RISK FACTORS FOR PULMONARY TB IN DIABETES MELLITUS TYPE 2 PATIENTS IN BULUKUMBA DISTRICT YEAR 2024

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Abstract

Tuberculosis (TB) and Diabetes Mellitus (DM) are public health disorders that often occur together and complicate each other at various levels. The relationship between diabetes mellitus and TB shows a significant increase, with many pulmonary TB cases occurring in diabetes mellitus sufferers. Objective: To determine the risk factors that influence and the risk factors that most influence the incidence of pulmonary TB in T2DM sufferers in Bulukumba Regency. Method: This research used a case-control design and was conducted in Bulukumba Regency. The case group consisted of 41 TB-DM patients and the control group consisted of 123 DM patients. A validated structured questionnaire (Kobotoolbox) was used for data collection and multivariate analysis with logistic regression in the STATA application. Results: The number of cases is 41 cases. (56.10%) male. Most were in the 41-50 year age group (36.59%). Education level 51.22% high school, 82.93% duration of suffering <5 years, type of oral medication 70.3% use oral medication. Bivariate analysis Body Mass Index (OR 4.79; 95% CI 1.80-12.8), Compliance with treatment (OR 3.01; 95% CI 1.36-6.70), Exposure to cigarette smoke (OR 1 .39; 95% CI 1.80-12.8), ; 95% CI 0.64-3.08), Family Support (OR 2.91; 95% CI 1.31-6.60), Household Contact (OR 2.17; 95% CI 0.99-4, 75 . Multivariate risk analysis is Body Mass Index (AOR 5.587; 95% CI 2.231-13.991). With a probability of (30.35%) causing TB-DM. Conclusion: Therefore, it is necessary to carry out an integrated examination of these two diseases, especially for T2DM patients who have a BMI < 18.5 in the examination.

Keywords: Diabetes Mellitus, Tuberculosis, TB-T2DM, Case-Control, BMI.

1. INTRODUCTION

Infectious diseases still account for the largest disease burden in most developing countries. Non-communicable diseases are responsible for a high proportion of deaths and disabilities in all countries. Non-communicable diseases (NCDs) account for around 50% of global deaths [1]

Tuberculosis (TB) and Diabetes Mellitus (DM) are public health disorders. DM mellitus and pulmonary TB often coexist and complicate each other at various levels. where there are many cases of pulmonary TB among DM mellitus sufferers [2]. DM often occurs in active TB patients [3.4].

The International DM Federation (IDF) notes that 540 million people worldwide suffer from DM. 90% are type 2 DM. It is projected to increase to 643 million in 2030 and 783 million in 2045. 3 out of 4 adults who suffer from DM live in low and middle income countries [5]. The prevalence of DM in Indonesia is 11.3% or the equivalent of 10.7 million sufferers [6].

Global TB Report reports an estimated 250,000 - 500,000 TB cases caused by DM worldwide. People with DM are at higher risk of developing TB and are more likely to experience poor TB treatment outcomes, including death [2] . There is a significant association between dysregulation of glycemic control and susceptibility to M tb infection . impact of TB and DM comorbidity on treatment and management [7]. The TB-DM group had a higher proportion of drug resistance than the TB and DM groups [8].

TB-DM sufferers face many barriers in accessing TB-DM services and support [9] . Frontline health workers have limited knowledge regarding TB-DM comorbidity and collaborative frameworks, which has a detrimental impact on the effectiveness of implementing these frameworks [10]. Nutritional support for TB-DM patients [11] One of the efforts to manage TB-DM patients related to the process and results of treatment is efforts to better monitor glycemic control [12].

Support in the form of integrated care efforts in the form of increased TB screening for DM patients, loss to follow-up from treatment for both diseases was reduced, and treatment success among TB patients increased with TB-DM integration efforts [13]. Greater efforts are needed to integrate TB-DM services into routine care [14,15].

The results of screening carried out in 38 regencies/cities with a DM-TB burden were carried out on 6485 (3%) respondents from 214,105 targeted DM sufferers . The number of TB suspects obtained was 1,907 people (29.4%). Then, TB cases were found in people with DM amounting to 707 cases of TB (10.9%) from people with DM who were screened for TB [16] . South Sulawesi Province since 2021-2023, TB-DM cases have continued to increase from 1,550 in 2021 to 2,133 in 2022 and 2,447 in 2023, where women are higher than men, 3,086 and 3,042 [17,18].

The high incidence and continuing increase in the incidence of TB in DM sufferers based on the above background is the reason we are researching the Risk Factors for the Incidence of Pulmonary TB in Type 2 DM Mellitus Patients in Bulukumba Regency.

2. MATERIALS AND METHODS

2.1 Types and Research Design

The design of this research is an analytical observational study called "Case Control" research on TB-DM sufferers in Bulukumba Regency in April - May 2024. The population in this study consists of all TB-DM sufferers who live in Bulukumba Regency.. Sampling technique used was Exhaustive sampling of all TB sufferers who suffered from DM. which means all TB-DM patients in Bulukumba Regency .

2.2 Ethical Aspects

Ethical permission has been obtained from the ethics committee of the Faculty of Public Health, Hasanuddin University with ethical approval certificate number: 935/UN4.14.1/TP.01.02/2024. All subjects provided informed consent before being given treatment

2.3 Sampling Technique

The number of samples in this study was 164 people with a ratio of 1:3. In total there were 41 cases and 123 control samples. The "Case" criteria are families whose members were diagnosed with TB-DM who were registered at Community Health Centers and Hospitals in the period January to December 2023. The "Control" group consisted of respondents suffering from DM and residing in the Bulukumba Regency area in 2024.

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2.4 Data Analysis

The data was analyzed using the Kobotoolbox application and the survey format was exported to an Excel file. for validation, editing, coding and cleaning purposes. Then, they are imported into STATA. Data entered into the STATA application is analyzed using univariate, bivariate and multivariate methods. Univariate analysis involves creating distribution and frequency tables of respondent characteristics, as well as dependent and independent variables.

Bivariate analysis was carried out by compiling a 2x2 table to calculate the odds ratio (OR) value. The significance test was used with *Confidence Interval (CI)* 95% and Chi-square (X^2). Multivariate analysis uses logistic regression, including variables that have a statistically significant 95% CI value in bivariate analysis. This helps determine domain variables that act as risk factors. In addition, the probability value of the independent variable that influences the incidence of TB which is the dependent variable is also assessed. The following steps were taken for the multivariate analysis: all independent variables that were statistically significant in the bivariate analysis were included. Stepwise elimination then, removed variables that had nonsignificant 95% CIs. This process helps obtain the final model fit to identify the dominant risk factors among the independent variables. Finally, the probability value is calculated using the formula: P = 1/ (1+ exp(-y)), so that the probability of the variables that are risk factors for TB incidence can be determined.

3. RESULTS

Table 1: Characteristics of respondents based on gender, age, education, duration of suffering and type of medication

Variable	Case		Control		Total	
	n	%	n	%	n	%
Gender						
Male	18	43.90	29	23.58	47	28.66
Female	23	56.10	94	76.42	117	71.34
Age						
31-40 Years	5	12.20	5	4.07	10	6,10
41-50 Years	15	36.59	31	25,20	46	28.5
51-60 Years	14	34.15	46	37.40	40	36.15
61-70 Years	4	9.76	32	26.02	36	21.95
> 70 Years	3	7.32	9	7.32	12	7.32
Level Of Education						
Elementary School	6	14.63	16	13.01	22	13.41
Junior High School	9	21.95	22	17.89	31	32.32
Senior High School	21	51.22	69	56.10	90	87.20
Bachelor	5	12.20	14	11.38	19	11.59
Master	0	0.00	2	1.63	2	1.22
Long Suffering						
Under 5 Years Old	34	82.93	67	54.47	101	61.59
Above 5 Years	7	17.07	56	45.53	63	38.41
Type Of Medicine						
Injection	12	29.27	20	16.39	33	20.12
Orally	29	70.73	102	83.61	131	79.87

Source: Primary Data, 2024

Based on Table 1, the distribution of respondent characteristics shows that the characteristics of respondents based on gender are 117 (71.34%) female, 60 (36.15%) in the age group 51-60 years. The highest level of education was at high school level 90 (87.20%), duration of suffering 101 (61.59%) < 5 years, and type of medication 131 (79.87) used orally .

Table 2: Distribution of Cases and Controls based on the independent variable T2DM without Pulmonary TB in the incidence of T2DM with Pulmonary TB in Bulukumba Regency

Independent Variable	Incidence of TB in DM				Total	
	Case		Control			
	n	%	n	%	n	%
BMI						
High risk	14	34.14	12	9.75	26	15.85
Low risk	27	65.85	111	90.24	138	84.14
Treatment Compliance						
High risk	25	60.97	42	34.14	67	40.85
Low risk	16	39.02	81	65.85	97	59.15
Exposure to cigarette smoke						
High risk	25	60.97	65	52.84	90	54.87
Low risk	16	39.02	58	47.15	74	45.12
Family support						
High risk	27	65.85	49	38.83	76	46.34
Low risk	14	34.14	74	60.16	88	53.65
Household contact						
High risk	21	51.21	40	32.52	61	37.19
Low risk	20	48.78	83	67.47	103	62.80

Source: Primary Data 202 4

Table 2: The BMI variable in the high risk category has the highest proportion in the case group (34.14%) compared to the control group, 9.75%. For the low risk category, the highest proportion was found in the control group at 90.24% compared to the case group at 65.85%.

Most of the TB-DM sufferers (cases) were exposed to cigarette smoke, 60.97% compared to the group who were not TB-DM sufferers (controls), 52.84%. In the low risk category (not exposed to cigarette smoke) the highest proportion was found in controls 47.15 compared to the case group 39.02%.

Variable Adherence to treatment in the case group, the proportion was greater in the high risk group, 60.90% compared to the case group, 34.14%, while in the low risk group, the highest proportion was in the Control group, 65.85%, compared to cases, 39.02%.

Family Support Variables in the Case Group, the proportion was greater in the high risk group, 65.85% compared to the case group, 38.83%, while in the low risk group, the highest proportion was in the Control group, 60.16%, compared to cases, 34.14%. Variables in the Case Group, the proportion was greater in the high risk group, 51.21% compared to the case group, 32.52%, while in the low risk group, the highest proportion was in the Control group, 67.47%, compared to cases, 48.78%.

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Table 3: Risk factors for T2DM without pulmonary TB in the incidence of T2DM with pulmonary TB in Bulukumba Regency

Independent Variable	Case		Control		Total		
	n	%	n	%	OR	*p*	CI 95%
BMI							
High risk	14	34.14	12	9.75	4.79	0.0002 *	1.80-12.6
Low risk	27	65.85	111	90.24			
Treatment compliance							
High risk	25	60.97	65	52.84	3.01	0.0025 *	1.36-6.70
Low risk	16	39.02	58	47.15			
Exposure to cigarette smoke							
High risk	25	60.97	42	34.14	1.39	0.3649	0.64-3.08
Low risk	16	39.02	81	65.85			
Family support							
High risk	27	65.85	49	38.83	2.91	0.0038 *	1.31-6.60
Low risk	14	34.14	74	60.16			
Household contact							
High risk	21	51.21	40	32.52	2.17	0.0319 *	0.99-4.75
Low risk	20	48.78	83	67.47			

Source: Primary Data, 2024

Based on Table 3 , it shows that the variables that are risk factors for the incidence of pulmonary TB in type 2 DM patients are BMI with a value of (OR 4.79; 95% CI, 1.80 – 12.6), Compliance with treatment with a value of (OR 3.01 ; 95% CI, 1.36 – 6.70) , exposure to cigarette smoke (OR 1 , 39 ; 95% CI, 0.641 – 3.084) Family support with value, (OR 2.91; 95% CI, 1.31 – 6.60), Household contact with value (OR 2.17; 95% CI, 0.99 – 4.75). Variables that were significantly related to p value <0.05 were BMI, adherence to treatment, family support and household contact.

Table 4: Model 1 Multivariate analysis of independent variables of risk factors for T2DM without pulmonary TB in the incidence of T2DM with pulmonary TB in Bulukumba Regency

Research variable	AOR	(95%CI)
BMI	5.399211	2.062491-14.13411
Treatment Compliance	1.953686	0.8455011-4.514349
Family support	2.136711	0.9191504-4.967125
Household contact	2.237184	1.003643-4.986825
Constanta	0.0827746	0.0374139-0.1831311

Source: Primary Data, 2024

Based on Table 4, the variables BMI, Treatment Compliance, Family Support, and Household Contact are risk factors for the incidence of pulmonary TB in type 2 DM mellitus patients and then carry out further multivariate analysis to get the final model that is fit to find out the dominant variables and obtain probability values for the factors. The risk of pulmonary TB in type 2 DM mellitus patients can be seen in the table below.

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Table 5: Model Fit Model Fit Multivariate Analysis of the Relationship between Dependent and Independent Variables T2DM without Pulmonary TB on the incidence of T2DM with Pulmonary TB in Bulukumba Regency

Research variable	AOR	Coeff	*p*	(95%CI)
BMI	5.587541	1.720539	0,000	2.23138-13.99162
Household contact	2.605707	0.9577041	0.015	1.204434-5.637261
Constanta	0.1575914	-1.847749		-2.436025--1259474

Source: Primary data 2024

Based on table 5 is the final model of the analysis of the main determinant variables that cause pulmonary TB in T2DM patients, namely BMI and household contacts . The most dominant variable is the risk factor for pulmonary TB in T2DM sufferers in Bulukumba Regency. The BMI variable is the highest with a value (AOR 5.58; 95% CI, 2.23138 – 13.99162) with a p value = 0.000. The results of this analysis can be concluded that T2DM sufferers with a BMI < 18.5 are at 5.58 times the risk of suffering from TB compared to T2DM sufferers with a BMI ≥ 18.5.

4. DISCUSSION

The discussion in the results of this research will provide a further description of the results of the data analysis that was stated previously. The research was conducted using *a case-control design* on 164 respondents consisting of 41 respondents in the case group and 123 respondents in the control group. This research was carried out on April 24 – May 22 2024 . Starting with holding meetings with each program manager, both the TB program manager and the non-communicable disease manager who handles DM mellitus to unify perceptions before conducting interviews with the case group and control group in the form of interviews and filling out questionnaires. Based on the results of our observations, the management of the two diseases between programs has not been fully integrated. Currently, it is still the responsibility of the tuberculosis program manager to record the management of the TB-DM program, while the management of the non-communicable disease DM mellitus program is still running in accordance with the currently applicable minimum service standards. This condition will impact the achievement of each program and influence the low control of both diseases.

Screening carried out by non-communicable disease management specifically for DM is limited to case finding, physical activity and therapy. Meanwhile, the prevalence of TB is higher among DM patients and DM among TB patients, when compared with the general population. Thus, active screening of DM patients for TB and vice versa is recommended [14]. DM is significantly associated with an increased likelihood of poor TB treatment outcomes in patients [19].

It is important to monitor blood sugar levels in DM patients and in patients with TB and DM co-infection, and this is very important. Adapting TB treatment protocols in DM patients can reduce morbidity, glycemic control and better TB outcomes. This will help towards the End TB Strategy and Sustainable Development Goals for TB elimination[7].

Body Mass Index (BMI) is a measurement used to determine a person's health status based on their height and weight. BMI is a simple, cheap, and non-invasive tool for screening weight categories, such as underweight, normal weight, overweight, and obesity.

Based on the results in this study, the BMI variable has an OR value of 4.79; 95% CI, 1.80 – 12.6, p= 0.0002, this shows that there is a relationship between BMI < 18.5 and is a risk factor for TB in DM sufferers. This is in line with the findings where the determining factors for pulmonary TB in DM sufferers are weight loss, decreased BMI, drug addiction, uncontrolled DM, high HbA1c numbers, increased insulin requirements, anemia, higher ESR, higher plates. let count and decrease serum protein and albumin[20].

Different things were found in prediabetic conditions associated with more types of lung lesions, higher bacillary burden, low hemoglobin (Hb), and high body mass index (BMI). Unfavorable TB treatment: Prediabetes was independently associated with unfavorable treatment and was significantly associated with a higher likelihood of unfavorable TB treatment outcomes. Control of dysglycemia during anti-TB treatment provides an opportunity to implement appropriate interventions for TB management [21].

TB screening with regular chest x-rays is feasible, but not economical in areas with low TB incidence. It is recommended that DM patients with low BMI, high FBG, and low triglycerides be selected as TB screening subjects [22].

The conditions of sufferers (TB) and (DM) are two diseases that influence each other. A person with DM has a higher risk of getting TB, and if they do get TB, treatment can be more complicated and take longer. Adherence to treatment in DM sufferers is very important to ensure the effectiveness of treatment and prevent drug resistance and more severe complications.

Based on the results of this study, treatment adherence was found with a value of (OR 3.01; 95% CI, 1.36 – 6.70), p = 0.0025, which means there is a relationship between treatment adherence and the incidence of TB-DM. This is in line with medication adherence is important in the management of DM treatment. The risk of acquired drug resistance increases significantly among recovered TB-DM patients compared to recovered TB-without DM patients, the need for more interventions during the clinical management of TB-DM cases [23].

This study also showed that 79.87% used oral medication. The use of Metformin has the potential to develop long-term immunity against TB infection and is responsible for its protective impact in patients with comorbid TB - DM. Metformin therapy improves T cells, Helper T cells and cytotoxic T cells in patients with comorbid TB - DM and can be prescribed as an adjuvant antitubercular drug unless there are contraindications [24]. In another study, it was found that DOT DM resulted in relatively better glycemic control (HbA1c) in TB-DM patients, although the programmed management of TB-DM patients did not have a significant effect on TB treatment outcomes [25] .

Another role in monitoring treatment compliance also requires family support and the role of health workers. Family support has a greater direct influence than health professional education on TB patient compliance. However, health workers still play an important role because the patient's family also receives education from health workers [26] . TB treatment and family support are very important in increasing the level of patient treatment compliance. Therefore, medical personnel who care for TB patients need to manage the treatment of TB patients with continuous consultation.

Exposure to cigarette smoke refers to a condition where a person inhales the smoke produced by burning tobacco from cigarettes, internally in the form of kretek, filter and electric which come from the two main sources of active cigarette smoke, smoke that is inhaled directly by smokers when smoking. Passive cigarette smoke is smoke inhaled by people around the smoker. Exposure to cigarette smoke has significant health impacts, both for active and passive smokers.

Exposure to cigarette smoke with a value of (OR 1.39; 95% CI 0.64-3.08) p = 0.3649, this means that there is no relationship between exposure to cigarette smoke directly causing TB. Our findings suggest that smokers are more likely to suffer from symptomatic and subclinical TB. Therefore, these individuals may be prioritized for intensive screening, such as the use of chest x-rays in the context of community-based screening. People with self-reported DM are also more likely to have symptomatic TB, but the association with subclinical TB remains unclear [27]. Quitting smoking has also been shown to have a negative impact on body weight, glycemic control, and increased risk of new DM. Smoking cessation may be beneficial for the prevention of DM and management of the disease and its macrovascular and microvascular complications. This narrative review examines the evidence for the impact of smoking and smoking cessation in patients with DM and specifically type 2 DM mellitus and its complications[28].

Smokers are at higher risk for type 2 DM and its complications. Smoking can increase blood sugar and cause insulin resistance. This is because when smoking the absorption of glucose by cells is slow, the effectiveness of insulin in the blood is reduced and the work of blood flow in the skin slows down. Heavy smokers (20 cigarettes/day) have twice the risk of developing Type 2 DM compared with non-smokers [29].

TB is a common comorbidity in DM patients. TB-DM comorbidity was significantly higher in smokers [30]. This research is also supported by other research on the incidence of TB on chronic kidney disease, number of medical visits, BMI, alcoholism and smoking, the risk remains higher in DM patients [31].

Family support is very crucial for TB-DM patients to achieve better health outcomes. This support can reduce the psychological and practical burden that patients face, improve adherence to treatment, and help patients manage their conditions more effectively and efficiently. Therefore, increasing the awareness and ability of families to support their members who suffer from TB-DM is an important step in the treatment and control strategy for these two diseases.

Family support in research with value, (OR 2.91; 95% CI, 1.31 – 6.60) p=0.0038. Based on this, support is a risk factor for TB in DM sufferers. This is in line with research where it is said that family support is very necessary for DM patients to continue to carry out self-management [32] . Family support is critical for managing chronic conditions but is often overlooked when designing behavioral interventions for type 2 DM mellitus (T2DM) .

The support received by T2 DM sufferers from their families and the role of this support in their efforts to implement DM management practices. In this study, sufferers received a lot of support from family members such as their partners and children. Their relatives encourage and motivate them to strive for health, they also provide instrumental support by preparing healthy meals, reminding them to take medication, and sharing physical activities. One of the obstacles in providing support to sufferers is that some sufferers also report that control measures are not always well received, including when visiting health facilities while still being independent. Therefore, any intervention that supports self-management practices needs to involve key family members. For this reason, interventions should be aimed at family members to ensure improved self-management practices of T2DM.

Good family support will increase compliance with self-care management so that the quality of life of DM patients will increase. Accompanying and empowering the family's role in caring for DM patients can maximize family support for the patient [33].

Family support is the variable that has the greatest contribution to the quality of life of type 2 DM patients, so it is hoped that the families of type 2 DM patients will provide high support to type 2 DM patients so that the patient's quality of life will be better [34]. Family support is significantly related to resilience [35]. Family support has an important role in improving the quality of life of DM patients. Therefore, efforts need to be made to increase family support for DM patients as part of the management of DM disease in health care settings both in hospitals and community health centers [36]. Providing health services and increasing the level of family support can contribute positively to the mood of elderly patients [37].

Household contact in TB sufferers refers to the concept where someone in the same house as a TB patient, household contact is said to have a higher risk of being infected with TB. This is due to continuous exposure to Mycobacterium tuberculosis which is released by the patient either through coughing or sneezing. The research results related to the household contact variable with the value (OR 2.17; 95% CI, 0.99 – 4.75). p=0.0319. This shows that there is a relationship between the incidence of pulmonary TB in sufferers of type 2 DM mellitus. This is in line with previous research. The significant risk factors for the incidence of pulmonary TB are a history of TB contact and a long history of suffering from DM [38].

Nearly 95% of DM cases and TB cases among household contacts were newly diagnosed. 64% of known DM cases among household contacts had poor glycemic control. DM among household contacts of TB patients with DM was significantly higher (OR—2.13, 95% CI: 1.10–4.12) compared to TB patients without DM. There was no difference in TB prevalence between patients with household contacts of TB patients with and without DM. Undetected and uncontrolled DM among household contacts of TB patients represents a strong index of the need for DM screening and intervention in this dual high-risk TB-DM population [39].

Contacts with people with pulmonary TB and dysglycemia are at higher risk of being QuantiFERON positive at baseline or month 6. Increased focus on close contacts can improve TB control [40]. HHC with DM are more likely to suffer LTBI Further investigation is needed to assess the mechanisms by which DM may increase the risk of LTBI after Mtb exposure [41].

5. CONCLUSION

Based on the results of the research that has been carried out, it can be concluded that the TB–DM cases in Bulukumba Regency are as follows:

a) T2DM sufferers with a BMI of 17-< 18.5 are at 4.79 times greater risk of suffering from pulmonary TB than those with a BMI > 18.5.

b) T2DM sufferers who have low medication adherence have a 3.01 times greater risk of suffering from pulmonary TB compared to patients with high medication adherence.

c) T2DM sufferers Exposure to cigarette smoke in T2DM sufferers did not show a significant relationship with the incidence of pulmonary TB.

d) T2DM sufferers who have good family support are 2.91 times more likely to suffer from pulmonary TB compared to sufferers who have low family support.

e) T2DM sufferers who have household contacts are 2.17 times more likely to suffer from new TB than T2DM sufferers who do not have household contacts.

f) BMI and household contacts are significantly associated with an increased risk of TB incidence. BMI is a significant predictor for the incidence of pulmonary TB with a probability of 30.35%.

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Reference

1) Nur Nasri Noor, Epidemiology of Infectious Diseases. Edition II. Makassar: Unhas Press, 2022.

2) WHO, Global Tuberculosis Report 2022. 2022. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022

3) J. Li *et al.* Prevalence and Risk Factors of Diabetes in Patients with Active Pulmonary Tuberculosis: A Cross-Sectional Study in Two Financially Affluent Chinese Cities. Diabetes, Metab. Syndr. Obese*.* Vol. 17(1), pp. 1105–1114, 2024, doi: 10.2147/DMSO.S450507.

4) A. Alemu, ZW Bitew, G. Diriba, and B. Gumi. Co-occurrence of tuberculosis and diabetes mellitus, and associated risk factors, in Ethiopia: a systematic review and meta-analysis, *IJID Reg.* Vol. 1 (9). pp. 82–91, 2021, doi: 10.1016/j.ijregi.2021.10.004.

5) IDF. Internation Diabetes Federation “https://idf.org/,” 2024.

6) Ministry of Health of the Republic of Indonesia. Infodatin Diabetes Mellitus.: Ministry of Health of the Republic of Indonesia. 2020. Available at: https://pusdatin.kemkes.go.id/download.php?file=download/pusdatin/infodatin/Infodat in-2020-Diabetes-Melitus.pdf," 2022.

7) U. Abbas *et al.* Tuberculosis and diabetes mellitus: Relating immune impact of co-morbidity with challenges in disease management in high burden countries, *J.* Clin. Tuberc. Other Mycobacteria. Dis. Vol. 29(1), pp. 100343, 2022, doi: 10.1016/j.jctube.2022.100343.

8) W.M. Song *et al.* Primary drug resistance among tuberculosis patients with diabetes mellitus: A retrospective study among 7223 cases in China, Infect. Drug Resist*.* Vol. 12(2), pp. 2397–2407, 2019, doi: 10.2147/IDR.S217044.

9) M. Arini, RA Ahmad, and A. Utarini, Tuberculosis and type 2 Diabetes Mellitus (TB-DM) comorbidity care: Barriers from the patients' perspective, Enferm. Clin. Vol. 30(3), pp. 174–178, 2020, doi: 10.1016/j.enfcli.2020.06.040.

10) RS Salifu and KW Hlongwana, Frontline healthcare workers' experiences in implementing the TB-DM collaborative framework in Northern Ghana, *BMC Health* Serv. Res. Vol. 21(1), pp. 1–11, 2021, doi: 10.1186/s12913-021-06883-6.

11) D. Girishbhai, T. Baral, S. Jacob, P. Malakapogu, K. Saravu, and S. Sekhar. Nutritional status in patients with tuberculosis and diabetes mellitus : A comparative observational study, J. Clin. Tuberc. Other Mycobacteria. Dis. Vol. 35(3). p. 100428, 2024, doi: 10.1016/j.jctube.2024.100428.

12) Wahiduddin, A. Pranoto, and Sudjarwo. Glycemic Control in Type 2 Diabetes Mellitus Patients with and without Pulmonary Tuberculosis. Health Media. Masy. Indonesia. Vol. 15(1), pp. 99–109, 2019, doi: 10.30597/mkmi.v15i1.5292.

13) JLZ Nyirenda, D. Wagner, B. Ngwira, and B. Lange. Bidirectional screening and treatment outcomes of diabetes mellitus (DM) and Tuberculosis (TB) patients in hospitals with measures to integrate care of DM and TB and those without integration measures in Malawi. BMC Infect. Dis. Vol. 22(1), pp. 1–12, 2022, doi: 10.1186/s12879-021-07017-3.

14) ZZ Araia, AB Mesfin, AH Mebrahtu, AG Tewelde, R. Osman, and HA Tuumzghi. Diabetes mellitus and its associated factors in tuberculosis patients in Maekel region, eritrea: Analytical cross-sectional study. Diabetes, Metab. Syndr. Obese. Vol. 14(3), pp. 515–523, 2021, doi: 10.2147/DMSO.S293557.

15) South Sulawesi Health Service, 2021 Health Profile of South Sulawesi Province . 2021. https://dinkes.sulselprov.go.id/document/Profil%20Kesehatan/

16) Indonesian Ministry of Health. 2022 Tuberculosis Control Program Report. 2022. https://tbindonesia.or.id/wp-content/uploads/2023/02/Factsheet-Country-Profile-Indonesia-2022.pdf

17) South Sulawesi Health Service. Provincial TB Management. 2024. https://tbindonesia.or.id/wp-content/uploads/2023/09/Laporan-Tahunan-Program-TBC-2022.pdf

18) Bulukumba District Health Service. Bulukumba District TB Management. 2023.

19) HT Adane, RC Howe, L. Wassie, and MJ Magee. Diabetes mellitus is associated with an increased risk of unsuccessful treatment outcomes among drug-susceptible tuberculosis patients in Ethiopia: A prospective health facility-based study. J. Clin. Tuberc. Other Mycobacteria. Dis. Vol. 31(4), p. 100368, 2023, doi: 10.1016/j.jctube.2023.100368.

20) NH Khalil and RA Ramadan. Study of risk factors for pulmonary tuberculosis among diabetes mellitus patients. Egypt. J. Chest Dis. Tuberc. Vol. 65(4), pp. 817–823, 2016, doi: 10.1016/j.ejcdt.2016.05.009.

21) RI Calderon *et al.* Persistent dysglycemia is associated with unfavorable treatment outcomes in patients with pulmonary tuberculosis from Peru. Int. J. Infect. Dis. Vol. 116(5), pp. 293–301, 2022, doi: 10.1016/j.ijid.2022.01.012.

22) Y. Ji *et al.* Screening for pulmonary tuberculosis in high-risk groups of diabetic patients. Int. J. Infect. Dis. Vol. 93(8), pp. 84–89, 2020, doi: 10.1016/j.ijid.2020.01.019.

23) W. Mei Song *et al.* Drug resistance of previously treated tuberculosis patients with diabetes mellitus in Shandong, China. Respir. Med. Vol. 163(1), pp. 1–7, 2020, doi: 10.1016/j.rmed.2020.105897.

24) R. Mishra *et al.* Effect and possible mechanisms of metformin as adjuvant therapy in the management of tuberculosis: A prospective study. Clin. Epidemiol. Globe. Heal. Vol. 16(6), p. 101106, 2022, doi: 10.1016/j.cegh.2022.101106.

25) P. Udaykumar, S. Kumar, C. N, RH Reddy, BM N, and SB Nagaraja. Daily monitoring of diabetic treatment among TB-DM patients under NTEP: Does it improve the treatment outcomes?. Clin. Epidemiol. Globe. Heal. Vol. 17(7), p. 101118, 2022, doi: 10.1016/j.cegh.2022.101118.

26) D. Anshar and G. Fadhilla. Correlation between Family Support and Health Professional Education on Tuberculosis Patient Compliance at Public Health Centers Tasikmalaya. Vol 9(42), pp. 314–319, 2023, doi: 10.25077/jsfk.10.3.314-319.2023.

27) Y. Hamada *et al.* Association of diabetes, smoking, and alcohol use with subclinical-to-symptomatic spectrum of tuberculosis in 16 countries: an individual participant data meta-analysis of national tuberculosis prevalence surveys. eClinicalMedicine. Vol. 63(6), pp. 1–13, 2023, doi: 10.1016/j.eclinm.2023.102191.

28) D. Campagna *et al.* Smoking and diabetes: Dangerous liaisons and confusing relationships. Diabetol. Metab. Syndr. Vol. 11(1), pp. 1–12, 2019, doi: 10.1186/s13098-019-0482-2.

29) RW Gayatri, AN Kistianita, and et al. Diabetes Mellitus in Era 4.0, Vol. 6(1). 2022.

30) AA Wagnew, F., Eshetie, S., Alebel, A., Dessie, G., Tesema, C., & Abajobir. Meta-analysis of the prevalence of tuberculosis in diabetic patients and its association with cigarette smoking in African and Asian countries. BMC research notes, Vol 11(1),pp. 298. 2018. https://doi.org/10.1186/s13104-018-3390-x.

31) V. Antonio-Arques *et al.* Subjects With Diabetes Mellitus Are at Increased Risk for Developing Tuberculosis: A Cohort Study in an Inner-City District of Barcelona (Spain). Front. Public Heal*.* Vol. 10(5), pp. 1–11, 2022, doi: 10.3389/fpubh.2022.789952.

32) Family Support for Diabetes Self-care Behavior in T2DM Patients who Use Herbs as a Complementary Treatment. Medico Legal Update, Vol 19(1), pp.238-243. 2020. https://doi.org/10.37506/mlu.v19i1.921

33) C. Yuliastuti, NM Astuti, DD Winarno, MA Sari, and N. John. Family Support Related to Quality of Life in Diabetes Mellitus Patients with Ulcer. Vol. 14(10), pp. 96–100, 2022, doi: 10.31674/mjn.2022.v14i02.016.

34) Chisalunda A, Ng'ambi WF, Tarimo NS, Banda NPK, Muula AS, Kumwenda J, Nyondo-Mipando AL. Quality of life among type 2 diabetes mellitus patients at Kamuzu Central Hospital in Lilongwe, Malawi: A mixed-methods study. PLOS Glob Public Health. Vol 3(10): pp.e0002367. 2023. doi: 10.1371/journal.pgph.0002367.

35) N. Agustini, N. Nurhaeni, H. Pujasari, E. Abidin, AW Lestari, and A. Kurniawati, Family Support towards Resilience in Adolescents with Type I Diabetes: A Preliminary Study in Indonesia. Vol. 4(2), pp. 66–71, 2019, doi: 10.31372/20190402.1028.

36) M. Ndama, RE Langitan, and DD Manggasa. The Role of Family Support in the Quality of Life of Diabetes Patients in the Internal Medicine Polyclinic at the Poso Regional General Hospital. Vol 5(2), pp. 108–119, 2023. https://doi.org/10.32734/ijns.v5i2.14345

37) B. Dastan and S. Hintistan. Exploring Problem Areas of Elderly Patients with Diabetes and the Support Provided by Their Family. Vol 12(1). pp.342-350. 2022, doi: 10.33808/clinexphealthsci.895039.

38) C. Destiany, A. Zulkifli, and RM Thaha. Relationship Between Time Term of Diabetes Mellitus, Age, and History of Lung TB Contact on the Event of Lung TB in Diabetes Mellitus Patients. J. Parasitol. Infect. Dis*.* Vol. 0982(4), 2019, doi: 10.36349/easjpid.2019.v01i04.001.

39) N. Zayar, R. Sangthong, S. Saw, ST Aung, and V. Chongsuvivatwong. Combined Tuberculosis and Diabetes Mellitus Screening and Assessment of Glycaemic Control among Household Contacts of Tuberculosis Patients in Yangon, Myanmar. Vol. 1(1), pp. 1–13, 2020.

40) MB Arriaga *et al.* The Effect of Diabetes and Prediabetes on Mycobacterium tuberculosis Transmission to Close Contacts. J. Infect. Dis. Vol. 224(12), pp. 2064–2072, 2021, doi: 10.1093/infdis/jiab264.

41) A.G.C. Smith *et al.* The Impact of Diabetes and Prediabetes on the Prevalence of Mycobacterium tuberculosis Infection Among Household Contacts of Active Tuberculosis Cases in Ethiopia. Open Forum Infect. Dis*.* Vol. 9(7), pp. 1–8, 2022, doi: 10.1093/ofid/ofac323.