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Diagnosis and Treatment Outcome of Smear Positive Pulmonary Tuberculosis: Retrospective study in Kpando Municipal, Ghana

Desmond O. Acheampong[1*], Richard Opoku[1], Alex Boye[2], Daniel S. Agyirifo[3], Isaac Dadzie[2], Prince A. Barnie[1], Godwin Kwakye-Nuako[1] and Francis Nyandzi[1]

[1]Department of Biomedical Sciences, School of Allied Health Sciences, University of Cape Coast, Cape Coast, Ghana.
[2]Department of Medical Laboratory Technology, School of Allied Health Sciences, University of Cape Coast, Ghana.
[3]Department of Molecular Biology and Biotechnology, School of Biological Sciences, University of Cape Coast, Ghana.

Authors' contributions

This work was carried out in collaboration between all authors. Authors DOA, AB and RO designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors PAB, DSA and GKN managed the analyses of the study and edited the final manuscript for intellectual content. Authors ID and FN managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Smear microscopy remains the primary tool for the detection of tuberculosis in Ghana. Laboratory diagnosis of active tuberculosis cases by sputum smear microscopy is a critical component of Directly Observed Treatment, Shortcourse (DOTS). Effective control of tuberculosis in Ghana at the rural level therefore hinges on the quality of local laboratory to provide accurate and reliable direct acid fast bacilli microscopy testing for diagnosis, treatment and monitoring.

**Corresponding author: E-mail: dacheampong@ucc.edu.gh, do.acheampong@gmail.com;*

Method: A retrospective trend analysis of laboratory entry records of tuberculosis (TB) cases from the Anfoega Catholic Hospital of the Kpando Municipal District in the Volta region from January 2013 to December 2015 was conducted. Patients were diagnosed according to the National TB programme Control guidelines. Data were computed into statistical software and analyzed for descriptive statistics, odds ratio and chi-square at 95% confidence interval. A p-value < 0.05 was considered statistically significant.

Results: Of the 116 cases recorded during the study period, 54 (46.6%) were found to be smear positive pulmonary tuberculosis and was highest among 21-40 year group. Annual prevalence generally decreased during the study from 31 (57.4%) to 11 (32.4%) with corresponding increase in treatment success rate. The proportion of new smear positives decreased from 27 (50.0%) in 2013 to 11(20.4%) in 2014 and 2015 respectively while new smear negatives also reduced from 19 (30.6%) in 2013 to 15 (24.2%) in 2014 but rose to 18 (29.1%) in 2015. High smear positivity was observed among males 33 (61.1%) than in females 21 (38.9%). 113(97%) of the 116 patients had their HIV status tested. Of these, 24 (21.2%) were HIV positive. 9 (7.9%) out of the 113 were found to be co-infected with Pulmonary tuberculosis.

Conclusion: Treatment outcome was statistically associated with age group but not with sex and was more successful among TB only patients compared to patients with TB/HIV co-infection, and HIV prevalence among smear negatives were higher than smear positives.

Keywords: Tuberculosis; TB/HIV co-infection; acid-fast bacilli.

ABBREVIATION

PTB : Pulmonary Tuberculosis
DOTS : Directly Observed Treatment, Short-course
TB : Tuberculosis
AFB : Acid Fast Bacilli

1. INTRODUCTION

Despite the availability of anti-tuberculosis chemotherapy, pulmonary tuberculosis (PTB) remains one of the commonest communicable diseases in Ghana. Currently, Ghana ranks among the high 30 TB/HIV endemic countries. [1] PTB caused by *Mycobacterium tuberculosis* is an airborne, contagious disease which primarily affects the lungs [2] and thus transmitted through inhalation of few droplets of tuberculosis (TB) bacilli to cause an infection. [3] People infected with PTB bacilli have a 10% lifetime risk of falling ill with TB [4]. The symptoms including a cough, fever, night sweats, and weight loss of active PTB disease may be mild for many months and thus lead to delay in seeking treatment, facilitating the spread to others. Over the course of a year, people with active TB can infect 10-15 other people through close contact [4].

With the evolution of a better symbiotic relationship with the human host, *Mycobacterium tuberculosis* has gained the ability to survive in a latent state and reactivate many years later, thriving in small populations for long periods after the infection. This has contributed significantly to the difficulty in controlling the disease from the community [5]. The interactive relationship between Human Immunodeficiency Virus (HIV) and tuberculosis facilitates a surge in their prevalence, morbidity and mortality. Infection with HIV-1 increases the risk of reactivating latent TB infection by 80- to 100-fold, and HIV patients who acquire new TB infections have higher rates of disease progression. Tuberculosis can occur at all points in the immunosuppressive spectrum of HIV disease, with variable presentations. In high-burden countries, TB may be the first presentation of HIV disease [6]. Previous hospital-based research in Ghana have indicated that prevalence of HIV in TB patients is 25-30%, and 50% of patients with chronic cough could be HIV positive. [7,8,9]

1n 2015, WHO reported an estimated prevalence rate of 356 per 100 000 population, an incidence rate of 160 per 100 000 population and a mortality rate of 19 per 100 000 population (due HIV+TB) in Ghana [1]. Thus, with a population of 27 million [1] an estimated 43,200 new cases are expected annually with 51,320 deaths with HIV/AIDS and TB as etiological agents without proper intervention. As such, the occurrence of both infections is of great public health concern in Ghana.

Tuberculosis diagnosis and treatment in Ghana depends heavily on the patients' self-report to health facility. Treatment of TB aims at curing patients, interrupting transmission and preventing the emergence of drug-resistant bacilli. Treatment outcome reflects on the quality of TB

treatment delivered by a health system [10]. Ghana has achieved high TB treatment success rate and case holding rate, however, case detection rate remains a challenge. At present, the Anfoega Catholic Hospital provides diagnostic and treatment services based on the DOTS program. In this study, we conducted a retrospective intended to investigate the prevalence and treatment outcomes of patients visiting Anfoega Catholic Hospital in the Kpando Municipal of Volta region of Ghana.

2. MATERIALS AND METHODS

2.1 Study Area

This is a hospital-based retrospective study comprising of available medical records of TB adult patients (aged >15) registered at Anfoega Catholic Hospital in the Kpando Municipal of the Volta Region of Ghana from 2013 January to December 2015. The hospital receives patients from about ten rural areas.

2.2 Diagnosis of Patients

The TB skin test was performed to determine first time exposure to the bacilli. This was done by injecting tuberculin into the skin on the lower part of the arm to identify first time exposures. A chest radiograph was then performed to support diagnosis. Subsequently, an early morning sputum is collected by patient (unless hospitalised) and a spot sputum mis also collected at site and processed the same day. Patients were categorised into seven (7) groups. Thus new, old, treated after treatment failure, treated after treatment default, treated after treatment relapse, TB patient with or without HIV, TB patient with or without pulmonary disease/other complications. Sputum microscopy test of tuberculosis was performed using Ziehl-Neelsen stain. Positive and negative control slides were included and used for internal quality control. The appearance of red straight, slightly curved rods with a blue background under the microscope (100x objective) was interpreted as a positive result. Both viable and non-viable bacilli were counted and quantified as being no acid-fast bacilli (AFB) seen, scanty, 1+, 2+ and 3+ AFB present A case of pulmonary TB was classified as positive (confirmed case of PTB) if at least one of the two two/three smears from the two /three sputum specimen received was acid fast bacilli positive and quantified as being scanty, 1+, 2+ and 3+ AFB present. Ethical approval was not required as the study was based on retrospective data. No particular identifiable group of patients were involved and their individual identities could not be traced. All the data were entered into and analyzed using statistical package for social science (IBM SPSS) statistics for windows version 20. Odds ratio and chi square test were calculated at 95% confidence interval (CI). A p-value <0.05 were considered statistically significant.

2.3 Definition of Associated Terms [11]

Pulmonary tuberculosis (PTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree.

New patient: a patient who has never received treatment for TB, or who has taken antiTB drugs for less than one month.

A bacteriologically confirmed TB case is one from whom a biological specimen is positive by smear microscopy, culture or rapid diagnostics.

Relapse: Patients who have previously been 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.

Treatment after failure: Patients who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.

Cured: A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.

Treatment completed: A TB patient who completed treatment without evidence of failure but with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.

Treatment failure: A TB patient whose sputum smear or culture is positive at month 5 or later during treatment

Treatment success: The sum of cured and treatment completed.

3. RESULTS

3.1 Prevalence of Tuberculosis

A total of 116 cases were filed during the period under study, of which 65 representing 56% males and 51 representing 44% females. As indicated in Table 1, 54 of the 116 cases were found to be pulmonary positive for *Mycobacterium tuberculosis* by smear microscopy, giving an overall prevalence of 46.6%. Also as presented in Table 1, 49 of the 54 positive cases representing 90.7% were new infections, 3 representing 5.6% were old cases while relapse and default cases were 1 respectively, representing 1.9%. Prevalence was higher in males (61.1%) compared to females with an M: F ratio of 1.5:1 showing a relatively higher burden of TB disease among men than females (Tables 2 and 3). The 21-40 and 41-60 year cohorts recoded the highest prevalence of 42.6% (Table 3). Also as shown in Table 3, the highest prevalence of 57.4% was observed in 2013. As presented in Table 4, the highest positive cases of only TB which represent a prevalence of 16.7% was observed at Aveme village. On the other hand, the highest prevalence 4.3% of only HIV was recorded at Anfoe village, whereas the highest prevalence of 5.6% of patients who tested positive for both TB and HIV was observed at Anfoega village (Table 4). Strikingly, annual prevalence decreased generally with time from 54.7% to 32.4% during the study period (Table 3).

3.2 Treatment Outcome

As presented in Tables 5 and 6, treatment outcome was significantly associated with age group but not sex and was relatively successful in TB only patients compared to TB/HIV patients. In Table 7, 42 of the 54 positive cases recorded in the study were successfully cured, representing a success rate of 77.8%. Only 1 treatment failure was recorded, representing 1.9% of the positive cases, and only 1 patient defaulted. Unfortunately, 4 deaths were recoded which represent 7.4% of the total positive cases (Table 7). As presented on Table 7, there was increasing treatment success rate from 2013 to 2015.

4. DISCUSSION

Smear microscopy remains the cornerstone tool for the laboratory diagnosis and in monitoring patients' response to treatment of TB in Ghana. Laboratory diagnosis of active tuberculosis cases by sputum smear microscopy is a critical component of DOTS. The purpose of sputum microscopy is to diagnose people with infectious TB, monitor progress of treatment and confirm that total cure has been achieved. It has been shown conclusively that good-quality microscopy of two consecutive sputum specimens will identify the vast majority (95-98%) of smear positive patients [12]. However, one positive result is required for a diagnosis of smear-positive pulmonary TB [1].

Table 1. General characteristics of the study

Characteristics	2013 N=54 n (%)	2014 N=28 n (%)	2015 N=34 n (%)	Total N=116 n (%)
Age group				
21-40	18 (33.3)	6 (21.4)	6 (17.6)	30 (25.9)
41-60	25 (46.3)	10(35.7)	17(50%)	52 (44.8)
>60	11(20.4)	12 (42.9)	11 (32.3)	34 (29.3)
Gender				
Male	33 (61.1)	14 (50.0%)	18 (52.9%)	65 (56.0)
Female	21 (28.9%)	14 (50.0%)	16 (47.1%)	51(44.0)
Type of patient				
New	46 (85.2%)	26 (92.9)	29(85.3)	101(87.1)
Old	5 (9.3)	0(0.0)	5(14.7)	10(8.6)
Treatment after relapse	2 (3.7)	1(3.6)	0(0.0)	3(2.6)
Treatment after failure	0(0.0)	1(3.6)	0(0.0)	1(0.9)
Treatment after default	1(1.9))	0(0.0)	0(0.0)	1(0.9)
Disease classification				
Pulmonary positive	31(57.4)	12(42.9)	11(32.4)	54(46.6)
Pulmonary negative	23(42.6)	16(57.1)	23(67.6)	62(52.6)
HIV Status				
Positive	9(16.7)	8(28.6)	7(20.6)	24(20.7)
Negative	43(79.6)	19(67.9)	27(79.4)	89(76.7)
Not done	2(3.7)	1(3.6)	0(0.0)	3(2.6)

Table 2. Annual diagnostic outcomes of patients

Patient category	Smear positive *(N=54)*			Total n (%)	Patient category	Smear negatives *(N=62)*			Total n (%)
	2013 n (%)	2014 n (%)	2015 n (%)			2013 n (%)	2014 n (%)	2015 n (%)	
New	27(50.0)	11(20.4)	11(20.4)	49(90.7)	New	19(30.6)	15(24.2)	18(29.0)	52(83.9)
Old	1(1.9)	0(0)	0(0)	1(1.9)	Old	4(6.5)	0(0)	5(8.1)	9(14.5)
Relapse	2(3.7)	1(1.9)	0(0)	3(5.6)	Relapse	0(0)	0(0)	0(0)	0(0)
Default	1(1.9)	0(0)	0(0)	1(1.9)	Default	0(0)	0(0)	0(0)	0(0)
Failure	0(0)	0(0)	0(0)	0(0)	Failure	0(0)	1(1.6)	0(0)	1(1.6))
Total	31(57.4)	12(22.2)	11(20.4)	54(100)	Total	23(37.1)	16(25.8)	23(37.1)	62(100)

Table 3. Prevalence of tuberculosis disaggregated by Gender, age group and year

	Disease classification		Total	Prevalence	*P*-value
	Pulmonary positive n (%)	Pulmonary negative n (%)			
Gender					> 0.05
Male	33 (61.1)	32 (27.6)	65	50.7%	
Female	21 (38.9)	30 (48.4)	52	40.4%	
Age group					< 0.05
21-40	23 (42.6)	7(11.3)	30	76.7%	
40-60	23(42.6)	29(46.8)	52	44.2%	
>60	8(14.8)	26(41.9)	34	30.8%	
Year					>0.05
2013	31(57.4)	23(37.1)	54	57.4%	
2014	12(22.2)	16(25.8)	28	42.9%	
2015	11(20.4)	23(37.1)	34	32.4%	
Total	54	62	116	46.6%	

Table 4. Distribution of TB cases among the village dwellers

Rural area	No of cases reported n (%)	HIV positive n (%)	TB only n (%)	TB/HIV n (%)
Anfoe	18	5(4.3)	3(5.6)	2(3.7)
Anfoega	18	4(3.4)	5(9.3)	3(5.6)
Aveme	15	1(0.9)	9(16.7)	1(1.9)
Gbefi	6	2(1.7)	2(3.7)	1(1.9)
Have	5	1(0.9)	2(3.7)	0(0.0)
Kpando	7	1(0.9)	4(7.4)	0(0.0)
Kpeme	7	1(0.9)	4(7.4)	0(0.0)
Nkonya	3	0(0)	2(3.7)	0(0.0)
Sovie	6	1(0.9)	4(7.4)	0(0.0)
Tafi	7	1(0.9)	4(7.4)	0(0.0)
Vakpo	10	3(2.6)	4(7.4)	1(1.9)
Wusuta	11	3(2.6)	2(3.7)	1(1.9)
Botoku	3	1(0.9)	0(0)	0(0)
Total	116	24(20.7)	45(83.3)	9(16.7)

The overall prevalence of the pulmonary TB in this study was 46.6% and was quite lower than the 62% of bacteriologically confirmed PTB cases in 2015 [1] and other studies elsewhere [13]. This was statistically associated with age (X^2 = 18.29, P <0.05) but not with sex. (OR=1.47, 95% CI 0.70-3.08). Prevalence in this survey decreased among the age group. 76.7% of TB prevalence was observed in 21-40 year cohort which forms the economically productive backbone of the communities. A general pool of infectious TB cases has been noted among young adults in Africa [13]. Thus the need for a close monitoring and targeting of this group for early case detection in order to reduce transmission and ease the decline in morbidity/mortality and also prevent the emergence of drug resistance. Using this age group as foci in TB control in relation to other environmental factors in various communities in Ghana and other sub-Saharan Africa will be significant in enhancing socioeconomic developments in rural areas.

High prevalence in males than females shows a relatively higher burden of TB disease among men than females. Lower smear-positive notification rates in females than males has also been observed in studies elsewhere [13,14]. Rhines [14] noted that sex-based differences in TB prevalence represent real epidemiological differences. Though the cause for this bias is uncertain, it appears to be influenced by divers factors such as less access to health facilities by women than men [15] robust immune system aiding in greater antibody production and cell-mediated immunity [16,17] and certain behavioral lifestyle such as smoking, alcohol consumption, social roles and contacts [18] that puts men at a higher risk of infection. Nonetheless, male predominance has been observed in countries with equal chances of health seeking behavior between sexes, [14] and a meta-analysis of 29 surveys in 14 countries showing male biasness in both case notification rates and prevalence rates indicated a strong evidence ruling out access to healthcare as a confounding factor [19].

Prevalence of TB/HIV co-infection was highest among the young and sexually active cohorts than in the older (above 60) folks. TB smear negative patients in this study had a higher HIV sero-prevalence rate than their other counterparts. The fact that TB has an atypical presentation in the end stage of HIV infection with a low sputum smear positivity which could result in delayed diagnosis, [20,21] may account for the observed low rate of smear positives among HIV positives. Moreover, such individuals have a higher mortality rate and are thus less infectious. This explains the observed high prevalence difference in both types of patients.

TB control in Ghana has seen improvements over the years in terms of case notification, case management and overall treatment outcome. Over the last two decades, treatment success rate has increased from 22% in 1996 to 70.1% in 2004 [22] and 85% in 2014 [1]. This is an indication of the effective efforts of the National Tuberculosis Programme and the commitment of other NGOs to eradicate TB in the country. Other favorable factors that have perhaps encourage patients' compliance to treatment such as the reduction in treatment duration from 18 months to 6 months [23] enablers package [24] fixed-dose combination [25] standardized treatment [26] and community treatment care [27] decline

Table 5. Treatment outcome stratified by gender, age group and types of patients (*N=54*)

Patient category		Treatment outcome						
		Successful		Unsuccessful			Total n (%)	*P*-value
		Cured n (%)	Treatment completed n (%)	Treatment failure n (%)	Died n (%)	Defaulted n (%)		
Gender	male	26(48.1)	2(3.7)	1(1.9)	4(7.4)	0(0)	33(61.1)	$>0.05^{\beta}$
	Female	16(29.6)	4(7.4)	0(0)	0(0)	1(1.9)	21(38.9)	
Age group	21-40	18(33.3)	3(5.6)	0(0)	1(1.9)	1(1.9)	23(42.6)	$<0.05^{s}$
	41-60	17(31.5)	2(3.7)	1(1.9)	3(5.6)	0(0)	23(42.6)	
	Above 60	7(13.0)	1(1.9)	0(0)	0(0)	0(0)	8(14.9)	
Types of patient	New	37(68.5)	6(11.1)	1 (1.9)	4(7.4)	1(1.9)	49(90.7)	$>0.05^{\beta}$
	Old	1(1.9)	0(0)	0(0)	0(0)	0(0)	1(1.9)	
	Relapse	3(5.6)	0(0)	0(0)	0(0)	0(0)	3(5.6)	
	Default	1(1.9)	0(0)	0(0)	0(0)	0(0)	1(1.9)	

$p< 0.05$ was considered statistically significant. s= significant; $^{\beta}$ = not significant

Table 6. Treatment outcome among TB only patients compared to patients with TB/HIV co-infection

Type of patient	Successful n (%)	Unsuccessful n (%)			Total n (%)
	Treatment completed + cured	Died	Defaulted	Treatment failure	
TB only	41(91.1)	3(6.7)	0(0)	1(2.2)	45(83.3)
TB/HIV	7(77.8)	1(11.1)	1(11.1)	0(0)	9(16.7)
Total	48(88.9)	4 (7.4)	1(1.9)	1(1.9)	54(100)

Table 7. Annual treatment outcome of TB patients

Year	Successful		Unsuccessful			Total n (%)
	Cured n (%)	Treatment completed n (%)	Treatment failure n (%)	Defaulted n (%)	Died n (%)	
2013	24(44.4)	2(3.7)	1(1.9)	0(0)	4(7.4)	31(57.4)
2014	8(14.8)	3(5.6)	0(0)	1(1.9)	0(0)	12(22.2)
2015	10(18.5)	1(1.9)	0(0)	0(0)	0(0)	11(20.4)
Total	42(77.8)	6(11.1)	1(1.9)	1(1.9)	4(7.4)	54(100)

in social stigma and improvement in diagnosis, [28] has been key in reducing defaulters' rate and thus the burden of TB on individuals and communities Treatment success rate in this study was found to be 88.9%, which is higher than similar studies conducted in rural parts of Ethiopia which were 70%, [29] and 80% [30]. However, it compares favorably with findings by Osei and his group [31]. Though there was no statistical association between treatment outcome and sex (OR= 0.28, 95% CI 0.03-2.58), treatment was however comparatively unsuccessful in males than in females. Treatment outcome in TB/HIV was more unsuccessful than patients with TB infection only. This observation has been reported by Osei and colleagues [31] in a study conducted in Volta region of Ghana and by several other studies elsewhere [21,32,33,34]. This observation may be attributed to the drug-drug antagonism between rifamycins and the antiretroviral drugs that result in low bioavailability of the drugs [35] and thus, resulting in unsuccessful treatment outcomes.

The mortality rate associated with TB (7.4%) was observed among males who were all new patients. This may be influenced by several factors such as severity of disease at the time of reporting to the hospital (delay between onset of disease and the start of treatment), HIV co-infection, and patients' compliance to treatment, malnutrition, physiological / immunological changes associated with aging and support provided to the patient to ensure that treatment is completed [36]. Mukadi and colleagues remarked that fatality rates are higher for TB/HIV co-infected patients receiving only anti-TB treatment but not antiretroviral therapy (16 to 35%) than for treated TB patients who are HIV negative (4 to 9%) [37] with the highest death rate occurring in coinfected patients with the lowest CD4 cell counts [38]. Moreover, Alobu et al also reported death to be associated with smear-negative TB, rural residence, HIV co-infection, not receiving antiretroviral therapy, or cotrimoxazole preventive therapy among TB/HIV patients in resource-poor areas [39]. Mortality rate was found to be higher in TB/HIV co-infected patients than in TB only patients. With its status as one of the ranking the high TB/HIV endemic countries, this calls for innovative and systematic or active case finding in the country especially in resource-limited areas like the Kpando Municipality. The villages of Aveme and Anfoega were highly prevalent for TB cases and least in Botoku village. It is possible that the source of infection in these rural areas may be mainly due to contacts outside these places [40] howbeit it would be necessary to conduct an intense case finding among household members living in these communities. Improvement in case finding among community dwellers will help to realize the United Nations Sustainable Development Goals of ending TB epidemic by 2030.

5. CONCLUSION

Overall, a high percentage of smear positive tuberculosis was commonly reported among males but showed a decreasing trend among the age group with statistical significance. Moreover, treatment success was high which reflects on patients' compliance to treatment, and was more successful among TB only patients compared to patients with TB/HIV co-infection. However, strategic methods which will be effective to encourage good healthcare seeking behavior among infected patients should be put in place and monitored to optimize early diagnosis and thus minimize the spread of infection among other community members.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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