

Prevalence of Tuberculosis in the North Indian Subcontinent Kashmir Valley: A Cross-sectional Hospital-based Study

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ABSTRACT

Introduction: Tuberculosis (TB) is an infectious bacterial disease caused by *Mycobacterium tuberculosis*, which most commonly affects the lungs. TB is one of the biggest public health challenges in the world especially in under-developing and developing countries.

Aim: To determine the prevalence of TB in the Kashmir valley.

Materials and Methods: The present cross-sectional study was conducted in the Department of Chest Medicine, Chest Diseases Hospital (CDH), Government Medical College, Srinagar and Intermediate Reference Laboratory (IRL), State TB Training and Demonstration Centre (STDC), CDH, Srinagar and in association with State TB Office (STO) Kashmir, India, from March 2019 to December 2020 in 10 districts. A total of 66,829 presumptive TB samples in 2019 inclusive of 450 samples of CDH and 63532 presumptive TB samples in 2020 inclusive of 400 samples of CDH were collected from Department of Chest Medicine, CDH,

Government Medical College, Srinagar and Revised National TB Control Programme (RNTCP) Centres of Kashmir valley under State TB office Director Health Kashmir as per World Health Organisation (WHO) criteria. It included both the positive and negative cases of TB registered during the year 2019 and 2020.

Results: The total prevalence of TB disease during the year 2019 was found to be 49.03 per 100,000 population and 37.31 per 100,000 population in the year 2020 respectively. There was no correlation among the surveyed demographics in the positive TB cases in the Kashmir valley ($p > 0.05$). Srinagar city reported highest cases whereas Budgam and Pulwama reported least cases in the year 2019 and 2020.

Conclusion: The respiratory precautionary measures like social distancing and use of face masks during the ongoing COVID-19 pandemic has reduced transmission and incidence of TB. Proper identification and treatment of infectious cases will prevent TB in the ethnic population. More studies are needed on large sample size.

Keywords: Acid fast bacillus, Chest diseases, *Mycobacterium tuberculosis*, Revised national tuberculosis control programme, Rural

INTRODUCTION

The TB is a global health problem and it is highly infectious airborne bacterial disease caused by *Mycobacterium tuberculosis*, which most commonly affects the lungs in the human respiratory system. TB is a challenge globally, and it is a major cause of morbidity and mortality in millions of people each year. TB is ranked among the 10 causes of deaths worldwide and regarded as one of the leading causes of death from infectious diseases. India accounts for 1/4th of the global TB burden and it is reported that around 4.8 lac people died due to TB of estimated 28 lac infected cases in 2015 [1]. As per latest TB report of WHO, TB remains a persistent developmental challenge worldwide and puts burden on exchequers [2]. The proportion of TB infected patients is higher in India because of poor socio-economic and environmental conditions. According to National Family Health Survey (NFHS-4), the prevalence of TB is 316 per 100,000 persons in India [3]. To achieve global target of "End TB 2035" is possible only due to decline of morbidity and mortality, new infections among population and elimination of economic and social burden of TB disease [4].

The first ever prevalence study on TB disease in Kashmir valley was conducted by Mayurnath S et al., and RNTCP was implemented in the valley in 2004 to stop further progression of TB disease in the Kashmir valley, which showed very good results and helped in decline of disease and removal of social stigma among patients regarding the disease and treatment [5]. The Kashmir valley is a demographically mountainous region, where around four to five months witnesses winter season due to which people remain inside and use wood, coal, gas for heating and cooking purposes. Many studies reported indoor air pollution as a significant risk factor for the occurrence of TB disease [6,7]. The present literature suggested a number of

factors associated with TB infection, including demographic, socio-economic and environmental factors, such as age, sex, level of education, marital status, place of residence, wealth, overcrowding, poor housing and household environment factors [8-11].

To get a more precise understanding of the current TB burden in the Kashmir valley, there was a need to conduct a new TB prevalence survey in the region. The primary objective of the survey was to estimate the prevalence of bacteriologically positive TB patients amongst the adult population (>15 years) in a regional representative sample and to improve quality life of infected patients in the society and help RNTCP to devise new strategies to control TB in Kashmir valley, India.

MATERIALS AND METHODS

The present cross-sectional hospital-based study was conducted in the Department of Chest Medicine, CDH Government Medical College, Srinagar and IRL, STDC, CDH, Srinagar, India. After acquiring the formal ethical clearance from the Institutional Ethical Committee (IEC) of Government Medical College Srinagar under Ref No: 138/ETH/GMC/ICMR, and informed consent from the participants, the present study was conducted in Kashmir valley from March 2019 to December 2020 in 10 districts.

1. Anantnag and Kulgam (considered as one for the study)
2. Baramulla and Bandipora (considered as one for the study)
3. Pulwama and Shopian (considered as one for the study)
4. Srinagar and Ganderbal (considered as one for the study)
5. Budgam
6. Kupwara

Inclusion criteria: Patients older than 15 years were taken for study after getting due consent. Patients of Kashmiri ethnic origin. Samples which follow WHO standard were included.

Exclusion criteria: Patients of non Kashmiri origin. Patients less than 15 years of age. Samples which are not as per WHO standard were excluded.

Sample size calculation: The sample size was estimated based on WHO 2018 guidelines [2,12,13]. The G power software tool, version 3.1 was used to calculate sample size.

A total of 66829 presumptive TB samples in 2019 (inclusive of 450 samples from CDH) and 63532 presumptive TB samples in 2020 (inclusive of 400 samples from CDH) were collected from Department of Chest Medicine, Government Medical College, Srinagar and RNTCP Centres of Kashmir valley district hospitals under State TB Office-Director Health Kashmir as per WHO criteria [14,15]. It included both the positive and negative cases of TB registered during the year 2019 and 2020. The total data of mid-year (mid-interval) population during the study period was estimated by using census 2011 figures and growth rates published in sample registration system bulletins [16,17].

Prevalence was estimated as the:

$$\frac{\text{Number of reported cases of TB}}{\text{Estimated mid-year (mid-interval) population}} \times 100000$$

Study Procedure

The cross-sectional study consists of patient's socio-demographic details and laboratory examinations. The participants having symptoms like cough >2 weeks, chest pain, fever more than two weeks, diabetes and age 15-65 years were taken for sputum examination and were asked to provide two sputum samples as per WHO criteria [18-22]. The RNTCP staff collected one spot sputum sample in a pre numbered sterilised sputum cup. A second vial was provided for morning sample collection. For people living in difficult terrain, two spot samples were taken one hour apart and transported to the nearest Designated Microscopy Centre (DMC). X-ray examinations were done at the nearest facility and the suspicious X-ray reports were tested using Acid Fast Bacillus (AFB) staining and were further confirmed by advanced technologies of diagnostics i.e., Cartridge Based Nucleic acid Amplification Test (CBNAAT) and TrueNat. Patients who were found positive were given treatment at the nearest hospitals using Directly Observed Treatment Short-course (DOTS).

STATISTICAL ANALYSIS

The data obtained was evaluated using Microsoft Excel 2011 and then analysed in Statistical Package for the Social Sciences (SPSS) version 16.1 (Chicago IL). The p-values were calculated as percentage by Student's t-test and Pearson's correlation analysis. A p-value of <0.05 was considered statistically significant. Prevalence estimations and 95% Confidence Interval (CI) for smear- and bacteriologically positive TB were calculated as recommended.

RESULTS

Between 2019 and 2020, 850 microscopic exams were performed at CD hospital Srinagar, which were included in regional data. Pulmonologists and clinicians examined 66,829 probable TB cases in the age group of 15-65 years in the ethnic community of Kashmir valley during the year 2019 [Table/Fig-1]. There were 3692 people diagnosed with TB infection among them. While the demographics of the participants were examined using the student's t-test, it was discovered that all of the participants have a relationship with demographics (age, gender, and residence) ($p > 0.05$), which is statistically insignificant [Table/Fig-2]. In bacteriologically, TB infected positive patients from Kashmir valley, there was no link between age, gender, or residence ($p > 0.05$) [Table/Fig-3]. As summarised in [Table/Fig-4], error-blot depicts the relationship of examined demographics in positive TB cases with 95% CI on AFB microscopy and molecular tests

and molecular testing and [Table/Fig-5] is correlation analysed by Pearson's correlation analysis which summarises with respect to demographics and positive tuberculosis rate which were insignificant where ($p > 0.05$) [Table/Fig-6,7] shows that the frequency was highest in Srinagar district among the 10 districts throughout both years. According to the data, the decrease in the number of positive cases detected in 2020 as compared to 2019 was attributable to ongoing surveillance, pandemic of COVID-19. The Standard Operating Procedure (SOPs) including social distancing, use of face masks and use of sanitisers helped in decrease the transmission and incidence of TB which shows that these SOP's (guidelines issued by WHO) can be used to reduce the transmission of TB.

Demographics	Total no. of participants 2019 (year)	Total no. of participants 2020 (year)	No of positive cases 2019 (year) by microscopy and molecular tests	No. of positive cases 2020 (year) by microscopy and molecular tests
Age (years)				
15-65	66829	63532	3692	2839
Residence				
Urban	9410	5869	1668	1123
Rural	57419	57663	2024	1716
Gender				
Male	35500	34520	1955	1472
Female	31329	29012	1737	1367
Clinical parameters*				
Chest pain	57419	57663	3692	2839
Fever	31329	29012	3692	2839
Cough >2 weeks	35500	34520	3692	2839

[Table/Fig-1]: Demographics of participants of study.

*More than one present

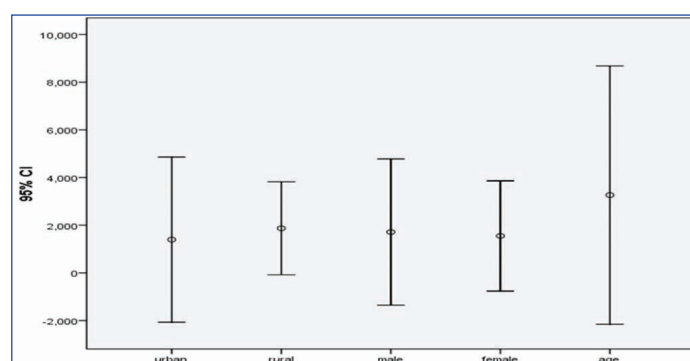
Demographics	N	Mean	Std. Deviation	Std. Error mean
Urban	2	1395.50	385.373	272.500
Rural	2	1869.50	217.082	153.500
Male	2	1713.50	341.533	241.500
Female	2	1549.00	257.387	182.000
Age	2	3265.50	603.162	426.500

[Table/Fig-2]: Demographics of TB cases.

Demographics	T	Df	Sig. (2-tailed)	Mean difference	95% Confidence interval of the difference	
					Lower	Upper
Urban	5.121	1	0.123	1395.500	-2066.94	4857.94
Rural	12.179	1	0.052	1869.500	-80.90	3819.90
Male	7.095	1	0.089	1713.500	-1355.05	4782.05
Female	8.511	1	0.074	1549.000	-763.53	3861.53
Age	7.657	1	0.083	3265.500	-2153.70	8684.70

[Table/Fig-3]: Detailed analysis of demographics.

Student's t-test



[Table/Fig-4]: Error blot depicts relationship of examined demographics in positive TB cases with 95% CI on AFB microscopy and molecular tests (CBNAAT/TrueNat).

Demo-graphics	Test	Urban	Rural	Male	Female	Age
Urban	Pearson's correlation	1	1.00	1.00	1.00	1.00
	Sig. (2-tailed)	
	N	2	2	2	2	2
Rural	Pearson's correlation	1.00	1	1.00	1.00	1.00
	Sig. (2-tailed)
	N	2	2	2	2	2
Male	Pearson's correlation	1.00	1.00	1	1.00	1.00
	Sig. (2-tailed)
	N	2	2	2	2	2
Female	Pearson's correlation	1.00	1.00	1.00	1	1.00
	Sig. (2-tailed)
	N	2	2	2	2	2
Age	Pearson's correlation	1.00	1.00	1.00	1.00	1
	Sig. (2-tailed)
	N	2	2	2	2	2

[Table/Fig-5]: Pearson's correlation analysis of examined demographics with positive Tuberculosis (TB) infection by AFB Microscopy and Molecular Tests (CBNAAT/TrueNat). **Correlation is significant at the 0.01 level (2-tailed).

In the year 2019, 1668 participants in the urban population were found to be TB infected, as confirmed by gold standard method (AFB, Ziehl-Neelsen staining microscopy) and molecular tests (CBNAAT/TrueNat), whereas 2024 participants in the rural population were found to be TB infected. The two key criteria studied to analyse the total prevalence were gender and region. In 2019, 1,955 males and 1737 females were infected with TB, according to gender distribution. In the Kashmir valley, the total prevalence of TB was found to be 49.03 per 100,000 people in 2019. In the Kashmir valley, 63,532 probable TB cases were assessed according to WHO criteria in the age category of 15-65 years in 2020. There were 2,839 people diagnosed with TB infection among them. In the year 2020, according to the distribution of habitation and gender, 1,123 participants in the urban population were TB infected as proven by microscopy and molecular tests, whereas 1,716 participants in the rural population were TB infected. In the year 2020, there were 1,472 males and 1,367 females affected, according to gender distribution. The total prevalence of TB analysed during the year 2020 was found to be 37.31 per 100,000 population in the Kashmir valley [Table/Fig-1].

Factor I: Total prevalence as per the regions (Rural/Urban)

The [Table/Fig-6] shows, in the year 2019, 66829 presumptive TB patients were seen in the Kashmir valley's hospitals and RNTCP centres. Gold standard AFB Microscopy and Molecular tests (CBNAAT/TrueNat) revealed that 63137 subjects were negative and 3692 were positive. Srinagar district had 1668 positive TB cases with a prevalence rate of 101.53 per 100,000 people, followed by Anantnag district with 713 positive cases and a prevalence rate of 43.27 per 100,000 population according to data analysis of 10 districts in Kashmir valley. With 175 cases and a prevalence rate of 21.08 per 100,000 people, the Budgam district of Kashmir valley had the lowest prevalence.

The [Table/Fig-7], shows that in the year 2020, 63532 probable TB cases visited the Kashmir valley's hospitals and RNTCP centres. The gold standard AFB Microscopy and Molecular testing (CBNAAT/TrueNat) identified 60693 subjects to be negative and 2839 to be positive. Srinagar district had 1123 positive TB cases with a prevalence rate of 67.79 per 100,000 people, followed by Kupwara district with 333 positive cases and a prevalence rate of 34.34 per 100,000 population according to data analysis of 10 districts in Kashmir valley. With 177 cases and a prevalence rate of 19.21 per 100,000 people, the Pulwama district of Kashmir valley had the lowest prevalence. The COVID-19 pandemic was to blame for the decrease in prevalence rate in 2020. Patients adopted WHO preventative measures such as social distancing and mask use, which may have lowered TB disease transmission and incidence rates. Due to the COVID-19 epidemic, fewer patients visited hospitals and health centres, resulting in fewer cases being screened.

Factor II: Age group

In 2019, the most afflicted districts were Srinagar, followed by Anantnag, and then Baramulla, with Budgam being the least affected district. Srinagar was again the most affected district in the year 2020, followed by Baramulla and Anantnag, and finally Kupwara. Budgam and Pulwama were the least hit areas [Table/Fig-8,9].

Factor III: Gender

Males were more impacted than females in Srinagar, according to a district-by-district TB case and gender-by-gender distribution in 2019. Similarly, males were impacted more than females in district Anantnag, but females were most affected in district Baramulla. In 2020, a map depicting district-by-district TB cases and gender-by-gender distribution revealed that males were more impacted than females in Srinagar. Males were also afflicted more than females

Districts	Mid-year population	Number of AFB microscopy done	Molecular tests (CBNAAT/TrueNat)	Total number of bacteriological examinations done	Number of positive cases	Number of negative cases	Rate (per 100,000 population)
Anantnag	1647707	13625	3548	17173	713	16460	43.27
Budgam	829887	4942	2387	7329	175	7154	21.08
Baramulla	1538856	9282	2889	12171	515	11656	33.46
Kupwara	958638	8713	2777	11490	354	11136	36.92
Pulwama	910622	6832	2424	9256	267	8989	29.32
Srinagar	1642851	9410	0	9410	1668	7742	101.53
Total	7528561	52804	14025	66829	3692	63137	49.03

[Table/Fig-6]: Prevalence of Tuberculosis (TB) in the Kashmir valley in the year 2019.

Districts	Mid-year population	Number of AFB microscopy done	Molecular test (CBNAAT/TrueNat)	Total number of bacteriological examinations done	Number of positive cases	Number of negative cases	Rate (per 100,000 population)
Anantnag	1665488	12581	2871	15452	534	14918	32.06
Budgam	839232	5085	2522	7607	169	7438	20.13
Baramulla	1555882	10498	3264	13762	503	13259	32.32
Kupwara	969472	7839	3515	11354	333	11021	34.34
Pulwama	920924	7026	2462	9488	177	9311	19.21
Srinagar	1656447	3819	2050	5869	1123	4746	67.79
Total	7607445	46848	16684	63532	2839	60693	37.31

[Table/Fig-7]: Prevalence of Tuberculosis (TB) in the Kashmir valley in the year 2020.

in districts Anantnag and Kupwara, although females were most affected in district Baramulla [Table/Fig-10,11].

Districts	Age group in the year 2019 (years)			
	15-30	31-45	45-60	>60
Anantnag	220	102	117	120
Budgam	67	32	35	31
Baramulla	228	87	81	89
Kupwara	163	42	58	73
Pulwama	76	53	59	50
Srinagar	543	312	339	352

[Table/Fig-8]: District wise TB cases- age wise distribution in 2019 year.

Districts	Age group in the year 2020 (years)			
	15-30	31-45	45-60	>60
Anantnag	173	108	78	109
Budgam	56	42	38	27
Baramulla	209	92	83	93
Kupwara	130	53	50	84
Pulwama	62	37	31	34
Srinagar	381	246	211	213

[Table/Fig-9]: District wise TB cases-age wise distribution in 2020 year.

Districts	Gender wise-2019 year	
	Males	Females
Anantnag	384	329
Budgam	92	83
Baramulla	228	284
Kupwara	169	184
Pulwama	139	128
Srinagar	943	729

[Table/Fig-10]: District wise TB cases and gender wise distribution in 2019 year.

Districts	Gender wise-2020 year	
	Males	Females
Anantnag	292	242
Budgam	79	90
Baramulla	211	292
Kupwara	181	152
Pulwama	98	79
Srinagar	611	512

[Table/Fig-11]: District wise TB cases and gender wise distribution in 2020 year.

In all districts of Kashmir valley in both 2019 and 2020, the most TB cases were reported in the 15-30 age group, with the majority of cases reported from Srinagar city, followed by Baramulla. According to present study findings, Srinagar had the greatest number of TB cases in both male and female sexes, followed by Anantnag, and Budgam and Pulwama had the lowest. The [Table/Fig-12] depicts the condition in Kashmir valley with regard to Extrapulmonary TB (EPTB) and the number of positive cases projected in 2019 and 2020.

District	2019	2020
Anantnag	277	243
Budgam	145	141
Baramulla	317	236
Kupwara	200	180
Pulwama	162	110
Srinagar	422	385
Total	1523	1295

[Table/Fig-12]: Number of positive Tuberculosis (TB) cases from Extra-pulmonary sampling in the year 2019 and 2020.

The [Table/Fig-13] clearly indicates here that the 17.72% of patients of urban population are TB positive in the year 2019 and whereas in [Table/Fig-14] reports that the 19.13% patients are TB positive in the urban population in the year 2020.

Demographics	Total No. of participants 2019 (Year)	Mid-year population 2019 (Year)	No. of positive cases 2019 (year) by microscopy and molecular tests	Percentage (%) of Tuberculosis (TB) cases 2019 (year)
Age				
15-65	66829	7528561	3692	5.52
Residence				
Urban	9410	1642851	1668	17.72
Rural	57419	5885710	2024	3.52

[Table/Fig-13]: Percentage of Tuberculosis (TB) cases in Kashmir valley in the year 2019.

Demographics	Total No. of participants 2020 (year)	Mid-year population 2020 (year)	No. of positive cases 2020 (year) by microscopy and molecular tests	Percentage (%) of Tuberculosis (TB) cases 2020 (year)
Age (years)				
15-65	63532	7607445	2839	4.46
Residence				
Urban	5869	1656447	1123	19.13
Rural	57663	5950998	1716	2.97

[Table/Fig-14]: Percentage of Tuberculosis (TB) cases in Kashmir valley in the year 2020.

DISCUSSION

This study enrolled 66829 presumptive TB samples in 2019 and 63532 presumptive TB samples in 2020, and it was a cross-sectional hospital-based study. The study was conducted to estimate the prevalence of TB in the Kashmir valley. Latest findings by the Rehman S et al., 2020 completed investigations on TB prevalence disease in the Kashmir valley [14]. As per recent research study analysis in 2018, India accounted for 25% of the worldwide TB burden, with an estimated 2.8 million new cases [16]. The Government of India, has set an ambitious goal of eliminating TB by 2025, well ahead of the 2030 sustainable development goals framework. In addition to implementing the National Strategic Plan to meet the goal, various additional initiatives have been launched, including notification of new cases to the government by private health providers, active case discovery, medication resistance surveys, and nutritional support for TB patients. The Ministry of Health, Government of India, has now initiated a countrywide TB prevalence survey to determine the disease's prevalence at the national and subnational levels [16,17]. In this study, it was found that the prevalence of TB disease in the Kashmir valley was 49.03 per 100,000 people in 2019 and 37.31 per 100,000 people among 2020, which was consistent with other study done by Rehman S et al., 2020 in Kashmir's ethnic community [14]. The annual risk of infection in Delhi is 2.4% (state TB officer, Delhi, pers. comm.) [18].

Traditional approaches for tracing TB transmission are imprecise and ineffectual in controlling the disease, necessitating the use of molecular diagnostics, which aligns with present study research model. It is one among the world's most deadly and widespread illnesses. The prevalence was highest in Srinagar and lowest in Budgam and Pulwama districts. This could indicate a higher prevalence of TB in the area, or a higher rate of case discovery and reporting, or both. Due to the COVID-19 pandemic and the WHO's preventive initiatives, the prevalence rate of TB was found to be lower in 2020 than in 2019. TB has been designated as a global public health emergency. It is a major cause of morbidity and mortality, particularly in under-developed nations. Sputum smear positive cases are the most worrisome because they can spread

the illness quickly and easily in the community through spitting. As a result, early detection and treatment are critical. The WHO's goal for reducing the disease's global burden includes early detection and treatment of such patients. This research looked into the TB condition in Kashmir in order to give a more accurate and realistic picture of the disease load in the valley. The age and sex were the main factors used to study the distribution in TB cases in Kashmir valley. The various studies reported on gender basis on different populations suggested that the males were highest predisposed to the disease as compared to females which was in line with other studies done in different ethnic populations of the world like China, Cambodia, Ethiopia, Bangladesh, Pakistan etc., [19-22]. The study reported by Mushtaq MU et al., showed that the prevalence of TB increased with age; a similar pattern can be seen in Pakistan's TB surveillance statistics [23]. Rather than rapid transmission, the greater TB prevalence among the elderly could be explained by return of TB due to endogenous reactivation in combination with a weakened immune system [24,25].

Limitation(s)

Every study has some limitations. In future course, more study will be taken with advanced molecular diagnostics with large sample size with clinical and laboratory parameters.

CONCLUSION(S)

The study emphasises the significance of incorporating sophisticated diagnostic technology such as CBNAAT/TrueNat as a critical diagnostic tool for presumed positive TB cases in Kashmir. CBNAAT/TrueNat is a nucleic acid-based molecular biology cartridge approach that is more precise and accurate than sputum smear microscopy. Accurate estimates of the TB burden at the regional and national levels aid policy makers in developing strategies to combat the disease, reduce the country's economic burden, and improve humanity's health index by reducing disease co-morbidity.

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