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Tuberculosis Mortality Hotspot Identification Tool

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Abstract : For more than a decade, tuberculosis (TB) has been the leading cause of death from a single infectious disease in Malaysia. The 2020 milestone of End TB Strategy of reduction of TB deaths by 35% compared to 2015 was not achieved by Malaysia. Instead the number of TB deaths reported in 2020 increased by 37% at national level and by 21% at state level of Selangor compared to their 2015 records. Spatial epidemiology has become indispensable in disease surveillance in developed countries. A tool to identify the Hotspots of TB mortality in Selangor state was developed in this research in alignment with the government's strategy of intensifying research and innovation as priority issues in TB control under its National Strategic Plan (NSP) for Tuberculosis control (2016-2020). The use of population in the denominator enhanced the original TB distribution maps making them more robust and standardized. The knowledge gained from this can be used by health policymakers to make more informed decisions about resource allocation, type of control and, or interventions, and specific targeted areas. As a result, the existing TB burden will be reduced. Other states can then incorporate successful TB control programmes in Selangor by deploying GIS alongside their existing TB control programmes.

Keywords: Tuberculosis, Mortality, Geographical Information System

1. Introduction

Tuberculosis (TB) is a chronic air-borne infectious disease caused by bacillus *Mycobacterium tuberculosis* and usually affects the lungs. TB is a curable and preventable disease however it is still one of the main cause of mortality and ill-health globally [1]. There is one new TB case every 4 seconds and more than 2 TB deaths every minute in the world [2]. The progress in provision of essential TB services and reducing TB disease burden was severly hampered by the recent Covid-19 pandemic. The

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number of people newly diagnosed and reported decreased from 7.1 million in 2019 to 5.8 million in 2020. Reduced access to TB diagnosis and treatment during the Covid-19 pandemic has led to an increase in the TB deaths across the globe [1]. Malaysia is currently not in the list of the 30 high TB burden countries but geographically is a neighbour to few of them (Indonesia, Thailand, Philipines, Cambodia and Vietnam). In 2020, Malaysia was reported to have TB incidence rate of 72.57 per 100000 population and TB mortality rate of 7.12 [3]. The TB mortality rate in Malaysia has increased from 5.56 per 100000 population in 2015 to 7.12 per 100000 population in 2020 [3,4]. The 2020 milestones of the End TB strategy were not met by Malaysia as seen in the **Table 1**. Instead of the reduction in the number of TB deaths by 35% in the year 2020 compared to 2015 baseline, Malaysia had an increase in the number of TB deaths by 36.8% at national level and 21% at the state level of Selangor and is above the 2020 milestone of less than 3 per 100000 population of the End TB Strategy [1]. Malaysia also could not meet the target of more than 90% of TB treatment success rate for both Malaysian and Non-Malaysian citizens. Lastly, the TB mortality rate in Malaysia was higher than the target of 3/100000 population both at national and state level in the year 2020.

Table 1: Current Malaysian TB situation

Indicators	2020 Milestones		Malaysia [3]	Selangor [6]
	WHO target[1]	MOH target[5]		
Reduction in the number of TB deaths compared with 2015	35%	25%	36.8%	21%
Reduction in the TB incidence rate compared with 2015	<85/100000		72.57/100000	74.81/100000
TB treatment success rate	>90%	90%[1]	78.3%[1]	69.5%[1]
		75%[2]	77%[2]	55.7%[2]
TB mortality rate	3/100000	≤5/ 100000	7.12/ 100000	7.18/ 100000

TB= tuberculosis, WHO= world health organization, MOH= Ministry of Health , Malaysia, [1]= Malaysian citizen, [2]= Non-Malaysian citizen

TB has remained among the top 5 communicable diseases and a leading cause of death from infectious diseases in Malaysia for more than 2 decades [7]. Selangor is one of the most populous and urban state of Malaysia [8]. Selangor state has the highest number of TB cases in the peninsular and three of its districts namely Hulu Langat, Gombak and Sabak Bernam had TB incidence of 94/100000, 93/100000 and 86/100000 respectively which is higher than the national TB incidence rate of 79.45 per 100000 population [9,10]. Urbanization favours TB transmission [11] and 76% of Malaysia is urban [12]. TB remains a serious public health problem not only in Malaysia moresoever in the state of Selangor as well as it accounts for $1/4^{th}$ of the total population of the country [8]. Geographical Information System (GIS) has proved its merit as an effective epidemiological tool in other developed countries [13,14]. There is scarcity of literature on use of GIS to understand the TB distribution and TB hotspots in Malaysia.

This study was conducted in alignment with the National Strategic Plan (NSP) for Tuberculosis control (2016-2020) to intesnsify the research and innovation as priority issues in TB control. The tool was developed to identify not only the hotspots of TB but also hotspots of TB mortality in the Selangor state. The knowledge obtained from this study could help the policy makers, researchers and practitioners to formulate more targeted and sound strategies to reduce TB mortality.

2. Materials and Methods

This was a cross-sectional study conducted in Selangor state of Malaysia. Selangor, is one of the 14 states in Malaysia which is spread across 7,931 km^2 of area and had total population of 6.29 million (3.27 million males; 3.02 million females) in 2021 [8]. It is located in the middle of the west coast of Peninsular Malaysia and is divided into nine districts comprising of [16]. The population consists of a majority of Malays (52.24%), followed by the Chinese (25.52%) and Indians (12.12%) [8].

2.1 Materials

The ethical approval was obtained from the National Medical Research & Ethics Committee, Ministry of Health Malaysia (NMREC) with the reference number NMRR-14-1956-22325. The study population was the tuberculosis patients registered into Malaysian National Tuberculosis Information System (MyTB) in Selangor from 1st January 2014 till 31st December 2017.The information on population demographics for the sub-district level of Selangor for the duration 2014-2017 was obtained from the Department of Statistics, Malaysia.

2.2 Methods

All TB cases registered with the State Health Department of Selangor for the duration of 2014-2017 were then scanned for the inclusion and exclusion criteria and only those which met the inclusion criteria were then included in the analysis of this study. The inclusion criteria was as follows

a) All new cases of TB patients (age > 18 years) registered for TB treatment in the state TB registry of Selangor from 1 January 2014 till 31 December 2017.
b) For patients who were registered more than once in the year for treatment due to default, relapse, or treatment failure, only the first instance will be considered and the rest will be excluded from the study.

The exclusion criteria was as follows:

a) The patients whose treatment outcomes were missing (missing data and outcome unknown) in the state TB registry of Selangor from 1 January 2014 till 31 December 2017.
b) The patients who did not have proper address in the state TB registry of Selangor from 1 January 2014 till 31 December 2017.

The TB data from JKNS was extracted to excel sheets (in accordance to the Standardized Data Collection Form) and cleaned. The excel sheet of Phase I data was converted into a comma separated values (csv) file and them added into the ArcMap 10.7.1. The addresses of the TB patients were entered in the ArcMap as multiple fields such as address, city, district, state, country and zip code and geocoded using the tool "geocode addresses". The tied and unmatched addresses were rematched by picking a point location on the map. The geocoded addresses were then added to the map of Selangor which was obtained from the department of Survey and Mapping, Malaysia (JUPEM). The geocoded addresses were validated as the points were within the boundaries of the Selangor state for each of the four years (2014-2017). Five points which fell in the region outside Selangor state were excluded from the study. The TB incidence rate was defined as per WHO [17] and MOH [18] guidelines which defined incident cases as inclusive of new and relapse cases of TB as shown in the **Eq. 1**.

$$TB\ Incidence\ Rate = \frac{Number\ of\ incident\ TB\ cases\ in\ a\ year}{Population\ in\ the\ same\ year} \quad X\ 100000 \qquad \boldsymbol{Eq.1}$$

The TB mortality rate was calculated as per the guidelines of MoH [18] as shown in the **Eq. 2**.

$$TB\ Mortality\ Rate = \frac{Number\ of\ TB\ deaths\ in\ a\ year}{Population\ in\ the\ same\ year}\ X\ 100000 \qquad \boldsymbol{Eq.2}$$

The data after cleaning was geocoded using the Arc-GIS software (version 10.7.1) and subsequently data sheet was created in the Arc Map. The process involved in developing the hotspot maps of TB mortality is depicted in **Figure 1**. The spatial attributes were created followed by geostatistical analysis and the final outcome was standardized TB hotspot and TB mortality hotspot maps.

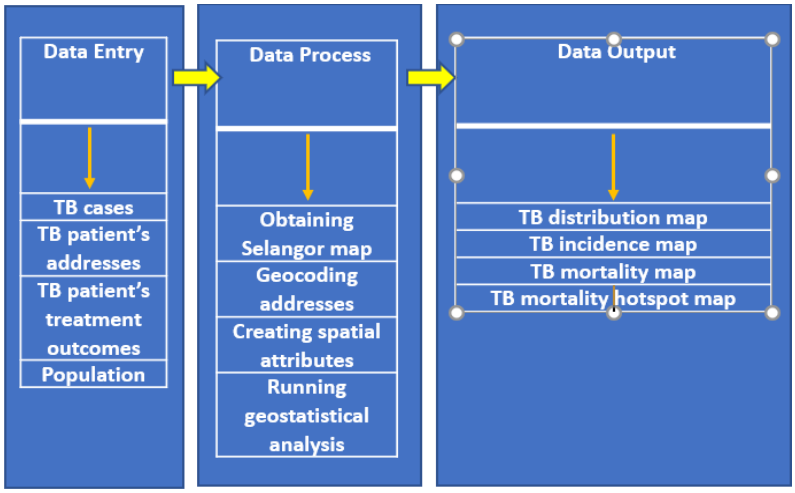


Figure 1: Flowchart of developing the Hotspot maps of TB mortality

2.3 Geostatistical Analysis

The method selected for spatial autocorrelation was Moran's Statistics, as this method retains the interval values of the data in its calculation and thus retaining all the information [19]. The null hypothesis (H_0) was that there is no spatial autocorrelation between TB mortality and the districts of Selangor, Malaysia. The alternative hypothesis (H_1) was that there is spatial autocorrelation between TB mortality and the districts of Selangor, Malaysia (clustered, dispersed or not random). The test of significance of the spatial autocorrelation was carried out under randomization sampling because we are considering the situation in the study area only. The Moran's coefficient I was calculated using the formula shown in **Eq. 3**.

$$I = \frac{n\sum_{i=1}^{J}(x_i - \bar{x})(x_j - \bar{x})}{J\sum_{i=1}^{n}(x_i - \bar{x})^2} \qquad \textbf{\textit{Eq.}}\ \mathbf{3}$$

where n is the total number of areas, J is the total number of joins, xi and xj are the values of the attribute variables for two contiguous areas and $\bar{x}$ is the mean of all the x values. The critical values were -1.96 and +1.96 as the significance level was 0.05. Since the test statistic, z falls outside the critical region the null hypothesis was rejected. There was spatial autocorrelation between TB mortality and the districts of Selangor, Malaysia (clustered, dispersed or not random). The values of Moran's I range between -1 and +1, with 1 for maximum positive association. Higher positive value indicates a stronger spatial autocorrelation. The z-score evaluates the significance of the estimate of the Moran's I. A disease is regarded spatially aggregated and statistically clustered if the Moran's I > 0 and Z-score >1.96. The Hotspot analysis was carried out further as the spatial autocorrelation showed clustering distribution in the previous test using Getis and Ordi (Gi*) statistics. The Getis Ordi statistics only assess positive spatial autocorrelation and a Gi value of ≥ 1.96 indicates that the district i and its neighboring districts have a TB prevalence rate that is statistically different (higher) than other districts. District i is the centre of that area with higher TB prevalence rate and is defined as a TB hotspot. The Getis-Ord statistic distinguished between hot and cold spots whereby the hot spots are places where the high values cluster while the cold spots are those where low values cluster. The Gi z-score test defines cluster at 90% CI, 95%CI and 99% CI in correspondence to the values of Gi z-score test ± 1.56, ± 1.96 and ± 2.58 respectively. A cluster is a hot spot when Gi z-score ≥ 1.56 but cold spot when Gi z-score ≤ -1.56.

3. Results and Discussion

3.1 Results

The first maps developed using this tool were TB distribution maps followed by hotspots maps of TB and TB mortality. However upon discussion with the State Health Department of Selangor, it was noticed that these maps were not useful as they were based on the number of TB cases which reflects the areas with higher population as the hotspots of the disease. Therefore, standardization was carried out and hotspot analysis was carried out on TB incident cases which reflected true picture of TB transmission in the area. Subsequently hotspot maps of TB and TB mortality were developed. The conceptual design of TB mortality hotspot identification tool is depicted in **Figure 2** whereby the map of Selangor can be seen at the sub-district level in the Arc-map. The marked areas of Kuala Lumpur and Putrajaya were not included in the study as they are not part of the Selangor state.

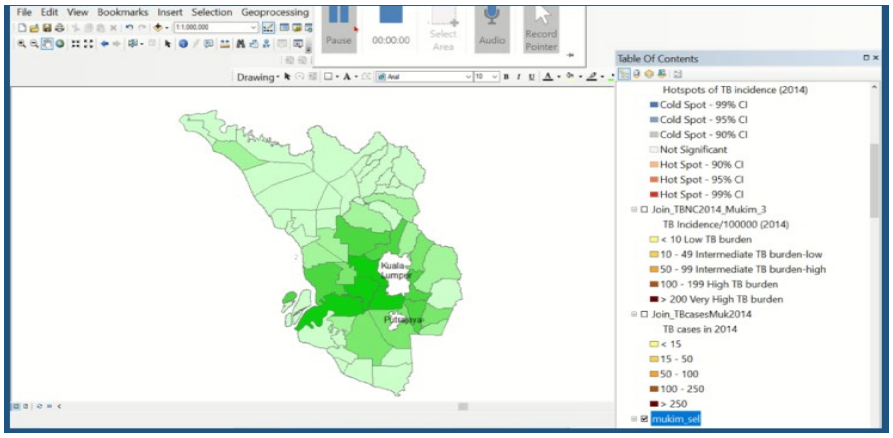
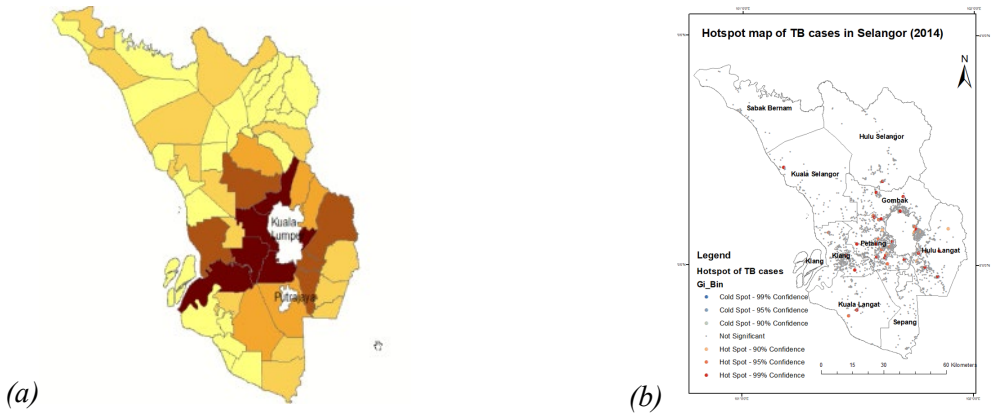


Figure 2: Conceptual Design of the TB mortality Hotspot Identification Tool

Figure 3 shows the TB distribution map which later produced false TB mortality hotspot as the hotspots coincide with the high population areas of Selangor.

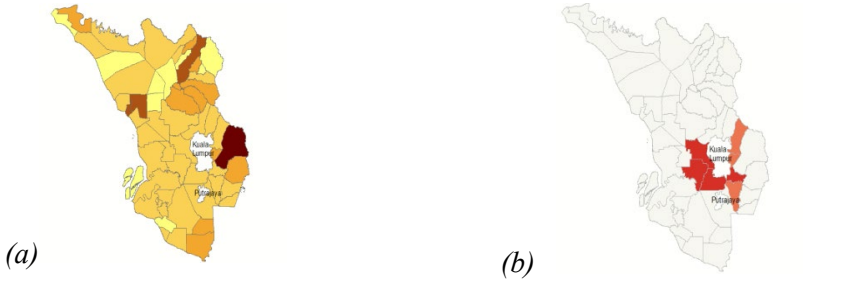


(a) TB distribution map

(b) TB Hotspot map based on TB cases

Figure 3: TB mortality Hotspot maps based on TB distribution where a) TB distribution map and b) TB Hotspot map based on TB cases

The standardized TB maps of TB incidence and subsequent TB hotspot maps based on TB incidence are shown in **Figure 4**.



(a) TB incidence map

(b) TB mortality Hotspot map based on TB incidence

Figure 4: TB mortality Hotspot maps based on TB incidence where a) TB incidence map and b) TB Hotspot map based on TB incidence

3.2 Discussions

The TB incidence rate of Selangor fluctuated over these four years and ranged between 70.20 and 75.85 per 100 000 populations. Incidence rate of a disease represents the actual risk of disease transmission of the disease in the population and its universal unit of per 100 000 population makes it easier for comparison with studies conducted elsewhere. The heterogeneity in the TB incidence rate at district level of Selangor implied that certain districts were faring better in terms of TB disease burden compared to others. So even though, the districts of Petaling and Hulu Langat were noted to have highest number of TB cases, the TB incidence rate was highest in the district of Gombak for each of the four-year ranging from 83.85 - 96.13 per 100 000 population. This TB incidence rate is even higher than the national TB incidence rate of Malaysia which was 82.10 per 100 000 population in 2014 and 80.78 per 100 000 population in 2017 [4, 20]. The spatial distribution of TB cases in Selangor state at sub-district (mukim) level also showed higher number of TB cases in the central region of the state. Six mukims which were identified to have very high (>250 TB cases) TB cases in each of the 4 years were Kelang, Damansara, Petaling, Sungai Buloh, Batu and Ampang. The mukim of Kajang was noted to have very high (>250 TB cases) TB cases only in the year 2014. The mukims with very low (<15 TB cases) TB cases in all the 4 years were distributed along the northern and western regions of the Selangor state. The proximity of the mukims to the Federal Territories makes them a more likely hub of internal immigration for people from other states, districts and mukims for trade, business, education, work related to government offices, tourism and entertainment [21].

The TB incidence was between 50-99 per 100000 population in almost all the districts of Selangor for the study period with exception of three districts namely Sabak Bernam, Kuala Selangor and Sepang which had TB incidence of 10-49 per 100000 population. The sub-district of Hulu Langat was identified as to have TB incidence of >200 per 100000 population in Selangor in each of the four-year study period. Majority of the sub-districts had TB incidence of 50-99 per 100000 population in Selangor in each of the first three years but then improved to 10-49 per 100000 in 2017. This reflects of successful efforts of the TB prevention and control programs in these areas. However, the TB patients need more close monitoring in Hulu Langat, Hulu Semenyih, Pasangan and Kerling sub-districts. The TB mortality >200 cases were located in the central districts (Petaling, Hulu Langat, Gombak and Klang) and central western sub-districts (Klang, Damansara, Petaling, Sungai Buloh, Hulu Langat and Ampang). The areas identified with high TB incidence are all noted to have high population density compared to the other areas of Selangor. Overpopulated areas increase the risk of TB transmission [22-25].

Seven hotspots (Sungai Buloh, Damansara, Petaling, Kajang, Cheras, Ampang and Hulu Kelang) of TB incidence were identified mainly in the central and eastern regions of Selangor district encompassing both the Federal Territories of Kuala Lumpur and Putrajaya in each of the four-years. However, Hulu Langat and Hulu Semenyih were TB incidence hotspots only in the year 2015 and 2017.

It was noted that these eight mukims comprised of half (52.93%) of the total population of Selangor in 2017. The hotspots of TB mortality among TB incidence cases were located in the central eastern region from 2014 till 2016 but changed to central western regions in the year 2017. This could be explained by the improved TB care in the sub-districts of Hulu Kelang, Hulu Semenyih, Semenyih and Sabak Bernam. This also implies that hotspots delineated at smaller unit scales are better. This spatial heterogeneity of the hotspots can be explained by the fact that the hotspots had higher population compared to the coldspots. The mukims identified as hotspots are among those with good infrastructure and healthcare services in place. These findings may be due to better accessibility to diagnostic services/ healthcare services in the areas being in close proximity to the capital city as also seen in the study conducted in Grande Comore, The Comoros [23]. The previous studies conducted in Malaysia have identified the two Federal Territories of Kuala Lumpur and Putrajaya as the areas with very high risk of TB [26]. TB being an airborne disease can be easily transmitted to those within close proximity and this can explain the hotspots in the mukims neighbouring the Federal Territories. To reverse the TB epidemic, many municipal authorities since 2014 have become part of Zero TB Cities Project, whereby they support their local communities to move to zero deaths as opposed to the central/ national government [27].

Hotspots created using Global Moran's I and Getis Ordi Statistics is novel as the previous maps have been created using other geostatistical methods in Malaysia. No published maps for TB mortality hotspot maps for Selangor at sub-district level in the literature are available. It offers a cheap, easy and fast depiction of large data that can be visualized and understood better. It provides insight into the areas where the TB prevention and control strategies should be targeted. This tool provides standardized maps as it was based on TB incidence cases making the findings more robust. This tool provides a convenient and reliable method to identify the hotspots of TB mortality. This tool has commercial potential to the following industry in Malaysia: National TB Department, Institut Perubatan Respiratori (IPR), State TB Department, Distric TB Department, Public Health Department.

4. Conclusion

The sub-district of Hulu Langat had highest TB incidence in each of the four-year study period making it a region with high TB transmission. Spatial analysis revealed that the hotspots of TB mortality were identical to hotspots of TB incidence and were located in the central region of Selangor encompassing the federal territories of Kuala Lumpur and Putrajaya. GIS provides an additional tool to the existing surveillance mechanism. It has huge potential in guiding the national TB programs to execute effective TB control interventions. This tool can be further used to develop TBGIS portal for more accurate and live detection of TB hotspots in the future.

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