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Frequency of *Mycobacterium tuberculosis* Isolated from Pulmonary Samples of Diabetes mellitus and Their Resistance to Rifampicin- Khartoum State

A dissertation submitted in partial fulfillment for the requirements of M.Sc. in medical laboratory sciences (Medical Microbiology)

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الآية الكريمة

يقول تعالى:-

(الَّذِي خَلَقَنِي فَهُوَ يَهْدِينِ (78) وَالَّذِي هُوَ يُطْعِمُنِي وَيَسْقِينِ (79) وَإِذَا مَرِضْتُ فَهُوَ يَشْفِينِ (80) وَالَّذِي يُمِيتُنِي ثُمَّ يُحْيِينِ (81) وَالَّذِي أَطْمَعُ أَنْ يَغْفِرَ لِي خَطِيئَتِي يَوْمَ الدِّينِ (82) رَبِّ هَبْ لِي حُكْماً وَأَلْحِقْنِي بِالصَّالِحِينَ (83) وَاجْعَلْ لِي لِسَانَ صِدْقٍ فِي الآخِرِينَ (84) وَاجْعَلْنِي مِنْ وَرَثَةِ جَنَّةِ النَّعِيمِ (85) وَاغْفِرْ لأَبِي إِنَّهُ كَانَ مِنْ الضَّالِّينَ (86) وَلا تُخْزِنِي يَوْمَ يُبْعَثُونَ (87) يَوْمَ لا يَنْفَعُ مَالٌ وَلا بَنُونَ (88) إِلاَّ مَنْ أَتَى اللَّهَ بِقَلْبٍ سَلِيمٍ (89)

صدق الله العظيم

(78 – 89) سورة الشعراء

Dedication

From the bottom of my heart I dedicate this work to my parents who spare no efforts until I reach to this stage.

I also won't forget the role of Dr. Hadia Abbas who kindly accepted to supervise and follow my work until it has reached this point.

The role of my college mates is also well appreciated ..

The consideration and understanding from my husband is a candle a head to me through a darkness bath.

I dedicate this work to everyone who stands by my side throughout my struggling and education.

Ebtihal Omer, my close friend who I consider a sister is always by my side done her best, supported me, helped and encouraged me.

Acknowledgment

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Abstract

Background:

Pulmonary tuberculosis (PTB) and diabetes mellitus (DM) are both important the most well known diseases predominated and health issues in Sudan and other world.

Objectives:

The aim of this study is to determine the dominance of pulmonary tuberculosis (PTB) in diabetic patients.

Method:

This is a cross-sectional study performed in *Omdurman Educational Hospital(Abdulla Khaleel Center) , Abu Anja hospital, & Mohammed Alameen Hamid for Infants* Hospital located in Omdurman, Sangat Elwehda health center in Elklaklla area- Khartoum state.

Khartoum state Sudan from August 2018 to December in the same year.

Results:

A total of patients with Diabetic mellitus were 73. Patients with signs and Symptoms of PTB infection were be included whereas they represent 23/73 patients while 50 out of 73 were excluded because they do not show signs and symptoms of PTB.

Result reveals that 10 /23 had (PTB), 9/23 were rifampicin resistance detected while 1/10(10%) rifampicin resistance was not detected. Positive samples by *Xpert® MTB/RIF* and ZN stain were 10 (43.4%). No significant association between PTB and diabetic duration. The association between PTB and level of glycated haemoglobin (HbA1c) in the study group was insignificant.

الملخص

خلفية:

مرض الدرن و مرض السكري من أكثر الأمراض الشائعة في السودان والعالم .إذ أن هذه دراسة أجريت بمستشفى أم درمان التعليمي مركز عبد الله خليل ومستشفى محمد الأمين حامد

الأهداف:

حيث أن الهدف من هذه الدراسة هو بحث العلاقة بين داء الدرن الرئوي ومرض السكري

الطريقة:

حيث شملت الدراسة 73 مريض بالسكري حيث 23 منهم بدت عليهم أعراض الدرن الرئوي وهي المجموعة موضع الدراسة و50 مريض تم استبعادهم لم تظهر عليهم الاعراض.

النتائج:

أظهرت النتائج أن عشره من مجموع 23 مصابين بالدرن 9 منهم مصابين بالسل المقاوم للعلاج . وكانت الاختلافات ليست لها قيمة ذات دلالة إحصائية. كانت نتيجة العلاقة بين مرض الدرن الرئوي (43.4%)10 الموجبة لاستخدام صبغة الزيل نلسون و الجين اكسبيرت ونسبة السكري التراكمي في المجموعة موضع الدراسة ليس لها قيمة ذات دلالة إحصائية. بالإضافة الى انه لم تكن هنالك دلالة إحصائية تدل على ارتباط فترة الإصابة بالسكري والإصابة بمرض الدرن الرئوي.

الخلاصة:

خلاصة هذه الدراسة هو أن هنالك خطورة نسبية علي المصابين بالسكري لإصابتهم مرض الدرن الرئوي

نوصى بإجراء مزيد من البحوث فى العلاقه بين مرض الدرن الرئوى والسكري فى السودان. ومعرفة نسبة إنتشار الدرن الرئوى وسط مرضى السكرى.

Conclusion:

this study found that consistent evidence for an increased risk of TB among people with diabetes despite heterogeneity in study design, and fundamental burden of TB, assessment of exposure and outcome.

We recommended a further research in an association between PTB and DM and determine the prevalence of PTB among diabetic patients.

List of Abbreviations:

Abbreviation	Full Meaning
TB	Tuberculosis
MTB	Mycobactrium Tuberculosis
MA	Mycobactrium Africanum
BCG	Bacille Calmette-Guerin
LTBI	Latent TB Infection
MDR-TB	Multi-Drug-Resistance Mycobactrium Tuberculosis
XDR-TB	Extensively Drug Resistant Mycobactrium Tuberculosis
TNF	Tumor Necrosis Factor
IL-12	Interleukin-12
IFNy	Interferon Gamma
DM	Diabetes Mellitus
IDDM	Insulin Diabetes Mellitus
NIDDM	Non-Insulin Dependant Mellitus
PMN	Polymorphouclear Leukocytes
PTB	Pulmonary Tuberculosis
ZN	Ziehl-Neelsons
T2DM	Type Two Diabetes Mellitus
HIV	Human Immune Virus
SPSS	Statistical Package for Social Science
NAA	Nucleic Acid Amphilification
MTBC	Mycobacterium TB Complex
RIF	Resistance to Rifampin
WHO	World Health Organization

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Chapter One

Introduction

Justification

Objectives

1. Introduction

1.1 Background:

Tuberculosis (TB) remains a major source of morbidity and mortality throughout the world (1, 2, 3). One-third of the world's population is estimated to be infected with *Mycobacterium tuberculosis* (MTB), whereby approximately 9 million people develop the disease each year, and almost 2 million of populations die annually as a result of TB(1,4).

TB is an infectious disease that is caused by a bacterium called *Mycobacterium tuberculosis.* The *M. tuberculosis* complex includes the following closely related organisms M. tuberculosis, *M. africanum, M. bovis* (subspecies bovis and caprae), *M. bovis* BCG (Bacille Calmette-Guérin), M. microti, *M.canettii*(5).

The symptoms of TB include a low- grade fever, night sweats, fatigue, weight loss and a persistent cough. Some people may not have obvious symptoms.

TB is contagious and can transfer easily when an infected individual coughs, sneezes, or talks closely with other persons and droplets more through the air (6).

A person who is exposed to TB may not necessarily develop disease. Most people are able to fight the infection with their immune system. In fact, healthy people who are infected with TB only have a 10% chance of converting to active disease over their lifetime. Some are able to control the infection, but unable to completely remove it from their bodies. In these cases, the infection remains, lying in an inactive or "latent" state. This is often described as Latent TB Infection or LTBI (7). A person with latent TB infection is described as following:

i. Usually has a skin test or blood test result indicating TB infection.
ii. Have a normal chest X-ray and a negative sputum test.
iii. Have TB bacteria in his/her body that are alive, but inactive.
iv. Does not feel sick.
v. Cannot spread TB bacteria to others.

LTBI is the source of most future TB disease so that the strategies to eliminate TB in industrialized countries hinge on diagnosis and treatment of LTBI (8).

LTBI may develop into active disease someday, often when the person's immune system becomes weakened. Active TB has a greater burden of TB bacilli than latent TB, and acts as an infection source for contacts (9).

Tuberculosis is treatable with a course of antibiotics. Two antibiotics most commonly used are rifampicin and isoniazid. Multi-drug-resistant tuberculosis (MDR-TB) is defined as resistance to the two most effective first-line TB drugs: rifampicin and isoniazid. Extensively drug-resistant TB (XDR-TB) is also resistant to three or more of the six classes of second-line drugs. Drug-resistant TB is a public health issue in many developing countries, as treatment is longer and requires more expensive drugs (10).

The relationship between diabetes mellitus (DM) and tuberculosis (TB), and the nature of their interaction with regards to co-morbidity are largely suggested by numerous epidemiological studies. In the early 20th century, the effect of DM on TB was a large concern to investigators, but this was slightly neglected in the second half of the 20th century with the emergence of proper treatment for both diseases. Recently, with the increasing prevalence of TB, particularly Multi Drug Resistant TB (MDR-TB), and DM cases in the world, the relationship is re-emerging as a significant public health problem. The link of DM and TB is more important in developing countries where TB is endemic and the prevalence of DM is rising.

M. tuberculosis is able to persist inside a host for extended periods due to its ability to survive inside macrophages and monocytes. MTB is able to manipulate both the innate and acquired immune response of the host so that the result can be an effective CD4+ T cell response limiting the disease but it can also promote the development of progressively destructive lesions in the lung.

1.2. Rationale:

Tuberculosis remains a major health problem in Sudan. Diabetes Mellitus is a known risk factor for tuberculosis. Very few studies have been conducted in Sudan on tuberculosis among diabetic patients; the exact prevalence of tuberculosis in this group of patients remains unknown.

1.3.Objective:

1.3.1. General Objective:

To determine the prevalence of pulmonary tuberculosis (PTB) in diabetic in *Omdurman Educational Hospital Abdulla Khaleel diabetic Center, Mohammed Alameen Hamid* Hospital and Abuanga which are located in Omdurman erea, Sangat Elwehda health center in Elklaklla area- Khartoum state 2018.

1.3.2. Specific Objectives:

- To detect M. tuberculosis (MTB) in sputum samples by Ziehl-Neelsons (ZN) stain and confirm by *GeneXpert*® System. s
- To detect resistant to rifampcin antibiotic.
- To determine association of the pulmonary tuberculosis with the diabetic patients.
- To determine association between Hemoglobin A1C level in diabetic patients and developing pulmonary tuberculosis.

Chapter Two
Literature Review

2. Literature review:

2.1. Tuberculosis and immune system:

M. tuberculosis is able to persist inside a host for extended periods due to its ability to survive inside macrophages and monocytes. MTB is able to manipulate both the innate and acquired immune response of the host so that the result can be an effective CD4+ T cell response limiting the disease but it can also promote the development of progressively destructive lesions in the lung (11).

Cellular immune responses to Mycobacterium tuberculosis progress in two stages. First, initial innate immunity involves the direct production of cytokines, such as tumor necrosis factor (TNF), interleukin- 12 (IL-12) and others, by infected macrophages activated via toll-like and other pattern receptors (12). Later, such mechanisms are amplified by adaptive responses of pathogen-specific T lymphocytes recruited to the site of infection, leading to the production of interferon gamma (IFNγ), useful both to amplify the immunological response and to activate intracellular antibacterial mechanisms (13). Therefore, the early macrophage- T-cell interactions result in inhibition of mycobacterial growth, and lead to the formation of granuloma.

2.2. Diabetes mellitus:

Diabetes mellitus (DM) is the most frequent chronic endocrine disorder(14) Classified into insulin dependent (IDDM) and non-insulin dependent (NIDDM) both of two classes are associated with a variety of genetically determined complications. In addition, infections have been listed as an important complication amongst diabetics (15).

Diabetics suffer from a number of pulmonary physiologic abnormalities including diminished bronchial reactivity. These Abnormalities lead to delayed clearance of microorganisms from the respiratory system and facilitate the spread of infections in the host (16).

The immune system of diabetics makes individuals more susceptible to infections. Specific immunological defects include abnormal polymorphonuclear leukocytes

(PMN) chemotactic response, impaired PMN adherence, phagocytosis, microbicidal activity and Lymphocyte mitogenesis is depressed in diabetes especially in the presence of hyperglycemia and hyperketonemia (17).

2.3. Tuberculosis & Diabetes mellitus:

The relationship between diabetes mellitus (DM) and tuberculosis (TB), and the nature of their interaction with regards to co-morbidity are largely suggested by numerous epidemiological studies. In the early 20th century, the effect of DM on TB was a large concern to investigators, but this was slightly neglected in the second half of the 20th century with the emergence of proper treatment for both diseases. Recently, with the increasing prevalence of TB, particularly Multi Drug Resistant TB (MDR-TB), and DM cases in the world, the relationship is re-emerging as a significant public health problem. The link of DM and TB is more important in developing countries where TB is endemic and the prevalence of DM is rising (18).

Diabetic patients have a significantly increased risk of active tuberculosis (TB), which is two to three times higher than in individual without diabetes (19). In 2013 there were 382 million people with diabetes worldwide. This number is expected to reach 592 million by 2035 (20).The World Health Organization predicts that diabetes will be the seventh leading cause of mortality worldwide in 2030 (21).The overall risk of death among people with diabetes is at least double the risk of those without diabetes (22) and type 2 DM (T2DM) will be responsible for 90% of diabetes mellitus cases. [1]

More recently, multiple persistent epidemiological studies investigating the relationship exhibit that DM is indeed positively associated with TB such as studies from Europe (23, 24), Asia (25) and Africa [1].

Investigators suggested that the association reflects the effect of DM on TB, some argument over the directionality of the association remains due to observations that TB disease induces temporary hyperglycemia, which resolves with treatment (26).

In a case-control study was conducted in Ribat University Hospital, Khartoum, Sudan found that, PTB among DM group was higher than in non-diabetic patients; 20% and 13.3% respectively, in addition to that this study exhibit the significant association between PTB and uncontrolled diabetic patients with high level of HbA1c [1] . Another study was performed in Southern Mexico; reveal the rate of TB among diabetics was significantly greater than non-diabetics (209.5 vs. 30.7 per 100,000 person-years, $p< 0.0001$). Co morbidity with diabetes may increase tuberculosis rates as much as co infection with human immunodeficiency virus (HIV) (27).

Stevenson et al carried out a systematic review of the subject finding that diabetes has been estimated to increase the risk of TB infection from 1.5 in one study up to 7.8 times in another(28).

Incomplete of TB treatment is a major cause of primary drug resistance. DM patients are thought to have impaired gastrointestinal drug absorption due to Gastroparesis which may affect treatments (29). A study by Nijland *et al* reported that Rifampicin is not absorbed as effectively in TB-DM patients, this could again be due to poor gastrointestinal uptake, or due to differences in metabolism, excretion and body weight (30). This poor intake of anti-TB drugs by DM patients could be a possible mechanism that leads to the development of drug resistance. However, whether DM presents any additional risk for the development of MDR-TB remains controversial (31, 32). Two case-control studies comparing DM/TB and non-diabetic TB patients from Iran and Turkey showed no significant association between DM and the risk of MDR-TB (33,34). Similarly, cross-sectional studies in Iran, and Taiwan have reported no association between DM and MDR-TB [35,36]. On the other hand, many studies have found 2.1 to 8.8 times increased the risk of MDR-TB among diabetic TB patients(37, 38). In addition, observational studies from Israel and Mexico have also shown patients with DM had a higher risk of developing MDR-TB (39, 40).

Chapter Three
Materials and Methods

3. Materials and Methods

3.1. Study Design:

This is a cross-sectionalstudy.

3.2. Study Area:

The study conducted in *Omdurman Educational Hospital Abdulla Khaleel diabetic Center*, *Mohammed Alameen Hamid* Hospital and Abuanga which are located in Omdurman erea, Sangat Elwehda health center in Elklaklla area- Khartoum state.

3.3. Study Population:

All diabetes patients were included during the period of study.

3.4. Study Duration:

This study was conducted between May - July, 2018.

3.5.Sample Size:

All samples presenting during the study period were included in the study.

3.5.1.Inclusion Criteria:

All patients diagnosed with diabetes mellitus.

3.5.2.Exclusion Criteria:

Patients, having risk factors for tuberculosis other than diabetes mellitus, were excluded on the basis of history, like HIV patients.

3.6.Tools of data collection:

Data were collected by questionnaire. Appendix (1).

3.7.Sample collection & processing:

A sputum specimen were collected in a dry clean container. Zeiln -Neelson staining of sputum smears was carried out after collection and preserve sample in ($-20C^0$) for *GeneXpert*® assay

3.8.Data analysis:

Data were analyzed using a computerized program Statistical package for social sciences (SPSS).

3.9. Ziehl-Neelsen (ZN) staining of samples:

Method:

The smear *slide* was placed on *the* staining rack *then* was filling *with* carbon-fuchsin staining solution. after that the torch was preparing by dipping its cotton wool end in burning; light it then all slide was heated keeping the torch a little below them and moving it continuously back and forth along the line until steam rises this step was repeated twice at intervals *of* 3-5 minutes. by using *the* forceps each *slide* was tilted *to* drain off *the stain solution* then *the slides* were rinsed well *with* distilled water and then *the* acid *solution* was poured over *the* smears covering them completely *and* allows it *to* act for 3 *minutes.* by *using the* forceps each slide was tilted *to* drain off *the* acid *solution and* gently rinse again with distilled water. After that, the smears were flooded with methylene blue solution for 1 minute. by using the forceps each slide was tilted to drain off the methylene blue solution and each slide was gently rinsed again with distilled water after that each slide was taken from the rack and let the water drain off then the slide was standing on edge on the drying rack and allow it to air-dry. The slide was examined for the presence of acid-fast bacilli [41]. Result interpretation illustrated in Table [1]:

Table [1]: The reporting of smears was based on the following criteria:-

Number of bacilli per filed	Report
0	No acid-fast bacilli were seen
1-9 bacilli per 100 filed	Report exact number
10-99 bacilli per 100 filed	+1 positive
1-10 bacilli per each filed	+2 positive
More than 10 bacilli per each filed	+3 positive

3.10. Molecular biology Processing:

3.10.1-GeneXpert MTB/RIF assay:

Is a nucleic acid amplification (NAA) test which simultaneously detects DNA of Mycobacterium tuberculosis complex (MTBC) and resistance to rifampin (RIF) *i.e.* ***(*mutation of the rpoB gene)** in less than 2 hours. In comparison, standard cultures can take *two* to *six* weeks for MTBC to grow and conventional drug resistance tests can add *three* more *weeks. This* system integrates and automates sample processing nucleic acid amplification and detection of the target *sequences. The* primers in the *xpertMTB/RIF* assay amplify a *portion* of the rpoB gene containing the 81 base pair core region. The probes are able to differentiate between the conserved wild-type sequence and mutations in the core region that is associated with rifampicin *resistance [42]*.

3.10.2- GeneXpert MTB/RIF sample processing:

1. 1mL of sputum was carefully transferred from the original container to another labelled leak-proof specimen container.
   - In a case of sputum is too viscous it was treated with Sputolysin.
2. Double volume of Sample Reagent was added by using a sterile transfer pipette to the sputum volume (2:1 Sample Reagent to Sputum)

3. Test sputum container was a vortex for 10s .then Allowed to stand for 10min at room temperature, and it was vortex again for at least 10s.
4. Test sputum container was allowed to stand for an additional 5min at room temperature before proceeding to inoculate cartridge.
5. A liquefied sample was transferred into the S-chamber of the Xpert MTB/RIF cartridge. Then cartridge lid was closed and proceed to GeneXpert instrument to load test, all processing from this point on is fully automated.

3.10.3-GeneXpert MTB/RIF result interpretation:

The GeneXpert Instrument system generates the results from measured fluorescent signals and embedded calculation algorithms.

Table [2]: GeneXpert MTB/RIF result interpretation [43]:

GeneXpert Instrument System generated result using Xpert MTB/RIF assay	**Interpretation of Xpert MTB/RIF assay result**
MTB detected, RIF resistance detected	MTB target is detected within the sample. A mutation in the *rpoB* gene has been detected.
MTB detected, RIF resistance not detected	MTB target is detected within the sample. A mutation in the *rpoB* gene has not been detected.
MTB detected, RIF resistance indeterminate	MTB target is detected within the sample. A mutation in the *rpoB* gene because of insufficient signal detection.
MTB not detected	MTB target is not detected within the sample.

Chapter Four

Results

4. Results

This study was done on 73 patients with Diabetic mellitus. Patients with signs and Symptoms of PTB infection were included where represent 23/73 patients while 50/73 were excluded because they do not show signs and symptoms of PTB. Total of 23 sputum sample were collected from selected patients. Zn staining was positive in 10 (43.5%), and confirmation assay *Xpert® MTB/RIF* display positive in 10 (43.4%) also. Whereas 9/10 (90%) were rifampicin resistance detected while 1/10(10%) rifampicin resistance was not.

Regarding gender, 14/23(60.9%) were male and 9/23(39.1%) were female, PTB was 6 (26.1%) in male and 4(17.4%) in female, p-value (0.637) was insignificant (Table 4-1).

In regard to age, distribution between (25-79) years the mean age was (52+_SD) years, the age group(58-68)years reveal higher frequent 6 (26%) and the most positive cases of PTB was 4(17.4%) present in age groups (36-46) years P-value (0.222) insignificant different (table 4-2).

Related to marital status, 19/23(82.6%) were married and 3/23(13%) were single while 1/23(4.3%) divorced (Table 4-3).

Regarding the present of symptoms, 17/23(73.9%) had a cough, fever, night sweating and weight loss P. values (0.100) were insignificant (Table 4-4).

The economic status was 13 (56.5%) were moderate, 9(39.1%) were poor and 1(4.3%) were rich, P-value (0.667) insignificant difference (Table 4-5).

Redard the mean duration of diabetes mellitus was (2.61years ± Std 1.076), The higher frequency of diabetes mellitus duration was 8(34.8%) in (10-14) years while the most positive PTB cases present in (15-19) years of duration, p-value (0.273) insignificant different(Table 4-6). The HbA1c (level = 8.9%) had majority of PTB positive which represent (12.5%), P-value (0.303) insignificant differences (Table 4-7).

Table (4-1) *Xpert® MTB/RIF* result of pulmonary tuberculosis against Gender:

Gender	Total	*Xpert® MTB/RIF* +ve		*Xpert® MTB/RIF* -ve	P-value
		RIF detected	*RIF not detected*		
Male	14	6	0	8	0.637
Female	9	3	1	5	
Total	23	9	1	13	

Table (4-2) Age groups Distribution& *Xpert® MTB/RIF* result

Age groups	Frequency	Percent	Gene xpert		P-value
			positive	negative	
25-35	4	17.4 %	1	3	0.222
36-46	5	21.7 %	4	1	
47-57	5	21.7 %	2	3	
58-68	6	26.1 %	3	3	
69-79	3	13.0 %	0	3	
Total	23	100.0	10	13	

Table (4-3) Incidence of pulmonary tuberculosis & marital status:

	Frequency	Gene xpert +Ve	Gene xpert -Ve	P-value
Single	3	0	3	**0.155**
Married	19	10	9	
Divorced	1	0	1	
Total	23	10	13	

Table (4-4) frequency of symptoms of pulmonary tuberculosis:

	Frequency	Genexpert +ve	Genexpert –ve	P-value
Cough	1	0	1	**0.100**
Weight loss	1	0	1	
cough Fever night sweating weight loss	17	10	7	
cough fever night sweating	4	0	4	
Total	23	10	13	

Table (4-5) Frequency of pulmonary tuberculosis in deferent socioeconomic classes:

Socioeconomic	Frequency	Genexpert +ve	Genexpert –ve	P-value
Poor	9	4	5	**0.667**
Moderate	13	6	7	
Rich	1	0	1	
Total	23	10	13	

Table (4-6) Duration of diabetes & result of *Xpert® MTB/RIF:*

	Frequency	Genexpert +ve	Genexpert –ve	P-value
Missing	1	0	1	**0.273**
0.5-4	2	0	2	
5-9	7	3	4	
10-14	8	3	5	
15-19	5	4	1	
Total	23	10	13	

Table (4-7) Pulmonary Tuberculosis & level of HbA1C:

	Frequency	Genexpert +ve	Genexpert –ve	P-value
4.1	1	1	0	
6.0	1	1	0	
6.1	1	1	0	
7.0	2	0	2	
7.1	1	0	1	
8.0	1	1	0	
8.9	2	2	0	
9.0	2	1	1	
11.0	1	1	0	
11.7	1	0	1	**0.303**
12.6	1	0	1	
17.0	1	0	1	
17.4	1	1	0	
Total	16	9	7	
Missing System	7	1	0	
Total	23	1	0	

Chapter Five
Discussion, Conclusion &Recommendations

5.1. Discussion

The most common underlying diseases that predispose to TB infection and development of the disease are diabetes mellitus, autoimmune diseases, and HIV serology positive status (44-46).

In the present study 23/73 (31.5%) diabetic patients reveal symptoms of pulmonary tuberculosis, 10/23(43.5%) of DM they had PTB Whereas 9/10 (90%) they had MDR-TB while 1/10(10%) had MTBC. the increase of this range of multidrug resistance it may be due to hypothesis. In type 2 diabetics, production of reactive oxygen species may be impaired, so strains with katG mutations may be better able to survive (47).

Some studies reported no relationship between DM and MDR- TB [35, 36, 33], On the other hand, few studies have found an increased risk of MDR- TB among diabetics (48, 32).

This study showed that no statistical differences between PTB in male and female (P= 0.637), despite that male display higher incidence than female and that might be due to their higher number in a study than female.

Some studies reported no difference in term of gender but some reported higher frequency among men (33, 49).

Also, no statically difference between age groups in this study, and the most infected age group was (36-46) years, which is similar to another study exhibit that relative risk of having pulmonary tuberculosis is higher among diabetics ageing less than 50-year-old, specifically (30-49)year-old (50).

Patients with duration of DM (15-19) years showed a higher pulmonary tuberculosis with no statistical differences' same as [1]. Besides, that elevated HbA 1c were not statistically significant risk factors for TB, This was comparable to other studies evaluating HbA 1c that found no association (51, 52).

Conventional methods for detection of MTBC in clinical specimens have low sensitivity (53). Molecular techniques, including the Cepheid GeneXpert system, have changed the field of TB with rapid diagnosis combined with high sensitivity

and specificity results. In December 2010, the WHO endorsed the Xpert MTB/RIF assay for the rapid diagnosis of TB and MDR-TB (54).

5.2. Conclusion:

The present study show relationship between tuberculosis infection of pulmonary tuberculosis with multidrug resistance according to gender, age and duration of diabetes militias have no effect in tuberculosis infection.

5.3. Recommendations:

i. Improved understanding of the relationship between the two diseases is necessary for proper planning and collaboration to reduce the dual burden of diabetes and TB.

ii. Screening of TB among diabetic patients and diabetic among TB patients.

iii. Surveillance is needed in the country to demonstrate the prevalence of diabetes in TB patients.

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Appendixes

Shandi University

Faculty of Medical laboratory science

Questionnaire

Dear Sir

This questionnaire is intended for educational and scientific purposes only; I assure you the information is confidential.

Association between Pulmonary Tuberculosis (PTB) and Diabetic Patients.

Number:- …….. Sex:- ……

Age: ……...years.

Marital Status:- single ☐ married ☐ divorced ☐

Residence:- ……..

Telephone:- …….

Socioeconomic Status:-

Poor ☐ Moderate ☐

Rich ☐

Job: …….. Duration of Diabetic ….

Years ……

Type of Treatment: -

Injection ☐ tabs ☐

Clinical Marks of TB:- Cough fever night sweating weight loss

History of Contact:- Family ……

Result ZN smear of AAFB ……

Result of GenXpert (Real Time PCR Type) ……

Ethical Consideration:

Approval from University of Shendi Khartoum State Ministry . Health Research Department and from health centers - Objectives of the Study: the ASSOCIATION Between Pulmonary Tuberculosis (TB) and Diabetic in Khartoum 2018. Participant has the right to voluntary informed consent. And he also has the right to withdraw at any time without any deprivation – he also has the sole right to no harm and confidentiality by using code questionnaire he has the right benefit from the researcher knowledge and skills. Investigation results will be received by the sputum immediately and the Questionnaire will be filled with their consent in their premises without any harm to their dignity.

ورقة استنيرة:-

أنا دكتورة ماجدة حسين أقوم بعمل دراسة بحث عن موضوعه العلاقة

بين مرض الدرن السكري بهدف معرفة العلاقة بين مرض الدرن

السكري ودراسة ذلك بولاية الخرطوم 2018م المدنة التي توجد في

هذه الدراسة هي اللعاب وسوف نأخذها في حاويه واسعة نظيفة وجافة

وسوف أقوم بملئ استبيان وسوف تكون المعلومات سرية تامة

مع الفرصة للمساهم بطوعية المشاركة .. للمشارك حق الانسحاب في

أي وقت من الدراسة ولن يؤثر على تلقي العلاج.

د. ماجدة حسين عبد الله

تلفون :- 0918145461