Print ISSN 1818-9741 Online ISSN 2091-0959 Vol.20, No 1, Year 2022

SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS

JOL
Journals online

Publishing since 2004
Free online access

SAARC TB and HIV/AIDS Centre (STAC)

SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS
An official publication of SAARC TB and HIV/AIDS Centre

TABLE OF CONTENT

SAARC Journal of Tuberculosis, Lung Diseases and HIV/AIDS

An official publication of SAARC TB and HIV/AIDS Centre

Vol. 20 No. 1 Year 2022

Editorial Board

Advisory Board

Published and distributed by:

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

Editorial

Tuberculosis in the SAARC Region: Prioritize control measures, strengthen health facilities

Globally, an estimated 10.0 million people fell ill with tuberculosis (TB) [127 cases per 100 000 Population] in 2020, a number that has been declining very slowly in recent years. About 6.1 million cases were notified in 2020 across the globe which means there was a gap of 3.9 million (39%) between incident and notified cases.

In the SAARC region, an estimated 3.6 million people fell ill with TB (198 cases per 100 000 Population). A total of 2.4 million TB cases were notified with a gap of 1.2 million (33%) between incident and notified cases. There were an estimated 0.6 million deaths (34 cases per 100,000). For the cases notified the treatment success rate was 86%. The region accounts for 36% of the global burden of TB incidence in 2020. Out of eight Member States three are high TB burden countries and four of them are high MDR-TB burden countries among 30 high burden countries. India accounted for 26%, Pakistan 5.7% and Bangladesh 3.6% of the world's TB Cases. The treatment success rate for new smear positive cases was 86% (2019 cohort). In 2020, the SAARC region had 4,24,869 estimated TB burden in children (0-14) years. Among them 2,19,493 were males and 2,05,376 were females. The region has 56% children (age <5 years) household contacts of bacteriologically-confirmed TB cases on Isoniazid treatment. In the year 2020, there were 54,578 MDR/RR-TB and 9,967 XDR-TB laboratory confirmed cases. Among them 46,746 MDR/RR-TB and 9,083 XDR-TB patients were started on treatment. Regarding the TB among HIV patients there were 31,309 TB Patients with known HIV status, among which 29,519 (94%) were on Antiretroviral Therapy. India accounts for 30,496 TB patients with known HIV status and 28,931(95%) patients were on ART. Afghanistan and Bhutan had provided 100% ART to TB patients with known HIV status in the region.

Hidden and unreported cases of tuberculosis are major challenges in SAARC region for tuberculosis control. In 2020, 10 countries collectively accounted for 74% of the global gap between estimated TB incidence and number of people newly diagnosed with TB and reported. In SAARC region Nepal accounted for highest percentage of gap (59.79%) with Bhutan having least (29.31%). Some of the major causes of gaps are underreporting and lack of access for diagnosis.

Every country and culture are different from their own aspects. SAARC member states have differences in human values. Therefore, each government body looking after their tuberculosis control program should identify innovative ways to find missing cases in their respective set ups. Rigorous brainstorming should be done with concerned stakeholders to figure out the ways before implementing at the grass root level.

Innovatively identifying cases will not work until it is supported by appropriate TB diagnostic, TB treatment and Preventive Services. Hence there is a need to scale up the recommended diagnostic (rapid molecular test or culture) in line with World Health Organization guidelines. This is critical because microbiological detection allows people to be correctly diagnosed and helps to start appropriate treatment regimen. Hence, it is imperative that these diagnostics be taken up to the lower level of health facilities. Innovation in treating tuberculosis is necessary in the future. Although a lot of new drugs have been discovered problems still exist in duration and complexity of treatment. This has led to suboptimal response and the emergence of resistance and continuous spread of the disease. Timely procurement of drugs and supply needs to be strengthened in the coming days. Another aspect which needs a major revision is in the preventive services. Three delays (Reaching, Seeking and Receiving) needs to be strengthened at all level of health facilities. It should especially be focused at the primary health care level and hard to reach areas in the SAARC member states. Awareness program to dilute the stigma and discrimination

should be done on a routine basis. Additionally, TB preventive therapy could be an important intervention to reduce the risk of TB infection progressing to active TB disease. Hence, there is a need of more TB screening at the household level. There is also a need of strengthening follow-up for TB screening at both household level and among people living with HIV and increase access to shorter (1-3) months regimen. Ensuring basic infection prevention and control should be prioritized. TB vaccine if discovered will be boon to the humanity.

COVID-19 devastated the world like anything else. Hence in this post COVID era there is a need for increased funding to bring back the tuberculosis control program in its original stature. High level of political commitment at the top level with team work and cooperation at the middle and the lower level is needed to make this happen. We all health professionals across the region must be committed and dedicated to bring that dream of ending TB into reality.

Chief Editor
Director, STAC

Original article

TUBERCULOSIS SANATORIUM OF 21ST CENTURY EXPLORING THE ADMISSION PATTERN AND DURATION OF STAY AT TB SANATORIUM BHOWALI, UTTARAKHAND, INDIA: A RETROSPECTIVE STUDY

Debnath Aninda [1]; Chandra Ankit [2]; Maroof Mohd.[3]; Awasthi Sadhana [4]; Arya Monika [5]

[1] Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India
[2] Centre for Community Medicine (CCM), All India Institute of Medical Sciences (AIIMS), New Delhi, India
[3] Department of Community Medicine, Rani Durgavati Medical College, Uttar Pradesh, India
[4] Department of Community Medicine, Government Medical College, Haldwani, Uttarakhand, India
[5] Government Doon Medical College, Dehradun, Pahadi Jan Swasth Sanstha, Haldwani (Nainital), Uttarakhand, India

DOI: https://doi.org/10.3126/saarctb.v20i1.52659
Received: 10th April Accepted: June 29th Published: 31th August
This article is available at:

ABSTRACT

Introduction: With time there have been major changes in the management of TB. No longer TB sanatoriums are preferred. However, in this 21st century, few sanatoriums do exist but are no longer in their original forms, to explore the admission patterns and duration of stay at the TB sanatorium Bhowali, Uttarakhand.

Methodology: We retrieved the data between 1st January 2018 to 31st July 2021 from the inpatient Department (IPD) of TB sanatorium Bhowali. Data were extracted in an extraction sheet and descriptive data analysis was done to see the admission patterns and duration of stay. The place of residence was analysed as per the district-wise distribution.

Results: There were 1247 admissions. These admissions were limited to six states, and the majority were from the state of Uttar Pradesh (50.7%) and Uttarakhand (46.7%). The highest cases were in the year 2018, and during April to July. As per the district-wise distribution, Udham Singh Nagar had the highest proportion of admissions (18.6%), followed by Bareilly (15%), Nainital (11.4%), and Rampur (10.9%). The mean (SD) and median (IQR) duration of stay were 22.7 days (SD–24.7) and 14 (IQR 7– 8) days, respectively. The median duration of stay was significantly higher for females (25.1 days) compared to males (21.6 days).

Conclusion: TB sanatorium Bhowali (Uttarakhand) caters majority of the patients from the neighbouring state of Uttar Pradesh. The admissions were high during the spring and summer seasons. The median duration of hospital stay for patients admitted with TB was two weeks.

Key words: TB, Sanatorium, Hospital admission, Duration of stay.

INTRODUCTION

Tuberculosis (TB) is one of the oldest diseases in India. For several years India is trying to control and eliminate this infectious disease.[1] In 1854, Hermann Brehmer started the sanatorium movement for the management of TB. This included isolation of a patient in a sanatorium for open-air, bed rest and providing a nutritious diet. These sanatoriums were mainly located at high altitudes for fresh air and health restoration.[2,3] India had its first TB sanatorium near Ajmer (Rajasthan) in 1906, followed by in Almora (Uttarakhand) in 1908. Thereafter several sanatoriums were constructed in India.[1] With the advent of chemotherapy these sanatoriums became superfluous and were closed. Also, studies had proved that the home treatment with chemotherapy at home is no different from

Correspondence:
Dr. Ankit Chandra
Centre for Community Medicine (CCM)
All India Institute of Medical Sciences (AIIMS)
New Delhi, India
Email: suniyal3151@gmail.com
Mobile +918754842645
Orcid ID – https://orcid.org/0000-0001-6872-2892

sanatorium treatment in terms of the clinical outcome and infection in the household contact.[4,5] This was a turning point for India where TB was a major public health problem and sanatoriums had limited beds.

TB sanatoriums were built before the discovery of drugs for the treatment of TB. These sanatoriums were associated with longer stays and substantial death rates. With time and scientific updates, they have incorporated the modern clinical treatment for TB.[4,6] Currently in the Uttarakhand state (India), there are a few TB sanatoriums, and one of them is TB sanatorium Bhowali which was established in the year 1912. It is located 11km away from the famous hill station Nainital (in Kumaon division). It is on the top of the hill at an elevation of 1706 meters above sea level.[7] It has a historical past, where the wife (Mrs Kamala Nehru) of the former prime minister of India (Jawaharlal Nehru) was admitted for the treatment of tuberculosis. In 1929 it was visited by Mahatma Gandhi.[8] There is a dearth of literature related to the admission and stay duration in these modern TB sanatoriums. We conducted this study to explore admission patterns and duration of stay among the hospital admissions in TB sanatorium Bhowali (Uttarakhand).

METHODOLOGY

It was a retrospective record review. This study was conducted at TB sanatorium, Bhowali, Nainital District, Uttarakhand (India). TB sanatorium Bhowali has 78 functional beds and a pulmonologist for specialist care. It is equipped with an X-ray machine and with the facility of GeneXpert testing. It plays a vital role in providing clinical management for stabilizing TB patients in terms of fluid and electrolyte imbalance, co-morbidity management. It also provides interventions for symptomatic relief for TB patients. We included the record of all the TB patients admitted to the TB Sanatorium Bhowali from 1st January 2018 to 31st July 2021. There were no exclusion criteria. We extracted the data related to the date of admission, date of discharge, gender, religion, and place of residence. The data were entered in a data extraction sheet in Microsoft Excel. We used a 'form' option with validation checks to minimise the errors related to the data entry. We did an analysis of secondary data using STATA 13 software (StataCorp,College Station, Texas, USA). Admissions numbers were presented in proportions for the year and state-wise distribution. The trend of monthly admission was depicted using a line diagram. We presented the duration of stay in mean (standard deviation - SD) and median (Interquartile range - IQR). The normality was assessed using the Shapiro-Wilk test and by plotting a frequency distribution. As the data were non-normal we used the Mann-Whitney test for the test of significance for comparing the duration of stay for males and females. The place of residence was analysed as per the district-wise distribution and it was represented using a heat map in Tableau software (Seattle, Washington, USA). Permission from the authorities was taken to access the records of the Inpatient Department (IPD) of TB Sanatorium Bhowali. The details of the participants were kept confidential and safe. This study has been carried out in accordance with declaration of Helsinki.

RESULTS

From 1st January 2018 to 31st July 2021, there were 1247 admissions. Out of these admissions, the maximum number of admissions (n= 510, 40.9%) were in the year 2018. There were only 158 admissions in 2020, and 152 admissions in 2021 (till 31st July 2021). We saw a decline in admissions in the years 2019 and 2020. The mean number of monthly admissions in the year 2018, 2019, 2020 and 2021 (till 31st July 2021) were 42.5 (SD – 19.9), 35.6 (SD- 22.2), 13.2 (SD – 11.3), and 21.7 (SD- 12.6), respectively. The mean number of admissions in the reference period was 29 (SD - 41.7). Considering 2020 and 2021 as not typical year; the mean and median admissions in the year 2018 and 2019 was 78 (SD- 40.3) and 74 (IQR – 46.5 – 103.5), respectively. Most of the admissions were in the month from April to July except in the year 2020 (**Figure1**). The majority of admissions were males (75.2%) and Hindu religion (79.9%). **(Table 1**)

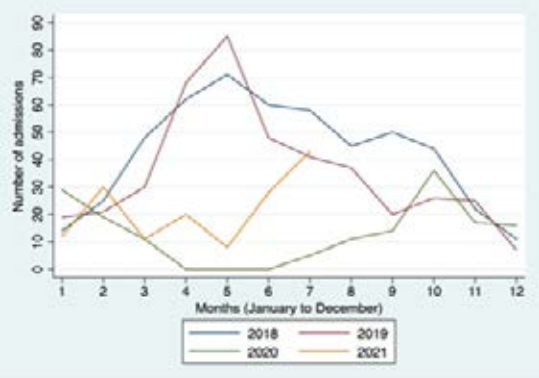


Figure 1: Distribution of admission numbers as per the month and year wise in TB sanatorium, Bhowali (Uttarakhand).

Table 1 – Details about the admissions done in TB sanatorium, Bhowali (Uttarakhand) from 1st Jan 2018 to 31st July 2021					
Variable	**Year**				
Gender	**2018 N(%)**	**2019 N(%)**	**2020 N(%)**	**2021 (till 31st July), N (%)**	**Total admissions N (%)**
Female	130 (25.5)	108 (25.3)	36 (22.8)	35 (23.0)	309 (24.8)
Male	380 (74.5)	319 (74.7)	122 (77.2)	117 (77.0)	938 (75.2)
Religion					
Christian	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Hindu	404 (79.2)	335 (78.5)	134 (84.8)	124 (81.6)	997 (79.9)
Muslim	103 (20.2)	91 (21.3)	24 (15.2)	28 (18.4)	246 (19.7)
Sikh	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)
State					
Delhi	3 (0.6)	1(0.2)	0 (0.0)	0 (0.0)	4 (0.3)
Haryana	12 (2.4)	6 (1.4)	0 (0.0)	2 (1.3)	20 (1.6)
Punjab	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Rajasthan	3 (0.6)	5 (1.2)	0 (0.0)	0 (0.0)	8 (0.6)
Uttarakhand	218 (42.8)	177 (41.5)	97 (61.4)	90 (59.2)	582 (46.7)
Uttar Pradesh	273 (53.5)	238 (55.7)	61 (38.6)	60 (39.5)	632 (50.7)
Total admissions	510 (100.0)	427 (100.0)	158 (100.0)	152 (100.0)	1247 (100.0)
Mean (SD) monthly admissions	42.5 (19.9)	35.6 (22.2)	13.2 (11.3)	21.7 (12.6)	*NA
Median (IQR) admissions in a month	46.5 (23.5 – 59)	28 (20.5 – 44.5)	12.5 (2.5 – 18)	20 (11 – 30)	*NA

**NA denotes not applicable*

The admissions were limited to the neighbouring six states of India. The majority of the admissions were from Uttar Pradesh (50.7%) and Uttarakhand (46.7%).(**Figure 2**).

As per the district-wise distribution, Udham Singh Nagar had the highest proportion of admissions (18.6%), followed by Bareilly (15%), Nainital (11.4%), and Rampur (10.9%) (**Table 2 & Figure 3)**.

Figure 2: Number of admission from 1st January 2018 to 31st July 2021 among six states

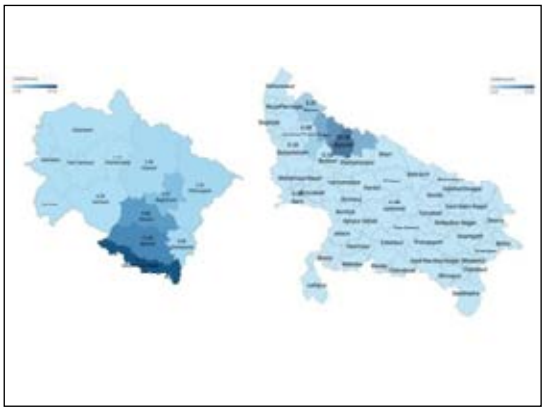


Figure 3: Heat map showing the proportion of admissions from the districts of Uttarakhand and Uttar Pradesh between the period 1st January 2018 to 31st July 2021

Table 2– District wise distribution of admissions done in TB sanatorium, Bhowali (Uttarakhand) from 1st Jan 2018 to 31st July 2021				
State	**District**	**Total Patient (n=1247)**	**Percentage (%)**	**State total (%)**
Delhi	New Delhi	4	0.3	4 (0.3)
Haryana	Ambala	19	1.5	20 (1.6)
	Faridabad	1	0.1	
Punjab	Amritsar	1	0.1	1 (0.1)
Rajasthan	Chittorgarh	7	0.6	8 (0.6)
	Jaipur	1	0.1	
Uttarakhand	Almora	112	9.0	582 (46.7)
	Bageshwar	52	4.2	
	Chamoli	13	1.0	
	Champawat	12	1.0	
	Nanital	142	11.4	
	Pauri Garhwal	4	0.3	
	Rudraprayag	1	0.1	
	Udham Singh Nagar	232	18.6	
	Pithorgarh	14	1.1	
Uttar Pradesh	Agra	1	0.1	632 (50.7)
	Bareilly	188	15.1	
	Bijnor	42	3.4	
	Budaun	13	1.0	
	Bulandshahr	2	0.2	
	Ghaziabad	1	0.1	
	Jyotiba Phule Nagar	25	2.0	
	Lucknow	1	0.1	
	Moradabad	96	7.7	
	Pilibhit	91	7.3	
	Rampur	136	10.9	
	Sambhal	36	2.9	

Table 3– Hospital outcomes about the admissions done in TB sanatorium, Bhowali (Uttarakhand) from 1st Jan 2018 to 31st July 2021					
Year wise distribution	**Death**	**Discharged**	**Leave Against Medical Advice**	**Referred**	**Total**
2018	17 (43.6)	446 (40.3)	7 (46.7)	2 (40.0)	472 (40.5)
2019	13 (33.3)	386 (34.9)	6 (40.0)	1 (20.0)	406 (34.9)
2020	7 (17.9)	142 (12.8)	1 (6.7)	0 (0.0)	150 (12.9)
2021 (till 31st July)	2 (5.1)	132 (11.9)	1 (6.7)	2 (40.0)	137 (11.8)
Gender wise distribution					
Female	9 (23.1)	276 (24.9)	1 (6.7)	0 (0.0)	286 (24.6)
Male	30 (76.9)	830 (75.1)	14 (93.3)	5 (100.0)	879 (75.5)
Religion wise distribution					
Christian	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
Hindu	35 (89.7)	880 (79.6)	14 (93.3)	4 (80.0)	933 (80.1)
Muslim	4 (10.3)	222 (20.1)	1 (6.7)	1 (20.0)	228 (19.6)
Sikh	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)
Total (%)	39 (100.0)	1106 (100.0)	15 (100.0)	5 (100.0)	1165 (100.0)

The hospital outcome data were available for 1165 (93.4%) admissions. Majority of the patients were discharged (94.8%), whereas 15(1.3%) patients took leave Against Medical Advice (LAMA and 6 (0.5%) patients were referred to higher centre for further management **(Table 3)**.There was total 39 deaths recorded in which 76.9% (n= 30) were male and 23.1% (n= 9) were female. The overall death rate at the TB sanatorium was 3.3%. The mean (SD) and median (IQR) duration of stay were 22.7 days (SD – 24.7) and 14 (IQR 7 – 28) days, respectively. It ranged from 0 to 170 days. The mean and median duration of stay for females was 25.1 days (SD- 24.1) and 18 (IQR 9 – 33) days, respectively. The mean and median duration of stay for males was 21.6 days (SD- 24.9) and 14 (IQR 7 – 26) days, respectively. There was a significant difference in the duration of stay for males and females (p-value – 0.0017).

DISCUSSION

We found that the median duration of stay at TB sanatorium was two weeks and with a death rate of 3.3%. The estimated death rate was almost half compared to the TB sanatorium where pulmonary TB patients were treated with isoniazid and p-aminosalicylic acid in India.[4] This could be due to the usage of better and effective drugs, and the short duration of admission as deaths occurring outside the sanatorium related to TB couldn't be captured. Considering the readmission rate as 16.9%, the mortality rate was estimated to be 4%.[9] This mortality rate was similar to the national mortality rate of TB patients (4%) followed up in the year 2019.[10] We couldn't estimate the readmissions, and the number of deaths that occurred outside the sanatorium which could have affected our estimates of mortality rate. The duration of stay was diminutive (2 weeks) compared to the sanatoriums of the 20th century where patients were admitted for almost 6 months to one year.[3,6] This huge difference was there because the TB sanatorium Bhowali admits patients only for stabilizing the health condition in the initial stage. The treatment completion is done near the residence of the patient as a daily observed treatment short course (DOTS). Also, TB sanatorium Bhowali does not admit a patient with drug-resistant TB (DR-TB). A study comparing the admission and duration of stay in TB sanitariums across various era have found a significant reduction in length of stay and deaths during the triple therapy era compared to the pre-chemotherapy era.[6] The admissions were higher during the spring and summer seasons (April to July) which could be due to the seasonal variation of TB transmission and incidence.[11] However, this could be also due to comfortable weather during summers. The number of admissions in the year 2020 was less. This was due to the stringent lockdown imposed due to the COVID-19 pandemic, as no were patients admitted in April, May, and June. Lockdown measures also resulted in a decrease in TB notification cases. In 2020, tumbling in the notification of cases was estimated to be 38% in India. Most of the admissions were from the nearby districts (Udham Singh Nagar & Bareilly). This could be due to higher TB incidence in these areas due to overcrowding and poor living condition.[12,13]

World Health Organization (WHO) and Sustainable Development Goals (SDGs) has set a target to eliminate TB globally by the year 2035 and 2030, respectively.[14,15] In line with these global commitments, National Strategic Plan for Tuberculosis Elimination in India has set a target to eliminate TB by 2025.[16] One of the key indicators for TB elimination is the reduction in mortality. For this several initiatives has been taken like real-time monitoring and patient tracing through Nikshay, daily drug regimen, decentralised DR-TB treatment services, active case finding, bi-directional screening and community awareness. Despite these initiatives, there is significant mortality of TB. In the 20th century, TB sanatoriums were considered as the backbone of TB treatment and now they seem to be forgotten. Currently, these TB sanatoriums no longer exist in their original form and have not been utilised to expand the TB care services. TB sanatoriums have certain advantages like supervised medications, a nutritious diet for patients and nursing care for people without caregivers. In the Madras trial, it was found that the weight gain of patients in TB sanatorium was 1.6 – 2 times higher and had a shorter time to sputum conversion compared to patients treated at home.[5] Studies in India have found a substantial non-medical cost borne by TB patients for diet, nutritional supplements and travel.[17,18] A sanatorium can address the financial problem which is considered a major socio-economic problem faced by TB patients,[19] as these sanatoriums provide a nutritious diet with a better living condition for the patient free of cost. There is a substantial burden of tobacco and alcohol use among TB patients which is often ignored. Alcohol and tobacco use have combined

effects and are associated with unfavourable outcomes in TB.[20,21] With the strengthening of staff and facilities these sanatoriums can provide the services for deaddiction, and behaviour change communication. These sanatoriums can be upgraded to Drug-resistant TB centres (DR-TBC), difficult-to-treat clinics and research centres to achieve the ambitious target of TB elimination in India by 2025.

This study explored and generated data related to admission patterns and duration of stay at the modern TB sanatorium of the 21st century. Findings from this study can be useful for the policymakers to plan an expansion and intervention for TB care services using these TB sanatoriums whose roles are undermined. We couldn't assess the readmission rates, age-specific mortality rates and treatment outcome. This was due to the limitation of the secondary data. Patient details records were outspread to multiple registers and lacked unique IDs. It was difficult to compile the data. Inability to assess the readmission rate could have affected the estimation of the death rate.

CONCULSION

TB sanatorium Bhowali at Uttarakhand state caters to the majority of the patients from the neighbouring state of Uttar Pradesh. The admissions were higher in the year 2018 compared to the years 2019 and 2020. The majority of the admissions were during the spring and summer seasons. The median duration of hospital stay at TB sanatorium Bhowali, Uttarakhand (India) for patients admitted with TB was two weeks. The median duration of stay was significantly higher for females compared to males. Further studies can be planned to explore the role of these tuberculosis sanatoriums.

ACKNOWLEDGEMENT

We would like to thank Mr Saurabh and the staff of TB sanatorium Bhowali for their help and cooperation. Also, we want to thank Pahadi Jan Swasth Sanstha, Haldwani (Nainital) for providing the support.

CONFLICT OF INTEREST

None

FUNDING

None

REFERENCES

1. Central TB Division, Ministry of Health & Family Welfare, Government of India. National Tuberculosis Elimination Programme [Internet]. [cited 2021 Sep 16]. Available from: https://tbcindia.gov.in/index4.php?lang=1&level=0&linkid=399&lid=2768

2. Martini M, Gazzaniga V, Behzadifar M, Bragazzi NL, Barberis I. The history of tuberculosis: the social role of sanatoria for the treatment of tuberculosis in Italy between the end of the 19th century and the middle of the 20th. Journal of preventive medicine and hygiene. 2018;59(4):E323.

3. Murray JF, Schraufnagel DE, Hopewell PC. Treatment of tuberculosis. A historical perspective. Annals of the American Thoracic Society. 2015;12(12):1749–59.

4. Dawson JJY, Devadatta S, Fox W, Radhakrishna S, Ramakrishnan CV, Somasundaram PR, et al. A 5-year study of patients with pulmonary tuberculosis in a concurrent comparison of home and sanatorium treatment for one year with isoniazid plus PAS. Bulletin of the World Health Organization. 1966;34(4):533–51

5. Tuberculosis Chemotherapy Centre, Madras. A concurrent comparison of home and sanatorium treatment of pulmonary tuberculosis in South India. Bulletin of the World Health Organization. 1959;21(1):51–144.

6. Zwick ED, Pepperell CS. Tuberculosis sanatorium treatment at the advent of the chemotherapy era. BMC infectious diseases. 2020;20(1):1–11.

7. District Administration, National Informatics Centre,Ministry Of Electronics & Information Technology, Government Of India. Bhowali | District Nainital, Government of Uttarakhand | India [Internet]. [cited 2021 Sep 16]. Available from: https://nainital.nic.in/tourist-place/bhowali/

8. The Times of India. Nehru's wife Kamala was treated for TB at Bhowali [Internet]. 2014 [cited 2021 Sep 16]. Available from: ttps://timesofindia.indiatimes.com/city/dehradun/nehrus-wife-kamala-was-treated-for-tb-at-bhowali /articleshow/45142507.cm

9. Frankel E, Heyer HE. Tuberculous Patients in New Jersey Sanatoriums. American Journal of Public Health and the Nations Health. 1930;20(9):969–77.

10. Central Tuberculosis Division, Ministry of Health and Family Welfare India. India TB report [Internet]. 2021 p. 1–352. Available from: https://tbcindia.gov.in/showfile.php?lid=3587

11. Fares A. Seasonality of tuberculosis. Journal of global infectious diseases. 2011;3(1):46–55.

12. Banerjee A, Harries AD, Salaniponi FML. Differences in tuberculosis incidence rates in township and in rural populations in Ntcheu District, Malawi. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1999;93(4):392–3.

13. Noykhovich E, Mookherji S, Roess A. The risk of tuberculosis among populations living in slum settings: A systematic review and meta-analysis. Journal of Urban Health. 2019;96(2):262–75.

14. Sustainable Development Goals [Internet]. United Nations Development Programme. [cited 2018 Oct 25]. Available from: http://www.undp.org /content/undp/en/home/sustainable-development-goals.html

15. World Health Organization. The End TB strategy: global strategy and targets for tuberculosis prevention, care and control after 2015. [Internet]. 2014 [cited 2019 Apr 30]. Available from: https://www.who.int/tb/strategy/End_TB_Strategy.pdf?ua=1

16. Central Tuberculosis Division, India. National strategic plan for tuberculosis elimination 2017 - 2025 [Internet]. [cited 2020 Aug 15]. Available from: https://tbcindia.gov.in/WriteReadData/NSP%20Draft%2020.02.2017%201.pdf

17. Chandra A, Kumar R, Kant S, Krishnan A. Costs of TB care incurred by adult patients with newly diagnosed drug-sensitive TB in Ballabgarh block in northern India. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2021 Apr 9;

18. Chandra A, Kumar R, Kant S, Parthasarathy R, Krishnan A. Direct and indirect patient costs of tuberculosis care in India. Tropical Medicine & International Health. 2020 Jul;25(7):803–12.

19. Aslan D, Altıntaş H, Emri S, Cesuro□lu T, Kotan O, Koyuncu S, et al. Self-evaluations of tuberculosis patients about their illnesses at Ankara Atatürk Sanatorium Training and Research Hospital, Turkey. Respiratory medicine. 2004;98(7):626–31.

20. Kumar R, Kant S, Chandra A, Krishnan A. Tobacco use and nicotine dependence among newly diagnosed pulmonary tuberculosis patients in Ballabgarh tuberculosis unit, Haryana. Journal of Family Medicine and Primary Care. 2020;9(6):2860–5.

21. Thomas BE, Thiruvengadam K, Kadam D, Ovung S, Sivakumar S, Bala Yogendra Shivakumar SV, et al. Smoking, alcohol use disorder and tuberculosis treatment outcomes: A dual co-morbidity burden that cannot be ignored. PLoS One. 2019;14(7):e0220507.

Original article

IMPACT OF STRATEGIC ADAPTATIONS DUE TO COVID-19 PANDEMIC ON A CAPACITY BUILDING PROGRAM: INSIGHTS FROM A DRTB PROGRAM UNDER NTEP IN INDIA

Manjari[1]; Lydia S Jasmine Beryl[1]; Sinha Atreyee[1]; Tripathi Ashutosh [1]; Sagil Karuna D.[1]

[1] International Union Against Tuberculosis and Lung Disease (The Union), India

DOI: https://doi.org/10.3126/saarctb.v20i1.52661
Received: 10th April Accepted: June 29th Published: 31st August
This article is available at:

ABSTRACT

Introduction: India has experienced high burden of drug resistant tuberculosis, under par treatment success rate and very high loss to follow-up despite continuous efforts to develop evidence-based policy to treat DRTB patients. However, it is challenging to translate policies into practice. The goal of this program was to build capacity of the program staff for effective management of DRTB in public sector through workshops, capacity building exercises, creation and dissemination of information, education and communication materials.

Methodology: The program was implemented in seven states; 11 state-level kick-off trainings were planned to reach 660 National TB Elimination Program staffs. Due to COVID-19 pandemic, on-field activities were replaced with virtual trainings with a set of 4-5 webinars per state. Pre and post training assessments were done to evaluate uptake of knowledge. Number of trainings conducted, staff trained and knowledge improvement were the indicators used to assess the outcome.

Results: A total of 34 webinars were conducted on revised Programmatic Management of Drug-Resistant Tuberculosis guidelines and 3000 staff was trained. The program organized three times more training and five times more staff were trained. Although retention of participants and their attention was challenging, transition to virtual platform provided increased coverage and targeted outputs. Proportion of participants answering correctly in pre/post-training assessments, increased from 47% to 65%.

Conclusion: Use of virtual trainings is an efficient high yielding method to build capacity of NTEP staff. Lessons learnt can help improve such interventions, benefit health programs and the end beneficiaries - the patients.

Key words: DRTB, Capacity building, NTEP, COVID-19, Webinars.

INTRODUCTION

Drug resistance strain of M. tuberculosis is more difficult to treat and is an obstacle to TB care and prevention. In 2019 globally 2,06,030 people with Drug Resistance Tuberculosis (DRTB) were detected[1]. India is one of the top ten countries in the world with a high burden of Tuberculosis and DRTB poses a huge challenge towards achieving the sustainable development goals (SDG) of eliminating TB by 2030 [2-5], as the estimated incidence of DRTB cases in the country is around 1.2 lakhs per year. In view of high burden of Multi Drug Resistant /Rifampicin Resistance Tuberculosis (MDR/RR-TB) with estimated case of 1,30,000 contributing to 27% of the global burden[1] and with a target to eliminate TB by 2025, National Strategic Plans (NSP)[6] have been proposed under the National Tuberculosis Elimination Programme (NTEP).[7] Under NTEP, MDR/RR TB case

Correspondence:
Ms. MANJARI
The Union South-east Asia
Project Assistant
B-211, 2nd Floor, Sector 26, Noida-201301
Email: manjari.singh0596@gmail.com
Mobile : 7679136160

finding and treatment initiation efforts registered remarkable improvement. Out of 66,255 MDR/RR TB cases diagnosed in 2019, 56,569 patients (85%) were put on treatment which is an increase from 71% in 2018.[8] However, treatment of DRTB across the country is in a weak state in terms of low treatment success rate and higher loss to follow up. In this context, it is pertinent to provide trainings to healthcare providers and ensure quality of care both in public and private sectors.

Rationale

Over a period of time, WHO has issued various evidence-based policy recommendations for DRTB care. The "Programmatic Management of Drug-Resistant Tuberculosis (PMDT) in India, 2019" was a detailed roadmap for diagnosis, care and management of DRTB patients in line with the global recommendations that integrates the use of shorter MDR TB regimen and all oral longer MDR TB regimen with new drugs under NTEP with the opportunity to modify regimen based on drug susceptibility test (DST) results.[9] There are also key updates on universal drug susceptibility testing, decentralised DRTB management, diagnostic technology, DRTB diagnostic algorithm and classes of anti-TB drugs recommended for treatment.[10,11] However, in a large country like India, which has a high burden of MDR-TB and extensively drug resistant (XDR) TB, suboptimal treatment outcomes along with a high loss to follow up pose serious challenges. Hence, it is vital to translate the policies into practice at the ground level for reducing the burden of the disease. Furthermore, there exists a prominent knowledge gap and capacity issues at provider level across both the public and private sectors which is a major challenge in the cascade of TB care in the country.

The Central TB Division (CTD) prepared the PMDT guidelines with an aim to provide high quality DRTB care to patients across India. With the roll-out of revised PMDT guidelines 2019, there was a pressing need of appropriate dissemination among key DRTB care cascade in public sector and implementation across India to enhance the clinical and programmatic acumen to diagnose all patients, put them on appropriate treatment and improve treatment outcomes. Inability to do so in a timely and systematic manner could lead to further deterioration in treatment outcomes and increased transmission of the disease. With increase in number of cases each year, it is pertinent therefore, to strengthen the health systems and create efficient human resource by training all health-care workers from physicians to grassroot level workers.[12] To address the emerging need and plug the knowledge gaps, the Union South-East Asia (USEA), in collaboration with Janssen India rolled out a plan to provide momentum to improvement of DRTB quality of care by rapidly percolating the information regarding key changes in PMDT at all levels of the health system.

The NTEP emphasizes on decentralized DRTB treatment services by strengthening of both Nodal DRTB centres (nDRTBC) and District DRTB centres (dDRTBC). While nDRTBCs are responsible for treatment initiation and management of Pre-XDR and XDR-TB patients, the dDRTBCs are responsible for initiation of treatment and management of Rif-Resistant TB Cases. The staffs of dDRTBCs are also crucial for field level follow-up, timely referral of Pre-XDR or XDR patients to nDRTBCs for management of serious adverse drug reactions (ADRs) and for treatment modification. Therefore, such training workshops will be critical as they are not undertaken by State NTEP and are currently not part of the state's training budget. Also, the format of the programme will help in hand-holding and strengthening of dDRTBCs by their respective nodal centres. In this paper, we present a brief account of how specific interventions were planned under the project and its course of implementation in a global pandemic scenario.

Objectives

The project aims to build capacity of public sector health care providers by advancing their knowledge for effective management of TB and DRTB.

METHODOLOGY

Study design

The project was planned to be implemented over a period of six months, from October 2019 to April 2020. In order to sensitize key clinicians and healthcare providers about the recent changes and improve their knowledge of revised PMDT

Guidelines 2019, the project adopted specific interventions as outlined below:

Intervention 1 - Quality improvement and cross-learning sessions/workshops/periodic meetings to disseminate latest PMDT guidelines: A total of 11 two-day long in-person state level kick-off trainings were planned for DRTB Committee members, nodal physicians and Senior Medical Officers (SMO) of all DRTB Centres and, all the state District TB Officers **(Table 1)**.

Table 1: Distribution of kick off meetings under Intervention – 1

State	**No. of State level kick off meetings (one for 20-25 districts)**
Andhra Pradesh	1
Karnataka	1
Punjab	1
Rajasthan	2
Tamil Nadu	1
Uttar Pradesh	3
West Bengal	2
Total	11

The trainings were to be facilitated by national, state PMDT experts, and WHO consultants. Through these meetings, a total of 660 key NTEP staff (60 NTEP staff per training) were targeted to be trained.

Intervention 2 - Creation and dissemination of material and job aid to disseminate latest PMDT guidelines: In order to facilitate dissemination of latest PMDT guidelines and its comprehension, assimilation and application by healthcare providers, it was planned to create job aides such as posters (showing decision trees/diagnosis and treatment algorithms, drug dosages, remedial actions for ADRs etc.), capacity building package comprising of ready reckoners, flyers, flipcharts, and short videos featuring eminent PMDT experts. These IEC materials based on respective core topics of latest PMDT Guidelines 2019, were planned to be extensively demonstrated and used during the various capacity building meetings and workshops organized under Intervention **1 (Table 2).**

Setting

The project was implemented in seven high DRTB burden states of India that account for 47% of the country's population i.e., 655 million, spread across 279 districts. In addition, these states contributed 47 percent of the DRTB case notification in the country in 2018 **(Table 3)**.[13] While majority of these selected states fall in the category of top 10 contributors to high burden in the country, they also show poor programmatic indicators such as low notification rate, low treatment success and high death rate as per recent statistics.[7,8] The sub-optimal DRTB case detection and treatment adherence in these states clearly points out the existing gaps and challenges in the TB care delivery in the country. Capacity building efforts for

Table 2: Details of planned IEC materials

Topic	**Type of IEC materials**	**Target Audience**
DR-TB integrated algorithm	Posters	Medical officers and Healthcare workers
DR-TB treatment regimen and Drug Dosage Table	Posters	Medical officers and Healthcare workers
DR-TB Pre-treatment Evaluation and follow up schedule	Posters	Medical officers and Healthcare workers
DR-TB Management - made simple	A 24-page flip book	Job-aids for healthcare worker training, includes counselling tool
PMDT at a glance	3-fold flyer	Medical officers
Ready Reckoner	A 24-page Booklet with illustrations	Medical Officers
DR-TB burden	1 Infographic flyer	Healthcare workers and private physicians
PMDT Presentation Deck	1 deck of 20 slides	Programme managers and clinicians
Short animation films & videos (3-6 minutes)	9 Videos	Programme managers and Healthcare workers

Table 3: DRTB Burden in the proposed states, 2018							
States	**Population (Lakhs)**	**No. of Districts**	**No. of DRTB centres**	**No. of notified DRTB patients**	**DRTB Notification Rate (No. of DRTB cases/ lac population)**	**No. of patient initiated on Shorter MDR-TB regimen**	**No. of Patient initiated Newer drug containing regimen**
Andhra Pradesh	515	13	13	1753	3.4	1318	148
Karnataka	660	31	31	1502	2.3	1069	68
Tamil Nadu	783	35	33	1529	2.0	1001	82
West Bengal	971	37	35	2700	2.8	1711	110
Uttar Pradesh	2215	75	77	10964	4.9	1032	35
Punjab	297	22	15	762	2.6	350	43
Rajasthan	761	34	35	2879	3.8	386	18

upgrading the knowledge of effective management of TB and DRTB was the need of the hour to ensure systematic strengthening of quality of TB care in the country.

Changes in study design during Covid-19 pandemic

The first case of COVID-19 in India was reported in later half of January 2020.[14] To curb the pandemic and prevent it from spreading further, a nation-wide lockdown was enforced since March 2020. The sudden lockdown posed a serious threat and collapsed the healthcare system of the country. The pandemic brought halt to all field level activities, thus affecting TB care services to a large extent.[15-20] This led to a drop in the TB notification and follow-up rate[8]. In order to tackle this situation, several risk mitigation plans were put in place in order to continue with the TB services to the patients. States quickly came up with standard protocols for TB patients, such as home-delivery of anti-tuberculosis drugs for about two months.[21]

The implementation of this program also encountered a major setback as the planned in-person trainings were put on hold. Keeping the objective of the project i.e., to build capacity of DRTB care providers as a priority, the activities under the planned intervention were re-strategized with certain adaptations in the mode of delivery. The key in-person capacity building activities were revised to virtual trainings and webinars.[22]

In order to compensate for the delay in initiation, the project period was extended by four months, till August 2020. State level kick-off workshops for DRTB committee members, nodal physicians, State TB Officers (STO), and District TB Officers (DTO) were converted into a series of 4-5 webinars for each state; each of the webinars was for the duration of 2-3 hours, facilitated by national and state PMDT experts. The scope of coverage was also broadened to include peripheral health workers as part of the webinars. In order to impart trainings on the latest PMDT Guidelines 2019, a total of nine topics were broadly identified and the intervention states chose two to three topics per webinar, according to their convenience and interest **(Box1)** Training materials were prepared in the form of smart presentations using graphics and animations to capture the attention of the participants. The experts incorporated innovative ideas to successfully facilitate the trainings such as, presentation of unique case studies and field experiences, open house discussions etc. Training materials were shared to all the participants for their future references and post execution of the trainings in their set-up.

Further, knowledge uptake among trained NTEP staff was assessed through pre- and post-training tests. These test sessions incorporated a structured questionnaire prepared by the respective PMDT experts involved in facilitating the particular webinar The questionnaires were administered to the participants ten minutes before the training and again for ten minutes after the completion of the trainings. Case finding approach, patient flow, and case studies based on the new treatment guidelines were some of the topics for which these tests were conducted. After the post-training test was completed, the speakers announced the results of the test and also explained the correct

Box 1: Selected topics for the webinars

1. PMDT Overview and newer initiatives
2. Updates on Case finding approach and Patient Flow
3. Updates on Newer Drugs
4. Updates on Treatment of DRTB
5. Data management on Nikshay and Supervision and Monitoring
6. Operation and programmatic challenges and solutions as per PMDT guidelines
7. Pre-Treatment Evaluation
8. Supply chain management
9. Private Sector Engagement
10. ADR Management, infection control and prevention
11. Case study from the nodal centers on the treatment based on PMDT guidelines
12. Continuity of TB service during lockdown

answers for understanding of the participants. For virtual implementation of the project, various online platforms like Go To Meeting (GTM), Microsoft Teams, and Zoom were evaluated. Comparing the accessibility, ease of use, budget and data security, GTM was preferred as a platform for virtual meetings and webinars. At a later stage Zoom meeting platform was selected for further webinars in order to utilize login registrations for participants and online polling feature for the knowledge assessment. The project team was trained through various demonstration sessions to operate and handle the platform for conducting webinars.

RESULTS

The measurable outcome indicators used for the project were the number of trainings conducted, number of participants who were trained through the webinars, and knowledge uptake among the trained NTEP staff, measured by the change in proportion of participants giving correct answers in the pre and post training tests.

Findings from intervention-1

The results underscored a significant increase in number of webinars conducted and the number of participants was more than that of original target, highlighting enormous success of the strategic adaptations. A total of 34 webinars were successfully conducted in the seven intervention states; these webinars were able to train nearly 3066 key NTEP staff comprised of three main groups, which included 1246 key clinicians viz. DTOs, SMOs, Medical Officers (MO), and other clinicians, 1294 DRTB Coordinators and Supervisors and 526 other DRTB staff including Statistical Assistants (SA), Pharmacists, Lab Technicians, Health Visitors (HV) and Counsellors. The project surpassed its planned targets in terms of completion and coverage; nearly three times more numbers of trainings were conducted and more than five times healthcare providers were trained

Figure-1 presents the participation of three main groups of NTEP staff over a series of five webinars.

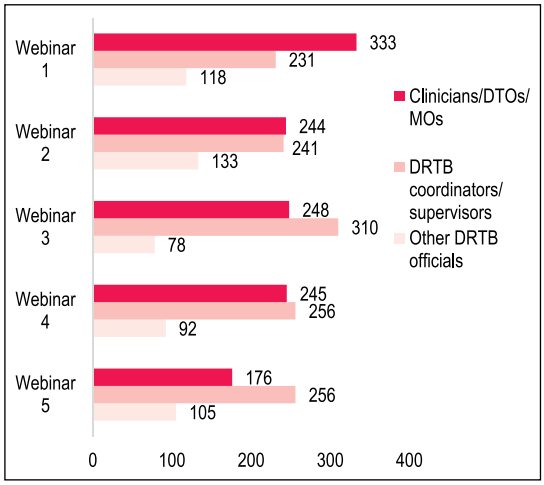


Figure 1: Numbers of key NTEP staff who attended the webinars from all intervention states.

Despite having surpassed the expected participation of healthcare providers, it was observed that the number of participants varied across the webinars and the numbers of NTEP staff in each group were slightly unstable.

Figure 2 depicts participation from seven intervention states. It revealed that participation of DTOs, MOs, Clinicians, and DRTB supervisors/ coordinators was higher than the third group in all the states.

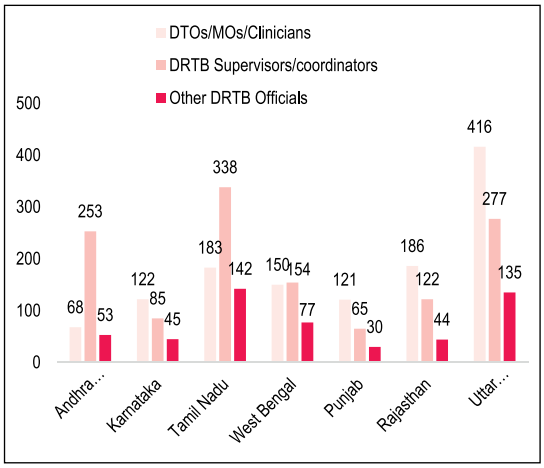


Figure 2: State-wise spectrum of NTEP staff who attended the webinars

In terms of numbers, Uttar Pradesh state registered highest participation (828) followed by Tamil Nadu (663), West Bengal (381), Andhra Pradesh (374), Rajasthan (352), and Punjab (216).

Results from the pre- and post-training tests

This exercise was done for five webinars in the states - Rajasthan, West Bengal, Punjab, Tamil Nadu, and Uttar Pradesh.

Figure-3 presents the overall outcome of the tests; out of the total participants undertaking the test (shown as 'n' in the graph), an average 20 percent increase in the proportion of correct answers in post-test was observed as compared to the pre-tests.

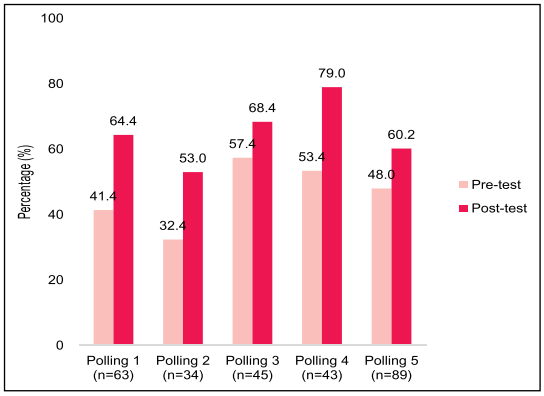


Figure 3: Proportion of participants who gave correct answers during the pre & post-training tests.

Results from intervention-2

As part of these activities IEC materials such as posters, flip book, 3-fold flyer, ready reckoners, presentation deck, and short videos were developed and disseminated among the states. The materials were initially developed in English and translated into six regional languages – Hindi, Punjabi, Bengali, Tamil, Kannada, and Telugu. To ensure effectiveness of the whole activity, feedback was sought from the STOs and other stakeholders on the content of the IEC materials and videos and the contents were modified further to ensure quality. Since the modalities of the project were changed and in-person trainings were not conducted, the IEC materials were shared with respective STOs in each of the intervention states and through the State NTEP Cell, they were widely distributed among Clinicians, Physicians, Program Managers, Medical officers, and Health Care Workers (HCW) at the peripheral level. We ensured successful dissemination through continuous follow-ups with the STOs and acquiring feedback from the recipients. Presentation deck and the videos were shared with the states as e-contents.

DISCUSSION

The COVID-19 pandemic had put massive repercussions in almost every corner of the world, including India, dividing the focus of health care between the pandemic and other important communicable and non-communicable diseases and caused a significant strain of the healthcare resources. However, ensuring quality of healthcare is extremely essential in recent times, to ensure adequate utilization of services and improved outcomes. The pandemic has altogether altered the face of healthcare delivery wherein medical practitioners have increasingly resorted to by adopting digital tools and technologies.[23] Similarly, DRTB which is one of the major health care concerns in India, cannot take a back seat at such a time. In this context, developing knowledge and skills of healthcare workers is also deemed necessary. This project gives an account of how effective risk mitigation plan and efficient strategies are vital to train maximum number of healthcare professionals and deliver the services in best possible way, at the time of global crisis.

The project achieved 100% completion rate and exceeded the planned outcomes in terms of its targeted number of trainings and coverage of participants. Findings of the present project conformed to existing studies and reaffirmed that virtual adaptation of various capacity building sessions can be successful and extremely productive in terms of its reach and finds support from existing research that explain role of web-based teaching technology and learning platforms in medical education. [24] Modern technology and learning platforms can bring together a large number of healthcare professions and facilitate collaborative learning and experience sharing when available resources are limited, face-to-face education is barred due to geographical isolation, especially at a time of national crisis.[25,26] Studies confirmed use of social media platforms to improve public health protection through public awareness.[27]

Few major drawbacks that need to be considered are that, the use of virtual platform does not ensure retention of participants and their interests throughout the span of the webinars. Although several measures were taken to make the webinars more interactive through introducing pre-post training polling sessions, open house discussions with the experts etc., the number of participants was highly unstable during and across the webinars. Another issue was interest of any particular group of NTEP staff in the particular topics being covered; although, virtual platform increased the coverage and key NTEP staff were instructed by the state NTEP cell to attend the trainings, there were chances that they don't derive any usefulness and lose interest over time. Thirdly, it was difficult to ensure full participation in the polling sessions; despite repeated requests, the number of participants undertaking the tests remained low and a challenge for effective assessment of knowledge and skill learnt.

CONCLUSION

Despite the few caveats, the project received wide acceptance and support from the intervention states which gave impetus to increase coverage and ensure success of the interventions. Although, retention of participants and their attention was a practical challenge, mainly because of the unavailability of the key NTEP staffs like clinicians due to their overwork with emergency COVID duties across the geographies and use of technology driven platform, the project was able to achieve its targeted outputs with 100 percent completion rate and beyond. Although ensuring uninterrupted internet availability and zero technical glitches was a challenging task, this strategic innovation was able to capture interests amongst the participants as it ensured attending the trainings programmes from the comfort zone of their environment without risking their safety. An added advantage was that the NTEP field supervisory staff were well-equipped with tablet computers and familiar with use of mobile apps (such as 99 DOTS) for program purposes and thus, the participation from all intervention states was overwhelming.

The success of the project provides a comprehensive understanding of how adaption of virtual platform can be a successful way out to be included as a risk mitigation plan in future capacity building programs. As suggested by other studies, virtual training of healthcare professionals is a viable, efficient, and effective alternative to traditional training programs that will play a vital role in building their competence to improve the healthcare system in post-COVID environment.[28] However, despite the successful completion of the project in terms of the activities, to ensure quality and continuity of knowledge uptake by public sector HCPs, refresher trainings and knowledge assessment of trained NTEP staff at regular intervals are pertinent.

ACKNOWLEDGEMENT

We acknowledge the continuous support received from Central TB Division and the State NTEP Cells in the project implementation. We are thankful to all the State TB Officers, WHO Headquarter/NTEP Consultants for their support to roll out the project in their respective states; National and State PMDT experts for facilitating the webinars and all other NTEP staff from the states for their active participation. We are also grateful to the senior management team, the finance and administration teams of The Union for their constant support during the course of the project

FUNDING

This project was supported by an educational grant received from Janssen India - Pharmaceutical Companies of Johnson & Johnson. The funders did not have any role in writing this paper.

ETHICAL APPROVAL

The current paper analyses the data from a project which is now completed. The paper does not involve any participants, and only uses project data and processes. Hence, the Ethics Advisory Group of International Union Against Tuberculosis and Lung Disease (The Union) has granted an ethics waiver.

CONFLICT OF INTEREST

None

REFERENCES

1. World Health Organization. Global tuberculosis report 2020 [Internet]. Geneva: World Health Organization; 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf.

2. Institute of Medicine. Facing the Reality of Drug Resistant Tuberculosis in India: Challenges and Potential Solutions: Summary of a Joint Workshop, 2012 [Internet]. Washington, DC: The National Academies Press; 2012. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92617/

3. Prasad R, Singh A, Balasubramanian V, Gupta N. Extensively drug-resistant tuberculosis in India: Current evidence on diagnosis & management. Indian J Med Res [Internet]. 2017;145(3):271-293. Available from: https://www.ijmr.org.in/article.asp?issn=0971-5916;year=2017;volume=145;issue=3;spage=271;epage=293;aulast=Prasad DOI: 10.4103/ijmr.IJMR_177_16

4. Chatterjee S, Poonawala H, Jain Y. Drug-resistant tuberculosis: is India ready for the challenge? BMJ Glob Health [Internet]. 2018; 3(4): e000971. Available from: https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC6089296/ DOI:10.1136/bmjgh-2018-000971

5. End TB Strategy [Internet]. Geneva: World Health Organization; 2015. Available from: https://www.who.int/tb/End_TB_brochure.pdf

6. Central TB Division. Revised National Tuberculosis Control Programme: National Strategic Plan for Tuberculosis Elimination 2017-2025 [Internet]. New Delhi: Central TB Division, Ministry of Health and Family Welfare, 2020. Available from: https://tbcindia.gov.in/WriteReadData/NSP%20Draft%2020.02.2017%201.pdf

7. Kanabus, A. Information about Tuberculosis [Internet]. GHE, 2020. Available from: www.tbfacts.org

8. Central TB Division. India TB Report 2020: National Tuberculosis Elimination Programme Annual Report [Internet]. Central TB Division, Ministry of Health and Family Welfare, New Delhi; 2020. Available from: https://tbcindia.gov.in/showfile.php?lid=3538

9. World Health Organization. WHO consolidated guidelines on drug-resistant tuberculosis treatment [Internet]. Geneva: World Health Organization; 2019. Available from: https://apps.who.int/iris/rest/bitstreams/1211676/retrieve

10. Chaudhuri AD. Recent changes in guidelines on programmatic management of drug resistant tuberculosis in India 2019: a paradigm shift in tuberculosis control. J of Assoc Chest Physicians [Internet]. 2020; 8:53-63. Available from: https://www.jacpjournal.org/article.asp?issn=2320-8775;year=2020;volume=8;issue=2;spage=53;epage=63;aulast=Chaudhuri DOI: 10.4103/jacp.jacp_47_20

11. Wares FD. Report on the review of Programmatic management of drug-resistant tuberculosis (PMDT) component of the Revised National TB Control Programme, India [Internet]. World Health Organization: New Delhi; 2019. Available from:https://www.who.int/docs/default-source/searo/tuberculosis/rglc-mission-report-india-2019.pdf?sfvrsn=9e4cf828_2

12. Institute of Medicine (US). Facing the Reality of Drug-Resistant Tuberculosis in India: Challenges and Potential Solutions: Summary of a Joint Workshop by the Institute of Medicine, the Indian National Science Academy, and the Indian Council of Medical Research [Internet]. Washington, DC: The National Academies Press (US); 2012. 2, Drug-Resistant TB in India. Available from: https://www.ncbi.nlm.nih.gov/books/NBK100386/

13. Central TB Division. India TB Report 2019: Revised National TB Control Programme Annual Report [Internet]. New Delhi: Central TB Division, Ministry of Health and Family Welfare, New Delhi; 2019. Available from: https://tbcindia.gov.in/WriteReadData/India%20TB%20Report%202019.pdf

14. Andrews MA, Areekal B, Rajesh KR, Krishnan J, Suryakala R, Krishnana B, et al. First confirmed case of COVID-19 infection in India: A case report. Indian J Med Res [Internet]. 2020; 151(5):490-492. Available from: https://www.ijmr.org.in/article.asp?issn=0971-5916;year=2020;volume=151;issue=5;spage=490;epage=492;aulast=Andrews DOI:10.4103/ijmr.IJMR2131_20

15. Visca D, Ong CWM, Tiberi S, Centis R, D'Ambrosio L, Chen B, et al. Tuberculosis and COVID-19 interaction: A review of biological, clinical and public health effects. Pulmonology [Internet]. 2021; 27 (2): 151-165. Available from: https://doi.org/10.1016/j.pulmoe.2020.12.012 DOI: 10.1016/j.pulmoe.2020.12.012

16. Shrinivasan R, Rane S, Pai M. India's syndemic of tuberculosis and COVID-19. BMJ Glob Health [Internet]. 2020; 5: e003979. Available from: https://gh.bmj.com/content/5/11/e003979

17. Husain AA, Monaghan TM, Kashyap RS. Impact of COVID-19 pandemic on tuberculosis care in India. Clin Microbiol Infect [Internet]. 2021; 27(2):293-294. Available from: https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7434422/ DOI: 10.1016/j.cmi.2020.08.014

18. Bhargava A, Shewade HD. The potential impact of the COVID-19 response related lockdown on TB incidence and mortality in India. Indian J. Tuberc [Internet]. 2020; 67(4):S139-S146. Available from: https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7348601/ DOI: 10.1016/j.ijtb.2020.07.004

19. Prasad R, Singh A, Gupta N. Tuberculosis and COVID-19 in India: Challenges and opportunities. Lung India [Internet]. 2020; 37(4): 292-294. Available from: https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7507925/ DOI: 10.4103/lungindia.lungindia_260_20

20. Jain VK, Iyengar KP, Samy DA, Vaishya R. Tuberculosis in the era of COVID-19 in India. Diabetes Metab Syndr Obes [Internet]. 2020; 14(5):1439-1443. Available from: https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/resource/en/covidwho-679821 DOI: 10.1016/j.dsx.2020.07.034

21. Tamil Nadu – National TB Elimination Program. Best Practices followed during the COVID 19 Pandemic [Internet]. Tamil Nadu: National TB Elimination Program; 2020. Available from: https://tbcindia.gov.in/WriteReadData/TNBest%20PracticeMay20.pdf

22. Agarwal S, Ferdousi S, John M, Nalven A, Stahl T. Effective Leadership in Virtual Teams during the COVID-19 Pandemic. Engineering and Technology Management Student Projects [Internet]. 2020; 2298. Availablefrom: https://pdxscholar.library.pdx.edu/etm_studentprojects/2298

23. Jnr BA. Use of telemedicine and virtual care for remote treatment in response to COVID-19 pandemic. J Med Syst [Internet]. 2020; 44(7), 1-9. Available from: 10.1007/s10916-020-01596-5 DOI: 10.1007/s10916-020-01596-5

24. Mehta R, Sharma KA. Use of learning platforms for quality improvement. Indian Paediatr [Internet]. 2018; 55(9), 803-808. Available from: https://www.indianpediatrics.net/sep2018/sep-803-808.htm DOI: https://doi.org/10.1007/s13312-018-1385-2

25. Bennett PN, Jaeschke S, Sinclair PM, Kerr PG, Holt S, Schoch M, et al. Increasing home dialysis knowledge through a web‐based e‐learning program. Nephrology [Internet]. 2014; 19(6), 345-351. Available from: https://pubmed.ncbi.nlm.nih.gov/24646191/ DOI: 10.1111/nep.12231. PMID: 24646191.

26. Sinclair PM, Kable A, Levett-Jones T, Booth D. The effectiveness of internet-based e-learning on clinician behaviour and patient outcomes: a systematic review protocol. Int J Nurs Stud [Internet]. 2016; 57:70-81. Available from: https://pubmed.ncbi.nlm.nih.gov/27045566/DOI: 10.1016/j.ijnurstu.2016.01.011

27. Al-Dmour H, Salman A, Masa'deh R, Abuhashesh M, & Al-Dmour R. Influence of social media platforms on public health protection against the COVID-19 pandemic via the mediating effects of public health awareness and behavioural changes: integrated model. J Med Internet Res [Internet]. 2020; 22(8), e19996.Availablefrom: https://www.jmir.org/2020/8/e19996/DOI: 10.2196/19996

28. Khurshid Z, De Brún A, Moore G, McAuliffe E. Virtual adaptation of traditional healthcare quality improvement training in response to COVID-19: a rapid narrative review. Hum Resour Health [Internet]. 2020; 18(1), 1-18. Available from: https://human-resources-health.biomedcentral.com/articles/10.1186/s12960-020-00527-2 DOI: https://doi.org/10.1186/s12960-020-00527-2

Original article

DESCRIPTIVE ANALYSIS OF THE PATIENTS WITH POST COVID INTERSTITIAL LUNG DISEASES IN A TERTIARY CARE HOSPITAL IN CENTRAL SRI LANKA: AN OBSERVATIONAL STUDY

Madegedara Dushantha [1]; Basnayake Lihini [2]; Bandara Damith Nissanka [3]

[1] Consultant Respiratory Physician, Respiratory Research Unit, National Hospital, Kandy, Sri Lanka
[2] Senior Registrars in Respiratory Medicine, Respiratory Research Unit, National Hospital, Kandy, Sri Lanka
[3] Research Assistant, Respiratory Research Units, National Hospital, Kandy, Sri Lanka

DOI: https://doi.org/10.3126/saarctb.v20i1.52663
Received: 29th March Accepted: 29th June Published: 31st August
This article is available at:

ABSTRACT

Background: To date, COVID-19 continues to remain at pandemic proportions. As of March 2022, COVID-19 has caused over 433 million infections and over 5.9 million deaths around the world. Long COVID associated complications were reported worldwide. COVID associated interstitial lung disease is a well-known, recognized long term consequence.

Methodology: A single centre observational study was carried out in the Respiratory Disease Treatment Unit two at National Hospital Kandy, Sri Lanka. Information regarding Demographic, clinical, biochemical and radio graphical characteristics were extracted from the medical records. An interviewer-administered questionnaire was used. Statistical analysis was performed using IBM SPSS statistics data editor.

Results: A total of 53 (13.6%) COVID-19 related ILD cases were analysed. Out of them, 38 (71.7%) were males. The median age was 59 years. The majority of patients (81.1%) were given a history of at least one underlying comorbid disease, while Diabetes Mellitus was the commonest (58.4%). Out of the male patients, 17 (47.3%) had a positive smoking history of varying pack years. Different pathological patterns, geographical and zonal distributions, occasionally asymmetrical patterns were observed in HRCT of patients with COVID-19 related ILD.

Conclusion: The majority of the COVID-19 related ILD patients were males with multiple comorbidities and had a positive smoking history. The progression of the disease is well displayed in the findings of HRCT. Detection of these findings should alert the clinicians to provide prompt and optimized care in order to minimize the morbidity and mortality of COVID-19 related ILD.

Key words: COVID-19, interstitial lung disease, Sri Lanka

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS –CoV- 2) or Novel Coronavirus is the causative organism for the coronavirus disease 2019 (COVID-19) pandemic which was first identified in Wuhan, China, in 2019.[1] As of March 2022, COVID-19 has caused over 433 million infections and over 5.9 million deaths around the world. [2] By March 1st, 2022, more than 0.6 million confirmed cases and 16244 deaths were announced by the Health Ministry of Sri Lanka.[3]

Correspondence:
Dr. Dushantha Madegedara
Respiratory Research Unit,
National Hospital, Kandy, Sri Lanka
Tel: +94 812 234220; Fax: +94 812 221270;
E-mail: dmadegedara@yahoo.com
Mobile: +94 812 234220

There is increasing evidence worldwide with long COVID-19 related post-acute and chronic persistent sequelae of multi-organ involvement.[4] The common symptoms encountered in long COVID-19 are fatigue, dyspnoea, cough, anosmia, brain fog and dysgeusia.[5] Moreover, organic system injuries involving pulmonary, cardiovascular,

cutaneous, and neuropsychiatric systems have also been reported.[4,5]

Secondary interstitial lung disease (ILD) is a well-known, recognized COVID associated complication adding further burden to pulmonary health.[6] According to the world health organization, post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually three months from the onset of COVID-19 with symptoms and that last for at least two months and cannot be explained by an alternative diagnosis.[7] ILD has a significant link with the viral pneumonia such as coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 and is characterized by the progressive scaring of the lung tissue, impaired lung function, and impaired gas exchange.[8] As there is a scarcity of publications locally describing the demographical, clinical, and radio graphical characteristics (Appendix 1) of the patients with COVID-19 related ILD, our endeavour was to fill the vacuum of the studies.

Appendix 1	
Radio graphical characteristics	**Definition**
Honey combing	Presence of small cystic spaces lined by bronchiolar epithelium with thickened walls composed of dense fibrous tissue.
Ground glass opacity	Filling of the alveolar spaces with pus, edema, hemorrhage, inflammation or tumor cells. Thickening of the interstitium or alveolar walls below the spatial resolution of the HRCT.
Fibrosis	Term given when there is an excess of fibrotic tissue in the lung. It can occur in a wide range of clinical settings and can be precipitated by a multitude of causes.
Crazy paving	Crazy Paving is a combination of ground glass opacity with superimposed septal thickening.
Mosaic attenuation	Density differences between affected and non-affected lung areas. There are patchy areas of black and white lung.
Linear atelectasis	Focal area of subsegmental atelectasis with a linear shape. It is normally horizontal and sometimes oblique or perpendicular.
Traction bronchiectasis	Irreversible dilation of the bronchi resulting from airway damage due to a variety of causes, including infection, airway obstruction, or fibrosis.
UIP- Usual interstitial pneumonia	Morphologic entity defined by a combination of (1) patchy interstitial fibrosis with alternating areas of normal lung, (2) temporal heterogeneity of fibrosis characterized by scattered fibroblastic foci in the background of dense acellular collagen, and (3) architectural alteration due to chronic scarring or honeycomb change.
NSIP- Nonspecific interstitial pneumonia	Chronic interstitial pneumonia with the homogeneous appearance of interstitial fibrosis and inflammation.
DIP- Desquamative interstitial pneumonia	Accumulation of numerous pigmented macrophages within most of the distal airspace of the lung and, sometimes, the presence of giant cells.

Material and methods

An observational study was carried out in the Respiratory Disease Treatment Unit two at National Hospital Kandy (NHK), Sri Lanka between 6th January 2021 to 12th January 2022. This is a training and research unit which carries out programmes for medical students and post-graduate students with the diploma in tuberculosis and chest diseases (DTCD). This is the second biggest unit in NHK, headed by the consultant respiratory physician.

The inclusion and exclusion criteria are:

Inclusion Criteria: (1) Patients ≥ 18 years (2) Confirmed infection with SARS COVID-2 (3) Confirmed post COVID-ILD within 6-20 weeks (Mean ± SD = 12.1 ±1.1) following the acute infection with SARS COVID -2.

Exclusion Criteria: (1) Patients who are < 18 years (2) Patients with pre-existing ILD (3) Patients with underlying connective tissue disorders and Haematological disorders which can cause ILD (4) Patients with chronic exposure to environmental and occupational agents and medications which are known to cause ILD (5) Patients with incomplete medical records (6) Patients who did not give consent for the study.

SARS COVID-2 cases were defined as a positive result by using real-time reverse-transcriptase polymerase chain reaction (RT-PCR) detection on a nasopharyngeal swab. Demographic, clinical, biochemical and radio graphical data were collected from patients who presented with COVID-19 related ILD, using existing medical records through a questionnaire consisted of necessary retrospective information.

COVID associated ILD was diagnosed in patients who developed persistent or worsening respiratory symptoms and High-Resolution Computer Tomography (HRCT) features favouring ILD pattern at least 6 weeks following the acute COVID infection. Spirometry and Six-minute walk test data were collected from patients who were diagnosed with COVID-19 associated ILD, using existing medical records.

All patients were examined by an expert respiratory team led by respiratory consultants. Imaging such as Chest X-Ray and HRCT chest were jointly interpreted by a consultant respiratory physician and a radiologist. Ethical clearance was obtained from the ethics review committee of NHK. Data analysis was carried out using the IBM SPSS version 25. The data were presented using descriptive statics in the form of frequency, percentage and mean.

RESULTS

A total of 387 COVID-19 confirmed patients were admitted of which, 53 (13.6%) post-COVID ILD patients were diagnosed. Out of them, majority 38 (71.7%) were males. The mean age of the study cohort was 59± 11.21 years ranging from 27 to 80 years. A little more than half of the patients, 27 (50.9%) were in the age group of 41-60 years. **(Table 1)**

Table 1- Age distribution of patients with COVID-19 related ILD (n=53)

Age category	Frequency	Percentage
01-20	1	1.9
21-40	4	7.5
41-60	27	50.9
61-80	21	39.6

Out of the male patients, 17 (47.3%) had a positive smoking history of which 9 (23.6 %) patients were current and eight (21%) were ex-smokers. The majority, 43 (81.1%), of patients had a history of at least one comorbidity. Diabetes Mellitus was the commonest comorbidity which accounts for 31 (58.4%), followed by Hypertension 25 (47.2%), Dyslipidaemia 6 (11.3%) and Bronchial Asthma 3 (5.6%) **(Table 2)**. Two comorbidities (Hypertension and Diabetes Mellitus) were found in 19 (35.8%) of the diseased patients. Three comorbidities (hypertension, diabetes mellitus, asthma) were found in 2 (3.8%) of the patients.

Table 2: Underlying comorbidities of patients with post COVID-19 ILD (n=53)

Underlying Comorbidity	Frequency	Percentage
Diabetes Mellitus	31	58.4
Hypertension	25	47.2
Dyslipidemia	5	11.3
Bronchial asthma	3	5.6
Ischemic heart disease	4	7.9
COPD	2	3.8
Chronic kidney disease	2	3.8

Multiple symptoms were observed in the majority of COVID-19 patients at the time of admission. The most common presenting symptom was shortness of breath, which account for 34 (64.2%) patients. **Table 3** summarizes the commonly observed initial symptoms of the patients diagnosed with COVID-19 related ILD. Furthermore, the post COVID symptoms have observed existentially at the three months follow-up including shortness of breathing 24 (45.2%), cough 17 (32%), fatigue 11 (20.7%), arthralgia/myalgia 5 (9.4%), wheezing 4 (7.5%) and headache 3 (5.6%) (**Figure 1)**.

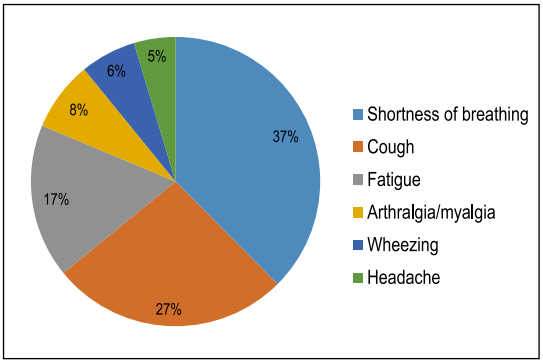


Figure 1: Post COVID symptoms of the patients at the 3 months follow-up (n=53)

Table 3: Presenting symptoms of the patients with post-COVID ILD (n=53)

Symptoms	Frequency	Percentage
Arthralgia/ myalgia	7	13.2
Anosmia	2	3.8
Dry cough	26	49.1
Productive cough	11	20.8
Fever	20	37.7
Headache	6	11.3
Loss of appetite	9	17
Sore throat	3	5.7
Shortness of breathing	34	64.2
Wheezing	5	9.4

During the first 15-30 days after recovery, abnormalities were observed on chest X-ray including bilateral patchy shadows 31 (60.3%), ground glass opacity 24 (45.2%), local patchy shadows 21 (39.6%), bilateral honeycombing 5 (9.4%), bilateral haziness 3 (5.6%), and secondary organizing pneumonia due to COVID-19 1 (1.8%).

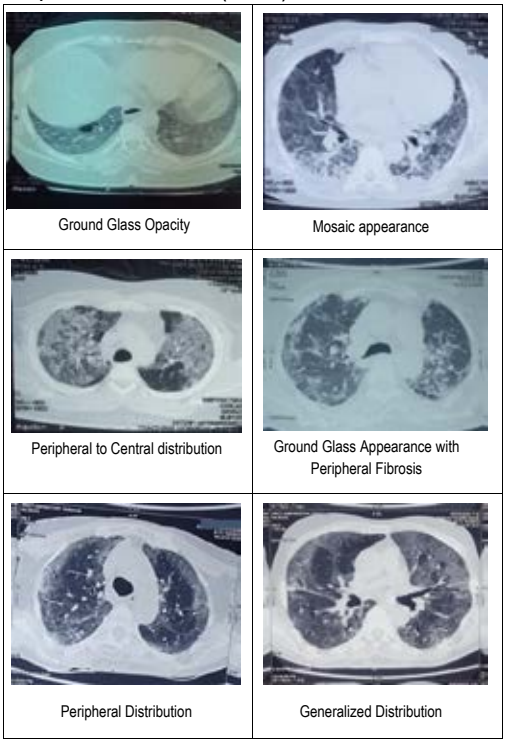
Table 4 illustrates the HRCT findings of the patients diagnosed with post-COVID ILD

Table 4- HRCT findings of the patients diagnosed with COVID-19 related ILD (n=53)

Variables		Frequency	Percentage
Distribution of Interstitial abnormalities	Asymmetrical	3	5.6
	Symmetrical	50	94.3
Geographical distribution	Patchy	2	3.7
	Generalized	49	92.4
	Peripheral	51	96.2
	Central	10	18.8
	Posterior	47	88.6
	Lower lobe	14	26.4
Zonal distribution	Apico basal involvement	42	79.2
	Lower to mid	11	20.7
	Upper to mid	4	7.5
Pathological Appearance	Ground glass opacity	50	94.3
	Fibrosis	52	98.1
	Honey combing	3	5.6
	Linear fibrosis	17	32.0
	Linear atelectasis	4	7.5
	Mosaic attenuation	7	13.2
	Crazy paving	9	16.9
	Traction bronchiectasis	22	41.5
Standard Pattern	UIP- Definite Problem	1	1.8
	NSIP- Definite Problem	13	24.5
	Organizing pneumonia	1	1.8
	Mixed	36	67.9
	DIP- Definite Problem	2	3.7

Definition of abbreviations- UIP: Usual Interstitial Pneumonia, **NSIP:** Nonspecific Interstitial Pneumonia, **DIP:** Desquamative Interstitial Pneumonia

Table 5- HRCT images of the patients diagnosed with post-COVID ILD (n=14)



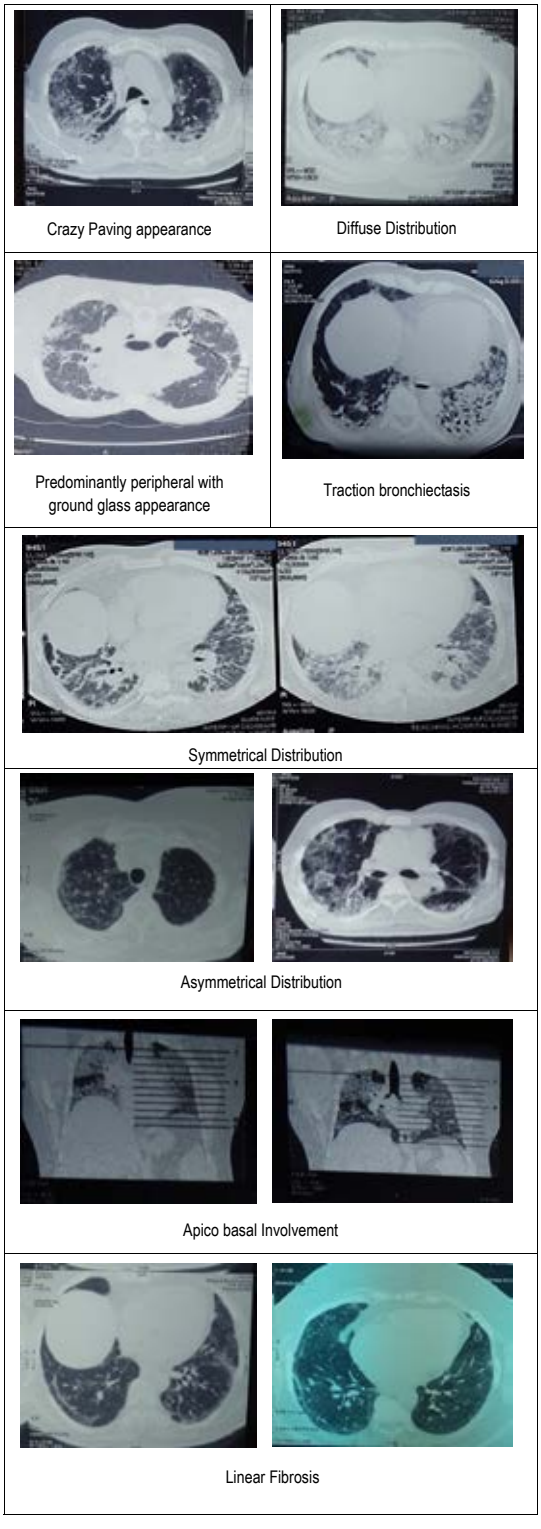


Table 6 illustrates the spirometry values at the initial diagnosis of post COVID-ILD. Three patients were unable to perform spirometry due to the worsening of breathlessness and fatigue.

Table 6: Spirometry values of the patients with COVID-19 related ILD (n=50)	
Descriptive statistics	Mean ± (SD) (N=50)
FVC (Pred)	1.74 ± 0.86
FEV1 (Pred)	1.49 ± 0.65
FEV1/FVC (%)	88.28 ± 17.9

Definition of abbreviations-FVC: Forced Cital Capacity, **FEV1:** Forced Expiratory Volume

Six-minute walk test results

At the diagnosis of the COVID-19 related ILD, the basic six-minute walk test was performed with the supplemental oxygen by measuring pre and post oxygen saturation, pulse rate and blood pressure changes. However, complete information was lacking at the time of analysis. The highest percentage difference of desaturation was 6-10%. **(Table 7)** Test was prematurely stopped due to worsening of breathlessness and general fatigue in five patients.

Table 7: Six-minute walk test results of the patients with COVID-19 related ILD (n=48)	
Percentage difference of desaturation	Number of patients
0-2% 2-4% 4-6% 6-10% >10%	3 7 14 23 1
The distance walked	
50-100m 100-150m 150-200m 200-250m 250-300m 300-350m 350-400m 400-450m	3 3 5 7 10 14 4 2

DISCUSSION

This descriptive analysis explored the demographical, clinical, biochemical and radio graphical characteristics of the patients with post-COVID interstitial lung disease in a single tertiary care center in Sri Lanka. It was found

that the COVID-19 patients in the age group of 41-60 years had the highest proportion to be a victim of COVID-19 related ILD. In the present study, the median age value of the diseased was 59 years. Consistent with recent literature, male predominance was observed in our study. Compared to nonsmokers, smokers were 1.4 times more likely to have severe COVID-19 symptoms, 2.4 times more likely to require ICU admission, mechanical ventilation, and to die [9]. Smoking is a contributing factor to the progression of COVID-19 related ILD.[9] Based on our data, 47.3% of the male patients had a positive smoking history.

In this study, more than three fourth (81.1%) of the diseased patients had at least one underlying comorbidity. This is consistent with the published literature.[6,10] The present study found that Diabetes Mellitus was the commonest comorbidity followed by Hypertension and Bronchial Asthma. However, other studies reported Hypertension as the commonest comorbidity.[11] González et al. (2021) conducted to investigate the incidence of restrictive lung disease and ILD in patients with pre-diabetes and type 2 DM reported increased risk for dyspnoea and ILD in patients with type 2 DM (Diabetes Mellitus).[12] When comparing patients with long-term type 2 diabetes to patients with pre-diabetes and non-diabetics on the mMRC (Modified medical research council) dyspnoea scale, patients with long-term type 2 diabetes had increased breathlessness.[12,13] These findings highlight the necessity of immediate screening for comorbidities. However, further studies need to be conducted with large cohorts to explore the association between Diabetes mellitus and increased risk for post-COVID ILD. At the diagnosis of COVID-19 related ILD, diseased patients had abnormal biochemical and haematological investigations, in particular Lymphocyte count, CRP, and serum creatinine. However, at the follow-up, biochemical markers indicated an improvement in systemic inflammation which is parallel with the reported literature .[6]

In our study, presenting symptoms of the patients who were diagnosed with COVID-19 related ILD are arthralgia/ myalgia, anosmia, dry cough, productive cough, fever, headache, loss of appetite, sore throat, shortness of breathing, and wheezing. These symptoms were presented within 15-30 days after the recovery of acute COVID infection. During the follow-up visits, the majority of the patients were presented with post COVID symptoms including shortness of breath, cough, fatigue, arthralgia/ myalgia, wheezing, and headache. Similar to our findings, Jessica González and colleagues found dyspnoea, muscular fatigue and wet and dry cough as the symptoms at the 3 months follow-up of their cohort.[12]

HRCT is an effective method to detect the progression of viral pneumonia and to classify the severity of the disease.[14] We have observed different pathological patterns, geographical and zonal distributions, occasionally asymmetrical patterns in HRCT of patients with COVID-19 related ILD. In our patients, the majority had a symmetrical distribution in HRCT which tallies with normal ILD entity. However, three patients had asymmetrical distribution. More than 80% of the patients were reported with generalized, peripheral and posterior geographical distributions. The majority of the cases had multiple zonal involvements, where the highest was noted as apicobasal distribution. Furthermore, lower to mid and upper to mid distributions were reported. Fibrosis was the most common pathological appearance followed by Ground Glass Opacity, Traction bronchiectasis, Linear fibrosis, Crazy paving, Mosaic, and Linear atelectasis. Similar to our findings, other studies also reported HRCT abnormalities including ground-glass opacities, consolidations, crazy-paving pattern, and linear opacities, primarily affecting peripheral areas[15,16] lower lobes and displaying a multilobar distribution[5,6]. More than half of the patients were reported with a mixed standard pattern. Moreover, definite cases of NSIP, DIP, UIP and organizing pneumonia were observed respectively.

In the present study, the main X-Ray findings of the initial phase of post-COVID-ILD were bilateral patchy shadows, ground-glass opacity, and local patchy shadows. However, chest X-rays could be used as an alternative radiological investigation method in patients with COVID-19.[17] At the 6-minute walk test, most of the patients had a 6-10% difference of desaturation with the highest distance walked being 300-350m. This is consistent with previous studies. [6,13]

CONCLUSION

This study reveals that males with multiple comorbidities and smoking history are at a higher

risk of being a victim of COVID-19 related ILD. These findings should alert the clinicians to provide prompt and optimized care in order to minimize the long-term complications of post-COVID ILD. The main limitation of this study was the small sample size. Hence, we recommend multicentre studies with a large cohort. This study reveals that males with multiple comorbidities and smoking history are at a higher risk of being a victim of COVID-19 related ILD. These findings should alert the clinicians to provide prompt and optimized care in order to minimize the long-term complications of post-COVID ILD. The main limitation of this study was the small sample size. Hence, we recommend multicentre studies with a large cohort.

CONFLICT OF INTEREST

None

REFERENCES

1 Huang, Chaolin, et al. "Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China." Lancet (London, England), vol. 395, no. 10223, Lancet, Feb. 2020, pp. 497–506, doi:10.1016/S0140-6736(20)30183-

2. Weekly Epidemiological Update on COVID-19 – 01 March 2022. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---25-january-2022. Accessed 03 March 2022.

3. Epidemiology unit, Ministry of Health, Sri Lanka http://www.epid.gov.lk/web/index.php?option=com_content&view=article&id=225&Itemid=518&lang=en

4. Aronson, Kerri I., and Anna J. Podolanczuk. "Lungs after COVID-19: Evolving Knowledge of Post–COVID-19 Interstitial Lung Disease." Annals of the American Thoracic Society, vol. 18, no. 5, 2021, pp. 773–74, doi:10.1513/AnnalsATS.202102-223ED.

5. Davis, Hannah E., et al. "Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact." EClinicalMedicine, vol. 38, Elsevier Ltd, Aug. 2021, p. 101019, doi:10.1016/J.ECLINM.2021.101019/ATTACHMENT/499C606A-AE36-49F5-87DD-09E3B87369C9/MMC1.DOCX.

6. Myall, Katherine Jane, et al. "Persistent Post–COVID-19 Interstitial Lung Disease: An Observational Study of Corticosteroid Treatment." Annals of the American Thoracic Society, vol. 18, no. 5, 2021, pp. 799–806, doi:10.1513/AnnalsATS.202008-1002OC.

7. Post COVID-19 Condition (Long COVID). https://www.who.int/srilanka/news/detail/16-10-2021-post-covid-19-condition. Accessed 25 June 2022.

8. Myall, Katherine Jane, et al. "Persistent Post-COVID-19 Interstitial Lung Disease. An Observational Study of Corticosteroid Treatment." Annals of the American Thoracic Society, vol. 18, no. 5, Ann Am Thorac Soc, May 2021, pp. 799–806, doi:10.1513/ANNALSATS.202008-1002OC.

9. Ojo, Ademola S., et al. "Pulmonary Fibrosis in COVID-19 Survivors: Predictive Factors and Risk Reduction Strategies." Pulmonary Medicine, vol. 2020, Pulm Med, 2020, doi:10.1155/2020/6175964.

10. Davis, Hannah E., et al. "Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact." EClinicalMedicine, vol. 38, Elsevier Ltd, Aug. 2021, p. 101019, doi:10.1016/J.ECLINM.2021.101019/ATTACHMENT/499C606A-AE36-49F5-87DD-09E3B87369C9/MMC1.DOCX.

11. Arnold, David T., et al. "Patient Outcomes after Hospitalisation with COVID-19 and Implications for Follow-up: Results from a Prospective UK Cohort." Thorax, vol. 76, no. 4, 2021, pp. 399–401, doi:10.1136/thoraxjnl-2020-216086.

12. González, Jessica, et al. "Pulmonary Function and Radiologic Features in Survivors of Critical COVID-19: A 3-Month Prospective Cohort." Chest, vol. 160, no. 1, Elsevier Inc, 2021, pp. 187–98, doi:10.1016/j.chest.2021.02.062.

13. Kopf, Stefan, et al. "Breathlessness and Restrictive Lung Disease: An Important Diabetes-Related Feature in Patients with Type 2 Diabetes." Respiration, vol. 96, no. 1, 2018, pp. 29–40, doi:10.1159/000488909.

14. Rubin, Geoffrey D., et al. "The Role of Chest Imaging in Patient Management During the COVID-19 Pandemic: A Multinational Consensus Statement From the Fleischner Society." Chest, vol. 158, no. 1, Chest, July 2020, pp. 106–16, doi:10.1016/J.CHEST.2020.04.003.

15. Bernheim, Adam, et al. "Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection." Radiology, vol. 295, no. 3, Radiology, June 2020, pp. 685–91, doi:10.1148/RADIOL.2020200463.

16. Hu, Qiongjie, et al. “Early CT Features and Temporal Lung Changes in COVID-19 Pneumonia in Wuhan, China.” European Journal of Radiology, vol. 128, Eur J Radiol, July 2020, doi:10.1016/J.EJRAD.2020.109017.

17. Li, Bingjie, et al. “Diagnostic Value and Key Features of Computed Tomography in Coronavirus Disease 2019.” Emerging Microbes & Infections, vol. 9, no. 1, Taylor & Francis, Jan. 2020, p. 787, doi:10.1080/22221751.2020.1750307.

Original article

COMPARISON OF GENEXPERT MTB/RIF ASSAY AND AFB SMEAR MICROSCOPY IN DIAGNOSIS OF PULMONARY TUBERCULOSIS AMONG HIV PATIENTS AT A TERTIARY CARE HOSPITAL

Bajracharya Najma [1]; Paudyal Rabin [1]; Bastola Anup [2]

[1]Kathmandu College of Science and Technology, T.U. (affiliated), Kamalpokhari, Kathmandu, Nepal
[2]Sukraraj Tropical and Infectious Disease Hospital, Kathmandu, Nepal

DOI: https://doi.org/10.3126/saarctb.v20i1.52665
Received: 31st May Accepted: 3rd July Published: 31st August
This article is available at:

ABSTRACT

Introduction: Tuberculosis (TB) has been the most common acute opportunistic infection in HIV-positive patients and accounts for more than half of all AIDS cases in underdeveloped nations. Hence, rapid laboratory diagnosis of M. tuberculosis is needed for vulnerable patients.

Methodology: In this study, 72 sputum samples were collected from ART-naive and patients using ART for 6 months. The samples were tested with the GeneXpert MTB / RIF assay to diagnose TB and drug resistance and AFB smear microscopy as per NTP guidelines.

Results: Among 72 sputum samples studied, males were more diagnosed with TB than females. People aged 25-56 years were more infected with HIV-TB co-infection. Four patients (5.56%) were found to be TB positive with both techniques, 7 (9.72%) were GeneXpert MTB/RIF positive but smear-negative and 61 patients (84.72%) were negative with both methods. The positivity for MTB detected for GeneXpert MTB/RIF method in females was 3 (15%) and the males were 8 (15.38%), while for the ZN staining method the positivity in females was 2 (10%) and the males were 2 (3.85%). The GeneXpert MTB/RIF assay was also capable of detecting TB in smear-negative cases.

Conclusion: This study showed that the GeneXpert MTB/RIF assay is an an effective tool for the early diagnosis of TB among HIV patients as compared to AFB smear staining method.

Keywords: Mycobacterium tuberculosis, Ziehl-Neelsen Acid Fast Bacilli staining (ZN-AFB), Human Immunodeficiency Virus (HIV), GeneXpert MTB/RIF.

INTRODUCTION

Tuberculosis (TB) is considered a highly significant infectious disease through the course of human history which can affect nearly any organ in the body but mostly affects the lung.[1] Tuberculosis is transmitted to people via minute droplets released through coughing or sneezing. The illness is typically chronic, and its main signs include persistent cough with or without expectoration, intermittent fever, loss of appetite, weight loss, chest pain, and hemoptysis.[2] Hence, it results in high global morbidity and mortality.[3]

Furthermore, according to 2017 WHO Global Tuberculosis report, 490,000 MDR cases were reported, with less than 50% survival in patients who received WHO-recommended treatment regimens possessing a serious threat to its management. While drug resistance (DR) continues to be a serious crisis and threatens health safety, TB / HIV coinfection is another major tuberculosis problem in Nepal.[4] The TB-HIV co-infection rate is 2.4% in Nepal.[5] According to the Global TB Report 2021, the TB mortality rate was 214000 among HIV-

Correspondence:
Ms.Najma Bajracharya
Kathmandu College of Science and Technology,
Tribhuvan University (affiliated), Kamalpokhari,
Kathmandu, Nepal
Email: bajracharya.naz@gmail.com

positive people globally. As a result, those with HIV have a 19-fold increased risk of developing active TB making it a deadly combination; accelerating each other's progression.[4]

For many decades, conventional methods such as smear microscopy and culture techniques were used to diagnose TB.[6] Culture is the gold standard and the most sensitive method for diagnosis of TB but has a limitation of a long turnaround time of 2-8 weeks as well as the complexity of the procedure demands highly skilled staff along with a biosafety level III lab.[7] Further, plenty of time is consumed to produce drug resistance patterns. As a result, its applicability as a diagnostic test gets limited.[8] Comparatively smear microscopy for acid-fast bacilli (AFB) is rapid and inexpensive but it has poor sensitivity. Bacilli concentrations as high as 5000-10,000 per ml of the specimen are normally required for the smear to be positive.[7]

Hence, WHO recommended the use of the rapid test GeneXpert MTB/RIF in 2010 that was implemented in Nepal in 2011/12. The GeneXpert MTB / RIF Assay is a unique hands-free integrated cartridge with incorporated chemicals and reagents for sample processing and hemi-nested real-time PCR analysis in a sequential manner for tuberculosis diagnosis and quick RIF resistance detection in clinical samples on GeneXpert platform.[9] This diagnostic has advantages of high sensitivity (79%) specificity (99%)[10], as well as determining rifampicin resistance as an indicator for MDR TB and providing the result in two hours. It is simple to conduct and is safe as it produces no cultivable aerosols. As a result, WHO has taken Gene Xpert MTB/RIF as one of the essential tests for all patients registering HIV care.[11]

There have been many types of research around the world to evaluate the effectiveness of the Xpert assay for tubercle bacillus culture, acid-fast bacillus staining and fluorescence microscopy, among TB suspected patients and the results show that the Xpert assay is an innovative invention.[12] But to the best of my knowledge, the study regarding the gene Xpert assay for prompt diagnosis, especially in ART-naive HIV patients is not conducted till now in Nepal. This study aims to provide valuable data regarding the application of gene Xpert assay for prompt diagnosis, especially in vulnerable populations such as HIV-infected patients. This study is carried out to compare AFB staining and GeneXpert MTB/RIF to consider whether Xpert service can be one of the baseline examinations for HIV-infected patients in TB-abundant countries like Nepal.

METHODOLOGY

This study was conducted at Sukraraj Tropical and Infectious Disease Hospital (STIDH), Teku, Kathmandu, Nepal from December 2019 to July 2020. This study compares the Genexpert MTB/RIF assay to AFB staining in the sputum samples of ART-naive HIV patients and patients using ART for 6 months. The samples were collected following stop TB guidelines.[13] A total of 72 sputum specimens were collected from clinically TB suspected HIV patients with their consent. While the sample containing only saliva and scanty sample were excluded for processing. Also, the occurrence of sample error during GeneXpert MTB/Rif assay analysis were excluded. Using the Ziehl-Neelsen technique, direct smear microscopy was used to detect the presence of AFB in sample II. Then, WHO criteria were used to report the AFB reports. Similarly, the GeneXpert MTB RIF assay was performed as per standard protocol provided by the manufacturer (Cepheid Inc., Sunnyvale, USA). The GeneXpert DX System interpreted the results from measured fluorescent signals and embedded calculation algorithms, which were displayed in the GeneXpert machine's "View Results" window.

Ethical Approval was taken from Nepal Health Research Council Reference number 110/2020 MT along with informed consent from all the suspected pulmonary tuberculosis HIV patients involved in this study by counseling and making them understand the study regarding the confidentiality and implication of the result.

All data were entered, structured and analyzed using SPSS 26.0 version software. Chi-Square test was employed to determine the associations between ZN AFB smear microscopy and GeneXpert MTB/RIF assay at a 95% confidence interval (95% CI).

RESULTS

Among 72 TB suspected HIV patients, 72.2% were males and 27.8% were females. More than half (69.4%) were in the age group of 15-45 years **(Table 1)**.

Table 1: Gender and age-wise distribution of patients (n=72)

Age group (in years)	No.	Male %	No.	Female %	No.	Total %
<15	2	3.9	-	-	2	2.8
15-45	37	71.2	13	65.0	50	69.4
>45	13	25.0	7	35.0	20	27.8
Total	52		20		72	100

Among 72 samples, 11 samples were found to be positive by GeneXpert assay whereas the remaining 61 samples were negative. Out of the 11 GeneXpert MTB/RIF assay positive samples, only 5.6% samples were AFB positive **(Table 2)**.

Table 2: Distribution of samples based on AFB staining and GeneXpert MTB/RIF assay results (n=72)

AFB smear	No.	%	GeneXpert assay	No.	%
1+	1	1.4	VL	3	4.2
2+	2	2.8	L	3	4.2
3+	1	1.4	M	4	5.7
N	68	95.8	H	1	1.4
			N	61	84.72
Total sample	72	100		72	100

Note: VL: Very low, L: Low, M: Medium, H: High and N: Negative

GeneXpert MTB/RIF assay gave positive result in seven AFB negative samples. Out of which 3 showed very low load, 2 showed low load and the next two showed a medium load of tuberculosis bacilli respectively. In this data, a statistically significant relationship was found between AFB smear results and gene Xpert test results **(Table 3)**.

Table 3: Comparative table showing M.tuberculosis load in AFB smear-positive and negative samples comparative to GeneXpert MTB/RIF assay (n=72)

AFB smear result	Gene-Xpert test results					Total (n)	p-value
	VL	L	M	H	N		
1+	-	-	1	-	-	1	0.001
2+	-	1	1	-	-	2	
3+	-	-	-	1	-	1	
Negative	3	2	2	-	61	68	
Total	3	3	4	1	61	72	

Note: VL: Very low, L: Low, M: Medium, H: High and N: Negative

In GeneXpert MTB/RIF assay, 7 samples were found positive in ART-naive whereas in patients using ART for 6 months 4 samples were positive. Similarly, 2 samples were found positive in both patients. In this data, a statistically insignificant relationship was found between ART-naive and patients using ART for 6 months as shown in **(Table 4**).

Table 4: Distribution of tuberculosis in ART-naive and patients using ART for 6 months as shown by GeneXpert MTB/RIF assay (n=72)

Types of HIV patients	Total no. of Samples (n %)	AFB smear Positive (n %)	GeneXpert MTB/RIF assay positive (n %)	p-value
ART naïve	27 (37.5%)	2 (2.7%)	7 (9.7%)	
Patients using ART for 6 months	45 (62.5%)	2 (2.7%)	4 (5.5%)	0.905
Total	72 (100%)	4 (5.5%)	11 (15.3%)	

Out of the 11 samples shown positive by GeneXpert MTB/RIF assay, 10 samples were found to be sensitive to rifampicin whereas 1 sample was found to be indeterminate. No samples were found to be resistant to rifampicin **(Table 5)**.

Table 5: Gene Xpert MTB/RIF assay rifampicin sensitivity results (n=72)

Rifampicin sensitivity	Gender		Total (n)
	Male (n%)	Female (n%)	
Sensitive	7 (70%)	3 (30%)	10
Resistance	-	-	-
Indeterminate	1 (100%)	-	1
Total	8	3	11

DISCUSSION

TB poses a concern to HIV-positive individuals both before and after starting antiretroviral medication, is difficult to diagnose, is rapidly lethal when drug-resistant, and is spreading in clinics and hospitals.[14] Thus, early diagnosis of TB is necessary to disrupt the disease transmission chain. In this study, among seventy-two samples from HIV patients suspected of pulmonary tuberculosis, smear

positivity was found to be 4 (5.6%) and GeneXpert positivity for MTB on the same samples remained 11 (15.3%) respectively which is similar to a study, that showed 67.5% smear positivity and 77.4% of GeneXpert.[15] However, a study conducted in Benin city[16] among HIV patients showed 41.6% positive cases by ZN microscopy and 62.1% positive cases by GeneXpert MTB/RIF. This is because sputum smear microscopy has a particularly low sensitivity for detecting TB among people living with HIV (PLHIV).[17] Diagnosis of TB among HIV patients are particularly challenging also because people hesitate to visit health facilities that delay not only their ART initiation but also screening for TB. Hence, people in later stages of HIV infection and with a weakened immune system often release fewer organisms into their sputum, at concentrations below the threshold for visual detection under a microscope.[17] However, the variation in this study and previous studies may be explained by differences in the physiological and thus medical conditions of the samples.

A predominance of co-infected people was observed in the economically active age range of 15-45 years. However, 4 (36.4%) out of 11 samples in the age group 25-45 were diagnosed MTB positive by both the ZN staining method and gene Xpert MTB/RIF assay. Likewise, a study was done in a South Asian general hospital in Nepal[18] that showed ages ranging from 33-68 years for MTB-positive cases. Correspondingly, the mean age of HIV-associated tuberculosis samples was 38.0 years.[8] This could be attributed to the weakening of the immune system due to HIV which quickly progress latent TB infection to TB disease. Even in the absence of HIV, this is the age group in the general population where reactivation of latent TB takes place.[16] In this study, of the total samples, 27 samples were from ART-naive patients whereas the remaining 45 samples were from patients using ART for up to 6 months. Two samples from ART-naive patients and another two samples from patients using ART for up to 6 months were found to be AFB positive. Similarly, in GeneXpert MTB/RIF assay, seven samples from ART-naive patients and four samples from patients using ART for up to 6 months were found to be positive. Statistically, an insignificant finding was observed between ART-naive and patients using ART for up to 6 months. The data indicate that there was no difference in diagnosis of TB despite of intiation of ART for up to 6 months.

In this study, the highest sensitivity for rifampicin was seen in male samples 7(70%) as compared to female samples 3(30%) but no samples were found to be resistant to rifampicin. The gene Xpert MTB/RIF assay is considered a good rapid testing technology for the detection of MDR-TB, and it detects mutations in the rpoB gene which occur in 95-99% of the RIF resistant isolates.[8] However, in subjects with no previous tuberculosis treatment, resistance was usually less frequent[19]; in a study carried out by Magar et al., 2019 (7), 66.67% and 28.85% were RIF-sensitive male and female cases respectively whereas 1.28% case was found to be RIF resistance which is higher compare to this study. Likewise, a wide range of resistance for MTB positivity by GeneXpert has been reported in earlier studies by Khunjeli et al.,[20], 3.2%, Bajrami et al.,[6], 11.7% and Atashi et al.,[21] , 3.1%. Further, in this study, 1 sample was found to be indeterminate. The basis for rifampicin indeterminate is when the first probe CT is >34.5 and the last probe CT is >38 cycles.[22] Though conventional culture-based drug sensitivity testing is considered a gold standard investigation to detect MDR, the sensitivity and specificity of GeneXpert MTB/RIF assay are comparable with conventional methods.[23]

Because every previous study and meta-analysis has consistently shown a 99 percent specificity, culture for mycobacteria was not performed due to the non-availability of the test. In areas of high TB prevalence such as Nepal, the majority of suspected TB cases are assessed by sputum smear microscopy and, where available, by tuberculin test, ESR, ADA, and CXR. Patients are frequently assigned to pragmatic practical treatment practices based on symptomatic analysis or abnormal CXR alone.[7,18] In these perspectives, GeneXpert excludes “false cases” from “true” smear-negative TB cases with cost-effectiveness reducing the burden out of the pocket of patients for their TB diagnosis and treatment.[7,18,24] In addition, Nepal Government has made GeneXpert test free of cost for the patients.

That being the case, this study backs up the notion that the gene Xpert MTB/RIF test is superior to conventional AFB smear microscopy for rapid identification of Mycobacterium tuberculosis in an HIV and tuberculosis-in endemic zone. Due to higher sensitivity, gene Xpert assay provides both TB and rifampicin resistance results which will greatly improve the early diagnosis of HIV-

associated TB compared to microscopy.[25] Hence, the gene Xpert assay is recommended in the diagnosis of TB among HIV-positive patients of every age.[11] Nevertheless, GeneXpert does not take the place of traditional microscopy, culture and anti-tubercular drug sensitivity which are necessary to track the effectiveness of treatment.

CONCLUSION

From this study, it can be concluded that GeneXpert MTB/RIF assay was effective in detecting Mycobacterium tuberculosis compared to AFB smear microscopy. Therefore, the implementation of gene Xpert as a baseline analysis can be very effective in detecting pulmonary tuberculosis in vulnerable groups such as HIV patients. Furthermore, it is a suitable technique to detect rifampicin resistance leading to early treatment of patients.

ACKNOWLEDGEMENT

The authors like to acknowledge all the staff of Sukraraj Tropical and Infectious Disease Hospital, Teku, Kathmandu, Nepal and all the faculties of the Department of Microbiology, Kathmandu College of Science and Technology.

CONFLICT OF INTEREST

None

REFERENCES

1. Azadi D, Motallebirad T, Ghaffari K, Shojaei H. Mycobacteriosis and Tuberculosis: Laboratory Diagnosis. Open Microbiol J. 2018 Mar 30;12:41–58.

2. Mahmood T, Dwivedi P, Shukla AD, Jain AK, Verma AK. An Observational Study of Follow Up of MDR Tuberculosis Patients after Successful Completion of Category 4 Treatment under RNTCP (PMDT) in Allahabad District. SAARC J Tuberc Lung Dis HIVAIDS. 2019 Jul 26;17(1):1–7.

3. Dhamnetiya D, Patel P, Jha RP, Shri N, Singh M, Bhattacharyya K. Trends in incidence and mortality of tuberculosis in India over past three decades: a joinpoint and age–period–cohort analysis. BMC Pulm Med. 2021 Nov 16;21(1):375.

4. Tuberculosis. Tuberculosis (TB) [Internet]. 2020 [cited 2020 Sep 27]. Available from: https://www.who.int/news-room/fact-sheets/detail/tuberculosis

5. Banstola A. Issues and threats of Tuberculosis in Nepal | Connecting our members with evidence and expertise [Internet]. 2012 [cited 2020 Sep 27]. Available from: https://www.ghdonline.org/ic/discussion/issues-and-threats-of-tuberculosis-in-nepal/

6. Bajrami, Mulliqi G, Kurti, Lila G, Iul. Assessment of diagnostic accuracy of GeneXpert Mycobacterium tuberculosis/rifampicin in diagnosis of pulmonary tuberculosis in Kosovo [Internet]. 2018 [cited 2020 Sep 27]. Available from: http://www.bmbtrj.org/article.asp?issn=2588-9834;year=2018;volume=2;issue=3;spage=191;epage=195;aulast=Bajrami

7. Magar ST, Ghimire G, Shah PK. Comparison of Led Fluorescent Microscopy and the Gene Xpert MTB/RIF Assay in Diagnosis of Pulmonary and Extrapulmonary Tuberculosis. Tribhuvan Univ J Microbiol. 2019 Dec 7;6:127–32.

8. Saeed M, Hussain S, Riaz S, Rasheed F, Ahmad M, Iram S, et al. GeneXpert Technology for the diagnosis of HIV-associated tuberculosis: Is scale-up worth it? Open Life Sci. 2020 Jun 30;15(1):458–65.

9. Zeka AN, Tasbakan S, Cavusoglu C. Evaluation of the GeneXpert MTB/RIF Assay for Rapid Diagnosis of Tuberculosis and Detection of Rifampin Resistance in Pulmonary and Extrapulmonary Specimens. J Clin Microbiol. 2011 Dec;49(12):4138–41.

10. Shrestha S, Shah N, Jha K, Pant R, Joshi L, Karki K. Challenges in the Diagnosis of Drug - Resistant Tuberculosis by Gene -Xpert MTB/RIF in Nepal. 2018;

11. HIV/AIDS Data Hub for the Asia Pacific [Internet]. HIV/AIDS Data Hub for the Asia Pacific. [cited 2022 Jun 19]. Available from: https://www.aidsdatahub.org

12. Shrestha P, Khanal H, Dahal P, Dongol P. Programmatic Impact of Implementing GeneXpert MTB/ RIF Assay for the Detection of in Respiratory Specimens from Pulmonary Tuberculosis Suspected Patients in Resource Limited Laboratory Settings of Eastern Nepal. Open Microbiol J [Internet]. 2018 Feb 28 [cited 2020 Nov 26];12(1). Available from: https://openmicrobiologyjournal.com/VOLUME/12/PAGE/9/FULLTEXT/

13. Guidelines for Submission of Sputum Specimens for Tuberculosis Testing. :7.

14. Chamie G, Luetkemeyer A, Charlebois E, Havlir DV. Tuberculosis as Part of the Natural History of HIV Infection in Developing Countries. Clin Infect Dis. 2010 May 15;50(Supplement_3):S245–54.

15. Kashif Munir M, Rehman S, Aasim M, Iqbal R, Saeed M. Comparison of Ziehl Neelsen Microscopy with GeneXpert for Detection of MycobacteriumTuberculosis. IOSR J Dent Med Sci. 2015 Dec 1;14:56–60.

16. Chinedum OK, Emwiomwan A, Ifeanyi OE. Comparative Analysis of Ziehl-Neelsen and Genexpert Techniques for the Diagnosis of Tuberculosis in Human Immuno-Deficiency Virus Positive Patients in Benin City. Ann Clin Lab Res. 2017;6.

17. WHO TB/HIV. TBHIV_Information_Note_final [Internet]. 2014 [cited 2021 Jun 16]. Available from: www.who.int › tb › tbhivresearchpriorities

18. Shrestha P, Arjyal A, Caws M, Prajapati KG, Karkey A, Dongol S, et al. The Application of GeneXpert MTB/RIF for Smear-Negative TB Diagnosis as a Fee-Paying Service at a South Asian General Hospital [Internet]. Vol. 2015, Tuberculosis Research and Treatment. Hindawi; 2015 [cited 2020 Dec 1]. p. e102430. Available from: https://www.hindawi.com/journals/trt/2015/102430/

19. Floridia M, Ciccacci F, Andreotti M, Hassane A, Sidumo Z, Magid NA, et al. Tuberculosis Case Finding With Combined Rapid Point-of-Care Assays (Xpert MTB/RIF and Determine TB LAM) in HIV-Positive Individuals Starting Antiretroviral Therapy in Mozambique. Clin Infect Dis. 2017 Nov 13;65(11):1878–83.

20. Khunjeli R, Mohsin U, Shrestha S, Adhikari S, Srivastava B, Shrestha B. Prevalence of Primary Drug Resistant Tuberculosis in a Tertiary Care Hospital, Nepal. J Chitwan Med Coll. 2015 Jan 28;4.

21. Atashi S, Izadi B, Jalilian S, Madani SH, Farahani A, Mohajeri P. Evaluation of GeneXpert MTB/RIF for determination of rifampicin resistance among new tuberculosis cases in west and northwest Iran. New Microbes New Infect. 2017 Sep 1;19:117–20.

22. Thapa A, Gurung P, Ghimire GR. Evaluation of Gene Xpert Mtb/Rif Assay for the Detection of Mycobacterium Tuberculosis in Sputum of Patients Suspected of Pulmonary Tuberculosis Visiting National Tuberculosis Centre, Thimi, Bhaktapur, Nepal. SAARC J Tuberc Lung Dis HIVAIDS. 2016;13(1):16–22.

23. Patil S, Microbiology, Nakate P, Microbiology, Patil S, Microbiology, et al. Comparison of diagnostic efficacy of GeneXpert MTB/RIF assay with Ziehl Neelsen staining & microscopy in diagnosis of pulmonary tuberculosis. IP Int J Med Microbiol Trop Dis. 2020 Jan 28;5(4):218–21.

24. Steingart KR, Ng V, Henry M, Hopewell PC, Ramsay A, Cunningham J, et al. Sputum processing methods to improve the sensitivity of smear microscopy for tuberculosis: a systematic review. Lancet Infect Dis. 2006 Oct;6(10):664–74.

25. Akanbi MO, Achenbach C, Taiwo B, Idoko J, Ani A, Isa Y, et al. Evaluation of gene xpert for routine diagnosis of HIV-associated tuberculosis in Nigeria: A prospective cohort study. BMC Pulm Med. 2017 May 30;17(1):87.

Case Report

COVID-19 IN ART NAÏVE HIV POSITIVE ADULT: COURSE OF PRESENTATION AND MANAGEMENT

Bastola Anup[1]; Pyakurel Prajjwal [2]; Shrestha Sanjay[3]; Maharjan Kijan [3]; Neupane Jenish[4]; Rijal Rishikesh[5]; Myneedu Vithal Prasad[6]

[1] Director, SAARC TB and HIV/AIDS Centre, Thimi, Bhaktapur, Nepal
[2] Research Officer, SAARC TB and HIV/AIDS Centre, Thimi, Bhaktapur, Nepal
[3] Consultant Physician, Sukraraj Tropical and Infectious Disease Hospital, Teku, Kathmandu, Nepal
[4] Medical Officer, Sukraraj Tropical and Infectious Disease Hospital, Teku, Kathmandu, Nepal
[5] Medical Officer, Shahid Gangalal National Heart Centre, Bansbari, Kathmandu, Nepal
[6] Sr. Microbiologist, SAARC TB and HIV/AIDS Center, Thimi, Bhaktapur,

DOI: https://doi.org/10.3126/saarctb.v20i1.52667
Received: 2nd May Accepted: 1st July Published: 31st August
This article is available at:

ABSTRACT

During the time of COVID-19 outbreak there is dilemma in diagnosis of acute lung infections. This is further hindered among immunocompromised patients due to bizarre clinical and radiological findings. We report young male severely immunocompromised HIV infected ART naïve patient presenting with acute onset of pneumonia and hypoxemia with SARS CoV-2 PCR positive.

Keywords: COVID-19, SARS-CoV-2, HIV, TB, Respiratory Infections

INTRODUCTION

The corona virus disease 2019 (COVID-19) was declared global pandemic on March 11, 2020 by World Health Organisation (WHO) after being first reported to the WHO China Country Office at the end of 2019 as pneumonia of unknown cause from the city of Wuhan in Hubei province, China.[1] The coinfection of the SARS-CoV-2 with other microorganisms may pose challenges particularly in terms of diagnosis and treatment, potentially affecting patient outcomes.[2] The role of HIV infection in contributing to risk of COVID-19 acquisition and disease severity have been less certain and current evidences does not suggest higher susceptibility to SARS-CoV-2 infection in HIV.[3-5] However people with HIV may have an increased risk for severe COVID-19 related outcomes, predominantly driven by comorbid medical conditions and opportunistic infections which may be more prevalent among people with HIV than in the general population.[6]

Pneumocystis pneumonia (PCP) is a one of the serious opportunistic infections in people living with HIV caused by the fungus *Pneumocystis jirovecii*.[7] The clinical picture of the fungal disease, Pneumocystis pneumonia, shares many overlapping features with the course of coronavirus disease 2019 (COVID-19) and hence possess diagnostic dilemma and presents diagnostic challenge in the COVID-19 pandemic.[8,9] Besides, Tuberculosis (TB) remains a main driver of morbidity and mortality among people with HIV and can accompany COVID-19.[6]

We present a case of 42 years Anti-Retroviral Therapy (ART) naïve male with advanced HIV who came to Sukraraj Tropical and Infectious Disease Hospital (STIDH), Kathmandu, Nepal with clinical and radiological features consistent with both pneumocystis pneumonia (PCP) and

Correspondence:
Dr. Sanjay Shrestha
Consultant Physician
Department of Internal Medicine
Sukraraj Tropical and Infectious Disease Hospital
Teku, Kathmandu, Nepal
Email: shrestha834@gmail.com

coronavirus disease 2019 (COVID19) . In this case report we discuss concern of Pneumocystis jirovecii, Tuberculosis and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coinfection and the difficulty in differentiating between the two diseases, especially in a resource limited setting where PCP is frequently diagnosed using case definitions and clinical experience.

CASE REPORT

A 42-year-old man from Kathmandu, Nepal presented with chief complaint of fever and cough for 8 days, shortness of breath for 7 days and anosmia for 6 days. Fever was mild to start with and was present throughout the day and not associated with chills and rigors. It was relieved on taking medications. Cough was dry in nature, more during night time, not associated with blood in the sputum. Shortness of breath was progressively increasing, more on exertion and relieved on rest. It was associated with bilateral wheeze. One day after the respiratory symptom, patient developed loss of smell. He was then suspected as a case of COVID-19 and tested for SARS-COV-2. RT-PCR showed positive results. Although, he was taking the medicines (Cefixime, Doxycycline, Paracetamol and Ibuprofen) his symptoms didn't improved and was increasing progressively. Later, he came to the emergency department of STIDH with complaint of respiratory distress.

Regarding the past history he was injecting drug user since 15 years of age together with his elder brother with regular practice of needle sharing. He was diagnosed with Human immunodeficiency virus (HIV) infection when one of his injecting drug partner fell ill and tested HIV positive. He didn't get Antiretroviral drugs (ART) in early days as National Program on HIV had limited supplies of ART. Later on, when ART was available, he was done multiple counselling, however he refused to take ART and remained ART naïve for many years.

Around 3 years back he developed painful vesicular lesions in the right side of the chest. Additionally, since few months he was having extensive seborrhoea of scalp and nasolabial folds. However, he didn't had history of weight loss, tuberculosis, opportunistic infections or history of chronic diseases. He was chronic alcoholic and denies smoking. He stays alone and works in an organization as a supervisor for living.

On presentation at emergency department, he had saturation of 67% in room air which improved to 97% on non-rebreathing mask (NRM) at 15 L/min, temperature recorded was 97°F, respiratory rate was 44 breaths/min, pulse rate was 115 beats/min and blood pressure was 100/70 mmHg.

On clinical evaluation patients had respiratory distress with use of accessory respiratory muscles. He was alert, conscious and responds to all the verbal communication. He had oral candidiasis, seborrheic dermatitis **(Figure 1 A)** and scar of past herpes zoster right at T 12 **(Figure 1 B)**. There was no lymphadenopathy. There were no neurological deficit and cardiovascular system looks normal on gross examination.

Figure 1 A: Seborrhei dermatitis

Figure 1B: Scar of past Herpes zoster

The condition of the patient deteriorated and was admitted in the intensive care unit on continuous positive airway pressure (CPAP). He was managed with antibiotics (Imipenem/Cilastin, Cotrimoxazole and Levofloxacin), Steroids, Heparin, Remdesivir and Convalescent plasma along with other

Table 1: Baseline Laboratory finding on admission to STIDH		
Lab findings	Findings	Reference
Complete Blood Count		
Total Leukocyte Count	9800/cumm	4,000-11,000/cumm
Neutrophils	84%	40%-75%
Lymphocytes	13%	20-45%
Platelets	5,85,000/cumm	150-400*1000/cumm
Haemoglobins	13.4 g/dl	13-17 g/dL
Liver function tests		
Alkaline Phosphatase	96 U/L	53-128 U/L
Alanine Aminotransferase	70 U/L	Up to 42 U/L
Aspartate Aminotransferase	138 U/L	Up to 37U/L
Renal function tests		
Urea	38 mg/dL	15-45 mg/dL
Creatinine	0.5mg/dL	0.4–1.4mg/dL
Serology		
HIV 1 and 2 Rapid	Positive	
Determine	Reactive	
Unigold	Reactive	
Statpack	Reactive	
HbsAg Rapid	Negative	
HCV	Negative	
Serum Cryptococcal Antigen	Negative	
Other tests		
Absolute CD3	265/uL	677-2383/uL
Absolute CD4	14/uL	424-1509/uL
Serum Ferritin	939ng/Ml	30-400ng/mL
D-Dimer	<0.1 mg/L	0-0.5 mg/L
C-reactive protein	Positive	
Serum Adenosine deaminase	57	0-15(Serum)
Sputum for AFB-1and 2	Negative	
Gene Xpert	MTB not detected	

supportive measures. Based on clinical, laboratory and radiological findings patient was started on ATT (HRZE).

Viral Load and CD4 count were also done to initiate the treatment in course with HIV. Antiretroviral Treatment (ART) was started according to National Guideline for initiating ART for people with HIV and TB coinfection which included 1)Tenofovir (TDF), 2) Lamivudine (3TC) and 3) Dolutegravir (DTG) with DTG given 50mg twice daily.(10) He was kept in CPAP for 13 days with additional 13 days in oxygen supplementation. Patient gradually improved and was discharged after 26 days of admission.

Absolute Lymphocyte count was 384 /uL (reference range: 990-3150), CD3 was 68.98% (reference range: 59-83), Absolute CD3 was 265 /uL (reference range: 677-2383), CD4 was 3.70% (reference range: 31-59) and Absolute CD4 was 14/uL (reference range: 424-1509). HIV-1 Viral Load via Quantitative PCR was 183555 copies/ mL.

Figure 2: Radiographic findings of patient after admission

Figure 2A: X ray findings

Figure 2B: HRCT Chest

Figure 2C: HRCT Chest

Chest X-ray showed diffuse infiltrations over bilateral lungs **(Figure 2A)**. High-resolution computed tomography (HRCT) showed diffuse ground glass opacities with vascular dilatations with diffuse areas of interlobular septal thickening and tiny nodular densities scattered in bilateral lungs along with bronchiectasis changes. The changes were more in the lower lobes compared to upper lobes. **(Figure 2B)** Few mediastinal lymph nodes were enlarged along with calcifications. **(Figure 2B and 2C)**

DISCUSSION

This case report represents the unique finding identified during COVID-19 pandemic in Nepal. The major highlights of the study were that the patient is ART naive HIV positive with RT -PCR positive for SARS-COV2, presenting with overlapping clinical and radiological features of COVID-19 Pneumonia, Tuberculosis and Pneumocystis Pneumonia. This picture gives us various dimensions of health conditions which has to be thought of before reaching the final diagnosis.

Our patient was had an underlying immune defect characterised by absolute lymphopenia and low CD4 count and was ART naïve, which could have predisposed the patient independently to SARS-CoV-2, P. jirovecii infection, Tuberculosis and other opportunistic infections. HIV infection without ART may be a very serious comorbidity of COVID-19 as COVID-19 was found to cause rapid augmentation of the process of T-cell exhaustion initially caused by HIV.[11] Patient with COVID-19 can become critically ill and develop Acute Respiratory Distress Syndrome (ARDS) and due to their immunocompromised status may have opportunistic infections leading to increased severity of the disease.[12,13] Besides, HRCT Chest was notable for diffuse bilateral ground-glass opacities with patchy bands of atelectasis and tiny nodular foci of consolidation along with bronchiectasis. Ground glass opacities have been described to accompany COVID-19 pneumonia, Tuberculosis as well as Pneumocystis Pneumonia, thus creating diagnostic dilemma. [7, 9, 14, 15]

This case reports highlights the important role of microbial coinfection in the occurrence and development of SARS-CoV-2 infection which can raise difficulties in diagnosis, treatment and

prognosis of COVID-19 in the context of resource limited settings.

CONCLUSION

Our case emphasized on the fact that other causes of respiratory distress should not be overlooked by the mere presence of SARS-CoV-2 infection and high index of suspicion should be done for opportunistic infections while treating immunosuppressed patient.

CONFLICT OF INTEREST

None

ACKNOWLEDGEMENT

None

REFERENCES

1. Organization WH. Rolling updates on coronavirus disease (COVID-19) Updated 31 July, 2020 2020 [Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen
2. Chen X, Liao B, Cheng L, Peng X, Xu X, Li Y, et al. The microbial coinfection in COVID-19. Appl Microbiol Biotechnol. 2020;104(18):7777-85.
3. Barbera LK, Kamis KF, Rowan SE, Davis AJ, Shehata S, Carlson JJ, et al. HIV and COVID-19: review of clinical course and outcomes. HIV Res Clin Pract. 2021;22(4):102-18.
4. Brown LB, Spinelli MA, Gandhi M. The interplay between HIV and COVID-19: summary of the data and responses to date. Curr Opin HIV AIDS. 2021;16(1):63-73
5. Karmen-Tuohy S, Carlucci PM, Zervou FN, Zacharioudakis IM, Rebick G, Klein E, et al. Outcomes Among HIV-Positive Patients Hospitalized With COVID-19. J Acquir Immune Defic Syndr. 2020;85(1):6-10.
6. Kerkhoff AD, Havlir DV. CROI 2021: Tuberculosis, Opportunistic Infections, and COVID-19 Among People with HIV. Top Antivir Med. 2021;29(2):344-51.
7. Harris JR, Balajee SA, Park BJ. Pneumocystis Jirovecii Pneumonia: Current Knowledge and Outstanding Public Health Issues. Current Fungal Infection Reports. 2010;4(4):229-37.
8. Szydłowicz M, Matos O. Pneumocystis pneumonia in the COVID-19 pandemic era: similarities and challenges. Trends Parasitol. 2021;37(10):859-62.
9. Broadhurst AGB, Lalla U, Taljaard JJ, Louw EH, Koegelenberg CFN, Allwood BW. The diagnostic challenge of pneumocystis pneumonia and COVID-19 co-infection in HIV. Respirol Case Rep. 2021;9(4):e00725.
10. National Centre for AIDS and STD Control M, Nepal. NATIONAL HIV TESTING AND TREATMENT GUIDELINES2020. Available from: http://ncasc.gov.np/uploaded/Banner/National-HIV-Testing-Guidelines-May-10-2020-WEB-Version.pdf
11. Sharov KS. HIV/SARS-CoV-2 co-infection: T cell profile, cytokine dynamics and role of exhausted lymphocytes. Int J Infect Dis. 2021;102:163-9.
12. Nagarakanti SR, Okoh AK, Grinberg S, Bishburg E. Clinical outcomes of patients with COVID-19 and HIV coinfection. J Med Virol. 2021;93(3):1687-93.
13. Kanwugu ON, Adadi P. HIV/SARS-CoV-2 coinfection: A global perspective. J Med Virol. 2021;93(2):726-32.
14. Coleman H, Snell LB, Simons R, Douthwaite ST, Lee MJ. Coronavirus disease 2019 and Pneumocystis jirovecii pneumonia: a diagnostic dilemma in HIV. Aids. 2020;34(8):1258-60.
15. Lee J, Lim JK, Seo H, Lee SY, Choi KJ, Yoo SS, et al. Clinical relevance of ground glass opacity in 105 patients with miliary tuberculosis. Respir Med. 2014;108(6):924-30.

Case Report

DISSEMINATED HISTOPLASMOSIS IN HIV-PATIENT IN NEPAL: A CASE REPORT

Bastola Anup[1]; Pyakurel Prajjwal[2]; Maharjan Kijan[3]; Shrestha Sanjay[3]; Bastola Rupak[4]; Myneedu Vithal Prasad[5]; Paudel Sunil[6]; Devkota Lina[6]

[1]Director, SAARC TB and HIV/AIDS Centre, Thimi, Bhaktapur, Nepal
[2] Research Officer, SAARC TB and HIV/AIDS Centre, Thimi, Bhaktapur, Nepal
[3]Consultant Physician, Sukraraj Tropical and Infectious Disease Hospital, Teku, Kathmandu, Nepal
[4] Medical Officer, Norvic Hospital, Kathmandu, Nepal
[5] Sr. Microbiologist, SAARC TB and HIV/AIDS Center, Thimi, Bhaktapur, Nepal
[6] Medical Officer, Sukraraj Tropical and Infectious Disease Hospital, Teku, Kathmandu, Nepal

DOI: https://doi.org/10.3126/saarctb.v20i1.52669
Received: 2nd May Accepted: 1st July Published: 31st August
This article is available at:

ABSTRACT

The risk of disseminated Histoplasmosis increases among immunocompromised HIV infected patients. It can clinically present with skin manifestation. We report a forty years HIV infected male with severe immunodeficiency clinically presenting as a disseminated Histoplasmosis with dermatological manifestation and diagnosis.

Keywords: COVID-19, Pandemic, Tuberculosis, Nepal

INTRODUCTION

Histoplasmosis is a systemic fungal infection caused by Histoplasma capsulatum, a dimorphic fungus. It is found in soil contaminated by bat and bird droppings. During farming, construction and chicken coups handling fungal microconidia are aerosolized which on inhalation reach the lung. In lungs conidia form a yeast causing localized or patchy infection. Furthermore, they are taken up by alveolar macrophages and reach the blood stream through the lymphatics. It is a self-limiting condition in immunocompetent person due to cell mediated immunity but in immunodeficient individuals it can disseminate to reticulo-endothelial organs such as liver spleen bone marrow and sometimes gastrointestinal system, bones, skin, eyes and brain. It manifests as acute, sub-acute, chronic and progressive disseminated disease.[1-4]

Histoplasma capsulatum is endemic in United states, certain parts of Mexico, Central and South America, Africa.[5-7] However, recently cases have been increasing in other non-endemic regions due to HIV, primary immunodeficiency, immunosuppressive drugs and solid organ transplantation. The cases are also in increasing trend in South East Asian region such as Bangladesh, India and China.[7-9]To the best of our knowledge only few cases were reported from Nepal. Hence, we report a case of 40 years old male with HIV and TB not improving inspite of appropriate treatment. He presented clinically with cutaneous nodules diagnosed as Histoplasmosis on microscopy.

Correspondence:
Dr. Kijan Maharjan
Consultant Physician
Department of Internal Medicine
Sukraraj Tropical and Infectious Disease Hospital
Teku, Kathmandu
Email: kijan1069@gmail.com

CASE REPORT

A 40 years male from Kusma, Parbat presented in local hospital in Pokhara with history of fever for 3 months and multiple episodes of loose stool for 2 months. Cervical lymph node biopsy showed

infectious reactive hyperplasia and treated with antibiotics. In spite of appropriate antibiotics course his symptoms did not improve. He was referred to a tertiary care center in Kathmandu. Repeat cervical lymph node biopsy showed granulomatous lymphadenopathy suggestive of TB lymphadenitis. He was put on category I ATT at National TB Control Center. He showed improvement for few days, however his symptoms persisted. Three months later he presented to Sukraraj Tropical and Infectious Disease Hospital (STIDH) with complaints of dysphagia, odynophagia, generalized weakness, anorexia, weight loss and multiple itchy skin lesions over the face and neck.

On examination patients was pale and cachectic (Weight=37kg). He had multiple papulo-nodular erythematous, painful, molluscum like lesions with central crusting over chin, cheeks, forehead and neck. Bilateral pitting pedal edema and anterior cervical lymphadenopathy was present. There were whitish patches on the buccal and pharyngeal mucosa with peripheral redness. Systemic examination showed no neurological deficit or any respiratory system findings. Abdominal examination showed hepatomegaly 4 finger below the right costal margins.

Blood parameters were Hb-6.1gm/dl, TLC 2700/ mm^3, Total bilirubin 3.6 mg/dL, Bilirubin direct 2.2 mg/dL, Serum ALT 27 U/L, AST 80 U/L, Sodium 125mEq/L. Potassium 4.3 mEq/Land random blood sugar 140mg/dL.Urine routine and microscopy were normal. Blood culture showed no growth. Serology for syphilis, serum cryptococal antigen, toxoplasmosis, rubella, cytomegalovirus and herpes simplex virus was negative. HIV serology was positive with CD4 count of 39/mm^3. Chest X-ray was within normal limit. Fine needle aspiration of the right cervical lymph node showed granulomatous lesion suggestive of tubercular lymphadenitis. Peripheral blood smear showed normocytic, normochromic and normal morphology of red blood cells and platelets. Sputum for AFB stain was negative. Fungal stain could not be done because of lack of facility at the hospital.

CT chest showed moderate bilateral pleural effusion with sub-segmental consolidation collapse of adjacent parenchyma and multiple small nodules scattered in bilateral lungs. CT abdomen and pelvis showed multiple discrete as well as coalesced necrotic lymph nodes in right paraaortic, periportal, peripancreatic, celiac, mesentery, retroperitoneal, paraaortic aortocaval and bilateral inguinal region.

Microscopy of scrapping from the skin lesions on the face showed fungal elements morphologically consistent with Histoplasma. **(Figure 2)**

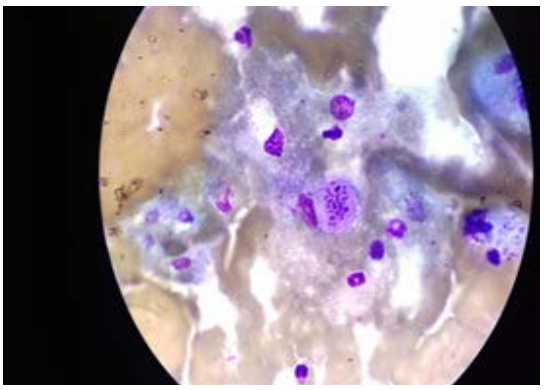


Figure 1: *Smear from skin scrapping shows structure with basophilic center and surrounding halo arranged in clusters and singly within and outside macrophages consistent with Histoplasmosis*

Figure 2: *Multiple papulo-nodular erythematous lesion with central crusting over chin, cheeks, forehead*

He was prescribed with Itraconazole 200mg/ day orally. However, patient deteriorated during treatment in the hospital and taken to High Dependency Care Unit (HDU) due to respiratory failure. Patients was later absconded from HDU management. The reason for abscondment was not known and he could not be traced for further management and the outcome was unknown.

DISCUSSION

The increasing trend of reported histoplasmosis cases have been observed in many Asian countries. First case in Nepal was reported from B.P.Koirala Institute of Health Sciences,Dharan,Nepal in a

male patient from Bihar, India.[10] Since then few cases have been reported[11,12] and hence the prevalence of the disease is yet to be studied. Histoplasmosis is an opportunistic infection in HIV that occurs when CD4 cell count is <200 cells/μL.[13] Histoplasmosis may be asymptomatic; an acute or chronic pulmonary infection; or disseminated histoplasmosis (DH). The acute form of DH is seen mostly in the immunocompromised people and is characterized by fever, malaise, weight loss, cough, dyspnea abdominal pain and diarrhea. Other clinical and laboratory findings include anemia, hepatosplenomegaly, lymphadenopathy, leucopenia and thrombocytopenia. The chronic form has an indolent course with focal lesions due to effective cell mediated immunity.[14] It presents as disseminated disease in 95% of cases.[15] Disseminated disease can involve gastrointestinal tract (GI) and skin. GI involvement can cause bowel obstruction, perforation and bleeding.[16] Skin lesions presents as polymorphic papules or plaque, pustules, nodules and ulcer like molluscum contagiousm or acne.[17] Due to clinical resemblance to TB and occurrence with TB in HIV patients, it is a diagnostic challenge in regions with high prevalence of TB. Lack of diagnostic facilities and low level of clinical suspicion leads to misdiagnosis of TB.[18] This patient also had diagnosis of Histoplasmosis delayed because of clinical and cytological features resembling Tuberculosis. Delayed diagnosis and treatment have poor outcome.

Diagnosis of Histoplasmosis requires understanding of test, their accuracy and limitations. The gold standard is growth of the H. capsulatum on specific culture media or direct visualization of the yeast in clinical specimens with the Gomori methenamine silver (GMS) and Periodic acid-Schiff (PAS). However, low sensitivity for mild cases and diagnosing invasive growth which requires 4 to 6 weeks are some of the limitations in routine laboratory set-up and requires Biosafety level 3 set-up. Antigen detection in serum and urine has higher sensitivity in disseminated histoplasmosis in HIV/AIDS. Among people living with HIV, it is recommended to diagnose disseminated histoplasmosis by detecting circulating Histoplasma antigens.[19] But the test is not widely available. Since antigen tests were not available in our setup, diagnosis in our patient was established using direct microscopy. Cytopathologic evaluation of bronchoalveolar lavage (BAL) alone has lower sensitivity however, combined with Histoplasma antigen testing the sensitivity rises to 97%.[20] Fine-needle aspiration cytology is safe and useful test for diagnosis from lymph nodes and adrenal glands. Antigen detection in serum when combined with urine is a very useful test in patients with severe acute or disseminated Histoplasmosis. Serological test takes 4 to 8 weeks to become positive so it is useful for subacute and chronic forms of Histoplasmosis.[21]

CONCLUSION

Although Nepal is non-endemic region for histoplasmosis it should be suspected in HIV patients who present with fever, weight loss and lymphadenopathy. High clinical suspicion and diagnostic facilities is key to early diagnosis. With high burden of HIV and increasing number of Histoplasmosis cases, there should be efforts to increase the availability of the test for urinary antigen detection in DH diagnosis and diagnostic center with well-trained medical personnel needs to be increased. Diagnostic facilities with microscopy examination of cutaneous lesion can aid in diagnosis of disseminated Histoplasmosis.

CONFLICT OF INTEREST

None

REFERENCES

1. Akram SM, Koirala J. Histoplasmosis. StatPearls. Treasure Island (FL)2021.
2. Myint T, Leedy N, Villacorta Cari E, Wheat LJ. HIV-Associated Histoplasmosis: Current Perspectives. HIV AIDS (Auckl). 2020;12:113-25.
3. Rahim MA, Zaman S, Amin MR, Uddin KN, Ma JC. Histoplasmosis: An Emerging or Neglected Disease in Bangladesh? A Systematic Review. Oman Med J. 2020;35(1):e91.
4. Lv X, Jiang M, He R, Li M, Meng J. Clinical features and endemic trend of histoplasmosis in China: A retrospective analysis and literature review. Clin Respir J. 2020;14(4):307-13.
5. Gupta A, Ghosh A, Singh G, Xess I. A Twenty-First-Century Perspective of Disseminated Histoplasmosis in India: Literature Review

and Retrospective Analysis of Published and Unpublished Cases at a Tertiary Care Hospital in North India. Mycopathologia. 2017;182(11-12):1077-93.

6. Oladele RO, Ayanlowo OO, Richardson MD, Denning DW. Histoplasmosis in Africa: An emerging or a neglected disease? PLoS Negl Trop Dis. 2018;12(1):e0006046.

7. Wheat LJ, Azar MM, Bahr NC, Spec A, Relich RF, Hage C. Histoplasmosis. Infect Dis Clin North Am. 2016;30(1):207-27.

8. Pan B, Chen M, Pan W, Liao W. Histoplasmosis: a new endemic fungal infection in China? Review and analysis of cases. Mycoses. 2013;56(3):212-21.

9. Antinori S. Histoplasma capsulatum: more widespread than previously thought. Am J Trop Med Hyg. 2014;90(6):982-3.

10. Amatya R, Koirala R, Khanal B, Gurung R, Rijal A, Dhakal KJHR. Histoplasmosis: first case from Nepal. 2010;7:61-3.

11. Sharma N, Adhikari RCJJoPoN. Adrenal involvement in histoplasmosis. 2019;9(1):1502-4.

12. Thapa S, Jha SC, Trotter AB. Persistent Fever and Skin Lesions Due to Histoplasmosis in a Boy from Rural Nepal. Am J Trop Med Hyg. 2016;94(2):249-50.

13. Tobon AM, Gomez BL. Pulmonary Histoplasmosis. Mycopathologia. 2021;186(5):697-705.

14. Limper AH, Adenis A, Le T, Harrison TS. Fungal infections in HIV/AIDS. Lancet Infect Dis. 2017;17(11):e334-e43.

15. Almeida MA, Almeida-Silva F, Guimaraes AJ, Almeida-Paes R, Zancope-Oliveira RM. The occurrence of histoplasmosis in Brazil: A systematic review. Int J Infect Dis. 2019;86:147-56.

16. Kahi CJ, Wheat LJ, Allen SD, Sarosi GA. Gastrointestinal histoplasmosis. Am J Gastroenterol. 2005;100(1):220-31.

17. Chang P, Rodas C. Skin lesions in histoplasmosis. Clin Dermatol. 2012;30(6):592-8.

18. Kirn DH, Fredericks D, McCutchan JA, Stites D, Shuman M. Serum ferritin levels correlate with disease activity in patients with AIDS and disseminated histoplasmosis. Clin Infect Dis. 1995;21(4):1048-

19. Perez F, Caceres DH, Ford N, Ravasi G, Gomez BL, Pasqualotto AC, et al. Summary of Guidelines for Managing Histoplasmosis among People Living with HIV. J Fungi (Basel). 2021;7(2).

20. Hage CA, Davis TE, Fuller D, Egan L, Witt JR, 3rd, Wheat LJ, et al. Diagnosis of histoplasmosis by antigen detection in BAL fluid. Chest. 2010;137(3):623-8.

21. Azar MM, Hage CA. Laboratory Diagnostics for Histoplasmosis. J Clin Microbiol. 2017;55(6):1612-20.

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