A Retrospective and Time Series Study of Cases of Tuberculosis: Evidence of Nnamdi Azikiwe University Teaching Hospital Nigeria

Abstract

Tuberculosis (TB) is one of the leading causes of mortality in developing countries in world. It is an airborne disease spread through inhaling. This study investigated the cases of tuberculosis at Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nigeria. TheTB data used in this study are secondary data sourced from NAUTH tuberculosis register from January 2005 to December 2021. This study is a retrospective cohort and time series analysis of all the cases of tuberculosis diagnosed and confirmed. The forecast methods used in this study are that of Box-Jenkins approach and Holt-Winters. Out of 395070 presumptive cases, 52311 (11.7%) were diagnosed with tuberculosis, and male had the highest rate. The age group that was most affected was the group 35-44 (24.68%). 8.4% of the tuberculosis diagnosed tested positive. ARIMA (0,0,1) (2,0,1) [12] was selected as the best model, used in forecasting tuberculosis cases for the next four years. Tuberculosis cases predicted showed that for the next four years, there will be a slight decrease.

Keywords: Tuberculosis, time series analysis, retrospective study, Nigeria

1. Introduction

Tuberculosis (TB) is one of the leading causes of mortality in the world, especially in the developing countries [1-4]. TB is a communicable disease that is caused by mycobacterium tuberculosis also known as TB bacilli [5,6], and it is spread through inhaling. It is an airborne disease that affects primarily the lungs, resulting to pulmonary TB, and if not settled in due time can affect other parts of the body like the kidneys, brain, and many other organs, resulting to extrapulmonary TB. TB is usually prevalent in denser areas and poor ventilated areas.TB affects all the age groups but the most vulnerable are adults especially in their productive years.

Sometimes, not all people infected with TB bacilli normally show the symptoms, this type of infection is known aslatent TB. However, a person with latent TB infection can graduate to active TB disease if there is any of these diseases diabetes mellitus, human immune deficiency (HIV), and cancer in his/her system, or if the person is aged or do not feed well [7]. HIV co-infection is one of the significant risk factors that can cause latent TB infection to easily progress to active TB disease [8, 9].

There have been huge efforts by countries and many health stakeholders to put to an end the transmission of TB due its great menace. However, because of these efforts, the World Health Organization (WHO) came out with a rapid molecular diagnostic tests for initial tests, and Xpert MTB/RIF Ultra and Truenat assayse [10].

In 2016, the World Health Organization (WHO) launched the ‘End TB Strategy’ with the aim of reducing the incidence and death of TB disease by 90% and 95% by 2035. However, for this strategy to succeed, it requires additional and critical actions from both local and international levels, with proper planning and understanding of current and past TB disease [11].In 2021, over 80% of TB cases and deaths are mostly in the low and medium income countries and about 187 000 people died of HIV association. The highest burden of HIV associated TB is higher in WHO African countries [11].

This current study assessed whether there were any variations in the TB epidemiology in Nnamdi Azikiwe University Teaching Hospital (NAUTH) under the period review and also to determine the best

time series model that will be used to obtain the forecasted number of TB cases for the next four years (48 months). The specific objectives of this study were to determine the (a) trend in the presumptive and notified TB cases; (b) trend in different types of TB cases; (c) variations in the cases of TB by sex and HIV status of diagnosed new pulmonary bacteriologically TB in NAUTH; (d) best linear time series for prediction; and (e) forecasted number of TB cases for the next four years (48 months).

2. Materials and Methods

2.1 Data

The number of presumptive, diagnosed TB, diagnosis and treatments were all carried out by NAUTH, and they were provided in line with the World Health Organization (WHO) [12], and recorded and stored in NAUTH tuberculosis register. Annual TB data (as an aggregation)for the period 2005-2021 were collected on the basis of sex of the TB patients, presumptive and diagnosed TB, types of TB, HIV status of TB patients, and age groups. Monthly data on TB cases from January 2005 to December 2021 were also collected.

2.2 Data analysis

Descriptive statistics – mean, standard deviation, proportion (%), and skewness was carried on aggregate of TB cases, while time series analysis – seasonal autoregressive integrated moving average (SARIMA) using Box-Jenkins methodology, Holt-Winters' additive, and Holt-Winters' multiplicative was carried on the monthly TB cases. The best SARIMA model was selected among the competing models using the Akaike information criterion corrected (AICC); the three forecast methods are first tested for adequacy and serial autocorrelation using the Box-Jenkins test. The measures of forecast performance are carried on the three forecast methods, should they be adequate. All the analyses are done using R 4.2.0 statistical package.

The SARIMA model is a time series model that is used to predict future values (TB cases) based on past observations (TB cases), and when there is seasonality in the data. It is denoted as ARIMA$(p,d,q)(P,D,Q)$ $[m]$, where m is the number of periods in each season, $p,d,q$are respective autoregressive, differencing, and moving average for the non-seasonal part of ARIMA, while P,D,Q are respective autoregressive, differencing, and moving average for the seasonal part of ARIMA. The model is written as

$$\nabla^d y = c + \varepsilon_t + \sum_{i=1}^{P} \Phi_i y_{t-im} + \sum_{i=1}^{p} \phi_i y_{t-i} + \sum_{j=1}^{Q} -(\Theta_j \varepsilon_{t-jm}) + \sum_{j=1}^{q} -(\theta_j \varepsilon_{t-j}) \quad (1)$$

where $\Phi_i : i = 1, \cdots, P$ are parameters of autoregressive for the seasonal part; $\phi_i : i = 1, \cdots, p$ are parameters of autoregressive for the non-seasonal part; $\Theta_j : j = 1, \cdots, Q$ are parameters of the moving average for the seasonal part; $\theta_j : j = 1, \cdots, q$ are parameters of the moving average for the non-seasonal part.

Holt-Winters is a time series model that is used to predict future values based on past values, especially when there trend and seasonality in the data. Holt-Winters – additive and multiplicative

Holt-Winters additive model is written as

$$y_{t+h} = l_t + hb_t + s_{t+h-m(k+1)} \quad (2)$$

where

$$\left.\begin{aligned} l_t &= \alpha(y_t - s_{t-m}) + (1-\alpha)(l_{t-1} + b_{t-1}) \\ b_t &= \beta(l_t - l_{t-1}) + (1-\beta)b_{t-1} \\ s_t &= \gamma(y_t - l_{t-1} - b_{t-1}) + (1-\gamma)s_{t-m} \end{aligned}\right\} \quad (3)$$

Holt-Winters multiplicative model is written as

$$y_{t+h} = (l_t + hb_t)s_{t+h-m(k+1)} \quad (4)$$

where

$$\left.\begin{aligned} l_t &= \alpha\left(\frac{y_t}{s_{t-m}}\right) + (1-\alpha)(l_{t-1} + b_{t-1}) \\ b_t &= \beta(l_t - l_{t-1}) + (1-\beta)b_{t-1} \\ s_t &= \gamma\left(\frac{y_t}{l_{t-1} + b_{t-1}}\right) + (1-\gamma)s_{t-m} \end{aligned}\right\} \quad (6)$$

where l_t is the level equation, b_t is the trend equation, s_t is the seasonal component, $m$is the number of seasonality, α is the smooth parameter for l_t, β is the smooth parameter for b_t, γ is the smooth parameter for s_t, t is the time, α, β, and γ all lie between 0 and 1.

3. Results

3.1 Analysis for retrospective study

Figure 1 shows the rate of TB cases in both male and female as reported. The rate of TB cases is higher in male than in female. The highest rate of TB cases reported for male was experienced in 2007 (41 TB cases per 100000), while the highest rate reported for female was experienced in 2013 and 2017 (26 TB cases per 100000 each). In Table 1, 60.1% of patients reported with TB cases are male with an average rate of 31 cases per 100000, while 39.9% are female with an average rate of 20 cases per 100000.

Figure 2 shows the number of presumptive TB cases and diagnosed TB cases reported. The number of presumptive TB cases is higher than the diagnosed TB cases. The highest number of presumptive TB cases was experienced in 2005 (18178 TB cases), while the highest number of diagnosed cases was experienced in 2010 (4110 TB cases). In Table 1, 81.6% of TB cases reported are presumptive TB cases with an average of 13664 cases, while 18.4% are diagnosed cases with an average of 3077 cases.

Figure 3 shows the proportions of the different types of TB diagnosed. TheNew pulmonary bacteriologically confirmed TBshowed the highest proportion of TB diagnosed. The highest proportion of New pulmonary bacteriologically confirmed TB was experienced in 2010 (66 %), the highestproportion of New pulmonary diagnosed clinically was experienced in 2009 (6%), the highest proportion of New extra pulmonary TB was experienced in 2007 (7%), and the proportion of Retreatment TB was experienced in 2013 and 2015 (6% each). In Table 1, out of TB diagnosed, 83.9% were New pulmonary bacteriologically confirmed TBwith an average of 58%, 5.2 % were New pulmonary diagnosed clinically with an average of 4%, 6.8% were New extra pulmonary TB with an average of 5%, and 4.1% were Retreatment TB with an average of 3%.

Figure 4 shows the proportion of HIV status among new pulmonary bacteriologically confirmed TB tested. In Table 1, the highest proportion of HIV tested among new pulmonary bacteriologically confirmed TB reported was experienced in 2007 (98%), while the highest proportion tested positive was experienced in 2017 (25%)

Figure 5 shows the rate of TB cases according to age group. In the age group 0-14, the highest rate was experienced in 2013, 2016, 2019, and 2020 (2 TB cases per 100000 each); in the age group 15-24, the highest rate was experienced in 2012 (29 TB cases per 100000); in the age group 25-34, the highest rate was experienced 2012 (75 TB cases per 100000); in the age group 35-44, the highest rate was experienced in 2016 (70 TB cases per 100000); in the age group 45-54, the highest rate was experienced in 2006 (60 TB cases per 100000); in the age group 55-64, the highest rate was experienced in 2007 (39 TB cases per 100000), and in the age group greater than or equal to 65, the highest rate was experienced in 2007 and 2011 (30 TB cases per 100000). In Table 1, among the TB reported, 0.45% was the age group 0-14 with average of 1 TB case per 100000, 8.31% was the age group 15-24 with average of 17 TB cases per 100000, 23.34% was the age group 25-34 with average of 48 TB cases per 100000, 24.68% was the age group 35-44 with average of 52 TB cases per 100000, 20.67% was the age group 45-54 with average of 43 TB cases per 100000, 11.96% was the age group 55-64 with average of 25 TB cases per 100000, and 10.59% was the age group greater than or equal to 65 with average of 22 TB cases per 100000.

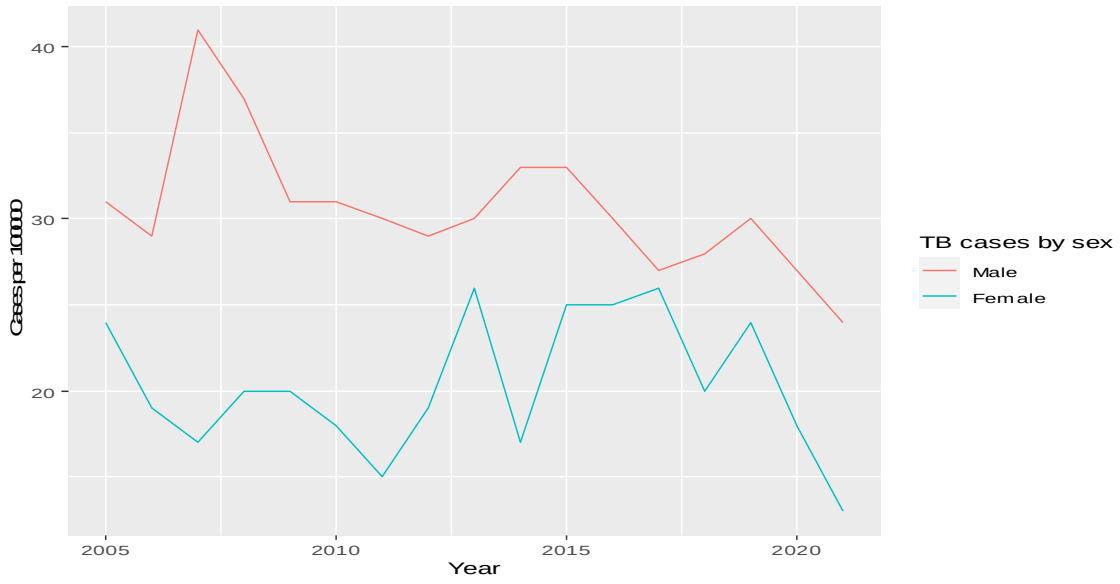

Figure 1. Time plot of TB cases per 100000 by sexfor the period 2005-2021

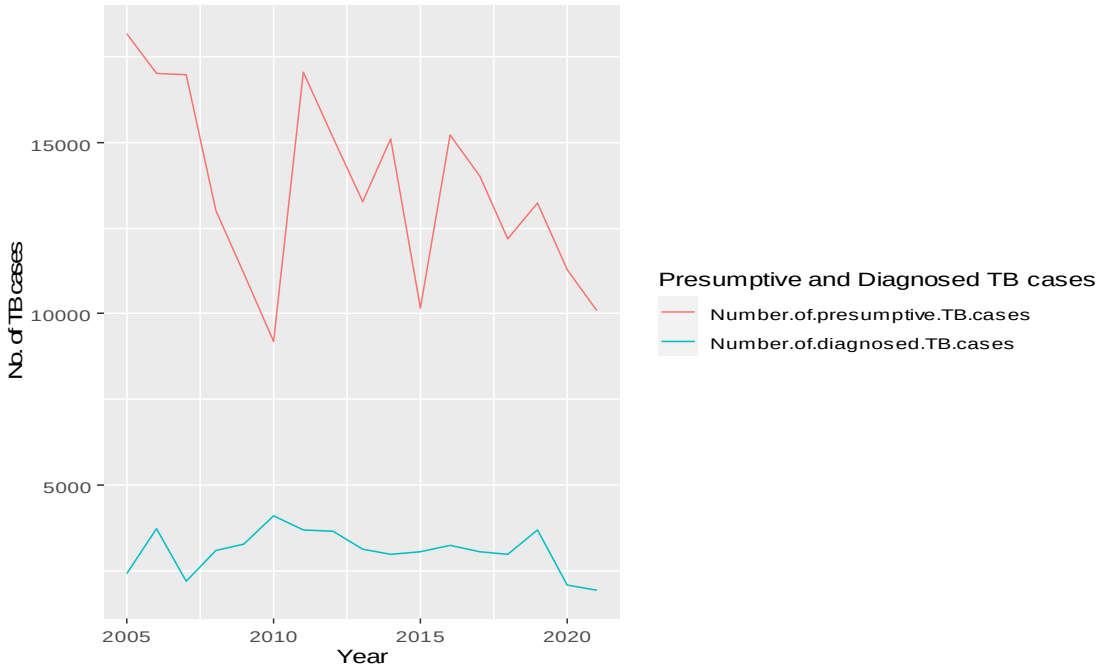

Figure 2. Time plot of number of presumptive TB cases and diagnosed TB cases for the period 2005-2021

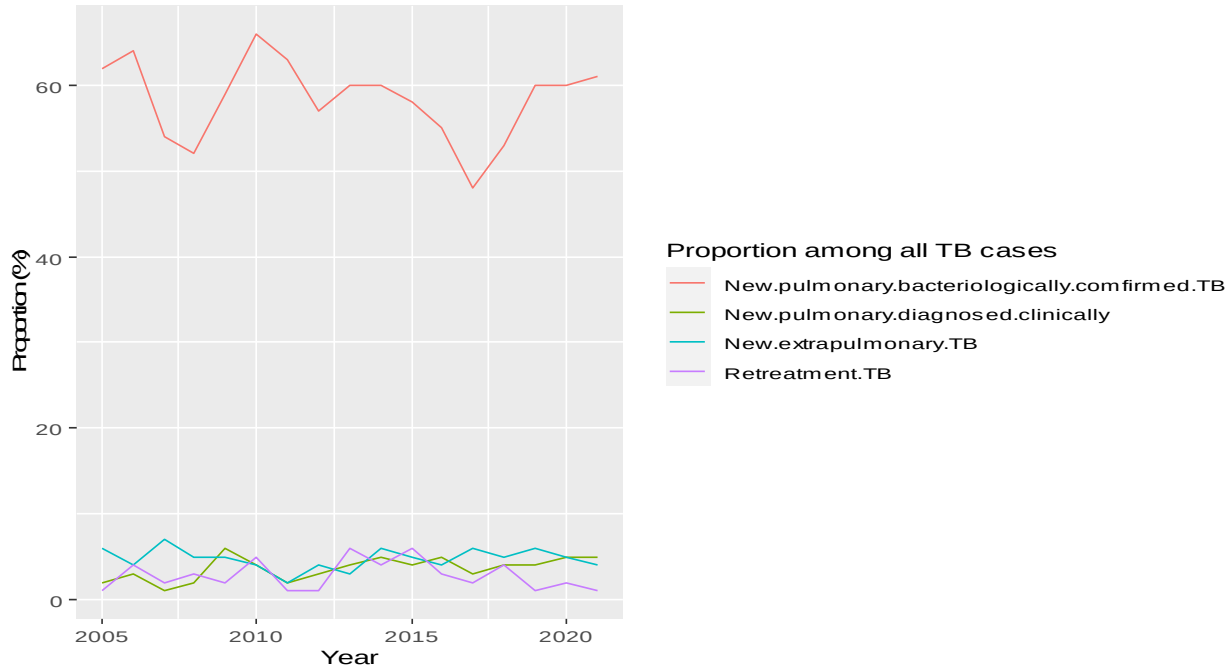

Figure 3. Time plot of proportions of the different types of TB diagnosed (%) for the period 2005-2021

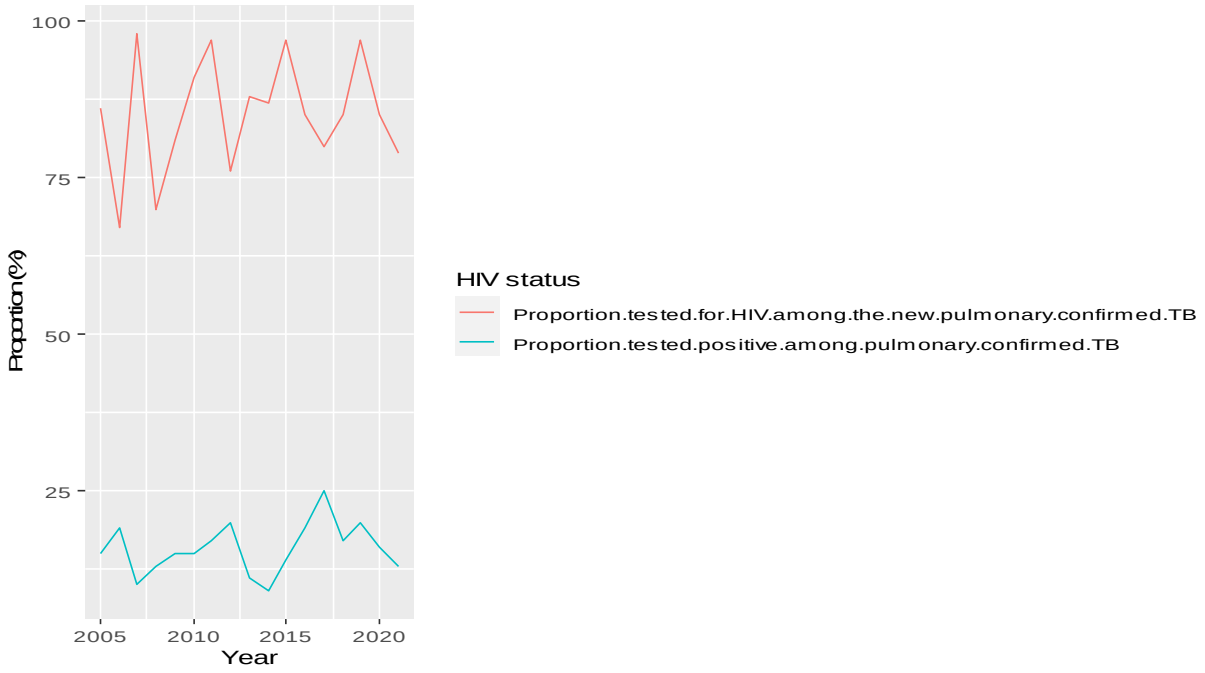

Figure 4. Time plot of proportion of HIV status among new pulmonary bacteriologically confirmed TB tested for the period 2005-2021

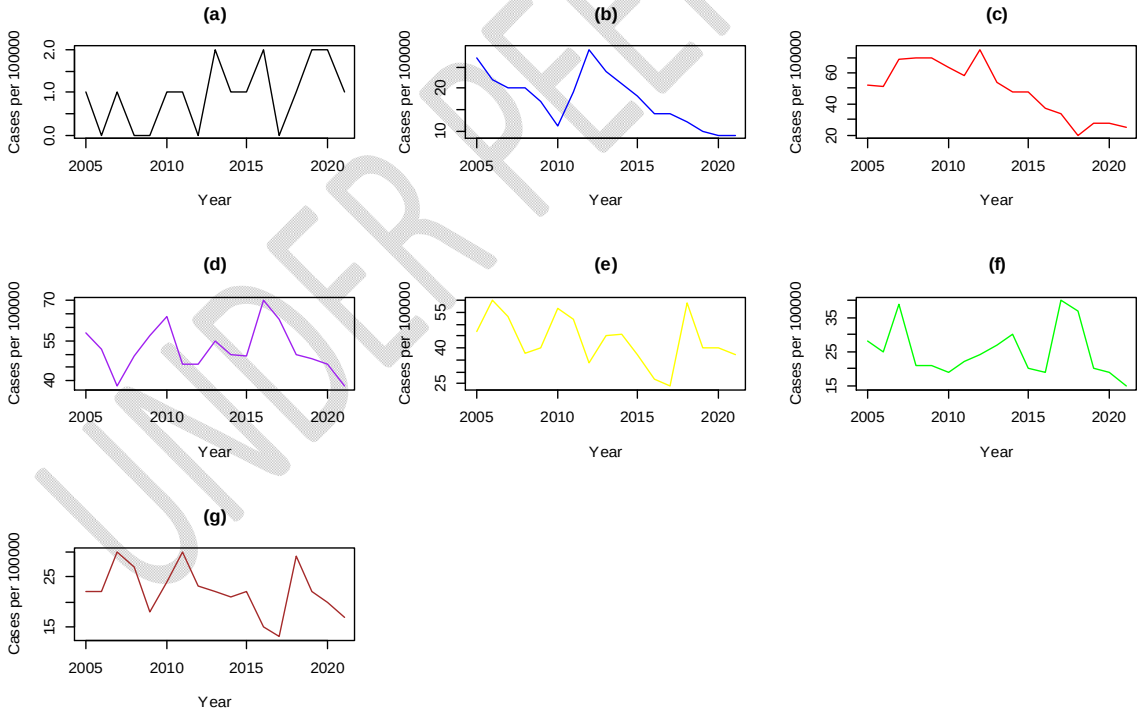

Figure 5. Time plots of TB cases per 100000 by age groups (a) 0-14; (b) 15-24; (c) 25-34; (d) 35-44; (e) 45-54; (f) 55-64; (g) greater or equal to 65 for the period 2005-2021

Table 1. Descriptive statistics for the data

Variable	Total	Mean	Standard deviation	%	Skewness
Sex					
Male	521	31	3.9	60.1%	1.1581
Female	346	20	4	39.9%	0.0005
Presumptive and diagnosed TB					
No. of presumptive TB cases	395070	13664	2746.3	88.3%	0.0156
No. of diagnosed TB cases	52311	3077	620	11.7%	-0.4218
Types of TB diagnosed					
New pulmonary bacteriologically confirmed TB	992	58	4.7	83.9%	-0.5696
New pulmonary diagnosed clinically	62	4	1.4	5.2%	-0.2668
New extra pulmonary TB	81	5	1.3	6.8%	-0.3646
Retreatment TB	48	3	1.7	4.1%	0.62809
HIV status from new pulmonary bacteriologically confirmed TB					
Proportion tested for HIV among the new pulmonary confirmed TB	1719	85	8.9	91.6%	-0.3325
Proportion tested positive among pulmonary confirmed TB	158	16	4.0	8.4%	0.3664
Age group					
0-14	16	1	0.73	0.45%	0.0986
15-24	296	17	5.99	8.31%	0.2425
25-34	831	48	17.1	23.34%	-0.1516
35-44	879	52	8.4	24.68%	0.4417
45-54	736	43	10.21	20.67%	-0.0185
55-64	426	25	7.29	11.96%	0.968
Greater or equal to 65	377	22	4.74	10.9%	0.0172

3.2 Time series analysis

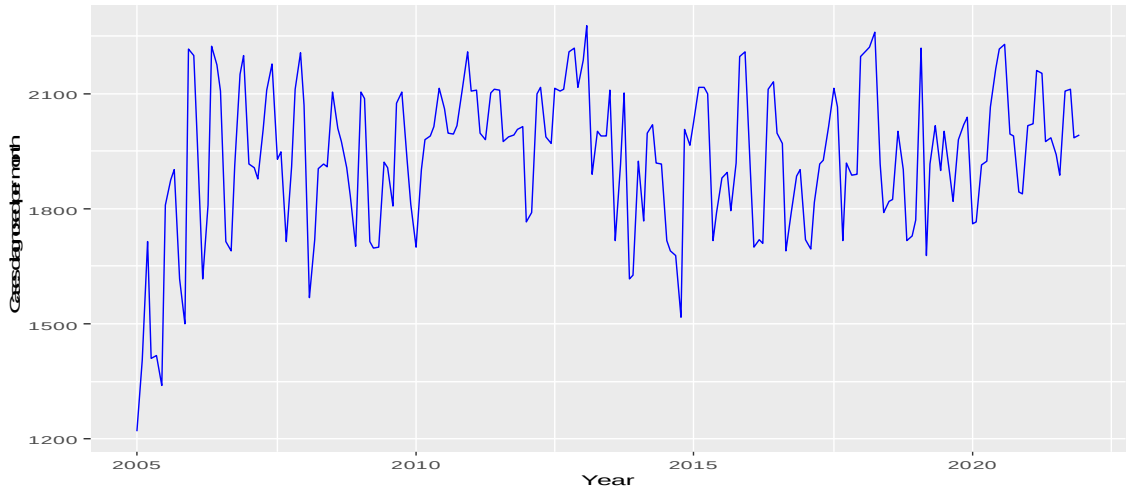

Figure 6. Time plot of cases of TB diagnosed per month for the period 2005-2021

The p-value in Table 2 is smaller than 0.05, indicating that the cases of Tuberculosis (TB) in Figure 6 are stationary, which means that the data on TB cases are not affected by time factor. However, there is no need for differencing.

Table 2. Unit root tests for stationarity

$Dickey - Fuller = -5.956$	$lag\ order = 5$	$p - value = 0.01$
Alternative hypothesis: stationary		

3.2.1 Seasonal ARIMA model fitting

The estimated sample autocorrelation function (ACF) and partial autocorrelation function (PACF) are plotted in Figure 7(a) and 7(b) respectively. The significant spikes in lag 0 and lag 1 in the ACF plot suggests a non-seasonal moving average (MA) component, while the significant spike in lag 0 and 1 suggests a seasonal autoregressive (AR) component and a seasonal moving average (MA) component.

The preferred seasonal ARIMA model is obtained by comparing the Akaike information criterion corrected (AICC) of all the competing models. This was done using the R 4.2.0 statistical package. The estimated parameters of the selected ARIMA model are shown in Table 3. The AICC of the preferred seasonal ARIMA model, that is ARIMA (0,0,1) (2,0,1) [12] is 2652.1, and it is the least AICC among the competing ARIMA models.

To confirm the adequacy of the model ARIMA (0,0,1) (2,0,1) [12], we referred to Figure 8. The time plot shows a stationary residual, while the histogram shows a normally distributed residuals. In the ACF plot, lag 5 is not within the significance limit, but the Ljung-Box test in Table 4 shows that there is no serial autocorrelation in the residuals, which is as a result of the p-value great than 0.05. However, this implies that the seasonal ARIMA selected is a good model for forecasting cases of TB.

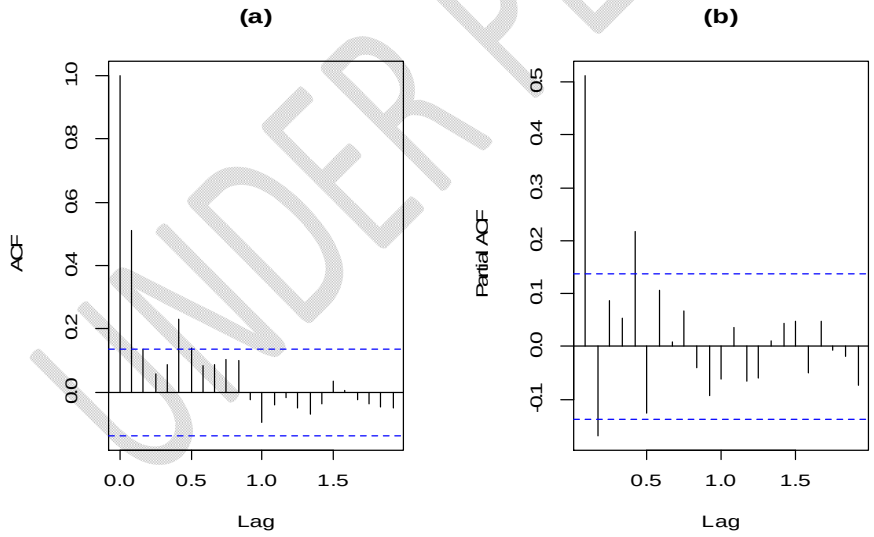

Figure 7. (a) ACF plot for cases of TB diagnosed per month; (b) PACF plot for cases of TB diagnosed per month for the period 2005-2021

Table 3. Estimated coefficients of ARIMA (0,0,1) (2,0,1) [12]

	Ma1	Sar1	Sar2	Sma1	mean
	0.601	0.045	-0.155	-0.200	1938.906
Standard error	0.0563	0.4861	0.1101	0.4907	12.9893

The seasonal ARIMA model using the information in Table 3 is written as

$$y_t = 1938.91 + \varepsilon_t - 0.601\varepsilon_{t-1} + 0.045y_{t-12} - 0.156y_{t-24} + 0.200\varepsilon_{t-12} \quad (10)$$

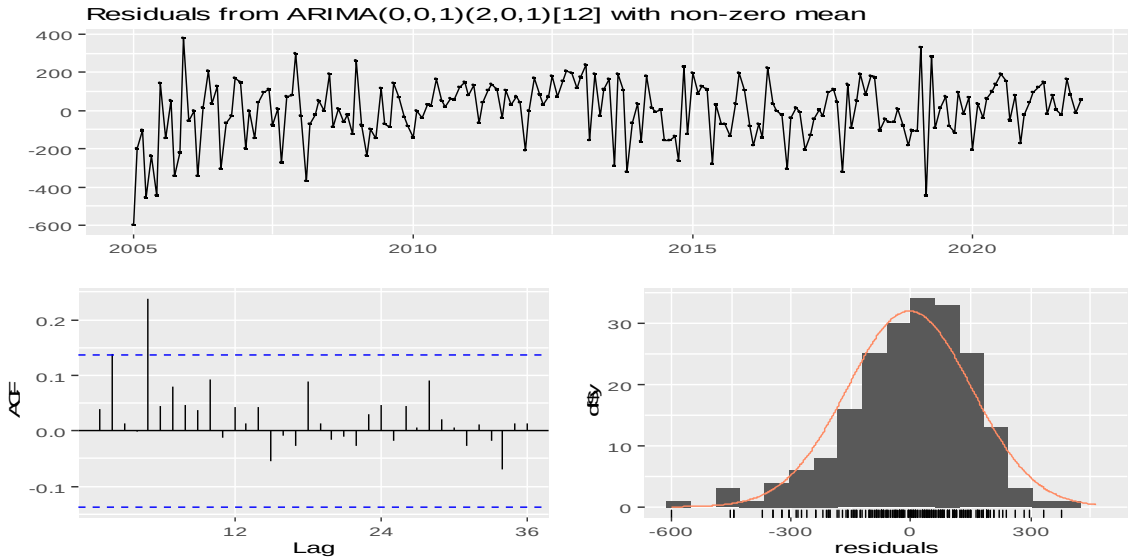

Figure 8. Model adequacy check for ARIMA (0,0,1) (2,0,1) [12]

Table 4. Test for serial correlation of forecast errors in ARIMA (0,0,1) (2,0,1) [12] with non-zero mean

Ljung-Box teste		
$Q^* = 25.219$	$df = 19$	$p - value = 0.1535$
$Model\ df = 5$	Total lags used = 24	

3.2.2 Holt-Winters' additive model fitting

Table 5 shows the estimated parameters of Holt-Winters' additive model. The estimated coefficients of the model are obtained using R 4.2.0 statistical package

To confirm the adequacy of Holt-Winters' additive model, we referred to Figure 9. Though the time plot shows stationary residuals, and the histogram shows a normally distributed residuals, but the ACF and the Ljung-Box test in Table 6 shows that the Holt-Winters' additive model is not a good model for forecasting cases of TB. This is because there are many lags that lie outside the bound of the significance limits, and the p-value of the Ljung-Box test is less than 0.05.

Table 5. Estimated coefficients of Holt-Winters' additive model

Smoothing parameters					
α = 0.2532	β = 1e-04	γ = 1e-04			
Initial states					
l = 1592.924	b = 3.2661				
s = 39.3071	−18.6877	1.7126	−64.0649	−11.1557	31.7645
45.3125	32.5391	12.8325	−59.4801	−12.5851	2.5052

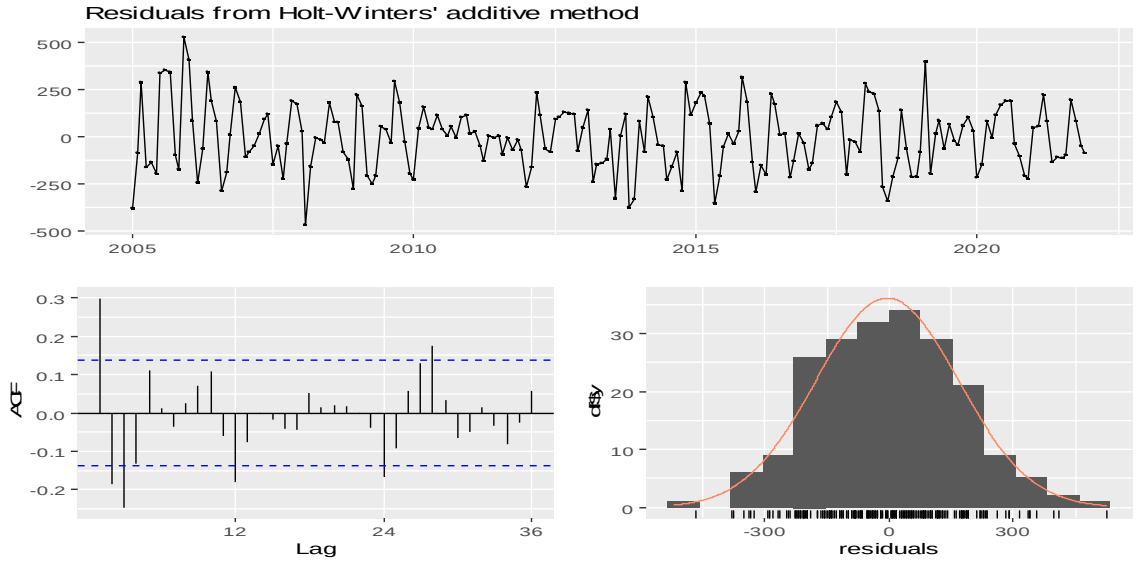

Figure 9. Model adequacy check for Holt-Winters' additive model

Table 6. Test for serial correlationof forecast errors in Holt-Winters' additive model

Ljung-Box test		
Q^* = 66.477	df = 8	$p-value$ = 2.462e-11
$Model\ df$ = 16	Total lags used = 24	

3.2.3 Holt-Winters' multiplicative model fitting

Table 7 shows the estimated parameters of Holt-Winters' multiplicative model. The estimated coefficients of the model are obtained using R 4.2.0 statistical package

To confirm the adequacy of Holt-Winters' multiplicative model, we referred to Figure 10. Though the time plot shows stationary residuals, and the histogram shows a normally distributed residuals, but the ACF and the Ljung-Box test in Table 8 shows that the Holt-Winters' multiplicative model is not a good model for forecasting cases of TB. This is because there are many lags that lie outside the bound of the significance limits, and the p-value of the Ljung-Box test is less than 0.05.

Table 7. Estimated coefficients of Holt-Winters' multiplicative model

Smoothing parameters					
α = 0.318	β = 0.0095	γ = 1e-04			
Initial states					
l = 1568.144	b = 30.4568				
s = 1.0105	0.9948	0.9939	0.9681	0.9875	1.0326
1.0203	1.0042	1.0127	0.9792	0.9986	0.9977

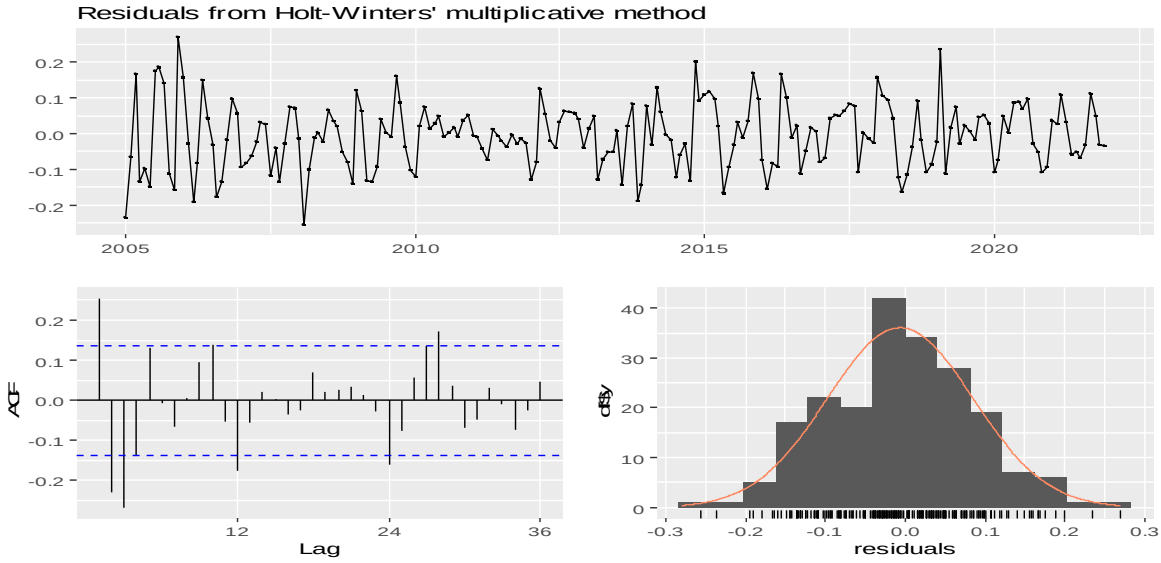

Figure 10. Model adequacy check for Holt-Winters' multiplicative model

Table 8. Test for serial correlation of forecast errors in Holt-Winters' multiplicative model

Ljung-Box test		
Q^* = 70.568	df = 8	$p-value$ = 3.788e-12
$Model\ df$ = 16	Total lags used = 24	

Figure 11 shows the out-of-sample forecast of the cases of Tuberculosis (TB) for a period of four years, that is from January 2022 to December 2025.In Table 9, by December 2022, the expected TB caseswill be1947, showing 46 (2.31%) cases less than that of December 2021; by December 2023, the expected TB cases will be 1931, showing 16 (0.82%) cases less than that of December 2022; by December 2024, the expected TB cases will be 1937, showing 6 (0.31%) cases greater than that of December 2023,and by December 2025, the expected TB cases will be 1940, showing 16 (0.31%) cases greater than that of December 2025. However, the TB cases are expected to reduce to 2.66% by December 2025, compared to December 2021.

Table 9. Predicted TB cases for the period 2022-2025 (48 months)

Year/Month	Forecasted	Year/Month	Forecasted	Year/Month	Forecasted	Year/Month	Forecasted
Jan-22	1999	Jan-23	1923	Jan-24	1929	Jan-25	1941
Feb-22	1946	Feb-23	1926	Feb-24	1937	Feb-25	1941
Mar-22	1917	Mar-23	1904	Mar-24	1941	Mar-25	1944
Apr-22	1907	Apr-23	1904	Apr-24	1942	Apr-25	1944
May-22	1907	May-23	1932	May-24	1944	May-25	1940
Jun-22	1892	Jun-23	1930	Jun-24	1946	Jun-25	1941
Jul-22	1885	Jul-23	1936	Jul-24	1947	Jul-25	1940
Aug-22	1895	Aug-23	1945	Aug-24	1946	Aug-25	1938
Sep-22	1907	Sep-23	1912	Sep-24	1943	Sep-25	1943
Oct-22	1907	Oct-23	1911	Oct-24	1943	Oct-25	1943
Nov-22	1948	Nov-23	1932	Nov-24	1937	Nov-25	1940
Dec-22	1947	Dec-23	1931	Dec-24	1937	Dec-25	1940

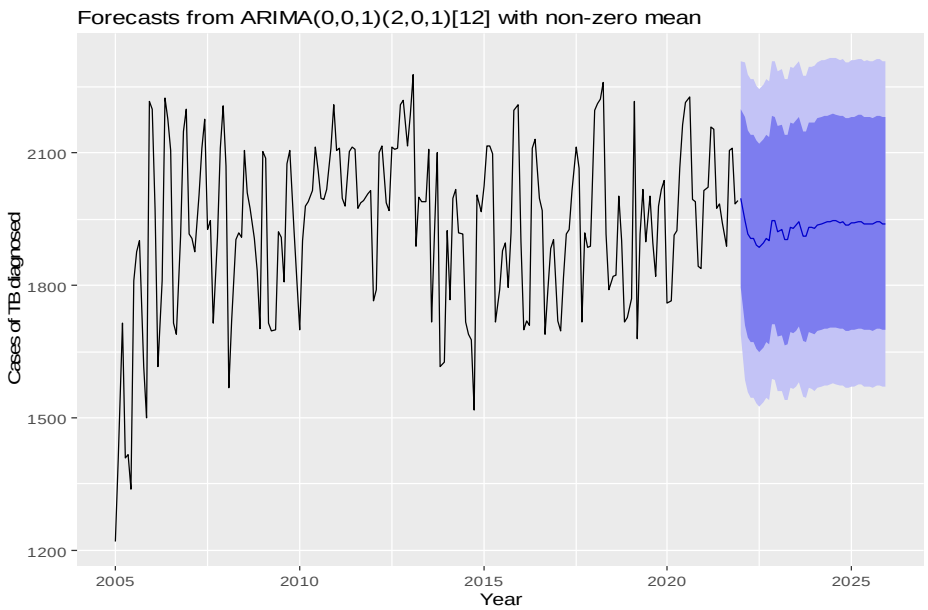

Figure 11. Time plot of cases of TB diagnosed and out-of-sample forecast of TB cases

4. Discussion

The study aimed at identifying and describing variations in the epidemiology of TB patients in Nnamdi Azikiwe University Teaching Hospital Nigeria. We found that male had the highest rate of TB cases compared to the female during the period under review. In the case of male, the highest rate of TB cases was experienced in 2007, while female experienced highest rates in 2013 and 2017. Meanwhile there was fluctuation in the rate of TB cases in both male and female from 2005 through 2020.

Furthermore, the burden of TB was higher in male than in female – thiswas because males have higher access to healthcare than females [13], have greater susceptibility to infection [14]becausethey smoke

more than females. Alcohol consumption is also a risk factor that contributed to the high rate of TB in males than in female [15].

We also found that the number of presumptive TB cases was higher than the number of diagnosed TB cases, meanwhile from 2005 to 2021 there was fluctuations in the cases, and in 2010, the number of number of presumptive TB cases was very high. In 2010, the proportion of new pulmonary bacteriologically confirmed TB was very high, the proportion of new pulmonary diagnosed clinically was very high in 2009, the proportion of new extra pulmonary TB was very high in 2007, while the proportion of retreatment TB was very high in 2013 and 2015. There was a fluctuation in the proportion of these types of TB under the period review. The burden of TB was very high in the age group 35-44 years and lesser in the age group 0-14 years.

91.6% of patients were tested for HIV per year, and out of those tested, the highest proportion of those tested positive to HIV was experienced in 2017. However, the findings showed that there will a slight increase in number of TB patients based on the forecasted number of TB cases. However, the proportion of HIV positive patients has not shown an increasing trend.

The limitation in this study is that not all the case files on the number of TB patients in Nnamdi Azikiwe University Teaching Hospital were included, that is because some of the files were missing. Again, the study was a retrospective one, it only centered on the data already recorded by the hospital itself and stored.

5. Conclusion

The TB cases in NAUTH Nigeria showed no trend over the period reviewed as compared to similar study carried by [16] that showed a rising trend of TB cases. The study showed that there was low proportion of TB patients diagnosed with HIV, and that those that bear greater burden of TB are people in the age group 35-44 years (Table 1), and that TB burden is higher in male than in female. However, alcohol consumption and smoking of cigarette are two major risk factors that increase the burden of TB in male and youths in general.Thus, from 2022 to 2025, NAUTH will be experiencing a decline in TB cases (Table 9).

However, in order to protect the vulnerable people of Anambra where we have NAUTH from the menace of TB as stipulated by WHO in 'The End TB Strategy' [10], this study suggests that Anambra State Ministry of Health should intensify their awareness campaign to the people of Anambra state on the causes of TB, the danger, the preventive measures, and how it can be treated.

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