184 patients, 12 (6.5%) developed TB-IRIS at a median (IQR) duration of 2.3 (1.7-4.4) months after ART initiation.[20]

Among HIV–ve TB patients, death rates were high among those on Re-treatment category. High proportion of deaths were seen among HIV+ve TB patients than HIV–veTB patients across all the RNTCP categories. According to RNTCP guidelines among New smear Positives, the Death rate should be <4%.[19] For New smear Positives, the Death rate among HIV+ve was 14.3% and among HIV-ve was 2%. The Death rate among HIV+ve TB patients on New smear Negative/Extra-Pulmonary category was also high as compared to HIV–veTB patients. The highest Death rate for Re-treatment category among HIV+ve TB patients could be due to emergence of drug resistance due to incomplete treatment. In a study done in Vietnam by H T Quy et. al., Death during treatment occurred in 15 of 50 HIV-infected patients (30%). Mortality was significantly associated with HIV infection, multidrug resistance and other resistance to two or more drugs .[21]

High death rates were noted in a study conducted by Vijay S. et al, among Re treatment HIV+ve TB cases. As per this study, Retreatment cases had a significantly higher probability of having 'unfavourable' treatment outcome.[22] Another study conducted at Malawi showed similar findings.[23]

The difference between the treatment success rates among HIV+ve and HIV-ve patients was high among patients belonging to Rural and Tribal areas compared to the Urban area. Urban areas have RNTCP trained TB health visitor(TB-HV) exclusively working under each STS(Senior Treatment Supervisor) of TU whereas Rural and Tribal area is manned by ASHA workers and volunteers(DOTS providers) at grass root levels, which may explain this difference. The long travelling distance for availing HIV services may affect the TB treatment outcome. These possible reasons reflect in terms of Death rates that are significantly higher in Rural and Tribal regions as compared to Urban region.

With regard to default rates, urban region shows high proportion of defaults among HIV+ve TB patients as compared to HIV–ve TB patients. The easy accessibility to TB treatment services out side RNTCP in urban areas as compared to rural and tribal areas make the patients more prone to switch over the treatment from RNTCP to one from Non-RNTCP sources. This is more likely among HIV+ve TB patients as the clinical presentation of TB among them is more severe than sero-negative TB patients.

The past history of TB and non-initiation of ART was the predictor variables significantly associated with treatment non-success. A study by Weerawat M et. al. also proved that non-initiation of ART was significantly associated factor for unfavorable treatment outcome and high mortality among HIV+ve TB patients, other factors being Re-treatment cases, Pulmonary-TB and non-initiation of CPT among HIV+ve TB patients.[24]

Poor treatment outcome (death) is significantly associated with non-initiation or delayed initiation of ART, which is in line with a study conducted by Vijay S. et al, which also showed that factors associated with 'Death' were non-initiation of ART. WHO guidelines (2010) for initiation of ART within 15 days of starting ATT among HIV+ve TB patients which have yet not been incorporated in NACO guidelines. The current study has also shown significantly higher mortality among HIV+ve TB patients who had delayed/non-initiation of ART.

CONCLUSIONS

TB treatment success rate was found to be significantly lower in HIV+ve TB patients as compared to HIV–ve TB patients.

Death rate is six times more and default rate is four times more common among HIV+ve TB patients as compared to HIV–ve TB patients.

The past history of TB and non-initiation of ART was the predictor variables significantly associated with treatment non success.

RECOMMENDATIONS

Patients with TB/HIV co-infection should receive specific focus (supervision and monitoring) under RNTCP as HIV+ve sero-status adversely affects the TB treatment outcome.

Other biomedical risk factors like severity of TB disease, drug resistance and severity of immune-suppression or any other co morbidity which could

have confounded the findings provide scope for further research.

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TUBERCULOUS ABSCESS OF PARAPHARYNGEAL SPACE: A CASE REPORT

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ABSTRACT

A tuberculous abscess of parapharyngeal space(PPS) without concomitant caries of cervical spine is an uncommon deep neck space infection. In recent scientific literature only five such cases have been reported, the last case was reported in an immunocomprised adult male.[1] We are reporting a case of tuberculous abscess of this deep neck space without caries of cervical spine in an immunocompetent adult male. The abscess was drained through intra-oral approach under local anaesthesia based on CT scan findings which suggested that abscess cavity was medial to great vessels of the neck. The diagnosis of *Mycobacterium tuberculosis* infection was confirmed with Mycoreal Real Time PCR performed using scrapings obtained from the abscess cavity. Patient was administered Anti-tubercular Treatment (ATT) using standardised Revised National Tuberculosis Control Programme guidelines. He made an eventless recovery and complete healing of the abscess was confirmed by post treatment CT scan of the neck. The case report reinforces that suspicion of tuberculosis of PPS,albeit a rare diagnosis, needs to be kept in mind by physicians while treating patients with a swelling in the lateral wall of oropharynx or upper part of neck, accompanied with odynophonia or dysphagia, respiratory difficulty, fever and generalised symptoms of asthenia, anorexia and weight loss.

CASE REPORT

Patient History

A thirty year adult male, school teacher by profession, presented with complaint of a visible alteration in the shape of the arch of his soft palate for past one month. He noticed that his soft palate on left side was swollen and getting gradually pushed downwards and inwards. This swelling which initially was the size of a walnut, slowly increased to the size of a pear within one month. There was no visible swelling on the outside of the neck. There was a mild pain in the throat especially during swallowing. However this pain did not radiate. He complained of off and on fever which ranged from 37.2 to 38^0C. Patient also complained of loss of appetite and loss of about six kilograms in weight over the past eight weeks. There was no history of cough with expectoration, difficulty in swallowing or respiration.

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The patient had prior history of recurrent attacks of sore throat accompanied with fever. He had been advised tonsillectomy about eight years ago which patient did not get done.

Local Examination

Examination of the throat revealed a visible elongated oval shaped swelling on the left lateral wall of oropharynx pushing the left tonsil and corresponding area of soft palate medially and distorting the shape of the arch of the soft palate. The uvula was in the midline. The movements of the soft palate on left side were hindered by the swelling. Indirect laryngoscopy examination showed a smooth surfaced swelling of the left lateral wall of the oropharynx extending downwards to a point just below the tip of the epiglottis. The mucosa over the swelling was reddish in colour. The swelling was cystic in consistency and non-tender. The left anterior pillar was pinkish red in colour and medial surface of tonsil was normal in appearance. No cheesy material could be extruded from tonsillar crypts. The right tonsil and posterior rhinoscopy examination was unremarkable.

Haematological and Biochemical tests

Haemoglobin was 11gms%, TLC was 7800 per cubic mm of blood, DLC Neutrophils 62%, Lymphoctes 34%, Monocytes 1% and Eosinophils3%. ESR was 78 mm in first hour by westergren method. Fasting Blood Sugar, liver and renal function tests were within normal parameters.Viral markers for HIV, Australia antigen and HCV were negative.

Radiological Investigations

CT scanexamination of the neck (figure 1 and 2) showed a well-defined hypodense lesion of 25 to 40 Hounsfield units intensity in left PPS measuring about 26 mm in transverse extent, 17 mm in antero-posterior extent and 50 mm in supero-inferior extent at the level of first cervical to third cervical vertebrae. It was causing partial compression of oropharyngeal airway medially. A single lymph node measuring about 11.5 into 10 mm in size with central necrosis was seen postero-lateral to the above lesion.Prevertebral space and visualized vertebrae were normal. No bony pathology was seen.

X-Ray Chest showed increased broncho-vascular markings in both lung fields.

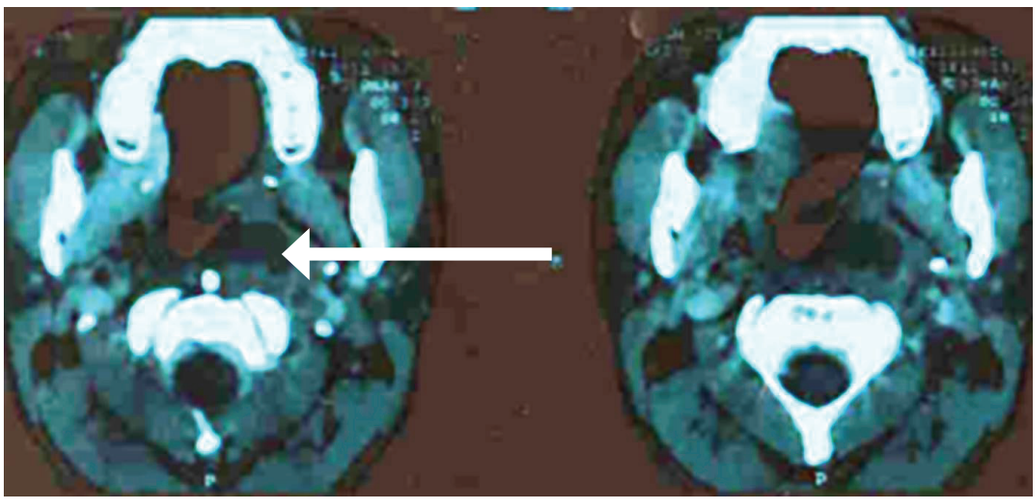

Figure1. Axial CT scan shows a well-defined hypodense lesion in Left Parapharyngeal Space (White Arrow)

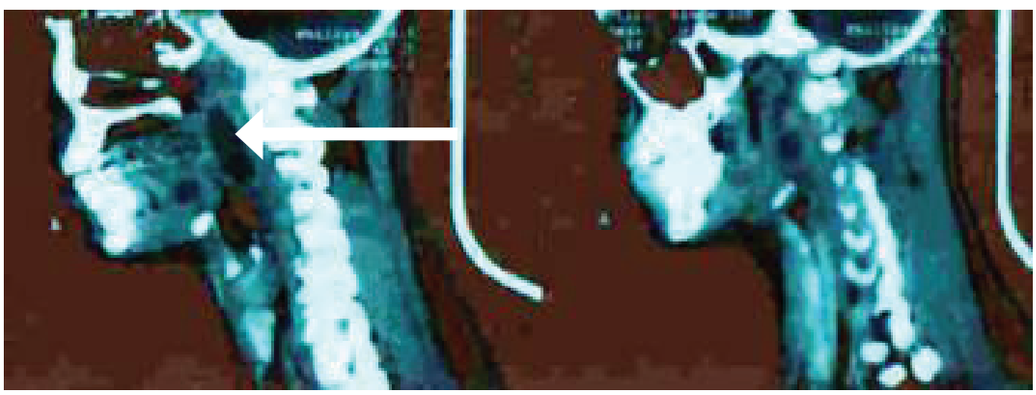

Figure 2. Saggital CT scan shows a well-defined hypodense lesion in Left Parapharyngeal Space (White Arrow)

Fine Needle Aspiration Cytology

About 2 ml of pus was aspirated from the abscess and sent for cytological and bacteriological examination. The smears prepared from material showed necrotic debris, degenerating cells along with acute and chronic inflammatory cells consisting of neutrophils, lymphocytes and a few histiocytes. No epithelioid granuloma was seen. The report concluded acute on chronic suppurative pathology. No Acid Fast Bacilli were detected. The culture

of the pus reported growth of *Staphylococcus epidermidis.*

Surgical Procedure

The patient was taken up for per-oral incision drainage of the abscess under local anaesthesia. The patient was placed in Rose's position with head end of the operation table lowered. Surface anaesthesia was obtained with Lignocaine Hydrochloride 2% viscous and infiltrative anaesthesia obtained as in standard tonsillectomy operation. A Boyle's Davis mouth gag was placed in patient's mouth and opened to obtain adequate view of oropharynx. A vertical incision about 2 cm long was given on the most prominent point of the abscess. Approximately 140 ml of pale coloured foul smelling pus was drained. A sinus forceps was inserted in the longitudinal plane of the abscess to break the loculi. Scrapings from the interior of the abscess cavity were obtained and sent for PCR for *Mycobacterium tuberculosis*. The abscess cavity was washed with hydrogen peroxide solution. No pack was placed in the abscess cavity. The wound was left open to allow continued drainage of abscess in to the oropharynx. Patient was put on intravenous broad-spectrum antibiotics as per the culture and sensitivity report along with hydrogen peroxide gargles. The patient was discharged in satisfactory condition on fifth day postop.

PCR Report

Mycoreal Real Time PCR detected *Mycobacterium tuberculosis*.

Anti-Tubercular Treatment Regimen

Real Time PCR based tests offer enhanced sensitivity and specificity in both pulmonary and extra-pulmonary specimens. It is recommended that a positive PCR in a symptomatic patient warrants active treatment for *Mycobacterium tuberculosis* infection. Patient was treated with anti-tubercular drugs as per Revised National Tuberculosis Control Programme (RNTCP) guidelines as category I patient. The anti-tubercular treatment (ATT) was started on third postop day. The patient (weight 60 kg) was put on a drug regimen comprising of Cap. Rifampicin 600mg, Tab Isoniazid 300mg, Tab Ethambutol 1200 mg and Pyrazinamide 2 gm. daily for two months and then Cap. Rifampicin 600 mg and Tab Isoniazid 300mg for the next four months.

FOLLOW UP

The incision healed by seventh day. The swelling subsided and normal contour of the palatal arch was achieved with in a fortnight and patient became asymptomatic (figure 3 and 4). The patient tolerated the ATT very well. No drug related adverse or side effects were reported. At the conclusion of treatment, patient had gained seven kilograms in weight. The CT scan of neck done at the conclusion of ATT showed complete healing of the lesion.

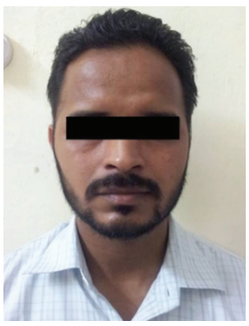

Figure 3. Patient at the conclusion of anti-tubercular treatment

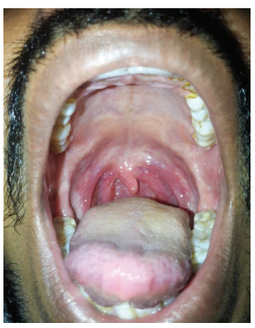

Figure 4. Normal contour of palatal arch at the conclusion of treatment

DISCUSSION

Head and neck tuberculosis is more of a diagnostic and therapeutic problem than is pulmonary tuberculosis, partly because it is less common and consequently less familiar to clinicians. In addition, most head and neck tuberculosis involves less accessible sites, and because of the nature of the sites involved, fewer bacilli can cause much greater damage. Small numbers of bacilli in inaccessible sites make bacteriologic confirmation more difficult, and final diagnosis is usually not made until after surgery.[2]

Tuberculosis of the head and neck can involve the cervical lymph nodes, larynx, temporal bone, sinonasal cavity, eye, pharynx, thyroid gland, and skull base. Cervical tuberculous lymphadenitis is the most common form of head and neck tuberculosis and accounts for approximately 5% of cases of cervical lymphadenopathy. In advanced cases, parapharyngeal or retro-pharyngeal abscess occurs in association with cervical lymphadenitis and characteristically manifests with rim enhancement on CT and MR images. Paravertebral abscess can be seen in patients with cervical tuberculous spondylitis.[2]

The PPS is a deep potential neck space shaped as an inverted pyramid extending from the base of the skull to the hyoid bone.The importance of the parapharyngeal space also lies in its relationship with the other spaces of the neck.The PPS may be divided into two compartments on the basis of its relationship to the styloid process. The contents of the prestyloid compartment include the minor or ectopic salivary gland, branches of the mandibular division of the trigeminal nerve, internal maxillary artery, ascending pharyngeal artery, and pharyngeal venous plexus, whereas those of the poststyloid compartment include the internal carotid artery, internal jugular vein, cranial nerves IX-XII, cervical sympathetic chain, and glomus bodies.[3]

Despite the wide use of antibiotics, deep neck space infections are commonly seen. Dental infections have been implicated as most common cause of deep neck infection (48.6%). Peritonsillar infections (19.7%) and tuberculosis (6.9%) have been reported as the other most common cause. Pain, odynophagia, dysphagia, and fever are the most common presenting symptoms.[4]

A diagnosis of suspected infection with *Mycobacterium tuberculosis* is based on history and clinical findings. Real Time PCR is a rapid and reliable method for the diagnosis of both pulmonary and extrapulmonary tuberculosis, with an overall sensitivity of 78.3% and a specificity of 100%. It enablesATT to be started early in more than half of the patients studied.[5]

The treatment of choice of abscesses in the PPS in adults is surgery with intravenous administration of antibiotics. The intra-oral approach to drain a PPS abscess is a safe and effective procedure provided the CT scan obtained preoperatively shows that the abscess is located medial to great vessels of neck.[6]

The diagnosis of PPS abscess in our case was prompted by complaints of gradually progressive swelling in oropharynx which was pushing the tonsil towards midline and odynophagia. The suspicion of infection with *Mycobacterium tuberculosis* was aroused by classical symptoms of loss of appetite and weight accompanied with low grade fever. A diagnosis of PPS abscess was confirmed by CT scan of neck which revealed a well-defined hypodense lesion of 25 to 40 Hounsfield units intensity in left PPS. The suspicion of tuberculous pathology was further strengthened by detection of a single lymph node measuring about 11.5 into 10 mm in size with central necrosis seen postero-lateral to the lesion.There are three patterns of nodal involvement in tuberculous lymphadenitis on CT or MR images. In the early course of the disease, the nodes are homogeneous in attenuation or signal intensity and enhance homogeneously after the injection of contrast material. This stage corresponds pathologically to a tuberculous granuloma with or without minimal necrosis. As the disease progresses, the second pattern, a node with a central area of necrosis is seen. This is the most common pattern encountered during the course of the disease. [(2)]The possible cause of PPS abscess in our patient was suppuration of lymph nodes along the upper part of the internal jugular vein.

The cytological and bacteriological examination of pus obtained from the abscess did not show any epthelioid granuloma or Acid Fast bacilli. The culture of the pus reported growth of *Staphylococcus epidermidis*. However keeping the suspicion index for a possible tuberculous pathology high, the scrapings obtained from abscess cavity after its drainage were sent for Mycoreal Real Time PCR which confirmed the presence of the *Mycobacterium tuberculosis*. Patient was treated with ATT as per RNTCP guidelines and CT scan confirmed cure obtained at the end of six months of treatment.

CONCLUSION

Tuberculous PPS abscesses have been reported in both immune-compromised and immune-competent patients. Local symptoms such as progressive swelling in oropharynx which push the tonsils medially and odynophagia accompanied by classical symptoms of appetite and weight loss and low grade fever shall arouse the suspicion of tuberculous pathology. CT scan is a useful diagnostic tool. Real Time PCR assay show a high degree of specificity, sensitivity and especially rapidity of detection of tuberculosis, the latter being a very important factor in patient management in terms of initiating appropriate anti tubercular therapy. Intraoral drainage of abscess followed by ATT as per RNTCP guidelines is the treatment of choice for tuberculos PPS abscess.

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SILICOTUBERCULOSIS IN AN OFFICE WORKER: A CASE REPORT

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ABSTRACT

Silicosis is an occupational disease that occurs in people who are exposed to silica dust for considerable period of time or amount.. High amount of suspicion is required to diagnose silicosis in a person who is not exposed to silica dust for significant time and who presents without any latency period. Even more diligence is required to diagnosis tuberculosis in a silicosis patient as the radiological and clinical features may overlap Although tuberculosis is the most important cause of miliary shadows in endemic countries, the possibility of silicosis coexisting with tuberculosis should be kept in mind and a detailed occupational and exposure history should be elicited. Quartz, the most common form of crystalline silica is responsible for majority of cases of silicosis. Chronic or classical silicosis is the most common clinical form of silicosis. In most circumstances, silicosis only develops subsequent to substantial occupational exposure in workers. The disease has a long latency period. It is known that exposure to silica causes a renewed multiplication of bacilli in the healing tuberculous lesions. We describe a case of silicotuberculosis in an office worker who was possibly exposed to environmental silica dust and who presented without a latency period.

Key words: Silicosis, Silicotuberculosis, Miliary, Quartz

INTRODUCTION

Silicosis is the most common occupational disease worldwide which results due to exposure to silica dust.[1,2] Two forms are known : amorphous and crystalline form. The three main crystalline forms are quartz, tridymite and cristobalite, the first being so abundant that it is often used in place of the general term crystalline silica (CS). Quartz is a common component of soil and rocks. Quartz can occur naturally and at varying concentrations in rocks such as sandstone (67% silica) and granite (25–40% silica.[1]

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Three forms of the disease have been recognized:

1. Acute silicosis

2. Accelerated silicosis

3. Chronic silicosis

Diagnosis of tuberculosis in silicosis patients is difficult because of two coexisting diseases that cause similar radiological findings. The incidence of silicotuberculosis is reported to be over 25% at autopsy[3] and even lower in clinical studies.[4]

Case Report: 31 year old male, a non smoker presented to outpatient department with complains of cough for 5 months, fever and chest pain bilaterally for 5 months. He had no history of breathlessness, wheezing, haemoptysis and sputum production. He had no comorbodity and had no history of tuberculosis treatment in the past. He was an office worker. There was a stone crushing (quartz) factory at a distance of one kilometre (0.62 miles) from his office through which he used to transit to work.

On examination his vitals were stable, chest examination revealed vesicular breath sounds with no added sounds. Systemic examinations were unremarkable. Blood investigations were normal, sputum Ziehl-Neelson stain for AFB, culture for mycobacterium tuberculosis and fungus were negative. HIV status was negative. Mantoux test done with 1 TU was negative (<5mm) Chest X-ray revealed bilateral miliary shadows (figure 1). Contrast enhanced CT scan of the thorax showed rightt paratracheal lymphadenopathy and subcarinal lymph nodes. These lymph nodes showed features of central caseation, rim enhancement and trabeculations suggestive of tuberculosis (figure 2). Lung field revealed some fibrotic areas in upper lobes and miliary nodules bilaterally in all lobes (figure 3).

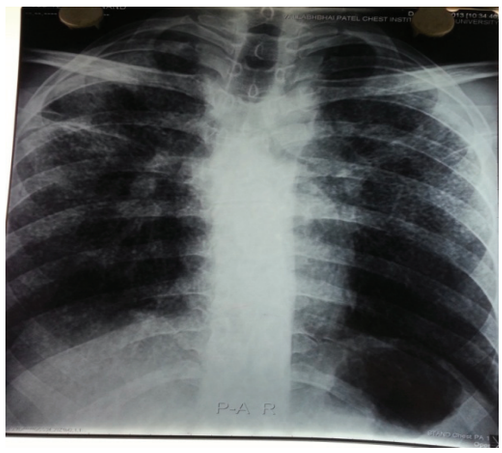
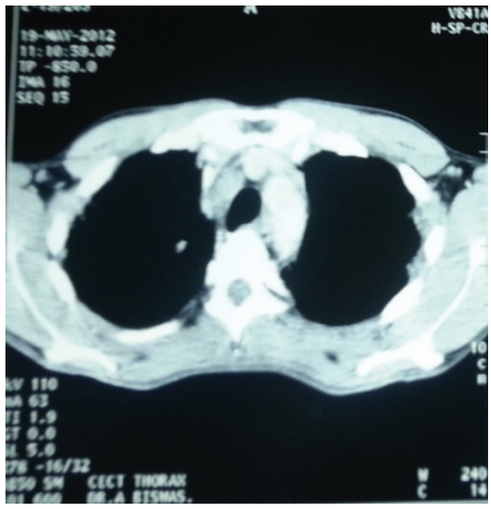


Figure 1. Posterior anterior chest x ray showing bilateral miliary nodules



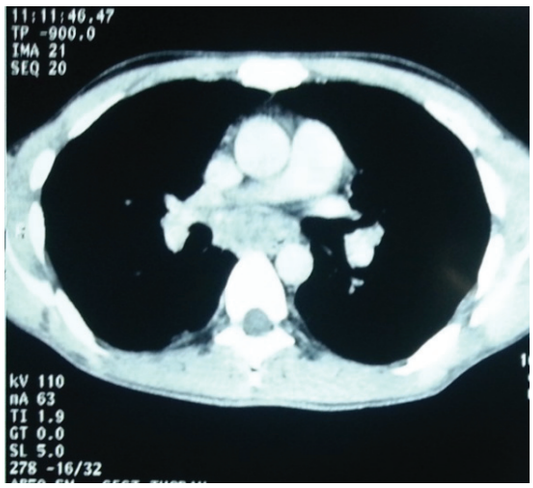
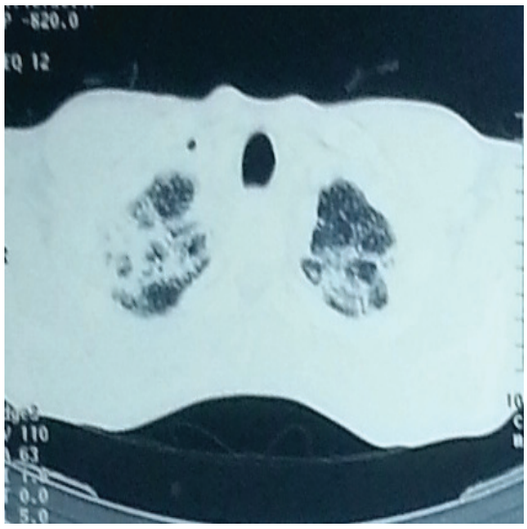


Figure 2. CT chest showing right paratracheal and subcarinal lymph nodes enlargement with caseation



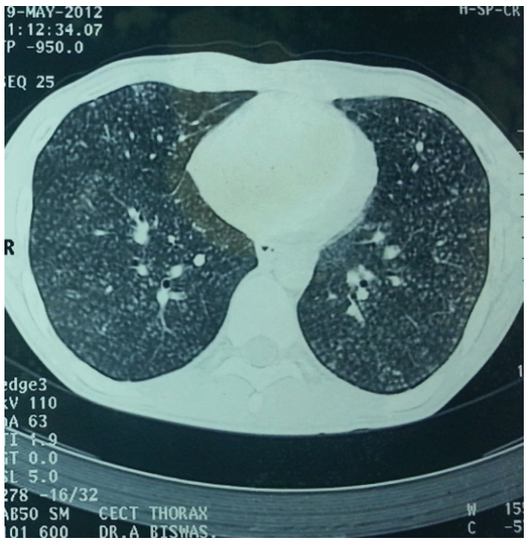


Figure 3. Lung window show upper lobe fibrotic bands and bilateral miliary nodules

He was diagnosed as a case of miliary tuberculosis and started on antituberculosis treatment of 4 drugs: isoniazid, rifampicin, pyrazinamide and ethmabutol according to his body weight. After two month of treatment there was relief regarding cough and fever subsided. He was then continued on rifampicin and isoniazid alone for 4 months. However radiological features did not improve. Patient completed 6 months of anti-tuberculer treatment. He presented after 8 months again with complains of cough and chest pain. When Chest x ray was repeated it revealed similar findings as before. Sputum was negative by smear and culture for Mycobacterium tuberculosis.

A review of diagnosis was done and fibreoptic bronchoscopy was done which showed few areas where the mucosa was granular. BAL was done from different segments which was unremarkable. TBLB revealed silicotic nodule (figure 4) made up of collagenised fibrous tissue and crystalline material was seen in these nodules. Pulmonary function tests revealed a restrictive pattern with an FVC of 37% of predicted, TLC (total lung capacity) of 42% of predicted and DLCO of 26% of predicted.

He was counselled regarding the etiopathogenesis and its prognosis. He was advised influenza and pneumococcal vaccination. He was advised relocation of his office.

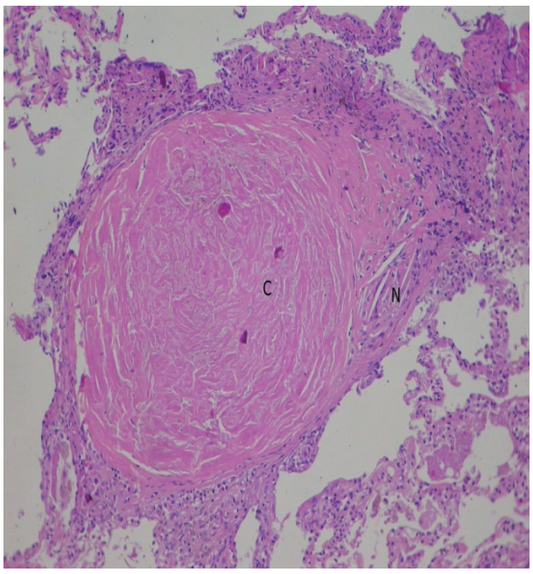


Figure 4. Histopathology of biopsy showing circumscribed nodule of collagen tissue (C). At 2 o'clock (N) needle shaped crystals surrounded by macrophages are seen.

DISCUSSION

In most circumstances, silicosis only develops subsequent to substantial occupational exposure. The disease has a long latency period.[1] Chronic or classical silicosis is the most common clinical form of silicosis. This form of silicosis develops only after decades of repeated exposure to high concentrations of silica dust. Chronic silicosis is not usually associated with mycobacterial infections and tends to be mild and not disabling but can progress to PMF.[1] Chronic silicosis can be radiographically distinguished from acute disease presentations by virtue of large upper lobe opacities in conjunction with small, diffuse nodular lesions.[1] Similar radiographic pictures were exhibited in our patient. Patients may also present with a condition known as accelerated silicosis. This condition is associated with profound silica exposures occurring over a relatively shorter time course when compared with chronic silicosis.

It is known that exposure to silica causes a renewed multiplication of bacilli in the healing tuberculous lesions as studied in guinea pigs.[5] This happens probably due to impaired response of the macrophages in presence of silica or accelerated growth of Tuberculer bacteria in presence of iron that has been absorbed by the silica particles.[6]

The accepted radiological findings to favour tuberculosis in a case of silicosis are rapidly developing nodulation, conglomerate masses and evidence of cavitation.[7]

Our patient was not exposed to silica dust substantially as would be expected in a patient of silicosis. He was an office worker and there was a stone crushing unit at a distance of 0.62 miles away from his office. This history suggestive of minimal exposure to silica and symptoms of fever, cough with upper lobe fibrosis along with mediastinal lymph node with features of caseation favoured the diagnosis of tuberculosis and he was started on anti-tuberculer treatment to which he responded initially. We could not find any acid fast bacilli in the biopsy taken by bronchoscopy. Our patient suffered from chronic silicosis as the symptoms were mild and radiologic picture matched the diagnosis. Finally histopathologic findings of chronic silicosis that is a silicotic nodule was demonstrated from the biopsy examination confirming the diagnosis. From these experiences

we can readily say that patient of silicosis presented to us with tuberculosis, the existence of two diseases camouflaging each other and making the diagnosis difficult for the physician.

None of the current treatment proposed have reduced mortality form silicosis. Only specific measure is to remove the individual from the exposure site.

CONCLUSION

It requires a high degree of suspicion to suspect Silicosis in a person not exposed substantially to silica dust. Usually there is long latency period observed in silicosis, which was not the case in our patient. Secondly tuberculosis in a silicosis patient is extremely difficult to diagnose especially in a endemic country like India and empirical anti-tubercular medications are likely to be prescribed if there are signs suggestive of tuberculosis.

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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.

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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. **Click here** for an example.

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.** 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.

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