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CHARACTERISTICS AND OUTCOMES OF TUBERCULOSIS PATIENTS WHO FAIL TO SMEAR CONVERT AT TWO MONTHS IN BUNGOMA COUNTY, 2012-2015.
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CHARACTERISTICS AND OUTCOMES OF TUBERCULOSIS PATIENTS WHO FAIL TO SMEAR CONVERT AT TWO MONTHS IN BUNGOMA COUNTY, 2012-2015.

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ABSTRACT

Background: **Tuberculosis (TB) remains one of the world's deadliest communicable diseases. Sputum smear positive patients are infectious for a variable period after start of treatment. Patients' receiving anti-TB treatment become non-infectious within the first two months, assessment of sputum smear conversion is by smear microscopy.**
Objective: **To determine the characteristics and treatment outcomes of TB patients who fail to smear convert at two months in Bungoma County, 2012-2015.**
Design: **Retrospective descriptive study.**
Setting: **All health facilities managing tuberculosis in Bungoma County.**
Subjects: **All patients treated for TB, January 2012-December 2016.** *Results:* **A total of 8393 patients developed TB of which 6998 (83%) had pulmonary TB, of those who had pulmonary TB 3008 (43%) initial smears were positive. After the intensive phase of treatment, 2380 (79%) had converted to smear negative, 141 (5%) were still smear positive and 487 (16%) sputum not done.**
Final outcome showed that those who smear converted at two month had a treatment success rate 2295 (96%) and those who delayed to convert treatment success rate was 108 (77%). Out of those who delayed to smear convert 7 (5%) patients developed drug resistant TB while those whose smear converted none developed drug resistant TB.
Conclusion: **The delay in sputum conversion at the end of intensive phase is associated with unfavourable outcome i.e. failure and drug resistant TB.**

INTRODUCTION

Tuberculosis (TB) remains one of the world's deadliest communicable diseases (1). In 2015, an estimated 10.4 million people developed TB and 1.4 million TB deaths were recorded, with an additional 0.4 million deaths resulting from TB among people living with human immuno deficiency virus (HIV) (1). Kenya is ranked 15th among the 22 high TB burden countries that account for 80% of the global TB burden.

It is ranked 4th in Africa (2). In the year 2015 there were approximately 88,000 new TB case notified in Kenya, 9,400 deaths among TB infected and 8,100 deaths among TB/HIV co-infection (3). TB case notification in Bungoma County was 1,515 with over 200 (10%) deaths, making it a high TB burden County in Kenya (3).Successful control of tuberculosis depends on early and effective control of the transmission of *Mycobacterium tuberculosis* from infectious patients. Sputum smear conversion at the end of the intensive phase of treatment is used as an important early predictor of treatment success (4). The World Health Organisation (WHO) recommends monitoring of all TB patients during anti-TB treatment to assess response to therapy (4). The parameters used for monitoring during TB treatment include: body weight and sputum smear examination which should be done at the Presence of several of these factors in an individual could increase the chances of delayed smear conversion and therefore increased duration of infectivity. The knowledge of factors associated with delayed sputum smear conversion at the end of the intensive phase of anti-tuberculosis treatment in our set-up is necessary, in order to prevent unfavorable outcomes. This study therefore set out to determine the characteristics and outcomes of tuberculosis patients who delayed to smear convert at two months' end of intensive phase of treatment (4). After starting effective anti-tubercular treatment, bacillary load should decrease rapidly (5). The proportion of smear positive patients with sputum smear conversion at the end of intensive phase is an indicator of TB program performance (5). Non-conversion of sputum smear at the end of intensive phase of treatment has been documented to be associated with unfavourable outcomes that is lost-to-follow up, failure, development of resistant TB and death (6-9). Some of the factors that have been associated with delayed smear conversion at two months include high bacillary load at diagnosis, cavitation on chest X-ray, old age at diagnosis, living far away from the health facility, male gender and treatment with non-standardized regimens or missed doses of anti-tuberculosis drugs (10-15)

MATERIALS AND METHODS

Study design: This was a retrospective descriptive study using routine collected programme data Setting, Bungoma County is located in the western region of Kenya and is one of the 47 counties in Kenya. It is 2,069 square kilometres and has a population of about 1.6 million, with 52.9% of the population living below the poverty line. Agriculture is the main economic activity (16).It is divided into 10 sub-counties namely Bumula, Mt Elgon, Kabuchai, Kanduyi, Kimilili, Sirisia, Tongaren, Cheptais, Webuye East and Webuye west.

Context: Bungoma County has 203 health facilities across the county, of which 176 are TB treatment sites while 86 are both treatment site and diagnostic i.e. smear microscopy can be accessed. The county has 3 genexpert sites. Treatment of TB is divided into 2 phases the intensive phase which is the initial 2 months and the continuation phase comprise of 4 months, a total of 6 months.

Follow up sputum is normally done at the end of intensive phase that is at 2nd month, 5th month and at the end of treatment 6th month

Study population: We reviewed the clinical records of patients who were treated for TB and notified on the electronic data base to the National Tuberculosis Program between January 2012 and December 2015 in health facilities in Bungoma County.

Data collection: The study used data from the TIBU, software that has consistency checks to ensure that data errors are minimized.

DATA ANALYSIS

Data was extracted from the TIBU database, cleaned and exported to Stata v11 for analysis. Descriptive analysis was undertaken. For continuous variables mean (SD) and median (IQR) was reported for normally distributed and non-normally distributed data respectively. Proportions were calculated for categorical variables.

ETHICAL APPROVAL

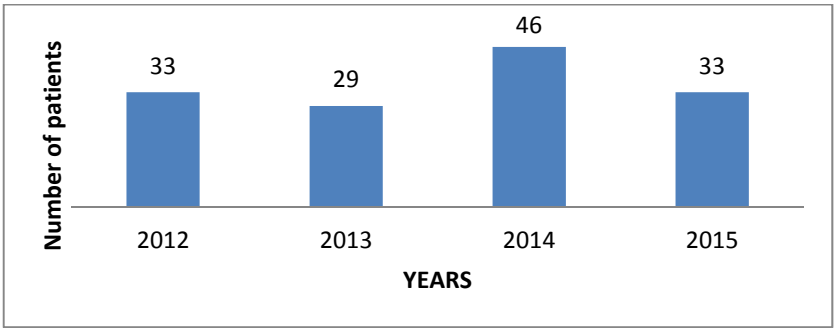
This study was approved by the Moi University College of Health Sciences (MU/CHS) and Moi Teaching & Referral Hospital (MT&RH) Institutional Review Board (IREC).

RESULTS

In the duration of the study, 8393 patients developed TB of whom 1395 (17%) had extraplumonary TB and 6998 (83%) had pulmonary TB. Of those who had pulmonary TB, 3008 (43%) had positive sputum, 3049 (44%) smears were negative and 941 (13%) had no sputum smears done. After the intensive phase of the pulmonary patients 2380 (79%) had converted to smear negative, 141 (5%) were still smear positive and 487 (16%) had no sputum smears. Of the 141 who delayed to smear convert at two month, only 2 had culture and drug sensitivity test done. The year 2014 had most of the patients who delayed to smear convert at two months (As shown in figure 1).

Figure 1

The number of tuberculosis patient who delayed to smear converts at month two of tuberculosis treatment-Bungoma County 2012-2015



Men had the higher number of patients who delayed to smear convert at two months 89 (6%), while in women it was 52 (5%) though the p value was not significant (p value= 0.52) Patients aged 65 years and above had the highest number who delayed to smear convert at two months 35 (9%) with a p value of <0.001, which was significant. Concerning the body mass index (BMI) BMI below 16.5 had 17 (9%) who delayed to smear convert at the end of intensive phase, with a significant p value of <0.001). Patients who decline HIV test 7 (11%) delayed to smear convert at two month followed by HIV positive at 36 (6%), smear conversion at two months was significantly associated with HIV status p value =<0.001. (As shown in table 1)

Table 1

Characteristics of sputum smear-positive tuberculosis patients, comparing the end of intensive treatment phase non-converters (delayed converters) with converters in Bungoma County, 2012-2015

Variable		Smear negative at two month n=2380 (%)	Smear positive at two month n=141 (%)	P value
Gender	Female	959(95)	52(5)	0.52
	Male	1421(94)	89 (6)	
Age group	<15	78 (95)	5 (5)	0.001[x]
	15-24	473 (97)	16 (3)	
	25-34	336 (96)	16 (4)	
	35-44	363 (93)	31 (7)	
	45-54	353 (94)	19 (6)	
	55-64	427 (95)	19 (5)	
	65+	350 (91)	35 (9)	
Body mass index	<16.5	163 (91)	17 (9)	<0.001[x]
	16.5-18.4	882 (93)	64 (7)	
	18.5-24	1045 (96)	46 (4)	
	>25	79 (94)	5 (6)	
	Missing	211 (96)	9 (4)	
X-ray	Not done	2255 (95)	128 (5)	0.463
	Done	125 (91)	13 (9)	
HIV status	Decline	7 (100)	0 (0.0)	<0.001[x]
	Not done	57 (89)	7 (11)	
	Negative	1755 (95)	98 (5)	
	Positive	561 (94)	36 (6)	
Cotrimoxazole preventive therapy (n=597)	No	1	0 (0.0)	0.875
	Yes	565 (95)	31 (5)	
Antiretroviral drugs(n=597)	No	27 (96)	1 (4)	0.947
	Yes	542 (95)	27 (5)	

P value significant at <0.05

Treatment success rate was better in patient who smear converted at two months 2295 (96%).(As show in table 2).

Table 2

Treatment outcome in relation to smears conversion after intensive phase of tuberculosis treatment in Bungoma County, 2012-2016

		Converted smear at two month n=2380 (%)	**Delayed to smear convert at two month n=141 (%)**
Treatment outcome	Treatment success rate	2295 (96)	109 (77)
	Died	33 (1)	4 (3)
	Loss-To-Follow-Up	40 (2)	3 (2)
	Failure	12 (<1)	17 (12)
	MDR	0	8 (5)

DISCUSSION

In pulmonary tuberculosis, the assessment of response to therapy is evaluated by disappearance of acid-fast bacilli (AFB) from sputum smear on completion of the intensive phase. Our study showed that Sputum smear of 2380 (94%) had converted and141 (5%) had not converted after completion of the intensive phase. Studies done in many settings have shown that proportions of sputum smear non-conversion at the end of the intensive phase of TB treatment range from 5% to 32% (10-15). Many reasons can explain the non-conversion of sputum smear at the end of the intensive phase of TB treatment. It can be due to non-viable bacteria which remain visible by microscopy but can be isolated through culture, poor supervision of the initial phase of therapy, poor patient adherence, poor quality of anti-TB drugs, doses of anti-TB drugs below the recommended range, co-morbid conditions, drug-resistant mycobacterium TB that is not responding to first-line treatment and heavy initial bacillary load (6,15). Results showed an association between age and two-month sputum smear non-conversion, with older TB patients showing high risk for non-conversion. These findings are consistent with studies conducted among TB patients in Cameroon, Korea and Burkina Faso (15, 17-18) Progressive age-related immune dysregulation and delayed TB diagnosis (19) could possibly account for the observed two-month sputum smear non-conversion among older patients. Results of this study showed an association between body mass index and two month sputum smear non-conversion, with body mass index below 16.5 showing high risk of non-conversion at two month. These finding are similar to study done in Cameroon (8).

This can be due to delay or lack of absorption of the drugs, reduced protein binding of some of the drugs or fluctuation in the volume of distribution of the drugs. This study showed unfavourable treatment outcome (failure and development of DR-TB) in patients, who delayed to convert at 2 months. These finding is consistent with studies done in Cameroon and Nigeria (8, 9). This can be attributed the fact that mycobacterium that is resistant will not respond to the first line TB treatment or it can be due to suboptimal therapy.

STUDY STRENGTHS

Large sample size: Adherence to the conduct and reporting of the study according to the Strengthening the Reporting of observational studies in Epidemiology (STROBE) guidelines (20).

LIMITATIONS

Use of routine programmatic records that may have inaccuracies, inconsistencies and missing data- though data validation is normally conducted on quarterly basis. Implications patients' characteristics including age, sex, and HIV status need to be considered when monitoring TB patients.
Active case finding is important towards early TB detection.

RECOMMENDATIONS

There should be a more organized approach to test and record HIV status according to policy guidelines. Patients who delayed to smear convert at two months are poorly followed, more attention to be paid to sending sputum specimens for culture and DST.

CONCLUSION

Our analysis showed that 5% of tuberculosis patients remained smear positive at the end of intensive phase. Risk factors for persistent positive smear at two months were old age, BMI below 16.5 and HIV status. The delay to smear conversion at the end of intensive phase is associated with unfavourable outcome that is failure and development of drug resistant TB. Active case finding in the old age, provision of food supplements and HIV screening should be put in place to minimize the delayed to convert which will reduce the unfavourable outcome thus making End TB strategy a reality.

Conflict of Interest: None

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AUTHORS' CONTRIBUTION

All authors participated in writing the study protocol, data analysis, report writing, drafted the paper with subsequent revision and approved the final manuscript.

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