TB-diabetes comorbidity and associated factors in Maekel Zone, Eritrea: A cross sectional study.

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Abstract

Background : In Eritrea, no study document the true burden of TB-diabetes comorbidity. However, diabetes has been constantly increasing with a prevalence of 3.4 %. Similarly, even though TB notification is showing a declining trend the prevalence is 123/100,000 population. With an increasing diabetes trend, the country is at higher risk of rising TB-diabetes comorbidity which can further complicate TB care, control and prevention activities. Thus, this study was conducted to assess the prevalence of diabetes among pulmonary positive TB patients and its influencing factors in Maekel zone, Eritrea.

Methods: This study was a cross sectional study conducted in all (11) TB diagnostic and treatment sites of Maekel zone. All consecutive pulmonary positive TB cases who were registered during the period of 2015-2018 in the national TB treatment register and were eligible included in the analysis. Pretested data extraction tool was used to collect the required information. Data analysis was done by SPSS version 23. Simple frequencies, percentages and means were used to describe the data. Chi-square test and logistic regression analysis was also performed.

Results: A total of 490 pulmonary positive TB cases were eligible for the study and the overall prevalence of diabetes among pulmonary positive TB cases was 4.3%. Univariate logistic regression showed that participants with an older age (45-90) were more likely to have TB-diabetes comorbidity (COR: 4.397[CI: 1.675-11.545], $p < 0.01$) than those aged 10-44 years old. In addition, subjects whose weight was 65kg and above were more likely (COR: 7.647[CI: 1.965-29.758], $p < 0.01$) to have TB- diabetes comorbidity than those with lower body weight.

Conclusion: TB-diabetes comorbidity observed in this study is low but given the growing diabetes trend in the country, an integrated TB-DM services should be given regularly on full scale at all health facilities.

Background

Tuberculosis is still a cause of much public fear and stigma in many parts of the world accounting for millions of morbidity and mortality each year [1]. The burden of this global epidemic is bore not by the developed countries where this disease is regarded as a disease of the past but by low- and middle-income countries where ending TB is still a distant reality [1–5]. One of the key challenges in putting an end to TB is its changing landscape of care and prevention spurred by the continuous epidemiological and demographic transitions the world is currently witnessing. Such transitions include the increase in the burden of non-communicable diseases as well as the aging populations adding to the existing pool of risk factors and giving importance to previously overlooked comorbidities [5, 6].

A quite preventable but incurable public health concern currently in the rise is Diabetes Mellitus with an estimated 425 million cases in 2017, with numbers predicted to increase to 629 million by 2045[3]. Countries found at the conjunction of TB and diabetes are faced with a double disease burden incurring catastrophic damages at the health system, family and individual level. Diabetes is a known risk factor for TB [3, 5, 6, 7, 8] and it triples the risk of developing Tuberculosis with 15% of the global TB

cases attributed to it [9, 10]. According to a recent systematic review on the co-prevalence of Type 2 diabetes mellitus and TB, high burdens of diabetes in TB patients were found in Mexico (36.1%), China (30.8%), India (44%), Marshall Islands (45%) and Malaysia (41.3%) followed by Kyrgyzstan (18.7%), Ethiopia and Tanzania (15%)[11]. The excess cases of TB attributable to diabetes have transcended the records set by the HIV-TB coinfection. Nowadays, globally there are now more TB patients living with concomitant diabetes than patients with concomitant HIV infection [8]. This increasing prevalence in TB-diabetes comorbidity offsets the expected effect of the intensified TB control efforts and represents a threat to the decades of progress made against TB [12].

Previously developed evidence base suggests that the relationship between TB and diabetes goes beyond an increased risk of developing TB with both diseases complicating each other at many levels. TB diagnosis among diabetic people could be challenging and TB patients with overlapping diabetes may experience adverse TB treatment outcome. In addition, diabetes may also accelerate the emergence of drug-resistant TB among those receiving TB treatment [3]. Conversely, TB may increase existing insulin resistance, trigger the onset of diabetes in predisposed individuals and worsens glycemic control in existing diabetes cases. Moreover, TB and DM medications may undermine each other's effectiveness through drug-drug interaction contributing to failure of TB treatment and glycemic control [3]. Thus, this double burden leads to substantial strain on individuals, families, health systems, and society [12].

According to the report of international diabetes federation, Eritrea has a diabetes prevalence of 3.4% which is constantly increasing [13]. At the same time, even though TB notification is showing a declining trend, the prevalence is 123/100,000 populations [14]. In response to these burdens, the country has adopted and implemented the provisional collaborative framework for the care and control of TB and diabetes which was launched by the WHO and the International Union against TB and Lung Diseases [9]. Among all TB cases registered in the 2018 in Maekel zone, 5.4% of them were also diabetic patients. [15]. With an increasing diabetes trend, the country is at higher risk of rising TB-diabetes comorbidity which can further complicate TB care, control and prevention activities. Thus, this study was conducted to assess the prevalence of diabetes among pulmonary positive TB patients and identify factors related to TB-diabetes comorbidity in Maekel zone, Eritrea.

Methods

Study design

The study was a cross sectional in design.

Study setting and participants

The study subjects were pulmonary positive TB cases who were treated for TB during the period 2015-2018 at all (11) TB diagnostic and treatment sites of Maekel zone. The study was conducted from June to August 2019. These health facilities include three community hospitals and eight health centers in which majority of them were located inside Asmara city. TB diagnosis was made based on the standard

diagnostic procedures as stated in the National TB Control Program Guidelines [16]. Thus, consecutive pulmonary positive TB patients diagnosed based on the standard diagnostic procedure by sputum smear microscopy for acid fast bacilli and or by Gene-x-pert were included in this study. Similarly, Diabetic status of all study cases was found from the record as a self-reported history of diabetes or fasting plasma glucose $\geq 126\text{mg/dl}$ or casual plasma glucose concentration $\geq 200\text{mg/dl}$ as Defined by WHO [17].

Inclusion criteria

All pulmonary positive TB cases who were registered during the period of 2015-2018 in the national TB treatment register were included for analysis.

Exclusion criteria

All pulmonary negative and extra pulmonary TB cases were not part of this study. In addition, pulmonary positive TB patients with unknown or undocumented (missing) diabetic status were also excluded.

Sampling technique and sample size

The sampling technique used in this study was census sampling in which a total of 490 consecutive pulmonary positive TB cases who meet the inclusion criteria were included in the final analysis.

Instruments and data collection

Pretested data extraction tool was used to collect the required information from the medical records (national TB treatment register, TB laboratory register and TB treatment cards) available at respective health facility. The data extraction tool was developed by the authors based on TB Laboratory register, TB treatment register and TB patient treatment card which are adopted from the standard recording tools recommended by WHO. The data extraction tool consisted two sections, with the first section containing information on socio demographic characteristics of patients such as age, sex and residence. Section two covers information on clinical variable such as type of patient, patient category, laboratory results (smear microscopy/Gene-X-pert), HIV status, diabetes status and treatment outcome.

Data analysis

Data cleaning was performed for the collected information, then it was coded, entered and analyzed by SPSS version 23. Subjects with unknown or missing diabetic status were excluded from the analysis. Simple frequencies, percentages and means were calculated to describe the data. Chi-square test has been done to test the statistical significance of association of different socio demographic and clinical variable to the probability TB-DM coinfection. Univariate logistic regression analysis was performed but multivariate logistic regression analysis was not done due to small number of TB-DM cases. In this study, $p \leq 0.05$ was considered as statistically significant.

Results

After excluding two ineligible cases, a total of 490 pulmonary positive TB patients treated for TB in Maekel zone at the 11 health facilities during the period of January 2015 up to December 2018 were included in the analysis. The overall prevalence of diabetes among the pulmonary positive TB cases was 4.3%. Male participants dominated in both TB patients with diabetes (66.67%) and those without diabetes (55.44%). Among TB-diabetes cases 71.42% were 45 and above years old whereas in TB cases without diabetes 49.04% were aged 25-44 years. Similarly, mean age among TB-diabetes cases was 51.04 years which is higher than the mean age of those without diabetes 40.60 years. The average body weight among TB-diabetes case was 53.4 kg but in subject with TB disease only, it was 46.8 kg (Table 1). Generally, almost three fourth (74.49%) of the study subjects and specifically 85.71% of the TB-diabetes cases and 73.98% of TB cases without diabetes were from urban areas.

Depending on their history of TB treatment, majority (85.71%, 89.34 %) of the cases were new in both TB with diabetes and without diabetes respectively. Previous TB treatment was reported among few (4.29%) TB-diabetes and in 10.66% of TB cases without diabetes. Among those previously treated cases only relapse were found among TB-diabetes but treatment after failure and after lost to follow up were reported only among TB cases without diabetes comorbidity.

According to patients' treatment category, 85.71% of TB-diabetes cases and 89.13% of TB cases without diabetes belonged to the first treatment category. The least number of cases were documented in category three in which only 2(0.43%) TB patients without diabetes coinfection and none of those with TB-diabetes coinfection fall in that category. The overall HIV positivity in this study was 10% in which comparable HIV positivity of 9.52% and 10.02% was found among TB-diabetes and without diabetes respectively.

More interestingly, 95.24% of TB-diabetes cases were cured and only 1 case (4.76%) died. Similarly, among TB case without diabetes, 92.75% were cured, 3.41% failed treatment, and 1.71% died (Table 2).

Regression analysis

The study found that age and weight of subjects were significantly associated with the presence of TB-diabetes comorbidity among pulmonary positive TB cases. Age of participants was categorized in to two groups as 10 – 44 and 45 – 90. Thus, univariate logistic regression showed that participants with an older age (45-90) were more likely to have TB-diabetes comorbidity (COR: 4.397[CI: 1.675-11.545], $p < 0.01$) than those aged 10-44 years old. Similarly, weight was categorized as 25-44 kg, 45-64 kg, and ≥ 65 kg. The finding revealed that subjects whose weight was 65kg and above were more likely (COR: 7.647[CI:1.965-29.758], $p < 0.01$) to have TB- diabetes comorbidity than those with lower body weight (Table 3).

Discussion

In the present study, overall prevalence of diabetes among the pulmonary positive TB cases was 4.3%. This was consistent to previous study that reported a prevalence of 4.7% in Zambia [18]. Higher prevalence of TB-diabetes comorbidity was also reported from Ethiopia 8.5% [19], Portugal 6% [20], Mexico 29.63% [21], Iran 24.3% [22], and India 25.3% [23]. The prevalence of diabetes among TB patients observed in this study is comparable to the occurrence of the disease in the general population. While the difference among countries could be due to the inherent difference in socio economic and demographic characteristics among their population and the existing burden of both diseases in general population.

Many studies showed that male TB patients were more likely to suffer from TB-diabetes comorbidity than female TB patients [19, 20, 22, 23,24]. The current study had also a consistent finding in which male subjects were proportionally dominant in both TB-diabetes cases and those without diabetes. In contrary to this, a study in Zambia described that majority of the TB-diabetes cases were females [18]. Presence of the comorbidity predominantly among male cases could be related to the relatively higher probabilities of smoking and alcohol drinking among men in Eritrea in which these risk factors could have increased the occurrence of both disease in this particular group.

Among TB-diabetes cases nearly three fourth were 45 and above years old whereas in TB cases without diabetes almost half of them were aged 25–44 years. Similarly, mean age among TB-diabetes cases was 51.04 years which is higher than the mean age of those without diabetes 40.60 years. Previous similar studies reported a consistent finding in which TB-diabetes cases were older than TB cases without diabetes and the difference was significant [20, 22, 25]. This could be described as age related diabetes because Type 2 diabetes frequently develops in older adults. This in turn could lead to the development of TB in infected individuals with the decreasing immunity due to diabetes. Opposing findings were also reported from Zambia where the mean age of participants was 33 and 37 years for TB-diabetes cases and those without diabetes respectively. None of the participants with coexisting TB-diabetes were above 50 years of age [18].

The present study failed to report BMI (body mass index) due to unavailability of height record for all patients. Thus, our result could not be compared to available literatures that reported MBI and should be interpreted carefully. Higher mean weight (53.4 kg) was observed among TB-diabetes cases in comparison to the TB cases without diabetes (46.8 kg). A likely description for effects of weight in relation to TB and diabetes has been documented in which higher risk of TB is detected in undernourished or underweight individuals and this risk decreases as individuals gain weight [12]. According to a study in Zambia, patients with coexisting TB-diabetes were more likely to have a normal or low BMI [19]. Likewise, a study from India reported lower mean BMI of TB-diabetes than those TB cases without diabetes [26]. Another study from UK found comparable BMI among TB-diabetes and those without diabetes [25]. Significant higher BMI in TB-diabetes patients was also reported [24, 27] that describes excessive weight gain predisposes to diabetes which is another independent risk factor for TB [3, 24]. People with diabetes could have been over weight and may remain in over weight status after being affected by TB. On the other hand, there could be weight loss among diabetes cases due to TB that is infection induced hyperglycemia.

Residential difference among study subjects had been related to varying occurrence of these diseases. Consequently, majority of the TB-diabetes cases and almost three fourth of TB cases without diabetes in the current study were residents of an urban areas. Earlier studies showed higher prevalence of diabetes among TB patients who were urban residents [19,26]. In contrast, a study in Northern India reported a higher number of study participants with TB-diabetes were living in rural areas [28]. The reason for higher TB-diabetes comorbidity among urban residents could be linked to the sedentary life style such as physical inactivity and unhealthy dietary intake. On the other hand there could be under diagnosis of these diseases in rural populations in relation to limited healthcare access or delay in healthcare seeking.

Depending on TB treatment history and category, majority of the cases were new case and in first treatment category in both TB-diabetes and without diabetes respectively. Previous TB treatment was reported among few (4.29%) TB-diabetes and in 10.66% of TB cases without diabetes. Among those previously treated cases only relapse were found among TB-diabetes but treatment after failure and lost to follow up were reported only among TB cases without diabetes comorbidity. In agreement to the present study results, a study from UK reported that almost all cases of TB-diabetes and those without diabetes were new TB case and only less than 2% of them were previously treated [25]. Nevertheless, relatively higher number of TB-diabetes in category two with comparable figures among those TB cases without diabetes was reported previously [24, 26]. This could be due to the fact that Eritrea has an excellent TB cases management and follow up reflected by very high TB treatment success rate which could have minimized the possibility of retreatment of TB cases.

Another health-related characteristic investigated by the study was HIV-infection. The overall HIV positivity in this study was 10% in which comparable HIV positivity was found among TB-diabetes and without diabetes. Studies in Zambia and Ethiopia had higher HIV positivity rate among TB-diabetes case [18, 19,22]. A study in Portugal reported discrepant results with absence of HIV infection being a factor significantly associated with diabetes among TB patients [20]. HIV positivity rate found in this study was almost double of the prevalence of HIV in TB and almost 10 times higher than the prevalence in the general population. This could be due related to the study setting (Maekel zone) which may contain the highest number of HIV cases in the country.

In the current study, univariate logistic regression showed that participants with an older age (45–90) were more likely to have TB-diabetes comorbidity (COR: 4.397[CI: 1.675–11.545], $p < 0.01$) than those aged 10–44 years old. In addition, subjects whose weight was 65 kg and above were more likely (COR: 7.647[CI: 1.965–29.758], $p < 0.01$) to have TB- diabetes comorbidity than those with lower body weight. It's expected that at an older age in the presence of immunity compromising infection people could be more prone to develop TB disease leading to comorbidity.

Prior study revealed that TB patients aged 41 and above had higher odds of having diabetes than younger patients [23]. Other literature also noted increasing age, family history of diabetes, sedentary occupation, body mass index, type of TB, category of TB, and smoking were significantly associated [24,26].

Conclusions

TB-diabetes comorbidity observed in this study is low but could not be ignored as increasing diabetes trend has been noticed in the country. Age ≥ 45 years and body weight of 65 kg and above were significantly associated to TB-diabetes comorbidity among pulmonary positive TB cases. Early TB screening for diabetic patients and diabetes testing for TB patients should be continued regularly on full scale at health facilities.

Limitations of the study

Data for this study was collected from medical records in TB diagnostic and treatment sites. Thus, some information may be missing in which it hindered analysis of some important variable like BMI. In addition, there were few TB cases with diabetes and thus multivariate logistic regression was not performed.

List Of Abbreviations

BMI- body mass index

COR- crude odds ratio

DM- diabetes mellitus

HIV- human immune deficiency virus

IUATLD – international union against TB and lung disease

MOH- ministry of health

TB- tuberculosis

WHO- world health organization

Declarations

Ethics approval and consent to participate

The study was approved by the research clearance committee of the Research department of the Ministry of Health, Maekel branch. The heads of the health facilities which were included in the study were informed on the objectives of the study and were provided with written consent prior to data collection. Individual consent from study participants was not required due to data collection nature of the study. The data was collected anonymously and did not include any personal identifiers.

Consent for publication

Not applicable

Availability of data and materials

The data set analyzed in this study is available from the corresponding author on reasonable request.

Competing interests

Not applicable

Funding

Not applicable

Authors' contribution

ZZ conceived the idea, designed the study, analyzed the data and wrote the manuscript. AH and HA participated in data collection and entry. AY and RO prepared literature review and draft proposal. AB critically assessed the manuscript. All authors have reviewed and read the final manuscript.

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Tables

Table 1. Background characteristics of study participants

Variable	Pulmonary positive TB		Total (%) N=490
	Diabetic(n=21)	Non diabetic(n=469)	
Sex (n=490)			
Male	14(66.67%)	260(55.44%)	274(55.92%)
Female	7(33.33%)	209(44.56%)	216(44.08%)
Age range(n=490)			
10-44	6(28.57%)	299(63.75%)	305(90.50%)
45-90	15(71.43%)	170(36.25%)	32(9.50%)
Mean age(years)	51.04	40.60	41.06
Body weight(Kg) (n=487)			
25-44	6(28.57%)	195(41.85%)	201(41.27%)
45-64	11(52.38%)	254(54.50%)	265(54.42%)
65 and above	4(19.05%)	17(3.65%)	21(4.31%)
Mean body weight	53.4	46.8	47.06%
Residence (n=490)			
Urban	18(85.71%)	347(73.98%)	365(74.49%)
Rural	3(14.29%)	122(26.02%)	125(25.51%)

Table 2. Clinical characteristics of study subjects

Clinical characteristics			
Variable	Pulmonary positive TB		Total (%)
	Diabetic (n=21)	Non diabetic (n=469)	(n=490)
Type of TB patient			
New	18(85.71%)	419(89.34%)	437(89.18%)
Previously treated	3(14.29%)	50(10.66%)	53(10.82%)
Patient category			
I	18(85.71%)	418(89.13)	436(88.97%)
II	3(4.29%)	49(10.450)	52(10.62%)
III	0(0.00%)	2(0.43)	2(0.41%)
HIV test result			
Negative	19(90.48%)	422(89.98%)	441(90.00%)
Positive	2(9.52%)	47(10.02%)	49(10.00%)
TB Treatment out come			
Cured	20(95.24%)	435(92.75%)	455(92.86%)
Treatment completed	0(0.00%)	2(0.43%)	2(0.41%)
Failed	0(0.00%)	16(3.41%)	16(3.36%)
Died	1(4.76%)	8(1.71%)	9(1.84%)
Not evaluated	0(0.00%)	4(0.85%)	4(0.82%)

Table 3. Regression analysis

Variable	Pulmonary positive TB		COR[95%CI]	p-value
	Diabetic(n=21)	Non diabetic(n=469)		
Sex (n=490)				
Male	14(5.11%)	260(94.89%)	r	
Female	7(3.24%)	209(96.76%)	0.622[.247-1.569]	0.351
Age range(n=490)				
10- 44	6(1.97%)	299(98.03)	r	
45-90	15(8.11%)	170(91.89%)	4.397[1.675-11.545]	0.003
Body weight(Kg) (n=487)				
25-44	6(2.99%)	195(97.01%)	r	
45-64	11(4.15%)	254(95.85%)	1.407[0.512-3.872]	0.508
65 and above	4(19.05%)	17(80.95%)	7.647[1.965-29.758]	0.003
Residence (n=490)				
Urban	18(4.93%)	347(95.07%)	r	
Rural	3(2.4%)	122(97.6%)	0.05[0.137-1.637]	0.238
Type of TB patient				
New	18(4.12%)	419(95.88%)	r	
Previously treated	3(5.66%)	50(94.34%)	1.397[0.397-4.909]	0.602
Patient category				
I	18(4.13%)	418(95.87%)	r	
II	3(5.77%)	49(94.23%)	1.422[0.404-5.000]	0.583
III	0(0.00%)	2(100%)	0.000[.000-]	0.999
HIV test result				
Negative	19(4.30%)	422(95.70%)	r	
Positive	2(4.08%)	47(95.92%)	0.945[0.213-4.185]	0.941