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CRP/LYMPHOCYTE RATIO AND CRP/ALBUMIN RATIO FOR PROGNOSIS OF HYPERGLYCEMIA IN PATIENTS TUBERCULOSIS WITH DIABETES MELLITUS

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ABSTRACT

The issue is complicated by the rise in Diabetes Mellitus (DM) cases, a known risk factor for pulmonary TB, with 15% of pulmonary TB patients having a history of DM. DM and chronic hyperglycemia impair immune function, leading to long-term inflammation and worsening TB prognosis. Diagnostic methods include blood culture, AFB examination, chest X-ray, and genotyping, but more accessible tests are needed. Inflammatory markers, particularly lymphocytes, play a crucial role in TB prognosis with DM. Lymphopenia indicates chronic inflammation and a shift to memory lymphocytes. CRP, an inflammatory marker, indicates chronic inflammation, and hypoalbuminemia in DM due to kidney damage further complicates TB prognosis. The ratios of CRP to lymphocytes (CLR) and CRP to albumin (CAR) are gaining attention to better illustrate TB prognosis with DM. This cross-sectional study analyzed CLR and CAR as prognostic indicators in 30 pulmonary TB patients with DM in Jambi City from May to June 2024. CRP was tested at Prodia Jambi Laboratory, while Albumin, Lymphocytes, and blood glucose levels were tested at Labkesda of Jambi Province. The results show a Comparison with each parameter based on treatment status. Both parameters show slightly higher average values in intensive (< 2 months), with an average of 5.55 for CLR and 1.82 for CAR, and there is a significant difference in CLR between intensive and follow-up treatment statuses, and ROC curve shows that CLR parameters have indicated high sensitivity and low false positive rate with AUC 0,692. A significant relationship is found between CLR and blood glucose levels with a p-value of 0.024 and an r-value of 0.411, indicating a moderately strong relationship where an increase in CRP-Lymphocyte ratio corresponds to an increase in blood glucose levels than each parameter.

Kata Kunci:

TB DM;
CLR;
CAR
Inflamasi

ABSTRAK

Kompleksitas meningkat dengan adanya Diabetes Mellitus (DM) sebagai faktor risiko TB Paru, dimana 15% pasien TB juga memiliki riwayat DM. Hiperglikemia kronis pada DM mempengaruhi fungsi sistem imun dan inflamasi, memperburuk prognosis TB Paru. Untuk diagnosis dan prognosis TB Paru, pemeriksaan seperti kultur darah, BTA, foto rontgen, dan genotyping digunakan. Namun, pemeriksaan ini memerlukan waktu dan fasilitas khusus sehingga diperlukan metode yang lebih praktis dan dapat diakses di semua pusat pelayanan kesehatan. Marker inflamasi pada TB Paru dengan DM menjadi fokus utama, terutama limfosit yang berperan dalam inflamasi kronis dan CRP sebagai penanda inflamasi. Limfopenia pada pasien TB DM menunjukkan inflamasi jangka panjang, dengan perubahan subset limfosit menjadi limfosit memori. CRP sebagai marker inflamasi juga digunakan untuk prognosis TB DM, di mana peningkatan kadar CRP menunjukkan inflamasi kronis. Parameter lain yang relevan adalah albumin, yang menekan respon inflamasi kronis tetapi seringkali rendah pada pasien DM dengan hiperglikemia kronis dan pengobatan TB Paru. Potensi rasio CRP terhadap limfosit (CLR) dan CRP terhadap albumin (CAR) menarik perhatian sebagai indikator prognosis TB DM dengan hiperglikemia jangka panjang. Penelitian cross-sectional dilakukan pada 30 responden TB DM di beberapa Puskesmas di Kota Jambi pada Mei-Juni 2024. Pemeriksaan CRP dilakukan di Laboratorium Prodia Jambi, sedangkan pemeriksaan albumin, limfosit, dan kadar gula darah dilakukan di Labkesda Provinsi Jambi. Hasil penelitian menunjukkan rata-rata nilai CLR adalah 4,91 dan rata-rata CAR adalah 1,95, dengan kadar gula darah rata-rata 251,10 mg/dl. Pada pengobatan intensif (<2 bulan), CLR dan CAR sedikit lebih tinggi, dengan perbedaan signifikan pada status pengobatan intensif dan lanjutan untuk CAR. Uji korelasi spearman menunjukkan hubungan signifikan antara CLR dan kadar gula darah (p-value 0,024, r 0,411), namun tidak signifikan untuk CAR (p-value 0,098). Ini menyimpulkan bahwa rasio CRP Limfosit dapat menjadi biomarker potensial dalam prognostik inflamasi, terutama yang disebabkan oleh kontrol glikemik yang buruk.

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INTRODUCTION

The increasing number of pulmonary infectious disease cases worldwide, particularly in developing countries, is becoming more alarming and remains a significant unresolved public health issue. Pulmonary infectious diseases, including pulmonary tuberculosis (TB), affect approximately 10 million people globally (WHO, 2021). The situation becomes more complex with the rising cases of Type 2 Diabetes Mellitus (T2DM) among patients with pulmonary TB (Batubara & Lukito, 2024). DM patients experience hyperglycemia, which creates a favorable environment for the proliferation of *Mycobacterium tuberculosis* (M.Tb) (Arliny, 2015). Additionally, DM leads to a weakened immune response, compromising the body's ability to fight bacterial infections (Harries et al., 2016).

The burden of co-infections involving TB and DM has been extensively reported, with the dual condition contributing to increased morbidity and mortality rates, particularly in low- and middle-income countries (Boadu et al., 2024). Despite global efforts, there remains a lack of accessible, timely, and reliable diagnostic tools for effectively managing this dual burden, particularly in resource-limited settings (Fernández et al., 2020).

The diagnosis of pulmonary TB is typically established through blood culture tests, acid-fast bacillus (AFB) smears, chest X-rays, and, more recently, genotyping examinations. However, these diagnostic methods are not yet available in all healthcare institutions and often require significant time, necessitating more efficient and effective diagnostic tools (Cheng et al., 2022).

The role of inflammatory markers in the pathophysiology of DM and TB has garnered significant attention, particularly in their prognosis. Leukocyte subtypes such as monocytes, neutrophils, and lymphocytes play a role in chronic inflammation, which is regulated by inflammatory cytokines during the course of TB and DM. Previous studies have shown a drastic reduction in lymphocyte counts, or lymphocytopenia, representing a high inflammatory state in both TB and DM patients (Nam et al., 2018). Other research investigating the absolute lymphocyte counts in DM patients with TB also found a decrease in total lymphocytes, CD4 T lymphocytes, and CD8 T lymphocytes, correlating with elevated blood glucose levels. However, the reduction in absolute B lymphocyte counts was not significant, suggesting that elevated blood glucose levels in TB-DM patients lead to the differentiation of memory B cell subsets. Moreover, the apoptosis of B lymphocytes is inhibited by high blood glucose levels (Wei et al., 2022).

C-reactive protein (CRP) is commonly used as a marker for systemic inflammatory responses. Previous studies have shown that CRP can predict the prognosis of DM and evaluate treatment progress in pulmonary TB patients. Elevated CRP levels reflect ongoing inflammation in the patient's body and are associated with chronic diseases (Harries et al., 2016). Meanwhile, albumin is often used as a predictor of disease progression in DM and pulmonary TB, as persistent hyperglycemia causes damage to the Bowman's capsule, leading to increased urinary albumin excretion and, consequently, high albumin levels in urine but low levels in the bloodstream (Rawat & Shrivastava, 2022).

Recently, the ratios of CRP to lymphocytes (CLR) and CRP to albumin (CRA) have gained attention for their prognostic value in various inflammatory diseases, including diabetes and pulmonary tuberculosis. A previous study by Qiyu et al. demonstrated that the CLR biomarker could serve as a predictive marker for diabetes mellitus in pulmonary TB patients (AUC: 0.621, $p<0.001$). Earlier research has proven that CLR and CRA can reflect the prognosis of various diseases. However, there are still few studies examining how these inflammatory biomarker ratios affect the prognosis of hyperglycemia in pulmonary tuberculosis patients (Yu et al., 2022).

Although significant progress has been made in understanding the inflammatory response in TB and DM, gaps remain in elucidating the specific prognostic value of inflammatory biomarkers, particularly CLR and CRA, in patients with concurrent TB and T2DM. Existing studies are limited in scope, with insufficient exploration of the relationship between hyperglycemia, immune dysregulation,

and inflammatory marker ratios. Additionally, data on the effectiveness of these biomarkers in predicting treatment outcomes remain scarce.

This study aims to investigate the prognostic value of CLR and CRA as biomarkers in patients with pulmonary tuberculosis and Type 2 Diabetes Mellitus. By providing a deeper understanding of these inflammatory markers, this research seeks to enhance diagnostic and prognostic approaches for managing the dual burden of TB and DM.

METHOD

Type of Research

This study is cross-sectional research aimed at analyzing the potential of the CRP lymphocyte and CRP albumin inflammatory biomarker ratios in the prognosis of TB disease accompanied by Diabetes mellitus.

Place and Time of Research

The study took place in Poltekkes Kemenkes Jambi (Health Polytechnic-Ministry of Health Jambi between February and July 2024.

Population and Sample

The population in this study consists of all TB patients with diabetes mellitus in several health centers in Jambi City, including Pakuan Baru Health Center, Simpang Kawat Health Center, and Paal 10 Health Center. The sample size was determined using Slovin's formula to ensure adequate statistical power and representativeness, resulting in a minimum required sample size of 30 participants. Participants were selected using a purposive sampling method, focusing on TB patients with diabetes mellitus who met the inclusion and exclusion criteria. The inclusion criteria included patients aged 18 years or older who were diagnosed with pulmonary tuberculosis and diabetes mellitus, who were in the phase of TB treatment with anti-tuberculosis drugs (OAT) of less than 2 months or more than 2 months and who were willing to participate in the study by providing informed consent. The exclusion criteria were patients suffering from other systemic diseases, such as cardiovascular or autoimmune conditions, and those undergoing routine corticosteroid therapy, as these factors could influence inflammatory markers. Patients with systemic diseases were identified through detailed medical histories, clinical examinations, and laboratory evaluations, ensuring the accurate exclusion of confounding conditions. This sampling approach was designed to focus on the target population, minimize bias, and enhance the validity of the study findings.

Data Collection

The collection of specimens or samples in this study was conducted using blood samples obtained from the research subjects through the vacutainer method. Two tubes were used: one purple-capped tube containing EDTA (for lymphocyte examination) and one yellow-capped tube with a gel separator (for albumin and CRP testing). The blood in the gel-containing tube was centrifuged at 3,000 rpm for 10 min to obtain serum for testing. CRP was then tested using High Sensitivity CRP (HsCRP) and the turbidimetry method at Prodia Laboratory. Albumin was measured using photometry, lymphocytes (differential blood cell count) were analyzed using an automatic analyzer, and blood glucose levels were measured with a photometer at the Jambi Regional Health Laboratory.

The Prodia Laboratory was chosen for CRP testing because it is the only lab in Jambi City currently offering hsCRP testing, as other laboratories are out of reagents. In regard to potential conflicts of interest, none of the authors are affiliated with Prodia Laboratory. If any potential conflicts exist, they will be disclosed in the conflict of interest section of the study.

Additionally, data collection was also carried out through questionnaires and direct interviews to obtain necessary information for the study, such as the duration of TB illness, duration of treatment, regular use of blood glucose medications, duration of diabetes, and other relevant details.

Data Analysis and Processing

SPSS software was used for statistical data analysis. Pearson or Spearman correlation analysis was conducted to explore the relationship between the potential inflammatory parameters and

hyperglycemia in subjects with lung infections. Additionally, an analysis and comparison of each parameter and ratio, both CLR and CAR, was performed based on the duration of treatment. The Receiver Operating Characteristic (ROC) curve was used to evaluate the value of the CRP to Lymphocyte Ratio and CRP to Albumin Ratio for predicting hyperglycemia prognosis in lung infection patients based on blood glucose levels.

RESULT

The results of the study are based on 30 respondents with pulmonary TB and diabetes mellitus, and the characteristics of the respondents can be seen in the table below:

Table 1. Frequency Distribution of Respondent

Respondent Characteristic	N (30)	Percentage (%)
Sex		
Male	17	**57**
Female	13	**43**
Age		
18-65 year	27	**90**
> 65 year	3	**30**
Duration of treatment		
≤ 2 month	12	**40**
> 2 month	18	**60**

Table 1 shows that the majority of TB patients with diabetes mellitus are male, with 17 individuals (57%). Most of the patients are of working age, between 18 and 65 years old, totalling 27 people (90%). The duration of treatment for more than 2 months has been observed in 18 respondents.

Table 2. Overview of C-Reactive Protein (CRP) Levels, Lymphocyte Count, and CRP to Lymphocyte Ratio in Pulmonary TB Patients with a History of Type 2 Diabetes Mellitus

	N	Mean	Min	Max	SD.
CRP (mg/L)	30	5.98	3.90	7.90	1.26
Limfosit (%)	30	25,76	10,2	40,1	7,47
Albumin (g/dl)	30	3.3	1.5	4.9	0.96
Blood Glucose (mg/L)	30	251,10	130	387	71,69
CLR	30	4,91	1,94	21,0	3,55
CAR	30	1.95	0.83	0.86	0.74

Based on Table 2, it can be seen that the average CRP level increased to 5.98 mg/L, while the average lymphocyte count and albumin levels were 25.76% and 3.33 g/dL, respectively. Blood glucose levels have also been measured in this study, with an average increase of 251.10 mg/dL. The CRP to Lymphocyte Ratio (CLR) is 4.91, and the CRP to Albumin Ratio is 1.95.

Table 3. Comparison of Each Parameter (CRP, Albumin, Lymphocytes, CLR, and CAR) Based on Treatment Duration.

	Variable	N	Mean	Min	Max	SD	*P-Value*
Level of CRP (mg/L)	≥2 month	18	5.56	3.9	7.9	1.2853	0.036
	<2 month	12	6.62	4.0	7.8	0.9752	
Level of Albumin (g/dl)	≥2 month	18	3.48	1.8	4.9	1.1184	0.628
	<2 month	12	3.29	1.5	4.9	0. 9498	
Lymphocyte (%)	≥2 month	18	24,90	18,0	39,0	6.28	0,453
	<2 month	12	27,04	10,2	40,1	40,1	
CLR	≥2 month	18	4.49	2.27	6.50	1.4796	0.262
	<2 month	12	5.55	1.94	21.00	5.5434	
CAR	≥ 2month	18	1.74	1.8	3.22	0.5056	0.050
	<2 month	12	1.82	0.84	2.90	0.6133	

From the table, it can be seen that for each parameter, CRP levels show a significant difference in TB patients with diabetes mellitus based on the duration of treatment. CRP tends to be higher during intensive treatment (less than 2 months). Regarding the CLR and CAR ratios, a significant difference is observed in the CAR ratio, with higher CAR values during treatment of less than 2 months compared to treatment lasting 2 months or more.

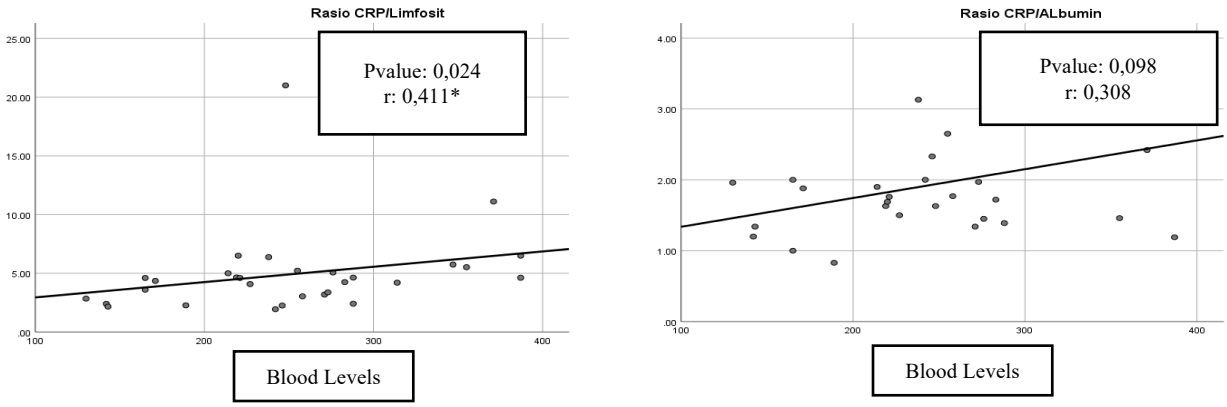

Figure 1. Relationship Between CLR, CAR, and Hyperglycemia Monitored Through Blood Glucose Levels in TB Patients with Diabetes Mellitus

Figure 1 shows that among the two parameters, CLR has a significant correlation with blood glucose levels ($p < 0.05$). This correlation is positive, indicating that an increase in CLR is associated with an increase in blood glucose levels, with a correlation coefficient of $r = 0.411$. No significant relationship is found between CAR and blood glucose levels in this study ($p > 0.05$).

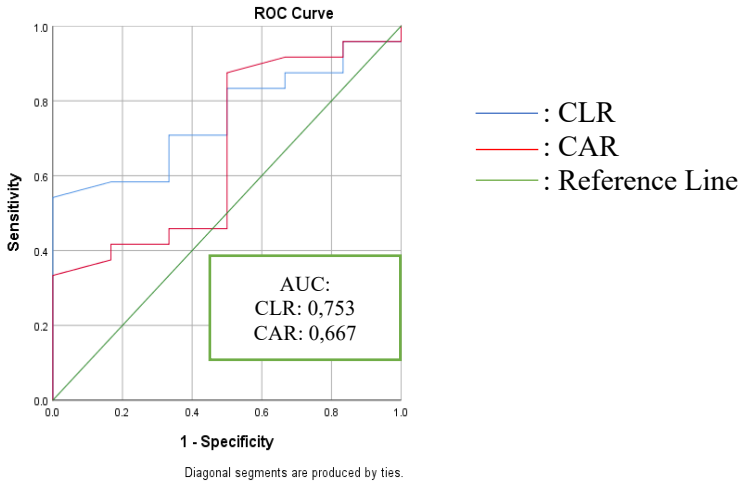

Figure 2. ROC Curve of CLR and CAR in Prognostic Identification of Hyperglycemia in TB Patients with Diabetes Mellitus

The diagnostic capability for hyperglycemia of the laboratory parameters has been assessed using the ROC curve to evaluate the potential of these parameters for identifying hyperglycemia in TB patients with diabetes mellitus. It is observed that the CLR parameter effectively indicates hyperglycemia in TB patients with T2DM. The AUC value of 0.753 suggests that CLR has a fairly good ability to distinguish between hyperglycemia and non-hyperglycemia. In contrast, the ROC curve for CAR shows that some of the lines remain along the diagonal, indicating that the diagnostic capability of CAR for hyperglycemia is not significant, with an AUC value of 0.667.

DISCUSSION

The aim of this study is to evaluate the diagnostic capability of various inflammatory parameters for identifying hyperglycemia in TB patients with diabetes mellitus, specifically focusing on comparing these parameters based on the duration of treatment. From the comparison of several inflammatory parameters based on the duration of treatment, it is statistically evident that CRP levels show a significant difference between the two treatment duration groups, with an average CRP level being lower in the group with treatment lasting more than 2 months. This finding is consistent with (Gao et al., 2020), which found a correlation between CRP levels and treatment duration in patients with TB complications and diabetes mellitus. A decrease in CRP levels indicates that CRP, as an inflammatory marker, decreases with prolonged treatment and is interpreted as a positive response to treatment (Jones et al., 2021).

For the ratio parameters, only the CRP to Albumin Ratio (CAR) shows a significant difference between treatment duration and the reduction in the CRP-Albumin ratio. Overall, the duration of treatment affects several inflammatory parameters, particularly CRP and CAR, but not albumin, lymphocyte percentage, or CLR. The study also demonstrates a significant relationship between blood glucose levels, as an indicator of hyperglycemia, and CLR, with a p-value of 0.024. This suggests that CLR has good sensitivity in detecting inflammatory changes associated with hyperglycemia in diabetes mellitus patients. This ratio is more responsive compared to CAR, which did not show a significant relationship with blood glucose levels (p-value 0.098).

The relationship between CLR and CAR with hyperglycemia in TB patients with a history of diabetes mellitus shows a positive trend; however, only the CLR graph correlates with hyperglycemia, indicated by increased blood glucose levels, whereas CAR does not. Previous research by (Cho et al., 2021) reported different results, where CAR was found to be a predictor of diabetes and positively correlated with TB incidence in diabetes mellitus. These results reflect that high blood glucose or hyperglycemia significantly influences inflammation in the body, as seen in diabetes mellitus patients

(Hasir et al., 2024; Xu et al., 2021). This condition may also indicate subclinical inflammation contributing to the development or exacerbation of TB in diabetes mellitus patients (Yu et al., 2022).

The study results, with an AUC value of 0.753, show that the CLR parameter has a 75.3% accuracy in predicting hyperglycemia in TB patients also experiencing diabetes mellitus (DM). Clinically, these results suggest that the CRP to Lymphocyte Ratio (CLR) has considerable potential as a prognostic tool for this disease. Compared to each parameter, such as CRP and lymphocytes, only CRP indicates inflammation (Wang et al., 2024), but the ratio of CRP to lymphocytes is more effective in illustrating the prognosis of the patient. Clinically, incorporating CLR into routine examinations could aid in the early identification and prognosis of TB in DM patients allowing for early intervention and strict monitoring to prevent more severe complications (Koc & Gullu, 2022).

However, further validation and development are needed to improve the accuracy of the model and its application in clinical practice, as well as to consider other factors that may contribute to more accurate predictions. The limitations of this study include the need for further validation and development to improve the accuracy of the model and its application in clinical practice. Additionally, other factors that may contribute to more accurate predictions should be considered. On the other hand, the strength of the study lies in its contribution to understanding the diagnostic capabilities of inflammatory parameters for identifying hyperglycemia in TB patients with diabetes mellitus, as well as its potential to improve clinical decision-making if validated in future studies.

CONCLUSION AND SUGGESTION

The study concludes that the CRP to Lymphocyte Ratio parameter has potential accuracy as a prognostic tool for hyperglycemia in pulmonary TB patients with diabetes mellitus, as evidenced by the AUC value of 0.753. Hyperglycemia can trigger long-term inflammation, thereby increasing the risk of complications. Further research is needed to evaluate the practical application of this parameter in the field and to ensure its accuracy in predictions.

REFERENCES

Arliny, Y. (2015). Tuberkulosis dan Diabetes Melitus Implikasi Klinis Dua Epidemik. *Jurnal Kedokteran Syiah Kuala*, *15*(1), 36–43. https://jurnal.usk.ac.id/JKS/article/download/3249/3064

Batubara, F. A., & Lukito, A. (2024). Hubungan Diabetes Mellitus Tipe II dengan Risiko Peningkatan Kejadian Tuberkulosis Paru di Rumah Sakit Umum Haji Medan Tahun 2022. *Ibnu SIna: Jurnal Kedokteran Dan Kesehatan Faklutas Kedokteran Universitas Islam Sumatera Utara*, *23*(2), 178–185. https://jurnal.fk.uisu.ac.id/index.php/ibnusina/article/view/615

Boadu, A. A., Yeboah-Manu, M., Osei-Wusu, S., & Yeboah-Manu, D. (2024). Tuberculosis and diabetes mellitus: The complexity of the comorbid interactions. *International Journal of Infectious Diseases*, *146*, 107140. https://doi.org/10.1016/j.ijid.2024.107140

Cheng, P., Wang, L., & Gong, W. (2022). Cellular Immunity of Patients with Tuberculosis Combined with Diabetes. *Journal of Immunology Research*, *2022*, 1–12. https://doi.org/10.1155/2022/6837745

Cho, A.-R., Lee, S., Hong, K.-W., & Jung, D. (2021). C-reactive protein-to-albumin ratio and 8-year incidence of type 2 diabetes: the Korean genome and epidemiology study. *Acta Diabetologica*, *58*(11), 1525–1532. https://doi.org/10.1007/s00592-021-01755-1

Fernández, R. D. V., Díaz, A., Bongiovanni, B., Gallucci, G., Bértola, D., Gardeñez, W., Lioi, S., Bertolin, Y., Galliano, R., Bay, M. L., Bottasso, O., & D'Attilio, L. (2020). Evidence for a More Disrupted Immune-Endocrine Relation and Cortisol Immunologic Influences in the Context of Tuberculosis and Type 2 Diabetes Comorbidity. *Frontiers in Endocrinology*, *11*(March). https://doi.org/10.3389/fendo.2020.00126

Gao, C., Zhao, M., Zhang, Y., Zhao, S., Zong, L., & Kan, Z. (2020). Correlation of Serum C-reactive Protein, IL-6, Blood Lipid and Blood Glucose in Patients with Type 2 Diabetes Mellitus Complicated with Pulmonary Tuberculosis. *Revista Argentina de Clínica Psicológica*, *XXIX*, 1001–1011. https://doi.org/10.24205/03276716.2020.926

Harries, A. D., Ade, S., Burney, P., Hoa, N. B., Schluger, N. W., & Castro, J. L. (2016). Successfully treated but not fit for purpose: paying attention to chronic lung impairment after TB treatment. *The International Journal of Tuberculosis and Lung Disease*, *20*(8), 1010–1014.

https://doi.org/10.5588/ijtld.16.0277

Hasir, H., Ruksin, H., & Nurbaya, N. (2024). Simulasi Latihan Fisik Berbasis Self-care pada Penderita Diabetes Mellitus. *Jurnal Masyarakat Mandiri (JMM)*, *8*(1), 1087–1093. http://journal.ummat.ac.id/index.php/jmm/article/view/20461%0A

Jones, T. P. W., Dabbaj, S., Mandal, I., Cleverley, J., Cash, C., Lipman, M. C. I., & Lowe, D. M. (2021). The Blood Neutrophil Count After 1 Month of Treatment Predicts the Radiologic Severity of Lung Disease at Treatment End. *Chest*, *160*(6), 2030–2041. https://doi.org/10.1016/j.chest.2021.07.041

Koc, İ., & Gullu, Y. T. (2022). C-reactive protein Lymphocyte Ratio in the Diagnosis of Pulmonary Tuberculosis. *Turkish Journal of Internal Medicine*, *4*(3), 121–128. https://doi.org/10.46310/tjim.1072714

Nam, H. W., Cho, Y. J., Lim, J. A., Kim, S. J., Kim, H., Sim, S. Y., & Lim, D. G. (2018). Functional status of immune cells in patients with long-lasting type 2 diabetes mellitus. *Clinical and Experimental Immunology*, *194*(1), 125–136. https://doi.org/10.1111/cei.13187

Rawat, K., & Shrivastava, A. (2022). Neutrophils as emerging protagonists and targets in chronic inflammatory diseases. *Inflammation Research*, *71*(12), 1477–1488. https://doi.org/10.1007/s00011-022-01627-6

Wei, R., Li, P., Xue, Y., Liu, Y., Gong, W., & Zhao, W. (2022). Impact of Diabetes Mellitus on the Immunity of Tuberculosis Patients: A Retrospective, Cross-Sectional Study. *Risk Management and Healthcare Policy*, *Volume 15*(April), 611–627. https://doi.org/10.2147/RMHP.S354377

Xu, F., Qu, S., Wang, L., & Qin, Y. (2021). Mean platelet volume (MPV): new diagnostic indices for co-morbidity of tuberculosis and diabetes mellitus. *BMC Infectious Diseases*, *21*(1), 461. https://doi.org/10.1186/s12879-021-06152-1

Yu, Q., Weng, W., Luo, H., Yan, J., & Zhao, X. (2022). The Novel Predictive Biomarkers for Type 2 Diabetes Mellitus in Active Pulmonary Tuberculosis Patients. *Infection and Drug Resistance*, *Volume 15*(August), 4529–4539. https://doi.org/10.2147/IDR.S377465