Trend analysis and seasonality of tuberculosis among patients attending Hiwot Fana Specialized University Hospital, Eastern Ethiopia: A retrospective study

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Abstract

Background : Tuberculosis (TB) is a worldwide public health threats caused by *Mycobacterium tuberculosis* in which about 10.0 million people globally infected in 2017. It is one of the top 10 leading killer diseases in the developing countries, particularly in Sub-Saharan Africa including Ethiopia. However, limited studies are available on seasonal variation and level of tuberculosis notifications in Ethiopia. Thus, the aim this study was to determine the prevalence, trend and seasonality of tuberculosis. **Methods:** A hospital-based retrospective study was conducted by reviewing all available patients' data from January 2015 to April 2019 at Hiwot Fana Specialized University Hospital. Socio-demographic characteristics and results of the GeneXpert assay were taken from the registration book. The data were entered into EpiData 3.1 and analyzed by using the Statistical Package for Social Sciences (SPSS) version 20. Bivariate and multivariate analysis with a 95% confidence interval was undertaken to check the association between prevalence of tuberculosis and dependent variables. **Result:** From a total of 8001 samples tested for Genexpert, the overall prevalence of *Mycobacterium tuberculosis* and rifampicin resistance was found to be 1,254 (15.7%) and 53(4.1%), respectively. Trend of tuberculosis proportion was downwardly decreased from 19.3% in 2015, 18.6% in 2016, 18.4% in 2017, 13.5% in 2018 to 13.0% in 2019 (P- value < 0.001) in all consecutive years throughout the study period. The maximum tuberculosis cases were reported during autumn 454(17.1%) and summer 310 (17.2%) season of calendar year. Age group of 15-29 (adjusted odds ratio (AOR) 1.7, 95% confidence interval (CI) 1.41, 1.98), male sex (AOR 0.84, 95% CI 0.75, 0.96), relapse of tuberculosis (AOR 0.51, 95% CI 0.35-0.78), and being HIV positive (AOR 0.51, 95% CI 0.3, 0.86) were found to be factors associated with tuberculosis. **Conclusions:** Trend of tuberculosis was decreased year to year. However, still high prevalence is observed with different seasonal variation. Thus, understanding and managing of tuberculosis in seasonal variation, improving case detection rate and controlling the most powerful factors are recommended steps to tackle the problem in Ethiopia.

Background

Tuberculosis (TB) is a worldwide chronic infectious disease mainly caused by *Mycobacterium tuberculosis*. It is highly transmitted by untreated smear-positive pulmonary tuberculosis when the infectious individual expels droplets of the bacilli which are produced during coughing, singing, and sneezing [1]. The disease occurs when the bacteria overcome immune defenses, multiply, and become enough in number to cause tissue damage. TB can attack all parts of the body. It typically attacks the lungs (pulmonary TB) as well as other parts of the body (extra pulmonary TB) [2].

Globally, about one-third of the world's population has dormant M.tuberculosis and hence at risk of getting an illness. So that it hinders socioeconomic development of a country as 75% of people with TB is within the economically productive age group of 15-54 years [3].

World Health Organization of 2018 global TB reported revealed that nearly10 million people have developed TB disease in 2017. Of these 3.2 million were women, 5.8 million were men and 1 million were

children. There were also an estimated 1.3 million deaths caused by TB and 300,000 deaths occurred in case of TB-HIV co-infection in 2017[4].

Globally, about 87% of all TB incident cases were covered by 30 high TB burdened countries. Amongst these, Africa shares one third by having nine countries from 22 high burdened countries and Ethiopia falls under this category [4]. Even though there has been a major decline in the incidence and TB associated death rates in Ethiopia, still the country is highly affected, and stands third in Africa with an annual estimation of TB incidence 172/100,000 and death rate of 24/100,000 population in 2017. Moreover, due to low socio-economic status, living conditions, poor nutrition, and lack of awareness to seek early diagnosis, ranks to TB third hospital admission and second cause of death from top ten diseases in Ethiopia [4-7].

Even though, TB was not well defined as a seasonal variation in different countries, some reports revealed that a peak of TB case was occurred in summer [8,9] and in spring [10,11] while lower in December and a peaks in July in Uganda [12] and rise up in autumn in Ethiopia [13]. TB was confirmed to be a seasonal disease with a low rate in the second and high in the fourth quarter of the calendar year in Ethiopia [13]. Geographical variation and healthcare-seeking behavior of patient causes high TB infection in the winter that profound the symptom and diagnosis of a disease at autumn and summer season [14].

Trend analysis and an assessment of TB seasonality help to allocate resource appropriately; clinical evaluation and research enrollment in high TB burdened areas. However, limited study has reported from Ethiopia. Therefore this study was aimed to assess the seasonality and trend analysis of tuberculosis among patients attended at Hiwot Fana Specialized University Hospital.

Methods And Materials

Study design, area, and period

A hospital-based retrospective study was conducted among patients diagnosed for TB using data recorded from January 2015 and April 2019 at Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia. Harar town is one of the historical places which found 526 km east to Addis Ababa, the capital city of Ethiopia. Based on the central statistical agency of 2007, the total population of Harari Regional state was 183,415, of whom females 91,099 and 92,316 are males. It has nine districts consist of three urban and six rural. There are six hospitals (4 governmental and 2 private), eight public health centers and 20 health posts in the region.

Hiwot Fana Specialized University Hospital (HFSUH) is one of the oldest hospitals in Ethiopia which was established during the occupation of Italian soldiers (1928-1933). Currently, the hospital has served to about 5.2 million people around Harar and neighboring regions like Dire Dawa administrative council, Oromiya and Ethiopia Somale Regional State.

It serves as a teaching center of eastern Ethiopia and delivering different health services to the community like internal medicine, surgery, gynecology and obstetrics, TB/HIV, etc. In the hospital, TB prevention and control program is coordinated by TB clinic staff with Harari regional health bureau.

Study populations

All patients with complete records of their demographic, clinical and laboratory data were included in the study. Individuals with an incomplete record were excluded from the study.

Sample size and sampling techniques

All available data that fulfill inclusion criteria from January 2015 to April 2019

Operational definitions

New patients: - Patients those have never been treated for TB or have taken anti-TB drugs for less than 1 month.

Relapse patients:- Patients previously treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB.

Laboratory investigation and data collection procedure

One sputum sample for the patient of age above five years and a gastric aspirate sample in case of children below five years and other samples like peritoneal, pleural, ascetic joint aspiration and cerebrospinal fluid were collected by an experienced health professional. Then the sample was processed for Genexpert modules tests, by following manufacturer protocols of Xpert MTB/RIF assay [5]. The sample reagent and specimen were added into 50 ml of falcon tube to dilute and treated, and then the tube was mixed by vortex at least twice in 15 minutes at room temperature till liquefied. Then 2 ml of the mixed sample was transferred to the cartridge by a sterile disposable pipette to load into the Xpert module with the remaining assay steps completed via an automated process [5].

Statistical data analysis

Data were coded and entered into EPI-data version 3.1 and analyzed by using SPSS version 20. Descriptive statistics of different variables were determined and presented in the form of texts, graphs and tables. Summary measures such as percentages and mean were used to generalize results accordingly. Bivariate logistic regression was carried out to identify the associated factors with tuberculosis. Variable with $p\text{-value} \leq 0.25$ was a candidate for the multivariate analysis. Finally, multivariate logistic regression analysis was performed for adjusted odds ratio with 95% confidence intervals and variables with a $p\text{-value} < 0.05$ were declared as statistically significant.

Result

Socio-demographic and Clinical characteristics of the study participants

From the total of 9060 TB suspected patients that have submitted their samples for TB diagnosis, 8001(88.3%) had complete data and were included in this study. The majority of the participants' HIV status was unknown in 7624(95.3%). The mean age of participants diagnosed for tuberculosis was 29.89($\pm$ 17.55) years ranging from 1 month to 95 years old, of which 4363 (54.5%) were males and 3638(45.5%) were females. The majority of them 6600 (82.5%) were in the age group of $\geq$ 15 years old. Most of the study participants lived in rural, 6362 (79.5%) and 1639 (20.5%) were urban dwellers (Table 1).

Prevalence of tuberculosis

The overall prevalence of MTB detected by using GeneXpert MTB/RIF assay was 15.7% (95% CI 14.9-16.5) in all age groups and the overall prevalence of rifampicin resistance was 4.2% (53/1254).

Trends of tuberculosis

The proportion of TB detected by GeneXpert MTB/RIF assay was decreased in all consecutive years of the study period. High rate of TB was presented 189(19.3%) in 2015 and with a low rate of 219(13%) in 2019 (P -value <0.001). Rifampicin resistance was slightly similar to 14(7.4%) in 2015, and 16(8.1%) in 2017. But decreased from 2017 to 2019 to reach 2(0.9%) (Figure 1).

Male participants have a high proportion of TB cases than female participants and age category of 15-29 was highly affected compared to the others. TB prevalence is high in previously treated patients compared to the new ones (Table 2).

Seasonality of tuberculosis

From January 2015 to April 2019 of the study periods, there were more than 16 seasons that a total of 8001 participants were recruited for TB diagnosis. The highest TB case was recorded in a May followed by June and August. January and December was the lowest month of tuberculosis documented (Table 3).

In general, the maximum proportion of tuberculosis was reported in summer 310 (17.2%) and autumn 454(17.1%). Rifampicin resistant of MTB was registered at all seasons without forming great fluctuation (Figure 2).

Factors associated with tuberculosis

A high proportion of TB prevalence was documented with patients lived in rural area 1015(16.0) compared to urban dwellers 239(14.4%). The positivity rate of a sample taken from pulmonary site 1235(15.7%) was slightly higher compared to extra pulmonary site 199(13.4%). From a bivariate analysis sex, age, history of TB, HIV status and resident of participants were recruited for multivariate analysis (p -

value < 0.25). In multivariate analysis, sex, age, history of TB and HIV status of patients were associated with tuberculosis (Table 4).

Discussion

Tuberculosis (TB) is a disease that continues to be a major public health problem amongst ten top disease causes to mortality. Millions of people continue to fall sick with TB each year, particularly in developing countries [4,15]. In this study, the overall prevalence of TB detected by Xpert assay was found to be 15.7%. This is comparatively similar to a study conducted at Felege Hiwot and Debre Tabor Hospitals, Northwest Ethiopia [16], Awi Zone, Northwest Ethiopia [17] and Addis Ababa, Ethiopia [18]. However, higher than a study report from Addis Ababa [6], Agaro (southwest Ethiopia) [19] and wollo, North East Ethiopia [20]. This difference might be due to the different methods of diagnosis that we used only GeneXpert assay while other study uses culture, microscopy and other molecular techniques for bacterial identification.

The trend of TB in this study was gradually decreased consecutively throughout the study period in which 19.3% in (2015), 18.6% in (2016), 18.4% in (2017), 13.5% in (2018) and 13% in (2019). This finding is consistent with a report from Agaro and Nekemte in Ethiopia [7,19] and in China [21] in which trend of TB was steeply declined. But it was contradicted with a study from Gambella, West Ethiopia [22] and in Nigeria [23] in which the trend of TB was fluctuated year by year. The difference might be due to the different status of TB co-infection of HIV, other diseases that disturb immune system which brings immune suppression and enhanced risk of developing tuberculosis, different level of awareness of people about early treatment and diagnosis. Moreover, in some parts of Ethiopia, the gradual decreasing of prevalence could be influenced by the health extension program that planned to achieve important basic health care to prevent the spread of tuberculosis by increasing community awareness.

In this study sex, age, previous history of TB, and HIV status of patients were found to be significantly associated with the cause of *Mycobacterium tuberculosis*. Male participants had significantly higher proportion of TB cases than female. This is agreement with a study reported from Jimma, west Ethiopia [24], Gondar, North west Ethiopia [25], Zambia [26], and Japan [27]. However, it is not consistent with the finding from Northwest, Ethiopia [17]. This might be, males are usually more social contact in the community than females that helps them to contract a disease.

The age group of 15–29 years was the most infected by TB, which was similar with a study reported from Ethiopia [13], Agaro, south west Ethiopia [19], Gondar, North west Ethiopia [26], Central Ethiopia [28], Pakistan [29] and Singapore [30]. This might be due to this age group is sexually active and hence infected with HIV, which predisposes to TB. Disproportionately, large burden of TB cases in this age group shares a high number of total workforces that could be contributed to poverty of one's country.

History of previously treatment is the other factor associated with the tuberculosis in the present study. This is similar with reports from Ethiopia [3] and Dessie, Northeast Ethiopia [20]. But it contradicts with

the study reported from Matahara, eastern Ethiopia [31]. This difference might be due to different implementation of DOTs (direct observed treatments) strategy and different awareness of the society.

People living with HIV are more likely to have TB compared to people without HIV in the present study. This is comparable to a study from other part of Ethiopia [32]. But not agree with a study from Sub Saharan Africa [33]. The difference might be due to different level of CD4 count and advanced WHO clinical stage that may determines the immunity of individuals' living with HIV.

Furthermore, living in rural area was not frequently identified factors associated with tuberculosis in this study, which is similar to a study from Pakistan [29] and North Ethiopia [20].

On the other side, the seasonality of tuberculosis was higher in the summer followed by the autumn compared to other seasonal year in this study. Similar ideas were reported from Addis Ababa, Ethiopia [6], Pakistan [29] and China [9] with a peak in summer. Concerning to TB by month, June and May shows high proportion while low proportion was documented in January in this study. In Uganda low proportion of TB was reported in December and high in July and October [12] and March was a Peak in Chile while October has a lower case [34].

Actually, the peak of TB cases in summer and autumn is influenced by the winter season that might be in winter, vitamin D deficiency is increased with parallel increases duration of contact with infection [35,36]. This makes reduce immunity, by increasing the susceptibility to the infection if exposed to an infected person [37]. Also, TB is a slow-growing bacterium and takes around 2 months to proliferate and showed symptoms with favorable conditions to be a diseased. Generally, during autumn and at the begging of the summer, most of the infected people particularly, rural residents have resources and time to seek medical care that increases TB cases in Ethiopia [13].

Limitation of the study

This research has some limitations. Since it was hospital-based, it would not have more representative of the general population. The right residence of study participants in Hiwot Fana Specialized University Hospital after diagnosis as well as information on rainfall and humidity to describe the seasonality of tuberculosis was not well-known.

Conclusion

The trend of TB proportion was decreased over study the period. The age category of 15-29 was the most affected and a high proportion of tuberculosis was observed in previously treated patients. Gender male and being HIV positive are other the most factors significantly associated with tuberculosis. High proportion of TB was detected in the summer and autumn season of the year. Moreover TB was not significantly associated with patient's living area.

Based on this study, attention should be given during summer and autumn seasonality in that high case of TB was recorded. Healthcare facilities should be improved for timely diagnosis, and treatment. Screen

all HIV positive patients with Gene Xpert which gives quickly results within two hours to identify new tuberculosis patients to reduce infection.

List Of Abbreviations

AOR: Adjusted odds ratio; HRERC: Institutional Health Research Ethics and Review Committee, HFSUH- Hiwot Fana Specialized University Hospital, HIV- Human Immuno Virus, RIR-Rifampicin resistant; MTB- *Mycobacteria Tuberculosis*, TB-Tuberculosis, WHO-World Health Organization

Declarations

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Availability of data and materials

The raw dataset used /analyzed during the current study is available from the author on reasonable request.

Authors' contributions

DB designed and conceived the study. DB, TT and ZA assessed the methodological quality of the included studies and wrote up of the final work. ZA and DB performed the statistical analysis and prepared the manuscript, TT supervise and reviewed the manuscript. All authors read carefully and approved the final manuscript.

Ethical consideration

The study clearance was obtained from College of Health and Medical Sciences, the Institutional Research Ethics Review Committee (IRERC), Haramaya University. Permission was obtained from HFSUH where the study was conducted.

Consent to participate

Not applicable

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interest.

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Tables

Due to technical limitations Tables 1-3 are available in the Supplementary Files as a download.

Figures

Figure 1

Trend of tuberculosis and rifampicin resistance in Hiwot Fana specialized University Hospital, Eastern Ethiopia, January 2015-April 2019 N.B- MTB- mycobacterium tuberculosis, RR-Rifampicin resistance

Figure 2

Graphical presentation of tuberculosis and rifampicin resistance at Hiwot Fana Specialized University Hospital, Eastern Ethiopia, January 2015-April 2019 N.B:-MTB-Mycobacteria tuberculosis, RR-Rifampicin resistance

Supplementary Files

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