

The Spatial-Temporal Epidemiology Analysis of Tuberculosis Disease in Pakistan

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Abstract

Despite significant progress, Tuberculosis (TB) remains a severe national health issue in Pakistan. However, very few studies have been done on the spatial-temporal appraisal of tuberculosis in Pakistan. The current research is based on the TB disease dataset obtained from the Pakistan Bureau of Statistics from 2015 to 2019. The study has focused on assessing Spatial epidemiology statistics to measure the TB Incidence rate (IR) (TB cases per 100,000 population) to identify the characteristics variations and spatial-temporal patterns. The global and local spatial autocorrelation detected the clusters of TB disease IR, Male, Female, and total TB patients at the provincial and territorial levels in Pakistan, by the Moran's Index and Local indicator of spatial association (LISA) using GeoDa software and ArcGIS tool. Results show that the IR in Pakistan exhibited a progressive decrease from 2015 to 2018 but showed an unexpected increase in 2019. It is also critically analyzed that the Punjab, Sindh, Khyber Pakhtunkhwa, Azad Jammu Kashmir (AJK), and Federally Administered Tribal Areas (FATA) provinces and territories were at high risk with a higher rate of IR. Despite this, the fact is that the global spatial autocorrelation has not been identified across provincial and territorial levels in Pakistan. In the five-year study, datasets have been observed the individual provinces and territories that indicate negative local spatial autocorrelation of Low-high provinces and territories, such as Balochistan and Islamabad Capital Territory (ICT).

Keywords—Tuberculosis; Incidence rate; Spatial auto-correlation; Temporal trends; Pakistan.

1 Introduction

TUBERCULOSIS (TB) is a life-threatening bacterial infectious disease typically caused by *Bacillus Mycobacterium* [1]. The *Mycobacterium* belongs to the phylum "Actinobacteria". TB classifies into two types active and latent TB. Active TB is symptomatic as well as harmful the contrary latent TB is asymptomatic as well as harmless [2]. There are many symptoms of active TB listed (fatigue, chronic headache, sputum coughing up and sputum with blood, fever, extreme weight loss, night sweat, shortness of breath, swollen glands, and more) [3]. The microbes usually target the lungs, although they can also affect different parts and organelles of the human body such as bone, brain, spine and internal organs, etc. *Mycobacterium* TB bacteria attacks the lungs is called pulmonary

TB and when the infection occurs in any other part except the lungs, it is known as extrapulmonary TB [4]. Many people infected with mycobacteria do develop the disease. It can show symptoms two to three months after infection or years later. However, many people infected with mycobacteria do not develop the disease. Patients with TB disease must take several medications for six months or more. TB patients can spread the infection as long as the patient has been on drugs. Latent TB infected patients provided treatment for usually (three to nine months). A patient with latent TB infection cannot spread the infection to anyone [5, 6]. TB is essentially transmitted through the respiratory plot and TB patients become the primary source of active disease. During speaking sneezing, coughing infected person-produced tiny droplets known as droplet nuclei, and many more sources like food handled by a TB patient, contaminated milk, and common huqqa smoking, etc. Several methods exist to detect TB depending on TB type like (biopsy,

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chest scan, x-ray, interferon-gamma blood test for TB infection, or more). People how were infected with TB within the past two years, health care workers, a person with HIV infection, interaction with the person infected with TB disease, people with weak immunity system at high risk of TB TB disease has existed globally in every country almost within the past two years, which is the reason for morbidity and mortality worldwide. According to the world health organization (WHO), in 2019, 1.4 million people were killed by TB, and approximately 10 million people could be at risk of TB disease. It exists in every age group 5.6 million men, 1.2 million children, and 3.2 million women [1]. Pakistan ranks in 5th place among 30 B high burden countries accounts for sixty percent of the TB cases in the Eastern Region [7-9]. According to National TB Control Program (NTP), approximately four lakh thirteen thousand four hundred and fifty TB cases (all types) arise each year in Pakistan. Epidemic data primarily consist of spatial attributes that have stimulated the curiosity of both epidemical and geographical backgrounds researchers. With the advancement of Geographic Information System (GIS) technology and its approach in epidemiology, spatial Epidemiology is a modern classification of epidemiology [10]. In Spatial Epidemiology, Spatial statistics are used to analyze the spread of endemic diseases. Spatial epidemiology aims to examine the spatial patterns of Homosapien diseases, and health situations, with the help of spatial information and mapping conception. In addition, spatial Epidemiology investigates spatial models to predict spatial and temporal disease trends. All the information mentioned can be applied to track and restrain disease, manage outbursts and provide medical facilities in a research-based way. The current study intends to explain the spatial distribution of TB at the provincial and territorial levels in Pakistan from 2015 to 2019. The study focused on assessing spatial statistics and spatial autocorrelation analysis on TB disease to detect the clustered regions in the country that are on the exposure of the disease at the provincial and territorial levels in Pakistan from 2015 to 2019. This study aimed to investigate, first, the temporal trends in TB incidence rate from 2015 to 2019; second, the Global Spatial Autocorrelation and the Local Spatial Autocorrelation of TB IR across the provincial and territorial level in Pakistan; third, the global and local spatial autocorrelation in male, female, and overall TB across and distinct provinces and territories of Pakistan.; fourth, the overall trend of TB in male, female, and total TB patients.

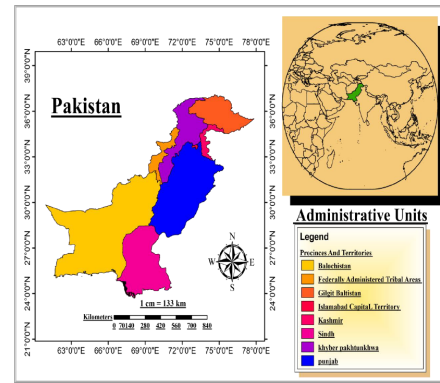


Fig. 1: Map of the administrative units of Pakistan created by ArcGIS (10.3)

2 Methodology

2.1 Study Area

The Islamic Republic of Pakistan is located in the northwestern portion of South Asia. According to the area, it is the 33rd-largest country. Geographically, Pakistan covers a landmass of 881,913km, within the 37°N latitude and 75°E longitude [11]. It is adjacent to India on the southeast, China on the northeast, Iran on the southwest, Afghanistan on the northwest. The study area comprised of 4 provinces (Sindh situated in the southeast, Punjab in the west, Baluchistan in the southwest, and Khyber Pakhtunkhwa in the North-West), Territories (Federally Administered Tribal Areas (FATA) in the northwestern, and Islamabad Capital Territory (ICT) in north-central) and 2 autonomous territories (Gilgit-Baltistan is attached to Azad Kashmir to the south, and Khyber Pakhtunkhwa to the west, Azad Jammu and Kashmir (AJK) is attached to Gilgit-Baltistan, Punjab and Khyber Pakhtunkhwa to the south and west) of Pakistan.

2.2 Data Description

2.2.1 TB Datasets

The National Institute of Health (NIH), Islamabad, Pakistan, is one of Pakistan’s most reputable autonomous organizations. The TB data were collected by the National Institute of Health (NIH), under National TB Control Programme (NTP). The Pakistan Bureau of Statistics published these reports. The TB data for administrative units from 2015 to 2019 were downloaded from the Pakistan bureau of statistics. These data consist of the number of New Sputum Smear Positive, relapse, gender, and the total TB patients for individual administrative units. Further information about the household, age, occupation,

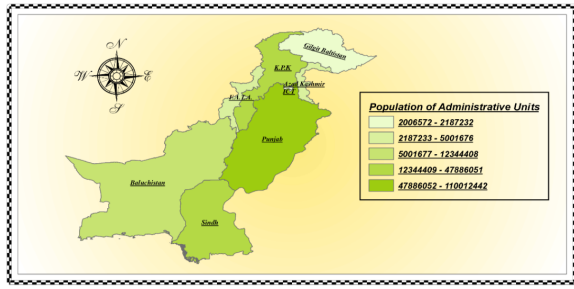


Fig. 2: Map of the population in administrative units of Pakistan

registration date was not mentioned in the reports. Private sector and Public health care facilities data were not included in reports.

2.2.2 Population Data

Pakistan ranked as the world’s 5th most populated country with 212.2 million inhabitants and exceeding with time. Provincial and territorial level population data were obtained from the Pakistan Bureau of Statistics. However, population data is based on the most recent census that ended in 2017 was considered a guide and increased 2.4%, which is the average annual growth rate between 1998 and 2017.

2.3 Methodology

2.3.1 Incidence Rate

In this study, IR represents, identifies, and captures the TB risk in provinces and territories in Pakistan, high and low levels of TB risk, and temporal and spatial clusters. The IR calculated as the new observed figure of TB patients (per 100,000 populaces) using the respective province and territory [12]. This rate is formulated as follows;

$$IR_i = \frac{O_i}{N_i} \times 100,000 \quad (1)$$

Where O_i and N_i are the new figure of TB patients and total populace in i^{th} province and territory each year correspondingly.

2.3.2 Spatial Auto-correlation Analysis

Spatial autocorrelation, known as the attribute values is being calculated is self-correlated and the correlation is attributable to the geographical collation of objects [13]. Spatial autocorrelation is categorized into 3 spatial forms: positive spatial autocorrelation appears when surrounding regions have similar values, negative spatial autocorrelation appears when surrounding regions have dissimilar values, and no spatial autocorrelation appears when surrounding regions has random

values. Thus, spatial autocorrelation can be a great method to analyze how spatial patterns change with respect to time.

Global spatial autocorrelation is used to calculate the autocorrelation of TB across the country. Moran’s I statistics is used to perform the Global Autocorrelation of TB IR in Pakistan from 2015 to 2019 [14-16]. The first stage in the spatial autocorrelation study is to create a spatial weight matrix that reflects the geographic neighbouring correlation among spatial provinces and territories. The w_{ij} is the binary spatial weight matrix, which is expressed as follows;

$$w_{ij} = \begin{cases} 0 & f_i \text{ is adjacent to } f_j \\ 0 & \text{otherwise} \end{cases} \quad (2)$$

Where w_{ij} representing the adjacent spatial correlation between different provinces and territories f_i and f_j .

- If f_i shares common boundaries and vertexes with f_j , w_{ij} is equal to 1.
- If f_i does not share any boundaries and vertexes with f_j , w_{ij} is equal to 0.

Moran’s Index is a well-known method for testing global spatial autocorrelation. The range of Moran’s Index lies from -1 to 1 [17-19].

- If $I > 0$, it would show positive autocorrelation
- If $I < 0$, it would show negative autocorrelation
- If $I = 0$, it would show no autocorrelation

The global Moran’s I formulated as follows:

$$I = \frac{n \sum_{i=1}^n \sum_{j=1}^n w_{ij} (y_i - \bar{y})(y_j - \bar{y})}{\sum_{i=1}^n (y_i - \bar{y})^2 \sum_{i=1}^n \sum_{j=1}^n w_{ij}} \quad (3)$$

Where n represents the number of provinces and territories, the values of TB (IR, Male, Female, and total TB patients) represented as y_i and y_j of the spatial provinces and territories i and j , the average value TB (IR, Male, Female, and total TB patients) of all provinces and territories represented as \bar{y} . The hypothesis testing of Moran’s I statistics carry out as follows:

- The null hypothesis (H_0) states that: no spatial autocorrelation
- The alternative hypothesis (H_1) states that: positive autocorrelation or negative autocorrelation.

Determine the test value by Z-score;

$$Z(I) = \frac{(I - E(I))}{\sqrt{Var(I)}} \quad (4)$$

Local spatial autocorrelation of TB calculates the autocorrelation of each province and territory individually. LISA is used to perform the local autocorrelation of TB (IR, Male, Female, and total TB patients) in Pakistan from 2015 to 2019. LISA is the local form of

the global Moran’s Index. LISA indicates the level of autocorrelation at the local scale. LISA is categorized into four Following categories [20, 21] such as;

- **High-High:** when, the province and territory with high (IR, Male, Female, and total TB patients) are neighboring for both provinces and territories with high IR.
- **Low-High:** when, the province and territory with low (IR, Male, Female, and total TB patients) are neighboring for provinces with high and territory with low IR.
- **Low-Low:** when, the province and territory with low (IR, Male, Female, and total TB patients) are neighboring for both provinces and territories with low IR.
- **High-Low:** when, the province and territory with high (IR, Male, Female, and total TB patients) are neighboring for low and territory with high IR.

LISA formulated as follows;

$$I_i = \frac{(y_i - \bar{y})}{(\frac{1}{n} \sum_{i=1}^n (y - \bar{y})^2)} \times \sum_{j=1}^n w_{ij}(y_j - \bar{y}) \quad (5)$$

where n is represent as number of provinces and territories, the values of (IR, Male, Female, and total TB patients) represented as y_i and y_j each of the spatial provinces and territories i and j , the average value of TB (IR, Male, Female, and total TB patients) of all provinces and territories represented as \bar{y} , and w_{ij} is the binary spatial weight matrix.

Determine the test value with the Z-score:

$$Z(I) = \frac{(I_i - E(I_i))}{\sqrt{(Var(I))}} \quad (6)$$

Positive I_i shows the level of the TB incident is indistinguishable to the neighboring provinces and territories (H-H and L-L), negative I_i shows the level of the TB incident is distinguishable to the neighboring provinces and territories (H-L or L-H) and I_i is approaching zero, which means the TB incident is random.

3 Results & Discussion

3.1 Spatial and Temporal Distribution

The Spatial distribution of average IRs for individual province and Territory in Pakistan from 2015-2019 in Figure 3 were examined by equation (1). The Natural Break Method is applied to aptly cluster similar IR values from the TB data set divided the IRs into five individual groups, and the color signifies the average IR of TB from 2015 to 2019. The average IRs were largest in Punjab (79.813 per 100,000 population) and

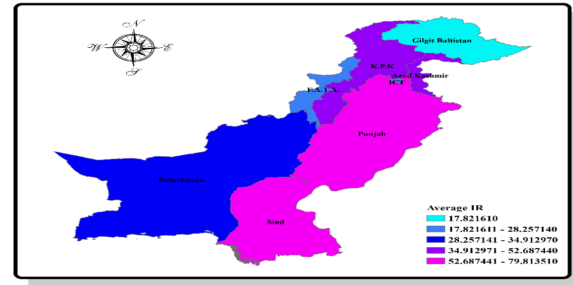


Fig. 3: Map of average IRs of TB from 2015 to 2019 at the provincial and territorial level of Pakistan

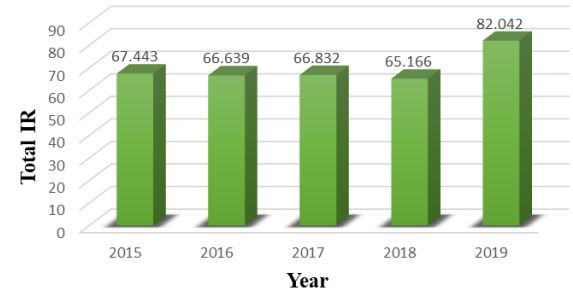


Fig. 4: The average IRs of TB overall across the provinces and territories of Pakistan from 2015 to 2019

Sindh (69.119 per 100,000 population), the average IRs was 2nd largest in Khyber Pakhtunkhwa (49.965 per 100,000 population), the average IRs were mid-range in Baluchistan (34.912 per 100,000 population), the average IRs of TB were 2nd smallest Federally Administered Tribal Areas (FATA) (28.198 per 100,000 population), the average TB IRs were smallest in Gilgit-Baltistan (34.912 per 100,000 population). The average IRs of TB across the provinces and territories of Pakistan from 2015 to 2019 in Figure 4 indicated a downward trend from 2015-2018 but suddenly showed an upward trend in 2019. Figure 5 indicated the highest incidence notifications were in Punjab, Khyber Pakhtunkhwa, Sindh, Azad Jammu Kashmir, and FATA provinces and territories. The dark red color highlighted the burden. On the other hand, the amount of notification in Balochistan, ICT, and Gilgit-Baltistan were not significantly shown by light pink color.

3.1.1 Spatial Autocorrelation Analysis

Table 1 shows the result of spatial autocorrelation by processing equations (2-4). on the data set of (IR of TB patients, Male, Female, and Total TB patients) registered in five years. The Global Moran’s I method illustrated negative values in all data sets of TB cases, which specify there was no autocorrelation under in-

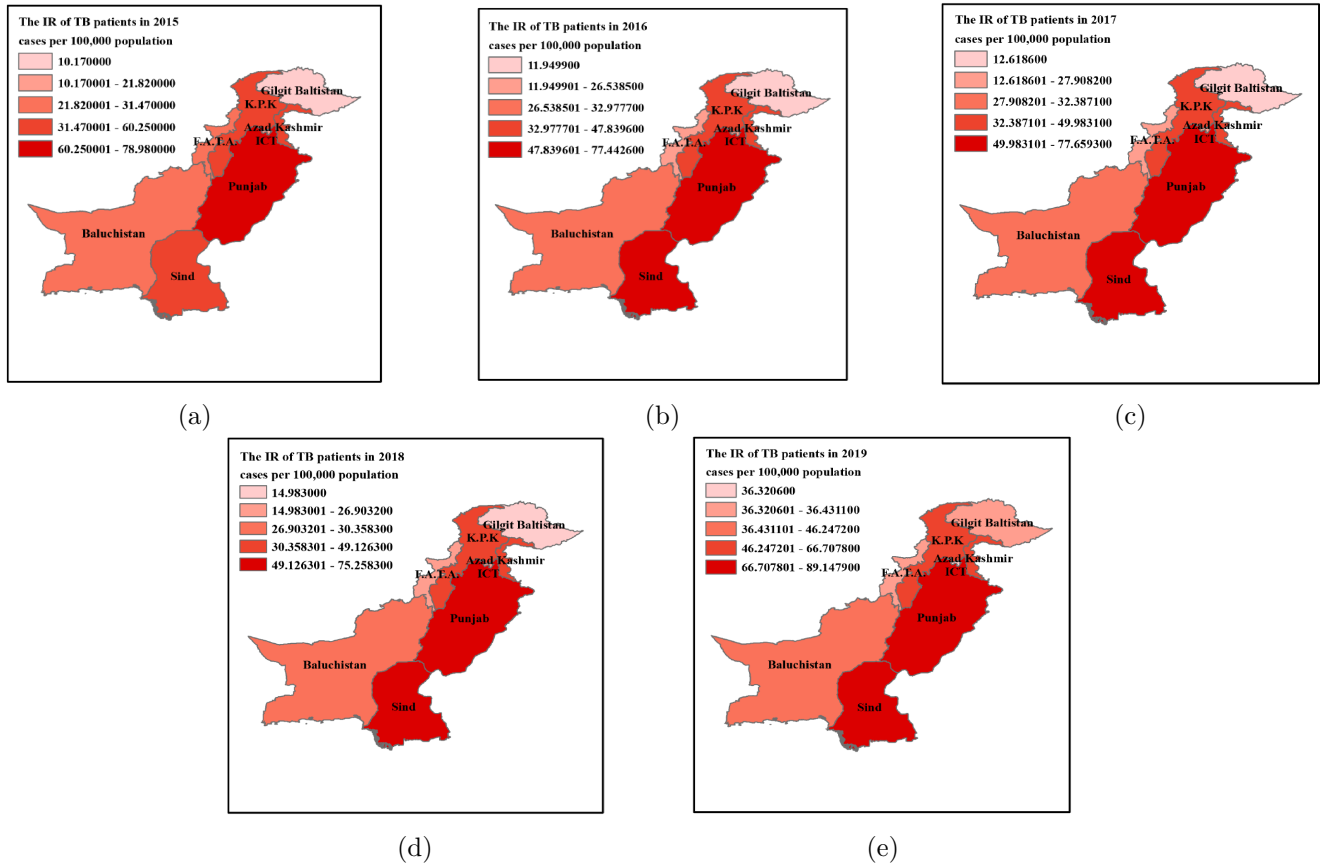


Fig. 5: Spatial distribution of incidence rate of TB cases (per 100,000 population) by each province and Territory in Pakistan from 2015 to 2019

vestigation and indicated the incidence of TB was spread randomly from 2015 to 2019. Furthermore, the p-value was ($p = 0.248$) the lowest value in all data sets and was failed to pass the significance level test also exposes the neighboring regions to have dissimilar values. Figure 6 presented the results of local spatial autocorrelation by applying equatins (5,6) the LISA method on all the datasets mentioned above. Figure 6 (a) the maps of the LISA cluster depicted Balochistan and ICT province and territory were low high province and territory in 2015, showing that the IRs of Balochistan and ICT were Low and were sharing the border with high IR provinces and territories. In 2018 Balochistan province was low high, showing that the IRs of Balochistan share the border with high IR provinces and territories. Maps of LISA in 2016, 2017, and 2019 have no significant and clustering phenomena. Figure 6 (b) illustrates the results of LISA on male TB patients' cases. In the study period (2015, 2016, 2017, 2018, and 2019), the maps of LISA showed Balochistan and ICT province and territory were low high provinces and territory presenting that the male TB cases in Balochistan and ICT were Low and were sharing the

border with the high influx of male TB cases provinces and territories. In 2016 Punjab province was high low, representing that the male TB cases in Punjab share the border with high male TB cases in provinces and territories. Figure 6 (c) and Figure 6 (d) display the LISA results using female TB cases and total TB cases in the five years of the study period. In both TB cases (female and total), LISA has given the same results that the Balochistan and ICT province and territory were low high provinces and territory that the female and total TB cases in Balochistan and ICT were Low and were neighboring with high (female and total) TB cases provinces and territories. The provinces and territories filled in with the color grey didn't represent Local Spatial Autocorrelation and displayed the distribution of TB were random. Annual reports of I_t in each year was negative in categories of TB and showed that the regions have dissimilar values to their surrounding regions.

3.2 Annual Trends Analysis of Tuberculosis

The current analysis interprets the annual increasing and decreasing trends of TB occurrence each year in

| | Year | 2015 | 2016 | 2017 | 2018 | 2019 |
|-----------------------|-----------|-----------|-----------|-----------|-----------|-----------|
| TBIR | Moran's I | -0.246772 | -0.155608 | -0.134823 | -0.135090 | -0.151578 |
| | Z-score | -0.506025 | -0.062522 | 0.039326 | 0.037443 | -0.041057 |
| | P-value | 0.612839 | 0.950147 | 0.968631 | 0.970132 | 0.967251 |
| Male positive cases | Moran's I | -0.230604 | -0.251099 | -0.254887 | -0.264497 | -0.277123 |
| | Z-score | -0.579726 | -0.775810 | -0.825428 | -0.919533 | -1.033170 |
| | P-value | 0.562099 | 0.437861 | 0.409129 | 0.357817 | 0.301525 |
| Female positive cases | Moran's I | -0.289484 | -0.275478 | -0.266216 | -0.263475 | -0.250836 |
| | Z-score | -1.132495 | -0.997304 | -0.925106 | -0.887395 | -0.744283 |
| | P-value | 0.257426 | 0.318617 | 0.354911 | 0.374866 | 0.456705 |
| Total positive cases | Moran's I | -0.283166 | -0.287053 | -0.260342 | -0.257059 | -0.240483 |
| | Z-score | -1.082238 | -1.153423 | -0.873246 | -0.828985 | -0.657442 |
| | P-value | 0.279147 | 0.248737 | 0.382529 | 0.407113 | 0.510896 |

TABLE 1: Summary of spatial autocorrelation by using Moran's I method on TB at provincial and territorial levels in Pakistan

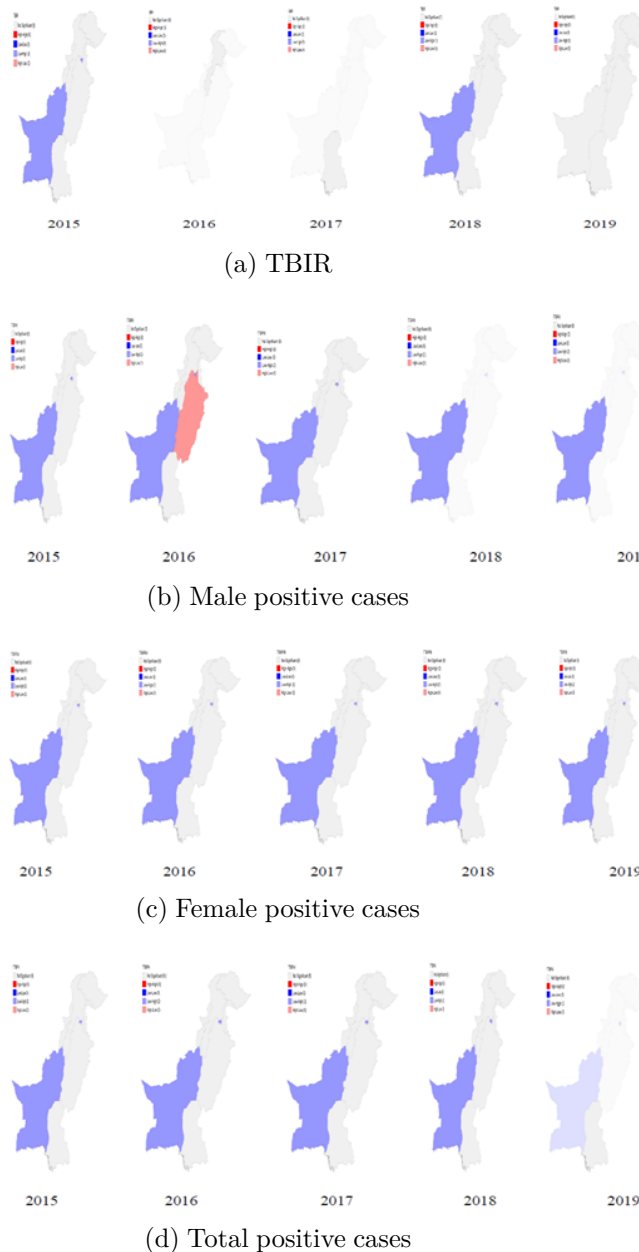


Fig. 6: LISA maps of Pakistan from 2015 to 2019

Pakistan from 2015 to 2019, categories into (male, female, and total positive cases). Figure 7 provides a detailed summary of TB cases in all data sets in individual provinces and territories. Punjab and Sindh provinces demonstrated the inclined waves with the high number of TB cases registered during five years of the study period concurrently Baluchistan, Khyber Pakhtunkhwa, Gilgit-Baltistan, FATA, ICT, and AJK provinces and territories displayed declined waves. In Figure 8, the bar arbitrated and amplified the possible look of TB cases in males and females. The graph presents the overall trend of TB among males, females and the total number of cases registered during five years. The bar expressed male, female, and the total number of TB cases was up high in the year 2018 and were low in 2015. Thus, the bar of male TB patients is slightly higher than female TB patients in the study interval. But male TB patients' bars were showed their low in 2015, and female TB patients were down in 2019.

4 Conclusion

This study examined the spatial-temporal evolution of tuberculosis in (IR of New TB patients, Male, Female and, Total TB patients) at the provincial and territorial level in Pakistan from 2015 to 2019 using ArcGIS tools, MS-Excel, and GeoDa software. The result displayed the IR of Pakistan unveiled a progressive decrease from 2015 to 2018 but showed an unexpected increase in 2019. There was no evidence of Global Spatial Autocorrelation all over Pakistan. There was negative Local Spatial Autocorrelation at the provincial and territorial levels, with Balochistan and ICT as the low-high provinces and territories throughout a five-year study period. Therefore, the health controller must closely adhere to preventative policies. To establish guidelines for the distribution

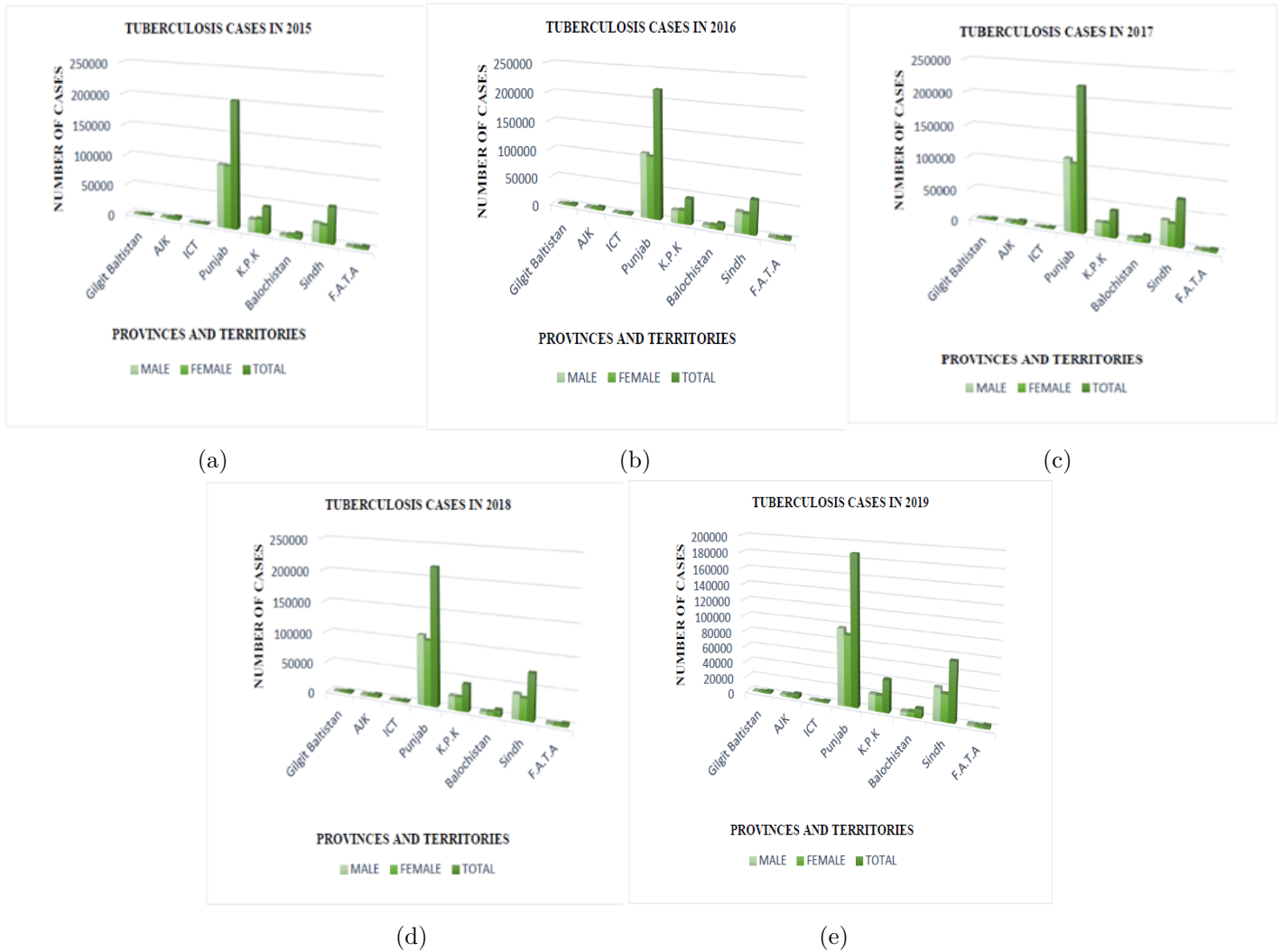


Fig. 7: Annual trends of tuberculosis in Pakistan

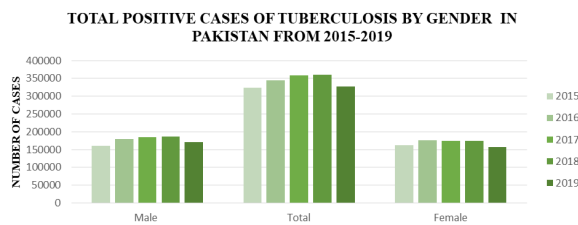


Fig. 8: graph of total positive cases of TB by gender in Pakistan from 2015-2019

of national health resources and to shape up health-related strategies. Provide education to TB patients related TB and guide them how to take their TB medications correctly, make sure that the vaccine name Bacillus Calmette-Guerin (BCG) should be provided to infants and children. Government responsibility and management, as well as monitoring and review of TB patients also the implementation of the strategy and

goals at the country level, with international partnership will help to control TB perversion. This study solely looked at the causes of TB distribution patterns qualitatively. Due to data limitations, detecting the latent components that lead to distribution features is difficult at this point. These limitations can be examined in the future, and further research is recurred to identify the risk aspect.

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