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The profile of tuberculosis infection at the Babcock University Teaching Hospital

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ABSTRACT

Background: Tuberculosis is the leading cause of death from any single pathogen and it has consistently continued to be a major public health challenge globally. Data show that Nigeria ranks tenth among the 22 high tuberculosis burden countries. **Aim**: This study intends to describe the profile of tuberculosis infections in Babcock University Teaching Hospital. **Methods:** This was a retrospective cross sectional study of patients presenting to the Tuberculosis Laboratory of Babcock University Teaching Hospital. **Results**: Patients presenting to BUTH were 2.29 times more likely to have a positive AFB sputum smear result when compared to samples from Primary Health Care Centers – $P = 0.05$, $\chi^2 = 3.83$, O.R = 2.29, R.R = 1.17, CI = 1.0 – 5.34. Patients presenting to BUTH were more likely to be HIV positive when compared to those from PHC's p = 0.00, $\chi^2 = 24.74$, df = 2. **Conclusion:** The burden of tuberculosis is still high in our environment and challenges in its rapid and accurate diagnosis still remain. In order to strengthen tuberculosis control, attention needs to be placed on rapid diagnosis and prompt treatment.

Key words: Tuberculosis, HIV, Primary Healthcare Centre, Ziehl Neelson stain, Directly Observed Treatment Short Course, pathogen

INTRODUCTION

Mycobacterium tuberculosis is a gram positive acid fast, slender-straight rod that is ubiquitous.[1] It is a strict aerobe and thrives best in organs with relatively high oxygen tension and thus thrives easily in the apices of the lungs.[1] The organism is transmitted exclusively by inhalation of infective droplets from patients with open pulmonary tuberculosis via coughing, sneezing, talking or expectorating.[1] The pathogen is found in human samples and also in water and soil. It is hardy and known to survive outside the human host for decades.[1]

Tuberculosis has been identified as the leading cause of death from any single pathogen and it has consistently continued to be a major public health challenge globally. Data available show that Nigeria ranks tenth among the 22 high tuberculosis burden countries with up to 98000 patients notified in 2012 accounting for an

estimated prevalence rate of 161 per 100,000 population thereby ascribing the country the status of a high disease burden nation.[2]

It has also been estimated by epidemiologists that about one-third of the world's population are currently infected or have been exposed to *Mycobacterium tuberculosis,* particularly those in Sub Saharan Africa and Asia and that about three million deaths are attributable to tuberculosis each year despite the availability of antibiotics that are potentially curative for this chronic infectious disease.[3]

A risk factor study showed that tuberculosis is strongly associated with the following variable; male gender, a family history of tuberculosis, absence of a BCG scar, cigarette smoking, alcohol use, chronic anaemia, HIV co-infection, and previous history and treatment of helminthic infections. In a multivariable model in that study that was based on 601 matched pairs of subjects, male sex, family history of tuberculosis, smoking, and HIV infection were independent risk factors of tuberculosis.[4]

Tuberculosis can affect any organ system.[5] Clinical manifestations vary accordingly but often include fever, night sweats, and weight loss.[5] Positive results on either a tuberculin skin test or an interferon-γ release assay in the absence of active TB establish a diagnosis of LTBI.[5] A combination of epidemiological, clinical, radiographic, microbiological, and histopathologic features is used to establish the diagnosis of active TB.[5]

The burden of tuberculosis in our local environment appears to be on the high side. At the moment Babcock University Teaching Hospital, being a fledgling medical institution, lacks baseline data on the profile of tuberculosis. The study thus sought to describe the burden of tuberculosis in Babcock University Teaching Hospital in order to better understand the presentation patterns for improved diagnosis. It also seeks to describe the epidemiologic profiles of tuberculosis infections at our local institution since no such previous study had been done in our institution.

This study will avail us the opportunity of knowing the true picture of the burden of disease in order for us to formulate rational measures in line with national programs towards addressing the problem. In addition, BUTH serves as a referral facility for at least three Primary Health Centers within its vicinity, thus this study will help to provide information on the picture within our local environment. The data obtained from this study will therefore act as baseline information for future studies to be conducted on tuberculosis and help us to conduct a trend analysis with respect to morbidity, drug resistance complications and mortality in our patients.

METHODOLOGY

Study setting

Ilishan is located in Ogun State in South West Nigeria. The Babcock University Teaching Hospital is a 140 bed facility that caters for the immediate community and surrounding environs. It has a Directly Observed Treatment Short Course (DOTS) clinic supported by the National Tuberculosis and Leprosy Control Project (NTBLCP).It also serves as a referral center for three Primary Health Care Centers (PHC's) – Ikenne, Iperu and Shagamu.

Study design and methods

This is a retrospective cross sectional study. Only patients with clinical features of tuberculosis were included in the study. Sputum smear examination on three consecutive specimens had been performed with the Ziehl Nelson method for staining acid fast bacilli and these records were recovered from laboratory data in the Medical Microbiology Tuberculosis Laboratory. The Ziehl-Neelson procedure was used to stain Mycobacterium tuberculosis and *Mycobacterium leprae*. The study was approved by the institution ethical committee.

A retrospective analysis of the profile and treatment outcomes of all tuberculosis patients registered from September 2013 to September 2015 at DOTS Clinic was retrieved. Reviewed data were patients' ages, genders, addresses, tuberculosis types, and sputum smear status as well as treatment outcome.

Sample size

The sample size was calculated using the Kish formula $N = Z^2pq/d^2$ where N is the sample size, p is the prevalence, d = 1-p and d = 0.05. With a prevalence of 15% [6] this results in a sample size of 200 patients.

Study population
This included both in- and out-patients receiving tuberculosis diagnostic services at the Department of Medical Microbiology, Babcock University Teaching Hospital. All patients within the time period of November 2014 to November 2015 were included in the study.

Statistical analysis
Data was entered and analyzed using Epi Info (WHO, version 3.5.1). Frequency distributions with 95% confidence intervals, and descriptive statistics - including mean/median shall be computed. The possible determinants (age, gender, residence, HIV status, smear status) shall be assessed. Significance tests are two-sided with *P*-values < 0.05 considered statistically significant. Chi-square test was used to evaluate differences in categorical variables. The Fisher's exact test was used when cell sizes were < 5.

Table 1: Frequency distribution of participants and variables

Variable		Frequency	Percentage
Ethnicity	Yoruba	145	80.1
	Ibo	18	9.9
	Others	11	6.1
	Hausa	7	3.9
Age Category	< 40	113	66.5
	> 40	57	33.5
Gender	Female	106	59.6
	Male	72	40.4
Sputum 1	+	7	4.0
	++	6	3.4
	+++	10	5.6
	0	152	85.9
	Scanty	2	1.1
Sputum 2	+	6	3.8
	++	13	1.9
	+++	14	8.9
	0	133	84.2
	Scanty	2	1.3
Sputum 3	+	3	4.1
	++	2	2.7
	+++	10	13.5
	0	59	79.7
HIV	Negative	50	27.9
	Not available	64	35.8
	Positive	65	36.3
Clinical Improvement	No	22	12.4
	Yes	155	87.6
AFB Seen	No	152	84
	Yes	29	16
Sample type	Aspirates	5	2.8
	Sputum	176	97.2
Treatment facility	BUTH	138	76.2
	PHC	43	23.8
Age group	Adult	152	89.4
	Pediatric	18	10.6

BUTH –Babcock University Teaching Hospital, PHC – Primary Healthcare Centre, HIV – Human Immunodeficiency Virus.

Table 2: Risk factors for acquisition of tuberculosis and HIV

Variable				*P* value	X^2	O.R	R.R	CI
Treatment facility		AFB Seen		0.05	3.83	2.29	1.17	1.0 – 5.34
		None	Yes					
BUTH		120	18					
PHC		32	11					
Treatment facility		HIV						
	Negative	NA	Positive	0.00	24.74			
BUTH	44	35	57					
PHC	6	28	8					
Age group		HIV						
	Negative	NA	Positive	0.11	4.38			
Adult	45	49	56					
Pediatric	5	10	3					
Gender		HIV						
	Negative	NA	Positive	0.09	4.74			
Female	24	37	43					
Male	26	26	20					
Age		HIV						
	Negative	NA	Positive	0.83	0.38			
< 40	32	41	39					
> 40	18	18	20					
Treatment facility		Improvement		0.23	1.41	2.13	1.97	0.60– 7.59
BUTH		None	Yes					
PHC		19	116					
		3	39					
Age		Improvement		0.55	0.35	1.31	1.36	0.50-3.71
		None	Yes					
< 40		15	94					
> 40		6	51					
Age group		Improvement		0.90	0.01	1.08	1.10	0.23-5.17
		None	Yes					
Adult		19	130					
Pediatric		2	15					
Age group		AFB Seen		0.52	0.42	0.93	0.61	0.13-2.80
		None	Yes					
Adult		126	26					
Pediatric		16	2					
Age		AFB Seen						
		None	Yes	0.14	2.20	0.90	0.49	0.19-1.28
< 40		91	22					
> 40		51	6					
Gender		AFB Seen		0.76	0.10	0.88	1.0	0.39-2.00
		None	Yes					
Female		88	18					
Male		61	11					

AFB – Acid fast bacilli, NA – Not available

RESULTS

In all, 181 patients' records from the laboratory register were analyzed. The predominant ethnic group in the study were the Yoruba's as they accounted for n = 145 (80.1%) of participants while the other tribes accounted for 29.1%. Regarding age stratification, most respondents, n = 113, (66.5%) were less than forty years with the rest older than forty years. Most participants, n = 106, (59.6%) were female, with males n = 72 (40.4%) accounting for the remainder. With respect to sputum analysis for Acid Fast Bacilli, 25 out of 177 1st samples, 35 of 166 2nd samples and 15 of 74 3rd samples were positive respectively (table 1).

The prevalence of HIV in the study is 36.3%. About 155 (86.7%) showed clinical improvement following two months of anti-kochs therapy. In addition 29 (16%) of all sputum samples were conclusively positive for Acid Fast bacilli by the Ziehl Nelson stain, as opposed to 152 (84%) that were negative. The predominant sample type for Mycobacterial analysis was sputum n = 176 (97.2%), with aspirates making up n = 5 (2.8%). Majority of patients received care in a tertiary hospital n = 138 (76.2%). Most cases seen were in adults n = 152 (89.4%) (table 1).

Concerning tests of significant statistical associations, patients presenting to BUTH 2.29 times more likely to have a positive AFB sputum smear result when compared to samples from Primary Health Care Centers; P = 0.05, χ^2 = 3.83, O.R = 2.29, R.R = 1.17, CI = 1.0 – 5.34. Patients presenting to BUTH were more likely to be HIV positive when compared to those from PHCs P= 0.00, χ^2 = 24.74, df = 2. There was no statistically significant association between HIV status and age or gender. Also there was also none seen with clinical improvement and either age or the location of the treatment facility. There was also no increased likelihood of recovering AFB based on age or gender (table 2).

DISCUSSION

Tuberculosis is a global emergency that is responsible for approximately two million deaths annually and is one of the leading causes of death among curable infectious diseases[6]. The tuberculosis and human immunodeficiency virus (HIV) epidemics are fueling each other in many African countries.[6] The data from our laboratory show a concomitant high burden of disease with HIV and tuberculosis similar with other series such as those of Beijerand his colleagues.[6]

Our rate of HIV in suspected tuberculosis patients was 36.3% representing more than a third of all patients. In addition, almost a third of patients did not have available retroviral screen results and this implies a break in the diagnostic chain of tuberculosis management as all patients with the disease condition must have a retroviral screen. The higher association of HIV with patients in our tertiary hospital compared to those from the PHCs might be due to higher transmission rates in a semi-urban environment than in a rural one, ditto for the higher detection rates of AFB in sputum samples in our Tertiary hospital.

Tuberculosis is a major opportunistic infection in HIV-infected persons and also represents an AIDS defining illness. As a result of this, the clinical conditions end up forming a lethal combination with each speeding up the other's progress. It is also observed that the present ongoing tuberculosis epidemic has been associated with several cases also in immune-competent individuals.[7]

The World Health Organization (WHO) estimates that 460,000 new cases of all forms of tuberculosis occurred in Nigeria in the year 2009 giving a grim picture despite concerted efforts geared at bringing down new cases to an acceptable minimum. In addition, the burden of the disease is further compounded by a relatively high prevalence of HIV in the country which is approximately 4.6% in the population. This high prevalence of HIV among tuberculosis patients indicates that the tuberculosis challenge will continue to be fueled by HIV.[8]

The findings from our study show that the burden of tuberculosis is still high in our environment and challenges in its rapid and accurate diagnosis still remain. The early diagnosis and prompt treatment remain essential components for effective tuberculosis control.[9] Any form of delay in the diagnosis of tuberculosis may increase infectivity to the immediate and remote communities, worsen the disease state, result in complications and enhance the risk of death. Delays in diagnosis

are usually due to late presentation on the part of patients, self medication, resorting to alternative forms of therapies as well as a low index of suspicion on the part of primary care givers.[9]

Studies have revealed that early diagnosis and prompt and appropriate management of infectious patients with pulmonary and extra-pulmonary tuberculosis help to reduce the transmission of *Mycobacterium tuberculosis* which would result in the elimination of the scourge. The higher rates of AFB detection in patients less than forty years show that understanding transmission patterns in individuals in this age group is key to the control of tuberculosis in our local environment. If tuberculosis is detected early and properly treated using effective combination chemotherapy, the patients usually become noninfectious within the first two months and are eventually cured. However, important challenges for tuberculosis control are human immunodeficiency virus (HIV) co-infection and drug resistance which is rapidly emerging even in treatment naïve patients.[10]

The present WHO international policy on tuberculosis case detection recommends the collection and examination of two sputum smears for the diagnosis of pulmonary tuberculosis as opposed to three previously used.[11] Our findings showed that most patients submitted two sputum samples and tuberculosis was reliably diagnosed with those two samples which is in line with studies conducted by *Parsons et al.* where almost 85.8% of tuberculosis cases were detected with the first sputum specimen.[11] With the second sputum specimen, the average incremental yield was 11.9%, while the incremental yield of the third specimen, when the first two specimens were negative was 3.1% which was negligible and added little information to the management of the patient.[11]

The accurate and rapid diagnosis of *Mycobacterium tuberculosis* infection and tuberculosis diseases is a formidable global challenge that is further complicated by HIV co-infection and the emergence of Multidrug Resistant (MDR) and Extensively drug Resistant (XDR) strains.[12] Delayed or absent tuberculosis diagnosis results in the delay and/or absence of appropriate treatment, therefore increasing morbidity, mortality, and mycobacterial transmission.[12] This is best evidenced by several recent autopsy studies from African countries, including South Africa, that revealed that up to 50% of persons with HIV infection or AIDS have unsuspected tuberculosis at the time of death.[12]

Globally, tuberculosis accounts for 1.2 – 1.5 million deaths each year, with 85% of this occurring in developing countries (such as Nigeria) and 26% in Sub Saharan Africa. Tuberculosis reemerged as a major global public health concern around the mid 1980s shortly after the onset of the HIV/AIDS pandemic.[13]

The other possible causes of re-emergence are due to rapid increase in poverty, poor living conditions with overcrowding, war, malnutrition, lack of drugs, the chronic problem of poor funding of local National Tuberculosis Programs, and non-adherence to program policies by some host governments.[13] These factors ultimately lead to increased transmission of *Mycobacterium tuberculosis* in the community and also to an increased risk of progression from latent to overt clinical tuberculosis.[13]

To impact on the high rates of both prevalent and incident tuberculosis in this and other resource poor settings, and to prevent associated high mortality and morbidity, a combination of strategies must be used.[14] This should include preventing late entry into HIV care and onto antiretroviral therapy, infection control measures around tuberculosis, targeted enhanced screening and enhanced adherence support for those on both tuberculosis and HIV treatment.[14]

Tuberculosis poses a severe challenge to public health globally but disproportionately affects resource constrained nations who have poorly developed Public Health systems. Individuals who have close contact with a patient who has active pulmonary tuberculosis and people from endemic regions of the world are at highest risk of primary infection, whereas patients with compromised immune systems have the highest risk of reactivation of latent tuberculosis infection from prior exposure.[15]

To stop the spread of the disease, treatment of active pulmonary tuberculosis patients remains the most effective strategy since a contagious person will infect up to 15 people every year if left untreated.[16] A World Health Assembly

resolution invigorated the tuberculosis control efforts and the internationally recommended control therapy, later named DOTS (Directly Observed Therapy Short Course) was launched.[16] However, interruption in tuberculosis treatment still remains the major barrier to its control and is the most important challenge for control.[16] Such interruptions are a breeding ground for Multidrug Resistant Tuberculosis even in treatment naïve patients.[16,17,18]

CONCLUSION

Although not all records were useable due to incomplete filling of biodata on the laboratory request forms, and samples providing in few instances were not suitable for analysis such as saliva instead of sputum. The observations from the present study revealed that tuberculosis in the 21st century still remains a huge public health issue despite gains and advances in diagnosis and chemotherapy. In order to strengthen tuberculosis control programs, attention needs to be placed on rapid diagnosis in rural and semi-urban areas as this will limit cross spread from such smaller communities to larger ones.

RECOMMENDATION

In the light of the emerging threat of Multidrug Resistant Tuberculosis (MDR), which is a huge cause for concern, concerted effort needs to be put in place to halt this trend and more sensitive equipment such as the GeneXpert should be made available in remote locations to help rapidly diagnose MDR Tuberculosis.

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