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Original Article **Open Access**

Diabetes and tuberculosis comorbidity: a cross-sectional study of patients attending diabetes clinic in Accra, Ghana

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Abstract:

Background: Diabetes and tuberculosis have significantly increased health-related and socioeconomic implications on individuals, families, health systems, and the global economy at large, making them a serious global health concern. The objective of this study is to determine the prevalence of diabetes-tuberculosis co-morbidity and the socio-demographic, behavioral and clinical factors associated with this comorbidity.
Methodology: This was a cross-sectional study of selected diabetic patients at the diabetic clinic of the Shai-Osudoku District Hospital-Dodowa in the Greater Accra Region, Ghana. Sputum samples from confirmed diabetics were screened for tuberculosis using GeneXpert MTB/RIF Test and Ziehl-Neelsen AFB Microscopy. The patients' awareness of their susceptibility to diabetes-tuberculosis, treatment compliance and care manager attentiveness, were assessed through semi-structured questionnaire. Statistical analyses of data were performed using Microsoft Analysis Tool Pak.
Results: The prevalence of diabetes-tuberculosis comorbidity in the study was 7.0% (7/100). The occurrence of diabetes-tuberculosis comorbidity among the participants seemed to be higher in males (11.1%, 3/27) as compared to female (5.5%, 4/73), with no statistically significant difference (p=0.327). The females with diabetes-tuberculosis comorbidity statistically demonstrated poorer glycaemic control (females: 17.08±0.79 mmol/L and males: 15.95±0.79 mmol/L; 95% CI; 7.15, p<0.001). Participants in the age group 61-80 years had the highest prevalence of 11.4% (4/35) for diabetics-tuberculosis comorbidity but this was not statistically significant (p=0.509), although their mean blood glucose was significantly higher than other age groups (p=0.0137). The mean of patients with no awareness of their susceptibility to diabetic-tuberculosis co-morbidity was 77±28.97% (95% CI=3.79-46.62, p=0.4648). Treatment compliance was observed in 91.0% of the study participants mainly due to high level of attentiveness by care providers at the diabetic clinic for 69.0% of the participants.
Conclusions: The prevalence of diabetes-tuberculosis comorbidity in this study is 7.0%, with majority of the diabetics not aware of their susceptibility to tuberculosis although there was high treatment compliance. There is the need for the adoption of a collaborative framework and integrated approach in the clinical management and control of diabetes and tuberculosis.

Keywords: Diabetes mellitus, tuberculosis, comorbidity, glycaemic control, Ghana

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Comorbidité du diabète et de la tuberculose: une étude transversale de patients fréquentant une clinique de diabète à Accra, Ghana

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Résumé:

Contexte: Le diabète et la tuberculose ont considérablement accru leurs implications sanitaires et socioéconomiques sur les individus, les familles, les systèmes de santé et l'économie mondiale dans son ensemble, ce qui en fait un grave problème de santé mondial. L'objectif de cette étude est de déterminer la prévalence de la comorbidité diabète-tuberculose et les facteurs sociodémographiques, comportementaux et cliniques associés à cette comorbidité.
Méthodologie: Il s'agissait d'une étude transversale portant sur des patients diabétiques sélectionnés à la clinique diabétique de l'hôpital du district de Shai-Osudoku-Dodowa dans la région du Grand Accra, au Ghana. Des échantillons d'expectorations provenant de diabétiques confirmés ont été dépistés pour la tuberculose à l'aide du test GeneXpert MTB/RIF et de la microscopie Ziehl-Neelsen AFB. La conscience des patients de leur susceptibilité au diabète-tuberculose, l'observance du traitement et l'attention du responsable des soins ont été évaluées au moyen d'un questionnaire semi-structuré. Les analyses statistiques des données ont été effectuées à l'aide de Ensemble d'outils d'analyse Microsoft.
Résultats: La prévalence de la comorbidité diabète-tuberculose dans l'étude était de 7,0% (7/100). La fréquence de la comorbidité diabète-tuberculose parmi les participants semblait être plus élevée chez les hommes (11,1%, 3/27) que chez les femmes (5,5%, 4/73), sans différence statistiquement significative (p=0,327). Les femmes présentant une comorbidité diabète-tuberculose ont démontré statistiquement un contrôle glycémique plus faible (femmes: 17,08±0,79 mmol/L et hommes: 15,95±0,79 mmol/L; Cl à 95%; 7,15, p<0,001). Les participants du groupe d'âge 61-80 ans présentaient la prévalence la plus élevée de 11,4% (4/35) pour la comorbidité diabète-tuberculose, mais cela n'était pas statistiquement significatif (p=0,509), bien que leur glycémie moyenne soit significativement plus élevée que celle des autres groupes d'âge (p=0,0137). La moyenne des patients n'ayant aucune conscience de leur susceptibilité à la comorbidité diabète-tuberculose était de 77±28,97% (IC à 95%=3,79-46,62, p=0,4648). L'observance du traitement a été observée chez 91,0% des participants à l'étude, principalement en raison du niveau élevé d'attention de la part des prestataires de soins à la clinique du diabète pour 69,0% des participants.
Conclusions: La prévalence de la comorbidité diabète-tuberculose dans cette étude est de 7,0%, la majorité des diabétiques n'étant pas conscients de leur susceptibilité à la tuberculose bien que l'observance du traitement ait été élevée. Il est nécessaire d'adopter un cadre de collaboration et une approche intégrée dans la gestion clinique et le contrôle du diabète et de la tuberculose.

Mots-clés: Diabète sucré, tuberculose, comorbidité, contrôle glycémique, Ghana

Introduction:

The world is currently focused on controlling emerging diseases and pandemics. However, long-term endemic infectious diseases such as tuberculosis, HIV, malaria, hepattis and neglected tropical diseases (NTDs) equally needs more attention (1). Tuberculosis is an infectious bacterial disease transmitted principally by airborne thus almost exclusively by person-to-person. The causal agent is *Mycobacterium tuberculosis* also known as human tubercle bacillus. There are seven closely related species of *M. tuberculosis*; *Mycobacterium bovis*, *Mycobacterium africanum*, *Myobacterium microti*, *Mycobacterium caprae*, *Mycobacterium pinnipedii*, *Mycobacterium canetti* and *Mycobacterium mungi*, all of which cause disease in humans (2-5).

Tuberculosis can cause impaired glucose tolerance which is a risk factor for developing diabetes. Diabetes is linked to about 15% of tuberculosis cases worldwide (6). People with diabetes have a threefold increased chance of contracting tuberculosis compared to those who do not have the chronic disease (7). Diabetes has been recognized as a separate entity risk factor for tuberculosis, and the two often coexist bi-directionally (8). Studies in 2010 by Ruslami et al., (9) suggest that 5–30% of tuberculosis patients have been associated with diabetes mellitus.

Diabetes is the most frequent chronic endocrine disorder. It is a non-transmissible pathological entity, characterized by disorders of carbohydrate, fat and protein metabolism, resulting from defects in insulin secretion, insulin action, or both (10,11). Chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs (12). Diabetes and tuberculosis remain the majority cause of mortality across the world with 415 million cases and 5.0 million deaths due to diabetes (13). About 95% of tuberculosis and 75% of the diabetes cases live in low-and-middle-income-countries (13, 14).

Africa has one of the highest rates of non-communicable diseases (NCDs) in the world. About a quarter of deaths (69% of deaths) across the sub-region are due to these diseases (13). Both diabetes and tuberculosis may simulate the symptoms of each other. Common symptoms for both include lethargy, fatigue, weight loss, fever, and loss of appetite. It is commonly seen with diabetic patients to present with complaints of worsening of blood glucose control only to find out later to be as a result of tuberculosis (15). A major challenge in diabetes management with active tuber-

culosis is the interactions of anti-tuberculosis drugs with oral anti-diabetic drugs (9).

This current study aimed to determine the prevalence of diabetes and tuberculosis comorbidity among patients who visited the diabetes clinic in Accra, Ghana and the association of socio-demographic characteristics, susceptibility awareness, treatment compliance and care providers vigilance of diabetes-tuberculosis comorbidity patients.

Materials and method:

Study design:

The study was a cross-sectional survey conducted among diabetes patients from May to July 2021 to determine the prevalence of diabetes-tuberculosis comorbidity, socio-demographic factors, susceptibility awareness, treatment compliance and care managers vigilance.

Study setting:

The research was carried out in the diabetic clinic at the Shai-Osudoku District Hospital-Dodowa in the Greater Accra Region, Ghana. The Shai-Osudoku District is situated in the South-Eastern part of Ghana in the Greater Accra Region. The district occupies about 968.361-kilometer square of land area, with Dodowa as its capital. The district is largely rural hence the predominant occupation is agriculture and trading. The industrial activities are those related to quarrying which takes advantage of the several inselbergs and rock outcrops that abound in the district (16).

Study population and participants:

Diabetic patients being treated at the diabetes clinic at the Shai-Osudoku District Hospital-Dodowa were included in the study. Newly diagnosed tuberculosis patients with fasting blood glucose (FBG) level of more than 7.0mmol/L, random blood glucose (RBG) level of over 11.2mmol/L and glycated haemoglobin (HbA1c) ≥ 6.5% were also included. The study focused on patients age 20 years and above.

Ethical clearance:

The protocol used for data collection was approved by the Ethical Review Committee of Accra Technical University. The objectives of the study, risks, benefits, right to refuse and confidentiality were explained to the respondents prior to obtaining written informed consent to voluntarily participate in the survey. The identity and information on the respondents were not disclosed. The authors do not have access to information that could identify individual participants during or after data collection.

Sample size:

The sample size (n) was calculated using the single proportion formula without correction for continuity; $n=Z^2P(1-P)/d^2$ (7). At 95% confidence interval, the 'Z' statistic was 1.96 and 'P' was determined to be 0.06 from previous prevalence studies (14,17). Assuming 'd' (the degree of precision) to be 0.05 (in proportion of one) and 5% non-response rate adjusted, 'n' was determined to be 100 participants.

Inclusion and exclusion criteria:

Diabetic patients who were 20 years of age and above with symptoms or history of coughing up blood or mucus, chest pain or difficulty with breathing or coughing, unintentional weight loss, night sweats, chills, loss of appetite, fatigue and fever. Diabetic patients with no symptoms or history suggestive of tuberculosis were excluded.

Diabetes mellitus screening:

Capillary blood of patients of 20 years and above irrespective of the diagnosis status was used to screen for fasting blood glucose (FBG) and/or random blood glucose (RBG) using glucometer. If patients have FBG level of more than 7.0mmol/L and/or RBG level of more than 11.2mmol /L, 5ml of venous blood was taken for glycated haemoglobin assessment within 4 hours of collection. A glycated haemoglobin (HbA1c) of ≥ 6.5% was confirmed as having diabetes mellitus (18).

Tuberculosis diagnosis:

Sputum samples collected from confirmed diabetic patients with symptoms or history of tuberculosis were used to screen for pulmonary tuberculosis using Ziehl-Neelsen AFB microscopy. Tuberculosis was confirmed in diabetic patients by the GeneXpert MTB/RIF test.

Questionnaire and data collection:

Questionnaires were developed, consisting of both closed and open-ended questions and in two parts. The socio-demographic characteristic, treatment compliance, susceptibility awareness and care managers' vigilance constituted the first part, and the second part was for data on diabetes-tuberculosis comorbidity during the study period. The respondents who agreed to participate in the study were interviewed for about 15–20 minutes in the health facility.

Data processing and statistical analyses:

The independent variables in the study were socio-demographic characteristics such as age, gender, behavioural and clinical characteristics such as treatment compliance, susceptibility awareness, care managers' vigilance and diabetes-tuberculosis comorbidity. The main outcome variable was diabetes-tuberculosis comorbidity among diabetic patients in the clinic. The data were presented as frequencies and percentages using univariate an-

alysis on the socio-demographic characteristics of respondents.

Statistical analyses were carried out using Microsoft Analysis Tool Pak, to establish association and variance between study parameters. Bivariate comparisons were done to determine the association between diabetes-tuberculosis comorbidity and independent variables using Chi-square test for categorical variables, and Student's '*t*' test and ANOVA for continuous variables. Associations were considered significant at 95% confidence interval with *p* value set at <0.05.

Results:

Prevalence and association of diabetes-tuberculosis comorbidity with age groups:

The prevalence of diabetes-tuberculosis co-morbidity was observed to be 7.0% (7 of the 100 participants). Of the one hundred participants, 35 were within the age group 20-40 years, with 1 (2.9%) had tuberculosis. Of the 24 diabetic participants within the age group 41-60 years, 2 (8.3%) had tuberculosis, and 4 (11.4%) of the 35 participants within the age group 61-80 years had tuberculosis, with no case of tuberculosis among the age group 81 years and above (Table 1).

There was no significant difference in the prevalence of diabetic-TB co-morbidity with respect to age groups (x^2=2.319, p= 0.509). Moreover, the mean blood glucose of the diabetic participants in 61-80 years (11.8± 2.18 mmol/L) and 41-60 years (11.3±2.18 mmol/L) age groups was significantly higher compared to those in the age group 20-40 years (8.2±2.18 mmol/L) and age group >80 years (7.5±2.18 mmol/L) (F-statistic=21.157, p=0.0137 by ANOVA).

Prevalence and association of diabetes-tuberculosis co-morbidity with gender:

The overall mean (±SD) blood glucose concentration among participants with diabetes-tuberculosis comorbidity was 16.52±0.79 mmol/L (95% CI=7.15, p=0.3404). This was statistically biased towards females; 17.08± 0.79 mmol/L than males; 15.95±0.79 mmol/L (t=-6.35, df=46.48, p<0.001).

In addition, the prevalence of diabetes-tuberculosis co-morbidity was higher in males (11.1%, 3/27) than females (5.5%, 4/73) although there was no statistically significant difference in the prevalence of diabetic-TB co-morbidity with respect to gender (p=0.327) as shown in Table 2.

Table 1: Age group distribution of diabetic participants and prevalence of diabetes-tuberculosis co-morbidity

Age group (years)	No of diabetes participants	Mean fasting blood glucose (mmol/L) (±2.18)	No of diabetes with tuberculosis	Percentage (%)
20 – 40	35	8.2	1	2.9
41 – 60	24	11.3	2	8.3
61 – 80	35	11.8	4	11.4
81 & above	6	7.5	0	0
Total	**100**		**7**	**7.0**
Statistics		p=0.0137* (ANOVA)	p=0.509 (x^2)	

ANOVA = Analysis of Variance; x^2 = Chi-square; * = statistically significant at p<0.05

Table 2: Gender distribution of diabetic participants and prevalence of diabetes-tuberculosis comorbidity

Gender	No of diabetic participants	Mean Fasting Blood Glucose (mmol/L) (±0.79)	No with diabetes-tuberculosis co-morbidity	Percentage (%)
Male	27	15.95	3	11.1
Female	73	17.08	4	5.5
Total	**100**	**16.52**	**7**	**7.0**
Statistics		(t value =-6.35; p<0.001)	p=0.327 (Z Score = 0.981)	

Mean fasting blood glucose for the 7 patients with diabetes-tuberculosis comorbidity is 16.52 ± 0.79 (95% Confidence Interval: 7.15, p=0.3404)

Table 3: Participants awareness of susceptibility to diabetes-tuberculosis comorbidity

Questions	**Number of participants responses**			
	Yes	**No**	**Not Aware**	**Total**
Do you have a family history of diabetes?	64	33	3	100
Are you aware you can get TB when you have diabetes?	19	81	0	100
Do you have a family history of tuberculosis?	1	93	6	100
Are you aware you can get diabetes when you have TB?	3	87	10	100
Mean of patients' responses	**21.75±29.30**	**73.5±27.44**	**4.75±4.30**	

Table 4: Diabetic participants treatment compliance and care managers vigilance level

Questions	**Number of participants responses**			
	Yes	**No**	**Not often**	**Total**
Do you take your medications on the scheduled time?	91	2	7	100
Does your care manager call/other form to check on your treatment update?	69	31	0	100

Patient's awareness of susceptibility to diabetes-tuberculosis comorbidity:

Assessing the patient's awareness of susceptibility to either condition (diabetes and tuberculosis) while managing one, the mean of the patients with no awareness of their susceptibility to either condition is 73.5±27.44 (95% CI=3.79–46.62, p=0.4648) as indicated in Table 3.

Patient treatment compliance and care managers attentiveness to diabetic participants:

A total of 91 (91.0%) of diabetic participants complied with the treatment schedules, 7 (7.0%) irregular and 2 (2.0%) not fully complied with treatment as shown in Table 4. There was high level of attentiveness by the care providers, as most of the respondents (69.0%) indicated being called to check on their treatment updates before their schedule visit to the hospital facility as shown in Table 4

Discussion:

In this study, 7 (7.0%) of the 100 diabetic participants screened for tuberculosis were positive. Previous studies have established interrelationship between diabetes and tuberculosis (18). The current prevalence of 7.0% for diabetes-tuberculosis comorbidity is comparable to other studies in some African, Asian and European countries which reported tuberculosis prevalence among diabetes mellitus patients to vary from 1.7% to 36.0% (14). This association could possibly be attributed to the metabolic effect of the two conditions.

Diabetes undoubtedly compromises the immune system of the body predisposing the individual to tuberculosis. Tuberculosis on the other hand, induces glucose intolerance and worsens glycaemic control in diabetics (14). This is the situation in this study with an overall mean blood glucose concentration among the 7 diabetes-tuberculosis co-morbidity patients of 16.52±0.79 mmol/L (95% CI 7.15, p=0.3404). These findings underpin the need for routine screening for tuberculosis among diabetics since early diagnosis of the disease will enhance its effective management.

In this current study, old age (61-80 years age group) seemed to be a risk factor for developing tuberculosis among diabetic patients as reported in previous studies in Ethiopia (19) and Malaysia (20). This may be due to reduced immune status which makes the elderly prone to TB infection. In this study, male gender was identified as an associated factor for diabetes-tuberculosis comorbidity, as corroborated by other studies (21,22). This may be due to the biological factors such as male sex hormones and genetic factors on host immunity during tuberculosis (23), and non-biological factors such as smoking, professional exposure, and health-seeking behaviours, known to be influenced by gender. However, it is inconsistent with previous study in some African countries (24), South Korea (25) and other Asian countries (7,14), which proposed that women seem to come into contact with TB patients due to their care-giving roles and may be vulnerable to TB infection due to the influence of oestrogen on cytokine production (26).

A high number of the patients demon-

strated ignorance about the possibility of diabetics developing tuberculosis and the vice versa. Knowledge is power and people perish for to lack of knowledge. Ignorance seems to the basis for significant increase in incidence of many communicable and non-communicable diseases among the population. When the population are sufficiently aware of their propensity of developing a particular condition, it may improve preventive measures and routine screening for tuberculosis among diabetics. Interestingly, majority of the diabetes patients (91.0%) complied with the treatment schedules, 7.0% being irregular and 2.0% not fully complying with the treatment regimen. These were evident on their blood glucose levels, even with diabetes-tuberculosis comorbidity patients showing an overall mean blood glucose concentration of 16.52±0.79 mmol/L (95% CI 7.15, p=0.3404).

The significant level of treatment compliance could be attributed to high level of attentiveness by the care providers towards susceptibility/comorbidity of the two diseases (diabetes and tuberculosis), as high proportion (69.0%) of the participants were contacted by their care managers/clinicians checking up on them for treatment update within their scheduled hospital visits via phone calls or other means. A major limitation of this study is the cross-sectional design that can only determine association, without establishing causality relationship between diabetic-tuberculosis comorbidity and the risk factors analyzed.

Conclusions:

There is a relatively high prevalence of diabetes-tuberculosis comorbidity in this study, with majority of the diabetic participants lacking knowledge of their susceptibility to tuberculosis although there was high treatment compliance. There is the need to adopt a collaborative framework and integrated approach in the clinical management and control of diabetes and tuberculosis.

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Contributions of authors:

HKH, LA and REA were involved in the study conceptualization; HKH, LA and BBB were involved in data curation; HKH, LA, WEKA, SA and BBB were involved in formal analysis; HKH, LA, REA and MA were involved in funding acquisition; HKH, LA and WEKA were involved in laboratory investigations; HKH, LA and WEKA were involved in the study methodology; HKH, LA, WEKA and MA were involved in project administration; HKH, LA and REA were involved in sourcing for resources; SA and BBB were involved in data software acquisition; HKH, LA and MA were involved in supervision; HKH, LA and MA were involved in project and data validation; HKH, LA and WEKA were involved in writing the original manuscript draft; and HKH, LA, REA and MA were involved in reviewing and editing of the manuscript. All authors approved the manuscript submitted for publication.

Availability of data and materials:

All data generated or analysed during this study are included in this published article.

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Conflict of interests:

No competing interest is declared.

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