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Research Article

Effect of Poor Glycemic Control with Length of Pulmonary Tuberculosis Treatment in Type 2 Diabetes Mellitus Patients

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Abstract
Type 2 Diabetes Mellitus (T2DM) is one of the leading risk factors in developing Pulmonary Tuberculosis (PTB) and associated with a higher risk in recurrence, treatment failure, and MDR-TB. Duration of PTB treatment usually takes six months with first line regimen, however in uncontrolled blood glucose confirmed by HbA1c, Fasting Blood Glucose (FBG), and Postprandial Glucose (PPG) the treatment takes longer than usual because of the difficulty to achieve an optimal management in both diseases. The aim of this study was to assess the correlation between glycemic control and duration of anti-tuberculosis treatment at Persahabatan General Hospital, Jakarta in 2019-2021. It was a non-experimental study with analytical observational design and retrospective approach by using medical records. Data were analyzed descriptively and by the chi square method. Odds ratio and relative risk measure the association between duration of treatment in PTB patients and their gylcemic controls. The results showed that 57 PTB patients with T2DM (69.5%) received nine months course of anti-tuberculosis therapy. Most patients tend to have poor glycemic control shown by HbA1c level >7% (79.3%), FBG >130 mg/dL (72%), and PPG >180 mg/dL (80.5%). Correlation between glycemic control and duration of PTB treatment are significant shown by p-value result 0,001. The OR result was found to be 8.74 (95% CI 2.45-31.11) which indicate that patients with poor glycemic control have a greater risk to experience longer duration of PTB treatment. In conclusion, duration of PTB treatment are mostly done in more than six months due to poor glycemic control.

Keywords: duration of treatment, glycemic control, HbA1c, pulmonary tuberculosis, type 2 diabetes mellitus

Pengaruh Kendali Glikemik yang Buruk dengan Lama Pengobatan Tuberkulosis Paru pada Pasien Diabetes Melitus Tipe 2

Abstrak
Diabetes Melitus Tipe 2 (DMT2) adalah salah satu penyakit komorbid yang menjadi faktor risiko Tuberkulosis paru dan dihubungkan dengan prognosis yang lebih buruk seperti terjadinya rekurensi, gagal terapi, dan TB-MDR. Pengobatan Tuberkulosis paru umumnya dilakukan selama enam bulan dengan pengobatan lini pertama, tetapi pengendalian DMT2 yang tidak optimal dinilai dari kadar HbA1c, Glukosa Darah Puasa (GDP), dan Glukosa Darah 2 Jam Postprandial (G2JPP) akan menambah lama pengobatan Tuberkulosis paru. Kendali glikemik pada pasien Tuberkulosis paru dengan DMT2 lebih sulit dilakukan salah satunya karena adanya interaksi obat antara Obat Anti Tuberkulosis (OAT) dan Obat Antidiabetes Oral. Penelitian ini adalah studi non eksperimental dengan desain analitik observasional dan pendekatan retrospektif menggunakan data rekam medik yang dilakukan untuk membuktikan adanya hubungan antara kendali glikemik pada DMT2 dengan lama pengobatan Tuberkulosis paru di RSUP Persahabatan pada tahun 2019-2021. Hasil penelitian ini menunjukkan bahwa sebanyak 57 pasien (69,5%) dari keseluruhan sampel mendapatkan pengobatan OAT selama sembilan bulan dengan mayoritas memiliki kendali glikemik yang tidak optimal dinilai dari kadar HbA1c >7% (79,3%), GDP >130 mg/dL (72%), PPG >180 mg/dL (80,5%). Nilai p 0,001 menyatakan adanya hubungan signifikan antara kendali glikemik dengan lama pengobatan Tuberkulosis paru. Pasien DMT2 dengan kendali glikemik buruk 8,74 kali lipat (95% CI 2,45-31,11) berisiko lebih lama menjalani pengobatan OAT. Kesimpulan dari penelitian ini terbukti bahwa lama pengobatan tuberkulosis paru umumnya dilakukan lebih dari enam bulan pada pasien dengan kendali glikemik yang tidak optimal.

Kata kunci: Diabetes melitus tipe 2, HbA1c, kendali glikemik, lama pengobatan, tuberkulosis paru

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Introduction

Tuberculosis (TB) cases in Indonesia are ranked third in the world. High morbidity and mortality rates of pulmonary TB are a problem in the world even though diagnostic tests vary and the disease can be treated with Anti-Tuberculosis Drugs (ATD) within a specified time.[1,2] World data shows that ten million people with TB with a mortality rate of 1.4 million people.[3,4] One of the comorbid diseases that are a risk factor for TB is Diabetes Mellitus (DM), especially type 2 Diabetes Mellitus (T2DM).

The number of DM patients in the world in 2019 is estimated at 285 million people and continues to increase. According to Indonesian basic health research (Riskesdas, 2018) there are 1,017,290 people diagnosed with DM and the number will increase to 21.3 million people by 2030.[3] However, only about two-thirds of the population receives treatment and receives education from the recorded data, this is because the course of DM disease is chronic and generally does not cause specific symptoms until it eventually hits the target organ. This will increase the risk of being infected with TB.[3,4] The majority of T2DM patients have a three times higher risk of suffering from TB-DM compared to those without DM.[4] Through various mechanisms it has been shown that DM provides a significant worsening of clinical TB patients, with the consequent increasing the length of use of ATD.[5] Therefore, glycaemic control must be carried out periodically through effective pharmacological and non-pharmacological therapies to prevent active pulmonary tuberculosis.

Glycaemic control assessment consisting of FPG, PPG, and HbA1c is the main examination carried out to assess the control of DM with the achievement of DM control goals.[4,6] Based on Indonesian basic health research's data in 2018, DM patients who routinely check blood glucose levels only amounted to 1.8%, then as many as 85.5% of patients never had an examination and 12.8% of patients did not routinely do an examination. This is often supported by the high dropout of treatment (50.4%) because DM patients feel that they are healthy so they no longer have regular check-ups and continue the treatment.[3] This causes glycaemic control in DM patients in Indonesia not optimal so that the risk of TB infection is increasing every year. TB patients with hyperglycaemia correlated with the risk of ATD resistance.[4] Slowing response to treatment can increase ATD side effects, therapy failure, reactivation, and eventually MDR-TB can occur.[4] Control of DM and TB must be carried out simultaneously so that optimal results are achieved. Glycaemic control through FPG, PPG, and HbA1c in DM patients is the main and most important determinant to achieve successful treatment of pulmonary TB.[4] This study aims to determine the association between glycemic control in T2DM and the duration of treatment for pulmonary TB as an effort to prevent pulmonary TB, especially in patients with T2DM. The Odds Ratio (OR) was done to measure the association between glycemic control and the outcome of TB treatment. The confidence interval is done to determine whether this odds ratio finding is correct. The confidence interval specifies the predicted range of the true odds ratio for the population. If the confidence interval for the odds ratio contains the number 1, the estimated odds ratio is not statistically significant. An odds ratio larger than one indicates that the exposed group has a higher chance of experiencing the event than the non-exposed group. An odds ratio less than one indicates that the exposed group has a lower chance of experiencing the event than the non-exposed group. An odds ratio of one indicates that the probability of the event occurring are the same in the exposed and

non-exposed groups.[7]

Methods

Study design

This is a retrospective observational analytical study. Subjects were obtained from medical record data year of 2019-2021 "Persahabatan" (Friendship) General Hospital, Jakarta. The research received permission from the Research Ethics Commission of the "Persahabatan" General Hospital No. 113/KEPK-RSUPP/12/2021.

Data collection

Data were collected by purposive sampling in populations that met the inclusion and exclusion criteria. The inclusion criteria are pulmonary TB patients with a history of T2DM who received ATD category 1 and have liver and kidney function within normal limits, complete blood glucose examination data (HbA1c, FPG, PPG), and data on the duration of treatment of TB. Exclusion criteria are patients with extrapulmonary TB, Drug-resistant tuberculosis (RO TB), Multidrug-resistant Tuberculosis (TB-MDR), Extensively drug-resistant Tuberculosis (TB-XDR), dropping out of treatment, ATD allergies, having other severe diseases such as HIV and AIDS, malignancy, hepatitis B and C, and renal failure.

The number of subjects obtained will be categorized into two parts, namely glycemic control and the duration of treatment of pulmonary TB. Glycemic control is divided into optimal and non-optimal while the duration of treatment of pulmonary TB is divided into exactly six months and more than six months. Optimal glycemic control is determined when the result of FPG, PPG, and HbA1c are in normal range while a non optimal glycemic control is determined when the result of the three main examination are above normal range for DMT2 patients.

Statistical analysis

Univariate data are analyzed descriptively and presented in the form of sums and percentages according to the type of data. Bivariate data were analyzed by the chi square method. Statistical Package for the Social Sciences (SPSS) version 16 was used for all analyses. The result of statistical test for bivariate analysis in this study showed a p-value: 0.001 (p-value: <0.05), this indicates a significant relationship between glycemic control and the duration of treatment of TB.

Results

The process of recruitment and sampling of subjects from the 2019-2021 medical records is depicted in Figure 1. Subject demographic data shown in Table 1. Data in Table 2. showed that 39 subjects (47.6%) of TB patients were examined using the TCM Xpert MTb/Rif method, this showed that there were subjects suspected of being resistant to ATD. Data on the duration of TB treatment in patients with comorbid T2DM was mostly carried out for 9 months, namely in 57 subjects (69.5%), 11 subjects (13.4%) underwent treatment for 12 months, and standard treatment for 6 months was carried out on 14 subjects (17.1%).

Data in Table 3. showed 65 subjects (79.3%) with a HbA1c value of >7%, 59 subjects (72%) with a FPG value of >130 mg/dL, and 66 subjects (80.5%) with a 2-hour after meal Blood glucose concentration value of >180 mg/dL. The results of the three examinations illustrate that the patient's glycemic control has not been optimal in most samples. A total of 33 subjects (40.2%) were given a combination treatment of Oral Anti Diabetics (OAD) and insulin injection.

Based on the data in Table 4. there were 17 subjects with optimal glycemic control, 8

Table 1 Demographic Characteristics of Research Subjects

Characteristics	Number (n)	Percentage (%)
Age (year)		
36–45	10	12.2
46–55	27	32.9
56–65	33	40.2
>65	12	14.6
Total	82	100.0
Gender		
Male	53	64.6
Female	29	35.4
Total	82	100.0
Employment		
House wife*	25	30.5
Private employee	16	19.5
Self employed	13	15.9
Retirees	12	14.6
Army	1	1.2
Fisherman	1	1.2
Delivery-service driver	1	1.2
Journalist	1	1.2
Others	10	12.2
Total	82	100.0

*In Indonesia, housewife is considered as "having a job"

subjects (47.1%) underwent pulmonary TB treatment for 6 months, while in 9 subjects (52.9%) underwent treatment for more than 6 months. Non-optimal glycemic control occurred in 65 subjects, the duration of pulmonary TB treatment extended to more than six months in 59 subjects (90.8%) and was carried out exactly 6 months in only 6 (9.2%) people alone.

The results of the bivariate analysis were carried out to determine the relationship between the duration of pulmonary TB treatment and glycemic control in T2DM patients. The results of statistical tests in this study showed a p-value: 0.001 (p-value: <0.05), this indicates a significant relationship between glycemic control and the duration of treatment of TB. The Odds Ratio (OR) value was obtained at 8,741 with a confidence interval (CI 95% 2.45-31.11) so it can be concluded that non-optimal glycemic control increased the duration of pulmonary TB treatment by 8,741 times compared to T2DM patients with optimal glycemic control. The confidence interval in this test is not equal to one so the relationship between glycemic control and the duration of treatment of pulmonary TB is proven at a significance level of 5%.

Discussion

Through this research, glycemic control has not been attained in the majority of PTB-DM patients with FPG values >130 mg/dL occurring in 59 individuals (72%), postprandial glucose levels >180 mg/dL occurring in 66 subjects (80.5%), and HbA1 values >7% occurring in 65 subjects (79.3%). The most common method of treating T2DM in patients with pulmonary PTB was a combination of antidiabetic oral medicines (AOD) and insulin injection, which was used in 33 individuals (40.2%),

Table 2 Characteristics of TB Patients

Characteristics	Number (n)	Percentage (%)
Types of bacteriological examination		
TCM Xpert MTb/Rif	39	47.6
Acid-fast bacillary	37	45.1
Both were checked	6	7.3
Total	82	100.0
Duration of treatment of TB		
6 months	14	17,1
9 months	57	69,5
12 months	11	13,4
Total	82	100,0

Abbreviations: TCM Xpert MTB/Rif: Test Cepat Molekular (Quick Molecular Test) Xpert Mycobacterium Tuberculosis/ Rifampicin

31 subjects (37.8%), and 18 subjects (22%). Fast-acting insulin and biguanid group was the most commonly used combination of AOD and insulin in 10 people (12.2%), metformin was the most commonly used AOD and insulin in 15 people (18.3%), and fast-acting and long-acting insulin was the most commonly used combination of AOD and insulin in 10 people (12.2%).

Complications of tuberculosis treatment in the T2DM population include lengthening the course of therapy, recurrence, failed therapy, more difficult glycemic control, and a higher risk of death.[8] In order to maintain glycemic control and avoid problems, such as the development of active pulmonary tuberculosis, T2DM patients can benefit from a blood glucose assessment that

Table 3 Characteristics of T2DM Patients

Characteristics	Number (n)	Percentage (%)
HbA1c		
<7%	17	20.7
>7%	65	79.3
Total	82	100.0
FPG		
80–130 mg/dL	23	28.0
>130 mg/dL	59	72.0
Total	82	100.0
2-Hour Post Prandial Blood Glucose Examination		
<180 mg/dL	16	19.5
>180 mg/dL	66	80.5
Total	82	100.0
Therapy of T2DM received		
AOD	31	37.8
Insulin	18	22.0
Combination insulin and AOD	33	40.2
Total	82	100.0

Abbreviation: AOD: Antidiabetic Oral Drugs

Table 4 Relationship of Glycemic Control with Length of Treatment of PTB

Glycemic control	Duration of treatment				p	Odds Ratio (95% CI)
	Subject	6 months	Subject	>6 months		
Optimal	8	47,1%	9	52,9%	0,001	8,741 (2,455-31,118)
Not Optimal	6	9,2%	59	90,8%		

includes FPG, PPG, and HbA1c.[4] FPG values between 80 to 130 mg/dL should be achieved for optimal glycemic control; failure to do so increases the risk of tuberculosis and lengthens the course of treatment.[4] According to Yoo, JE et al.'s research, there was an increase in TB cases in patients who had an increase in FPG, particularly at a value of 220 mg/dL.[9] The research of Siddiqui et al. said that the T2DM population with FPG values of 110 mg/dL had more pulmonary TB and was shown to decrease the conversion rate of sputum containing Fast-acid Tuberculosis Bacilli (FTB), so the prognosis of pulmonary PTB treatment was much worse compared to patients with normal FPG values.[10]

Two-hour after meal blood glucose concentration is useful for assessing the function and quality of the hormone insulin which functions to maintain glucose homeostasis in the blood after eating.[4] PPG values affect glycemic control in avoiding microvascular and macrovascular complications as well as the risk of infection including PTB.[4,11] The risk of PTB and worsening of the patient's prognosis occurs not only at uncontrolled FPG levels, but also at PPG levels.4 This is supported by research conducted by Khalil NH, et al., which shows that the dominant TB-DM population has a non-optimal PPG value with an average value of 391.01 mg/dL when compared to the DM population that does not have PTB. The findings of this study indicate that glycemic control is not optimal to be a risk factor for PTB.[12]

The results of a study in Hong Kong found that T2DM patients with HbA1c levels more than 7% were more likely to develop PTB.[12] Khalil NH, et al. investigation also revealed that the average HbA1c value in PTB-DM patients was 9.88%.[12] Chronic hyperglycemia in T2DM patients alters the immune system by impairing chemotaxis and phagocytic abilities of TH1 lymphocytes, macrophages, and inflammatory mediators such as TNF-, IL-1, and IL-6. Hyperglycemia over time causes thickening of the layers of the alveolar

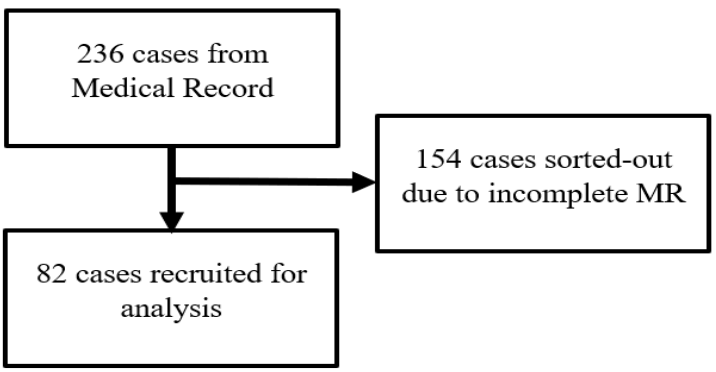

Figure 1 Recruitment process and sampling of subjects from medical records in 2019–2021

epithelium as well as the basal lamina of the pulmonary capillaries.[13]

The combination of rapid-acting insulin injection and metformin was the commonly utilized for PTB-DM patients in this study compared to other drug combinations. Initiation of insulin therapy is administered immediately when glycemic control of T2DM patients with PTB is not optimal. Insulin can be given in the form of a basal regimen, long-acting insulin, or a combination insulin (premixed insulin) that combines basal and prandial insulin. Insulin with rapid action is more commonly utilized, particularly in ketosis patients with uncontrolled hyperglycemia.[14] The use of metformin with insulin injection is carried out mainly when FPG levels are controlled but the values of HbA1c and PPG have not been reached, other oral drugs such as repaglinide and acarbose can also be used but the decrease in HbA1c with such treatment only reaches about 0.5-1%, therefore, metformin is more widely used alongside insulin injection.[15]

Putra ON, et al. stated that the risk of failure in treatment of PTB-DM patients was nine times greater than that of pulmonary PTB patients who did not have DM because it was proven that ATD rifampicin (RIF) concentration were 53% lower in PTB-DM patients.[16] The interaction between sulfonylureas as well as thiazolidinedione (TZD) with RIF affects the outcome and duration of treatment PTB. A decrease in sulfonylurea concentration by 22-30% and about 54-64% of TZD in the blood plasma due to an increase in the metabolism of both drugs by rifampicin.[17] Insulin becomes the main option to lower blood glucose levels without affecting the effectiveness of ATD.[15] Research in Pontianak showed that the dominant drug interactions that occurred in PTB-DM patients were glimepiride and RIF with a total of 20 cases (52.63%). Drug interactions occur due to induction in CYP-450 isoenzymes that increase CYP2C9 enzyme which decreases the concentration of AOD.[18]

Treatment of PTB with ATD consists of two stages, namely the initial (intensive) stage for two months and the advanced stage for four months. The duration of PTB treatment depends on the patient's clinical state, type of PTB, and comorbid diseases.[5] T2DM is a comorbid disease that can affect the duration of treatment of PTB to at least nine months, this occurs when glycemic control is not optimal, while PTB-DM patients with optimal glycemic control can undergo TB treatment for six months.[8] The ATD regimen given to T2DM patients is the same as patients who do not have T2DM even though the duration of treatment for PTB becomes longer, up to 9-12 months. Large number of TB bacteria, drug interactions between ATD and AOD, and side effects due to ATD are the reasons for the lengthening of the PTB treatment.[17] Decreased AOD levels due to ATD consumption decreases the effectiveness of AOD so that the duration of ATD administration extends.[16]

Glycemic control assessed through HbA1c examination is important to determine the duration of treatment for PTB in the hope that the duration of therapy will be the same as that of TB patients without DM. HbA1c examination is more individualized by assessing the patient's age and life expectancy, length of time suffering from DM, history of hypoglycemia, comorbidities and cardiovascular complications, as well as other factors such as purchasing power ability and drug availability. Elderly patient who has a condition that does not allow to maintain the HbA1c value of <7% then the therapy target is changed to 7.5-8.5%.[15] The duration of treatment for PTB in T2DM patients is determined by observing the patient's glycemic control, namely HbA1c <7% but if the patient has a therapeutic target with

an HbA1c value of >7% then the duration of treatment must be considered through clinical conditions, bacteriological examination, and X-ray photo.[15,19]

According to Wang JY, et al. PTB treatment in T2DM patients is better given for nine months because the data shows TB-DM patients experience more recurrence after two years of completion of TB treatment for six months. Nine-month ATD treatment prevented and lowered the previous 3.54% pulmonary TB recurrence rate to 1.19%. The decrease in the patient's clinical symptoms and the slow response to treatment are also considerations for extending the duration of treatment to 9 months. Macrovascular and microvascular complications, are also signs of the ineffectiveness of treatment and it shows glycemic control has not been achieved that PTB treatment will be extended. The slow response of treatment can be assessed by the non-occurrence of FTB sputum conversion at the end of the intensive phase of treatment due to chronic hyperglycemia that occurs.[19]

In this study, 6 subjects (10.3%) with non-optimal glycemic control did not experience prolonged lengthening of pulmonary TB treatment, these results were contrary to the theory mentioned previously. The duration of treatment for pulmonary TB is not only determined through the glycemic control of T2DM patients, clinical improvement and thoracic photo and the occurrence of FTB sputum conversion in the first two months of treatment shows a better TB prognosis, hence, treatment for 6 months can be done.

There were 9 subjects (52.9%) with optimal glycemic control undergoing treatment for more than six months, consisting of 8 people with treatment for 9 months and 1 person with treatment for 12 months, consecutively. The duration of treatment for pulmonary TB was appropriate for 6 months in 8 people (47.1%), and this did not match the theory that T2DM patients with optimal glycemic control could undergo TB treatment for 6 months like patients who did not have T2DM. The duration of treatment for pulmonary TB can extend in controlled T2DM patients if other parameters used to determine the duration of TB treatment show unexpected results such as extensive and persistent lesions in the thoracic photo image, especially when tuberculosis has occurred and late conversion of FTB sputum.

The strength of this study is that it can identify the number of diabetes mellitus patients with optimal and non-optimal glycemic management, which is valuable for those interested in the incidence of pulmonary tuberculosis. This study also demonstrates the importance of glycemic control in T2DM patients with pulmonary tuberculosis treatment duration for maintaining the patient's quality of life. This study additionally aims to assess the correlation between T2DM patients' glycemic control and the length of treatment for pulmonary tuberculosis by excluding T2DM patients who have not been diagnosed with pulmonary tuberculosis or have extrapulmonary tuberculosis, RO TB, TB-MDR, and TB-XDR, patients who develop Drug Induced Liver Injury (DILI), drop out of treatment, ATD allergies, and patients who have a history of other significant illnesses can lengthen the period of treatment for pulmonary tuberculosis. The limitations of this study are in the form of low data on routine blood glucose examinations in PTB patients with a history of T2DM, especially HbA1c examinations which are not carried out periodically every three months so that the average HbA1c value of patients during suffering from PTB cannot be determined. Glycemic control is determined on the patient's last blood glucose examination. Recommendation for further research include develop research indicators, characteristics, and methods, looking for other factors that enhance the time of treatment for pulmonary

tuberculosis in T2DM patients, looking for direct and indirect correlations between glycemic control and length of pulmonary tuberculosis treatment.

Conclusion

There is a relationship between glycemic control in T2DM and the duration of treatment for PTB because most patients with a history of T2DM at Persahabatan General Hospital undergo PTB treatment for more than six months (90,8%). Treatment of PTB over six months has been shown to be effective in preventing recurrence, but good glucose control must be done optimally to avoid dropping out of treatment due to the length of treatment.

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Conflict of Interest

All authors state that there is no potential conflict of interest with research, authorship, and or publication of this article.

References

1. Setiati S, Alwi I, Sudoyo A, Simadibrata M, Setiyohadi B, Syam A. Buku Ajar Ilmu Penyakit Dalam. VI. Setiati S, editor. Jakarta: Interna Publishing; 2014. 883–863 p.
2. Silva DR, Muñoz-Torrico M, Duarte R, Galvão T, Bonini EH, Arbex FF, et al. Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. Kementeri Kesehat Republik Indones [Internet]. 2018;53(9):80. Available from: https://www.researchgate.net/publication/334255803_Kendali_Glikemik_pada_Pasien_Diabetes_Melitus_Tipe_2_dengan_dan_tanpa_Tuberkulosis_Paru
3. Kementerian Kesehatan RI. Laporan Riskesdas 2018. Lap Nas Riskesdas 2018 [Internet]. 2018;53(9):154–65. Available from: http://www.yankes.kemkes.go.id/assets/downloads/PMK No. 57 Tahun 2013 tentang PTRM.pdf
4. Pranoto A, Studi P, Jenjang K, Fakultas D, Universitas K, Epidemiologi D, et al. Kendali Glikemik pada Pasien Diabetes Melitus Tipe 2 dengan dan tanpa Tuberkulosis Paru Glycemic Control in Type 2 Diabetes Mellitus Patients with and without Pulmonary Tuberculosis. J MKMI [Internet]. 2019;15(1):99–109. Available from: https://www.researchgate.net/publication/334255803_Kendali_Glikemik_pada_Pasien_Diabetes_Melitus_Tipe_2_dengan_dan_tanpa_Tuberkulosis_Paru
5. Kementrian Kesehatan Republik Indonesia. Pengobatan Pasien Tuberkulosis. Kementeri Kesehat Republik Indones [Internet]. 2017;1–117. Available from: http://www.ljj-kesehatan.kemkes.go.id/pluginfile.php/4607/coursecat/description/Pengobatan Pasien TB.pdf
6. Soelistijo SA, Novida H, Rudijanto A, Soewondo P, Suastika K, Manaf A et al. Pedoman pengelolaan dan pencegahan diabetes melitus tipe 2 di Indonesia. Perkeni. 2019. 133 p.
7. Tenny S, Hoffman MR. Odds Ratio.

[Updated 2023 May 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431098/
8. Kemenkes RI. Konsensus Pengelolaan Tuberkulosis dan Diabetes melitus (TB-DM) di Indonesia. 2015. p. 51.
9. Yoo JE, Kim D, Han K, Rhee SY, Shin DW, Lee H. Diabetes Status and Association with Risk of Tuberculosis among Korean Adults. JAMA Netw Open. 2021;4(9):1–11.
10. Siddiqui AN, Khayyam KU, Sharma M. Effect of Diabetes Mellitus on Tuberculosis Treatment Outcome and Adverse Reactions in Patients Receiving Directly Observed Treatment Strategy in India: A Prospective Study. Biomed Res Int. 2016;2016(Dm).
11. Punthakee Z, Goldenberg R, Katz P. Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. Can J Diabetes. 2018;42:S10–5.
12. Khalil NH, Ramadan RA. Study of risk factors for pulmonary tuberculosis among diabetes mellitus patients. Egypt J Chest Dis Tuberc [Internet]. 2016;65(4):817–23. Available from: http://dx.doi.org/10.1016/j.ejcdt.2016.05.009
13. Susilawati made dewi, Muljati S. Hubungan Antara Intoleransi Glukosa dan Diabetes Melitus dengan Riwayat Tuberkulosis Paru Dewasa di Indonesia (Analisis Lanjut Riskesdas 2013). Media Litbangkes. 2016;26(9):71–6.
14. Niazi AK, Kalra S. Diabetes and tuberculosis: A review of the role of optimal glycemic control. J Diabetes Metab Disord. 2012;11(1):1.
15. Soelistijo SA, Lindarto D, Decroli E, Permana H, Sucipto KW, Kusnadi Y et. al. Pedoman pengelolaan dan pencegahan diabetes melitus tipe 2 di Indonesia 2021. 2021;46.
16. 1Putra ON, Hardiyono H, Rizkiyah F, Yuniar N.H A. Impact of Uncontrolled HbA1C on The Outcome of Tuberculosis Treatment in TB Patients With Diabetes. J Profesi Med J Kedokt dan Kesehat. 2020;14(2):210–20.
17. Wijaya I. CONTINUING MEDICAL EDUCATION Tuberkulosis Paru pada Penderita Diabetes Melitus. Cdk-229. 2015;42(6):412–7.
18. Sari WDP, Nurmainah, Untari EK. INTERAKSI OBAT HIPOGLIKEMIA ORAL (OHO) DENGAN OBAT ANTITUBERKULOSIS (OAT) PADA PASIEN DIABETES MELITUS TIPE 2 YANG TERINFEKSI TB PARU. Tanjungpura Univ J. 2020;14–6.
19. Wang JY, Lee MC, Shu CC, Lee CH, Lee LN, Chao KM, et al. Optimal duration of anti-TB treatment in patients with diabetes: Nine or six months? Chest [Internet]. 2015;147(2):520–8. Available from: http://dx.doi.org/10.1378/chest.14-0918