Prevalence of Tuberculosis Among High Altitude Residents of Nepal

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INTRODUCTION
Tuberculosis (TB) is a global health concern, and its prevalence can vary widely from one region to another. Factors such as altitude, climate, population density, and healthcare infrastructure can all influence the dynamics of TB in a particular area. It is caused by the Mycobacterium tuberculosis (MTB) bacteria which mostly affects the lungs and is spread through air via coughing, sneezing, or spitting and requires few germs to infect the person by inhalation. Worldwide, TB is the 13th leading cause of death and the second infectious killer after Corona Virus Disease-2019 (COVID-19) (above HIV/AIDS).1 The first-ever National TB Prevalence Survey (2018-19) conducted in coordination with the World Health Organization

ABSTRACT

Introduction: Tuberculosis is a global health concern, and its prevalence can vary widely from one region to another. Factors such as altitude, climate, population density, and healthcare infrastructure can all influence the dynamics of tuberculosis in a particular area. This study aimed to provide insights into whether altitude played a role in the occurrence of tuberculosis and its different forms in the specific region of Jumla the western rural district of Nepal.

Methods: Jumla is a high-altitude mountainous region ranging from 915m-4679 m with a population of 119,337 (2021) having 8 municipalities. Data were collected from all the municipalities over a period starting from July 15th 2021-July 14th 2022 and were compared with prior years in number and diagnosis with national data of Nepal.

Results: A total of 84 cases were recorded of which 52.4% (n=44) were females. The group affected most was between the ages 16-30 years (34.5%) and 61-75yr (22.6%). The cases detected by the sputum Xpert MTB/RIF testing were 54.7%, with positive sputum Acid-fast bacilli being 27.4%. Most of the patients were diagnosed to have pulmonary bacteriologically confirmed (PBC) tuberculosis 52.4%, PCD (Pulmonary clinically diagnosed) 16.7%, Extra-pulmonary 28.6% with one case of each multi-drug resistant tuberculosis (MDR-TB), and Pre-XDR (Extensive drug resistant) TB. Among them, 12% of people had a history of TB undergone ATT (anti-tuberculosis drugs) in the past with 6% having a close contact history.

Conclusions: Tuberculosis infection, disease, and mortality seem to be less common at high than low altitudes. As in Karnali Province, Humla with the second being Jumla has the lowest number of TB patients than other parts of Nepal, affecting younger people.

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(WHO) found an estimated 3% annual reduction in TB incidence though the burden seems to be higher (1.6 times) than previously estimated. According to the survey conducted in 2020 (Nepal), 69000 people developed TB (2018), 17,000 died out of which 32,474 cases were reported and 54% of cases were missed to be diagnosed and treated. The incidence of TB seems to be 245 per 100,000 population (2019) thus to achieve the target of reducing incidence to 20 per 100,000 population by 2050, missing cases should be traced and risk factors contributing to illness and reasons for delay in diagnosis and treatment should be recognized. TB and its forms are classified into three categories: Pulmonary Bacterially Confirmed (PBC), Pulmonary Clinically diagnosed (PCD), and Extra-pulmonary TB (ETB) by the Nepal TB Center (NTC) with the help of the Minister of Health and Population (MOHP) department of health services. Risk factors such as diabetes, alcohol, malnutrition, tobacco smoke, and indoor air pollution impact both individuals and populations to TB infection and disease. Whereas, delay in the diagnosis and treatment spreads the infection, increases the severity of the disease, and results in a higher risk of mortality. The idea that TB might be less prevalent at high altitudes is interesting and has been explored in various scientific studies. The reasoning behind this hypothesis is that lower oxygen pressures at high altitudes might inhibit the growth and survival of Mycobacterium tuberculosis. This is because the bacterium relies on oxygen to reproduce and thrive. At high altitudes, the partial pressure of oxygen (PO2) in the atmosphere is lower compared to lower altitudes. This lower oxygen availability could potentially limit the ability of the TB bacteria to multiply and cause active disease. However, it’s important to note that the relationship between altitude and TB prevalence is complex and can be influenced by various factors, including socioeconomic conditions, healthcare access, and population density. High altitude settings have historically been recommended for protection from TB and there is evidence from many countries which state that an increase in altitude above 1000 m has been associated with a decrease in latent TB infection and morbidity. A study done by Mansoer et al in Kenya revealed that tuberculosis notification rates were strongly associated with altitude. At altitudes of 1000 m or more, the notification rates were less than 30% of those in districts at altitudes below 500 m. Likewise in Nepal, following geographical division, notification rates were found to be lowest in the mountain areas to the North and highest in the terai in the South and rates seem to be higher in older age groups. This study aimed to provide insights into whether altitude played a role in the occurrence of TB and its different forms in this specific region, Jumla, the western rural district of Nepal comparing the findings with the national data.

**METHODS**

**Study Population:** This was an observational, retrospective study conducted in Jumla district of Nepal. Jumla lies in Karnali Province and is a high-altitude mountainous region that ranges from 915m-4679m, with a population of 119,337 (2021) having 8 municipalities (Fig: 1) with various elevations (Table 1).

**Table 1: Elevations of municipalities of Jumla**

<table>
<thead>
<tr>
<th>Municipalities</th>
<th>Elevations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chandannath</td>
<td>2575 m</td>
</tr>
<tr>
<td>Hima</td>
<td>982 m</td>
</tr>
<tr>
<td>Tila</td>
<td>1572 m</td>
</tr>
<tr>
<td>Tatopani</td>
<td>1190 m</td>
</tr>
<tr>
<td>Guthichaur</td>
<td>3667 m</td>
</tr>
<tr>
<td>Sinja</td>
<td>915 m</td>
</tr>
<tr>
<td>Kanakasundari</td>
<td>2801 m</td>
</tr>
<tr>
<td>Patarasi</td>
<td>4097 m</td>
</tr>
</tbody>
</table>

The study area covers all these municipalities of Jumla district and data were collected from the health posts of all the municipalities and the district health office helped us in the data collection process. Ethical clearance was taken from the Institutional Review Committee of Karnali Academy of Health Sciences (KAHS) (Ref No- 079/080/41) which lies in Chandannath municipality.

**Background and adjustment variables:** The data of the people who were diagnosed with TB in any form and were either under an anti-tubercular drug treatment or had completed treatment as per the Nepalese treatment protocol and instructions to fill the record as per the policy were collected. The format
was provided by the Nepal government for collecting the data of TB patients.

Outcome Variable: It will give the prevalence of TB patients and its forms in the Jumla district and compare it with previous data of Jumla and all over Nepal. The prevalence of TB following the geographical distribution of Nepal was then compared with high-altitude regions.

Statistical Analyses: Data were collected from all the municipalities of Jumla district for the fiscal year of 2077/78 (July 15th 2021-July 14th 2022) and were compared with prior 2 years' data of Jumla in number and diagnosis with annual data of Nepal. Data were also compared by the geographical distribution. All the patients had undergone sputum Acid Fast bacilli test and Gen Xpert for the sensitivity testing of the drugs Isoniazid (INH) and rifampicin (RIF) with other routine tests and Chest X-ray before starting the therapy.

Data were entered in Microsoft Excel 2010 and statistical analysis was done in the form of mean, median, and correlation. Data was compared with the previous old data of TB under Provinces, data of high altitude districts were compared with Jumla district data, and previous year data of TB of Jumla district was also analyzed comparing with the national data.

RESULTS

A total of 84 cases were recorded from July 15th 2021-July 14th 2022 from the Jumla district of which mean age was mean ± SD (38.57 ± 21.5) among which 52.4% (n=44) were females. The group affected most was between the age 16-30 years (34.5%) and 61-75yr (22.6%) rest as shown in Table 2.

Table 2. Distribution of TB patients according to age

<table>
<thead>
<tr>
<th>Age</th>
<th>Frequency (n)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-15</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>16-30</td>
<td>29</td>
<td>34.5</td>
</tr>
<tr>
<td>31-45</td>
<td>13</td>
<td>15.5</td>
</tr>
<tr>
<td>46-60</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>61-75</td>
<td>19</td>
<td>22.6</td>
</tr>
<tr>
<td>&gt;75</td>
<td>2</td>
<td>2.4</td>
</tr>
</tbody>
</table>

The cases were mostly detected by the sputum Xpert MTB/RIF testing (54.7%) with positive sputum Acid-fast bacilli cases being 27.4%. Most of the patients were diagnosed to have PBC and rest as shown in Fig 2.

Among them, 12% of people had a history of TB who had undergone ATT (anti-tuberculosis drugs) in the past with 6% having a close contact history. Among them, most of the patients were current smokers (68%) and 32% alcoholics.

Similarly, TB prevalence recorded in Jumla district compared with over the last two years (Fig 3) appears to be increasing.

DISCUSSION

Tuberculosis has remained a public health challenge in Nepal and large numbers of deaths have been reported every year though it’s a preventable and curable disease. Most TB cases were seen among young and productive age groups (15-54 years). In our study too, the most affected age group was 16-30 Years (34.5%), and the second being above 61 years (24%) in the Jumla district for the year 2021/22. Similarly, data for 2018/19 of Nepal also showed that the burden of disease was highest in the age 15 to 24 years and second being age group above 65 years. Females between the ages of 15 to 24 had the highest
TB compared to other age groups and males highest in the age group of more than 65 years.13 Whereas, Kakchapati et al study showed that the incidence of TB was more prevalent in males (M: F), incidence ratio was 1.86 in Nepal.14

The most prevalent form of TB that existed as classified by NTC was PBC, the second being EP which was seen both in Jumla and all over Nepal.13 The trend of PBC cases in the Jumla district seems to be increasing (fig 2) which was comparable with the data of Nepal (fig 3); this might be due to the microscopic positivity rate of the sputum and use of GeneXpert for detection of bacteria. In our study, 54.7% of cases had positive results using GeneXpert resembling the Gurung et al study where positive tests using GeneXpert (5.5%, n= 859/15,637) were significantly higher than sputum microscopy testing 2% (n=120/6309).15 The findings were similar to the data of the whole country of Nepal, which showed an increased rate of yield of MTB cases in GeneXpert (18%) than microscopy positivity rate (5%).13

TB notifications vary with altitude and temperature, the causative agent MTB being a facultative aerobic bacillus, its oxygen consumption and growth slow down by exposure to hypoxia. It replicates more readily at higher temperatures and high airflow in hot conditions provide an environment favourable for the spread of TB.16, 17 Our study center also lies in high altitude which which might be the reason that the low prevalence of TB was seen compared with the other region of Nepal.13 Eisen et al. (2013) reported that among 15 healthy low landers ascending to 3400m and 47 high altitude residents their whole blood in vitro showed reduced growth of a BCG strain of MTB by > 75% while comparing with blood from the lowlanders at sea level.9 Similarly, national data also revealed that only 3% cases were notified in mountain region compared to terai region (59%). The greater number of cases in terai region might be due to high temperature, poor socio-economic status, high density, malnutrition and social deprivation which plays role in spreading TB infection.18 Tamrakulu et al study also highlighted that the incidence of TB was lower in cities of Turkey which were located at high altitude (P < 0.000) and higher in cities with a high population density (P = 0.000).19 Similar findings are seen in study from Vietnam which reveals that tuberculosis notification rate are low in mountainous setting which reflects true low incidence, might be due to low transmission rates or altitude-related differences in pathology.20

Gelay et al study reviewed that risk of TB notification increased with increasing effect of temperature which supports the view that lower altitudes are beneficial for TB transmission, since TB notification declined with increasing altitude as shown by study done in Mexico, Turkey and Kenya.16 It might be due to the ultraviolet ray exposure which has bactericidal effect and 10–12% higher intensity for every 1000 m of elevation leading to higher levels of Vitamin D which might enhance immune response and decrease consequent reactivation of TB. It might also be due to increase production of cells (lymphocytes) in high altitudes which plays an important role in the cure of tuberculosis resulting high degree of immunity.17

Thus, in Karnali Province, Humla with the second being Jumla has the lowest number of TB patients than other parts of Nepal, affecting younger people.2

LIMITATIONS

In this study we only compared the data of Jumla district with the other parts of Nepal though we could not determine the effect of altitude directly as it was a retrospective study.

CONCLUSIONS

Tuberculosis incidence showed a steady decreasing trend, 3% annual reduction but the number of cases was still very high (1.6 times) than previously estimated. Gender differences existed in TB incidence in Nepal. Most prevalent form was PBC due to use of GeneXpert. Higher rates were observed in the Terai Region and urban areas whereas only 3% cases were notified in mountainous region. Tuberculosis infection, disease, and mortality seem to be less common at high than low altitudes. As in Karnali Province, Humla with the second being Jumla has the lowest number of TB patients than other parts of Nepal, affecting younger people

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DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position.

COMPETING INTERESTS

None

REFERENCES


