



Analysis Of The Relationship Between HBA1C and Serum Galectin-3 Levels in Subjects With Type 2 Of Diabetes Mellitus

Zaifah Firayanti¹, Yuyun Widaningsih², Liong Boy Kurniawan², Himawan Sanusi³, Andi Alfian Zainuddin⁴, Tenri Esa²

¹Program Studi Ilmu Biomedik, Sekolah Pascasarjana, Universitas Hasanuddin Makassar

²Departemen Patologi Klinik, Universitas Hasanuddin Makassar

³Departemen Ilmu Penyakit Dalam, Fakultas Kedokteran, Universitas Hasanuddin Makassar

⁴Departemen Ilmu Kesehatan Masyarakat, Fakultas Kesehatan Masyarakat, Universitas Hasanuddin Makassar

Email corespondensi : 01zaifah@gmail.com

<p>Track Record Article</p> <p>Accepted: 30 March 2023 Revised: 28 April 2023 Published: 19 June 2023</p> <p>How to cite: Firayanti, Z., Widaningsih, Y., Kurniawan, L. B., Sanusi, H., Zainuddin, A. A., & Esa, T. (2023). Analysis Of The Relationship Between HBA1C and Serum Galectin-3 Levels in Subjects With Type 2 Of Diabetes Mellitus. Contagion : Scientific Periodical of Public Health and Coastal Health, 5(2), 493–502.</p>	<p style="text-align: center;">Abstract</p> <p><i>Type 2 diabetes mellitus is a disease characterized by increased blood glucose levels known as hyperglycemia. This disease can be diagnosed by examining HbA1c (glycated hemoglobin). Hemoglobin A1c is a minor component of hemoglobin related to glucose. Meanwhile, galectin-3 is a protein encoded in humans by the LGALS3 gene. This study aimed to clarify the relationship between HbA1c and serum galectin-3 levels in patients with type 2 diabetes. This study was conducted using an observational analysis technique with a cross-sectional study design. This research was conducted at the Clinical Pathology Laboratory, Hasanuddin University State University Hospital, and Laboratorium Universitas Hasanuddin Medical Research Center State College Hospital Universitas Hasanuddin Makassar. This research was conducted from January to March 2023. The population in this study were all patients with type 2 DM who visited the Hasanuddin University Hospital (RSPTN-UH) for treatment a total of 112 patients. Research sampling technique with non-probability purposive sampling. The sample of this study was 60 patients. Data analysis with the Independent T-test or Mann-Whitney test. The results of the study were that serum Galectin-3 levels in uncontrolled type 2 diabetes mellitus had a higher average value of 20.18 ± 6.15 ng/mL compared to controlled type 2 diabetes mellitus, namely 14.80 ± 6.41 ng/ mL although there was a statistically significant difference ($p=0.012$) but no significant correlation was found between HbA1c and serum Galectin-3 levels in type 2 diabetes mellitus subjects ($r=0.176$ $p=0.179$) with the distribution of data in the Scatterplot not forming a linear relationship pattern. It is recommended that type 2 Diabetes Mellitus patients carry out an HbA1c examination as an effective test to control glucose levels, reduce the risk of complications, and maintain a healthy lifestyle to avoid type 2 DM.</i></p> <p>Keyword: HbA1c, Serum Galectin-3, Type 2 Diabetes Mellitus</p>
--	---

INTRODUCTION

Diabetes mellitus is a chronic disease in the world of health (Zheng et al., 2018). According to the World Health Organization, diabetes is a disease characterized by elevated blood sugar levels, which in humans can lead to complications including heart, blood vessels, eyes, kidneys and nerves, with chronic consequences (WHO, 2016). Diabetes is ranked seventh in Indonesia which contributes to the chance of developing Diabetes Mellitus as many as 10.7 million people in Southeast Asia (Kemenkes RI, 2020). Based on Basic Health Research data

for 2018, the prevalence of Diabetes Mellitus sufferers in Indonesia is 2.0% (Kemenkes RI, 2018).

Type 2 diabetes mellitus can be indicated by impaired insulin secretion. This disease is attributable to increased insulin resistance. Type 2 DM is still considered a serious global health issue because this disease's prevalence increases yearly (Decroli, 2019). Hemoglobin A1c (HbA1c) is the small component of hemoglobin that binds glucose. HbA1c is called glycosylated or glycated hemoglobin. Hemoglobin is an oxygen-carrying pigment that gives red blood cells (HR) a red color and is the dominant protein in HR (Que et al., 2015).

Hemoglobin A1c is a glycated and sub-fractionated hemoglobin formed from glucose bonds to the HbA molecules (hemoglobin in adults), which will increase according to the average blood glucose levels. Normal erythrocyte lifespan ranges from 90-120 days. Thus, HbA1c reflects the average blood glucose levels over the last 2 to 3 months (Donnelly & Bilous, 2014). Screening and determination of glycemic control status (HbA1c) are used to predict the development of DM complications (Powers, 2005).

The results of HbA1c and blood glucose examinations are considered for treating patients with diabetes mellitus (Owora, 2018; Punthakee et al., 2018). People with DM must get serious treatment. Furthermore, they must undergo regular examinations and treatment to monitor their metabolic status. The levels of HbA1c are expected to be less than 7% as a guideline for therapy monitoring in DM (Wang et al., 2020). In addition, the HbA1c value can also be used to assess high tissue damage caused by high blood glucose levels. Therefore, it is necessary to routinely measure HbA1c to see the severity of type 2 diabetes mellitus (Driyah et al., 2020).

Galectin-3 (Gal 3) is a protein encoded by the human LGALS3 gene. Galectin-3 is a member of the beta galactoside binding family known as carbohydrate binding protein-35 (CBP-35) (Li et al., 2022). This protein is involved in cell activation, proliferation, migration, apoptosis, oxidative stress, and inflammation in various pathological conditions such as obesity, cardiovascular disease, and Diabetes (Ma et al., 2020). Galectin-3 is 26 kDa and consists of C-terminal carbohydrate and N-terminal domains (Johannes et al., 2018).

Increased Gal-3 levels have been observed in type 2 DM Lin et al., (2021) report that patients with type 2 DM experienced an increase in Gal-3 levels. Previous research had associated Gal-3 with atherogenesis and the development of heart failure. High plasma levels of Gal-3 are associated with renal dysfunction and increased risk of death in patients with chronic heart failure with stable acute decompensation (Lok et al., 2010).

Based on research conducted by Zulfian et al., (2022) It is known that there is an association between HbA1c levels and serum creatinine levels in patients with type 2 DM. 6.3 fold higher HbA1c is a risk factor for elevated serum creatinine in patients with type 2 diabetes. Galectin-3 is a biomarker associated with inflammation and fibrosis in heart disease, liver and kidney. It was revealed that overweight and obese individuals possess higher levels of galectin-3 (Vora et al., 2019).

METHODS

Types and Research Design

This research was carried out using observational analytic methods with a cross-sectional research design. This study aimed to determine the relationship between HbA1c and serum Galectin-3 levels in type 2 diabetes mellitus subjects.

Location and Time of Research

The research samples were collected at the Clinical Pathology Laboratory, Hasanuddin University Hospital. The research was then conducted at the Hasanuddin University Medical Research Center (HUM-RC) Laboratory, Hasanuddin University Hospital, Makassar. This research was conducted from January to March 2023.

Population and Sample

The population in this study were all patients with type 2 DM who visited the Hasanuddin University Hospital (RSPTN-UH) to treat 112 patients. The inclusion criteria utilized were type 2 DM patients aged ≥ 30 years willing to be research subjects. Meanwhile, the exclusion criteria consisted of pregnant and lactating women and patients who have cancer, liver disorder (HEPAR), and autoimmune disease.

Patients determined as research samples were those who met the inclusion criteria. They were taken until the required number was met. An appropriate formula to calculate the sample size is presented as follows:

$$n = \left\{ \frac{Z\alpha + Z\beta}{0,5 \ln \left[\frac{(1+r)}{(1-r)} \right]} \right\}^2 + 3$$

Information :

$Z\alpha$ = Standard derivative α (type1 error), type 1 error was set for 5 percent = 1.64

$Z\beta$ = Standard derivative β (type 2 error), with a power of 90 percent, type 2 error was set for 10 percent = 1.28

r = 0.40 (correlation coefficient)

n = sample size

$$n = \left\{ \frac{1,64+1,28}{0,4 \ln\left[\frac{1+0,33}{1-0,33}\right]} \right\}^2 + 3 = 51$$

The calculation result shows that the minimum number of samples was 51. Considering the dropout factor, the sample size was made into 60 samples divided into two groups consisting of controlled type 2 DM and uncontrolled type 2 DM.

Sampling Technique

The sampling method utilized in the current study was non-probability purposive sampling. It is a sampling technique that selecting samples among the population according to the conditions set by the researchers. Thus, the sample can represent the characteristics of the previously known population. This study was conducted after ethical approval from the Health Research Ethics Commission Faculty of Medicine, Hasanuddin University-Hasanuddin University Hospital with ethical number 85/UN4.6.4.5.31/PP36/2022.

Venous blood sampling, as much as 3 mL of venous blood was drawn. The plasma was obtained after the blood sample tube was frozen for 30 minutes at room temperature and centrifuged at 3000 rpm. The samples were then stored at 80°C and thawed at 25°C prior to analysis. Examination of galectin-3 serum levels was performed using the Human Galectin-3 (GAL-3) kit from Assay Genie (the Irish Factory), with the sandwich method of Enzyme-Linked Immunosorbent Assay (ELISA). It was carried out at the Hasanuddin University Medical Research Center (HUM-RC) laboratory. Meanwhile, the HbA1c examination used the Boronate Affinity Assay at the Clinical Pathology Laboratory of Hasanuddin University Hospital, Makassar.

Data Analysis

Data analysis was carried out by utilizing the SPSS software version 22. The bivariate analysis was employed to analyze the data. Meanwhile, the statistical test was performed using the Independent t-test or the Mann-Whitney test. The Pearson correlation test is used if the data is normally distributed. On the other hand, the Spearman Rank correlation test is applied if the data is not normally distributed.

RESULTS

Table 1. Characteristics of Research Subjects

Category	Type 2 Diabetes Mellitus		
	n	%	Mean
Gender	Male	28	46.7
	Female	32	53.3
Age	36 - 45 years	6	10.0
	46 - 55 years	13	21.7
	56 - 65 years	32	53.3
	> 65 years	9	15.0
HbA1c levels (%)	60	100	9.01
Galectin-3 levels (ng/mL)	60	100	19.20

Source: the primary data

Based on the table 1. This research was conducted from February to March 2023 at Hasanuddin University Hospital (RSPTN), Makassar. A total number of 60 people with type 2 Diabetes Mellitus consisting of 28 males and 32 females, were involved as the research subjects. They were aged between 37 years to 84 years, with average HbA1c levels of 9.01% and average galectin-3 levels of 19.20 ng/mL.

Table 2. Normality Test of HbA1c and Galectin-3 Levels

Type 2 DM	HbA1c level			Galectin-3 level		
	Statistic	N	p	Statistic	n	p
	0.119	60	0.033	0.099	60	0.200*

Source: Primary Data

Note: *p= the Kolmogorov-Smirnov test significance

Based on the table 2. The normality test for HbA1c levels with galectin-3 in type 2 Diabetes Mellitus was carried out to determine whether the data distribution was normal or not normal. The Kolmogorov-Smirnov test was employed with a significant ($\alpha = 0.05$) value. Based on the test, the p-value of serum galectin-3 levels was 0.200 ($p > 0.05$), indicating that the data were normally distributed. Meanwhile, the p-value for HbA1c levels was 0.033, indicating that the data was not normally distributed.

Table 3. Comparison of Galectin-3 Levels in Subjects with Type 2 Diabetes Mellitus

Type 2 Diabetes Mellitus	N	Galectin-3			
		Range	Median	Mean \pm SD	p-value
Control (HbA1c <7%)	11	0.18 - 23.23	15.25	14.80 \pm 6.41	0.012
Uncontrolled (HbA1c > 7%)	49	1.08 - 29.01	20.84	20.18 \pm 6.15	

Source: Primary Data

Note: *p= Independent t-test

Based on the table 3. Based on the normality test on the data of serum galectin-3 levels, it can be concluded that the data were normally distributed. An Independent t-test was

performed to compare serum galectin-3 levels in controlled and uncontrolled type 2 DM subjects with normally distributed data. According to the statistical test, the median galectin-3 levels in controlled type 2 DM subjects was 15.25 ng/mL, while the uncontrolled type 2 diabetes mellitus subjects were 20.84 ng/mL. Furthermore, the mean serum galectin-3 levels in controlled type 2 diabetes mellitus patients were 14.80 ng/mL, while the mean galectin-3 levels in uncontrolled type 2 diabetes mellitus patients were 20.18 ng/mL. This points out that serum galectin-3 levels in wild type 2 DM patients were higher than in controlled type 2 DM patients. The statistical test with the independent t-test obtained $p = 0.012$. Because the value of $p < \alpha$ ($\alpha = 0.05$), it can be concluded that there was a significant difference between serum galectin-3 levels in controlled and uncontrolled subjects with type 2 diabetes mellitus.

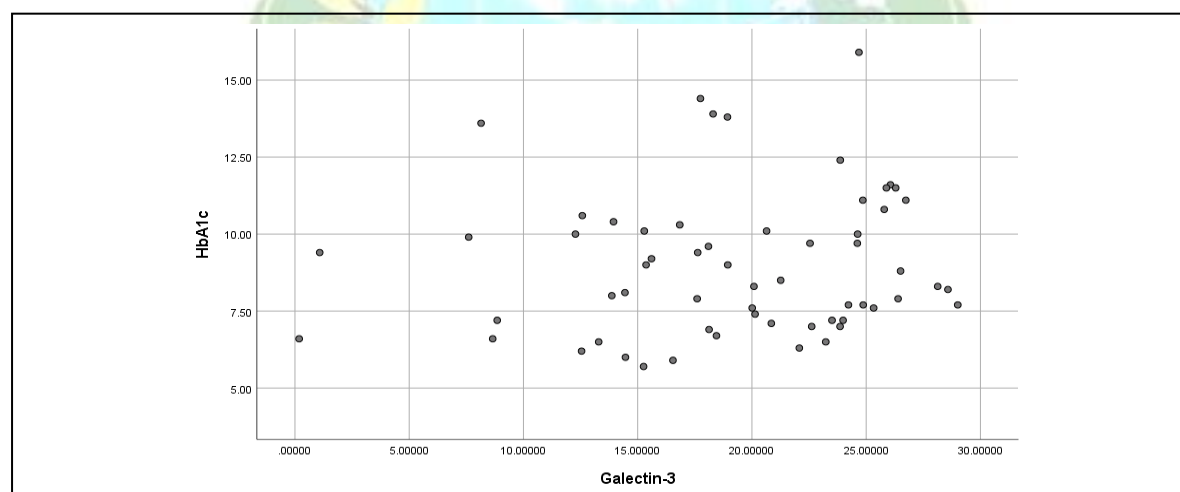
Table 4. Correlation Test of HbA1c Levels and Galectin-3 Levels

Variable	HbA1c Levels
Galectin-3 levels	$r = 0.176$ $P = 0.179$ $n = 60$

Source: Primary Data

Note: * $p =$ Spearman Correlation Test

Based on the table 4. The result of the normality test on the HbA1c levels revealed that the data was not normally distributed. The Spearman correlation test was performed to determine the correlation between serum galectin-3 levels and HbA1c levels, and $p=0.179$ was obtained. Because α ($\alpha=0.05$), it can be inferred that there was no significant correlation between HbA1c levels and serum galectin-3 levels in patients with type 2 diabetes mellitus



Picture 1. Scatterplot Graph of HbA1c and Serum Galectin-3

Based on picture 1. Data exploration can be performed using the Scatterplot graph to determine the pattern of the linear relationship between HbA1c and serum galectin-3. Based on the Scatterplot image, it can be seen that the distribution of data does not form a linear

relationship pattern. It suggests no correlation between HbA1c and serum galectin-3, considering that the scatter plot points form a random pattern.

DISCUSSION

Diabetes mellitus is a metabolic disorder with a multifactorial etiology. This disease is characterized by chronic hyperglycemia and affects carbohydrate, protein and lipid metabolism (Ermawati et al., 2022). People with this disease will be found with various symptoms such as polyuria (urinating a lot), polydipsia (drinking a lot), and polyphagia eating a lot) with weight loss (Rahmawati et al., 2019). Prolonged duration of this disease can lead to a number of metabolic disorders leading to macrovascular and microvascular pathological abnormalities (Sa'diyah et al., 2018)

The current study determines the relationship between HbA1c and serum galectin-3 levels in subjects with type 2 DM which was conducted from February to March 2023 at Hasanuddin University Hospital, Makassar. Based on gender characteristics, there were 60 research subjects consisting of 28 males and 32 females. Meanwhile, according to their age, they were aged between 37 years to 84 years.

As can be seen from Table 3, the Independent t-test obtained $p = 0.012$ ($p < 0.05$), indicating that a significant difference was found in serum galectin-3 levels from controlled and uncontrolled subjects. There were 11 controlled subjects ($HbA1c < 7\%$) with an average Gal-3 level of 14.80 ng/mL, and there were 49 uncontrolled subjects ($HbA1c > 7\%$) with an average level of 20.18 ng/mL. This is because respondents with controlled HbA1c values ($HbA1c < 7\%$) in this study may have taken medications that can suppress and control blood sugar levels in patients with Type 2 DM. HbA1c is used as a predictor of the development of DM complications. Subjects with uncontrolled HbA1c values ($HbA1c > 7\%$) will develop complications. Several studies have shown a correlation between HbA1c with microvascular and macrovascular complications. Increased HbA1c levels can reduce the risk of nephropathy by 25-44%, retinopathy by 35%, and neuropathy by 30% (Powers, 2005).

According to Table 4, the Spearman correlation test conducted in subjects with type 2 DM obtained $p = 0.622$ ($p > 0.05$), and the Scatterplot graph (Figure 1) did not form a linear relationship between HbA1c and serum galectin-3. The distribution points between HbA1c and serum galectin-3 form a random pattern, indicating no correlation between HbA1c and serum galectin-3 levels. This could be because the respondents had undergone treatment, so the serum galectin-3 levels did not experience an increase. In addition, this is because the respondents

were influenced by variables such as having a smoking habit or alcohol consumption. The researchers did not classify or record these variables. Smoking can increase oxygen radicals through exposure to both exogenous and endogenous Reactive Oxygen Species (ROS). Thus, ROS formation can be inhibited so that cell adhesion, inflammation, and production can be suppressed. This can cause Gal-3 to be unable to increase significantly (Weigert et al., 2010). Antioxidant consumption in vitamins can also capture and inhibit the performance of enzymes that produce ROS (Widowati, 2007).

Other studies also report that increased galectin-3 levels were not only affected by type 2 DM but also attributable to other diseases not examined in this study. Saeed et al (2021) suggested that galectin-3 is significantly associated with coronary artery disease. Moreover, increased serum galectin-3 also occurs in patients with coronary artery occlusion or coronary artery disease (CAD) (Ozturk et al., 2015). Galectin-3 also plays an important role in autoimmune diseases such as autoimmune encephalomyelitis (EAE), rheumatoid arthritis (RA), and systemic sclerosis (Li et al., 2022). Other studies found that apart from certain diseases, age, genetics, gender, and diet can also affect Gal-3 levels (Li et al., 2020).

Based on the direct observation conducted by the researchers, some limitations arose. Those limitations should be considered, especially for those who want to conduct further research so that they can refine their research further. The current research certainly has some drawbacks that must be continuously improved in future studies. Another limitation was that during the interview session, the answers provided by the informants sometimes needed to be to the questions asked by the researcher. Besides, there needed to be more information about how long the patients had been carrying out treatment, and the medicines are taken, and their treatment adherence. In addition, the unbalanced distribution of gender might influence the results statistically. Variables such as smoking habits, drug consumption, alcohol consumption, duration of Diabetes, hypertension, and heart disease, which can affect the results, were not analyzed. Furthermore, because the cross-sectional study design only looks at data at a single point, serum Gal-3 levels in patients with type 2 DM may have decreased or changed after undergoing treatment.

CONCLUSIONS

There is a significant difference between serum galectin-3 levels in controlled and uncontrolled diabetes, and it can be concluded that there is no association between HbA1c and serum galectin-3 levels in patients with type 2 diabetes. In the future, researchers may use a healthy control group to compare to prove an increase in galectin-3 levels in patients with type

2 DM. In addition, further research is expected to compare serum galectin-3 levels by grouping type 2 DM based on complications by controlling the factors affecting the galectin-3 levels.

It is recommended that type 2 Diabetes Mellitus patients carry out an HbA1c examination as an effective test to control glucose levels, reduce the risk of complications, and maintain a healthy lifestyle to avoid type 2 Diabetes Mellitus.

REFERENCE

- Decroli, E. (2019). Diabetes melitus tipe 2. *Padang: Pusat Penerbitan Bagian Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Andalas*, 1–52.
- Donnelly, R., & Bilous, R. (2014). Buku Pegangan Diabetes Edisi Ke-4. *Yogyakarta: Bumi Medika*.
- Driyah, S., Oemiati, R., & Riyadina, W. (2020). Indikator HbA1c pada Responden DM pada Studi Kohor Faktor Risiko Penyakit Tidak Menular di Kota Bogor, Indonesia 2017: Korelasi Kadar Glukosa Darah dan Kolesterol Total. *Jurnal Biotek Medisiana Indonesia*, 9(2), 81–89. <https://doi.org/https://doi.org/10.22435/jbmi.v9i2.4411>
- Ermawati, N., Prakoso, S. A., Shofi, M., & Andayani, A. (2022). Hubungan Kadar HbA1c dengan Nilai Laju Endap Darah Pada Penderita Diabetes Mellitus Di RSUD Daha Husada Kota Kediri. *Jurnal Sintesis Penelitian Sains Terapan Dan Analisisnya*, 3(2), 1–8. <https://doi.org/https://doi.org/10.56399/jst.v3i2.30>
- Johannes, L., Jacob, R., & Leffler, H. (2018). Galectins at a glance. *Journal of Cell Science*, 131(9), 1–9. <https://doi.org/10.1242/jcs.208884>
- Kemkes RI. (2018). *Laporan Nasional Riskesdas 2018*. Jakarta : Kementerian Kesehatan RI. Retrieved from <https://www.litbang.kemkes.go.id/laporan-riset-kesehatan-dasar-riskesdas/>
- Kemkes RI. (2020). *NFODATIN Pusat Data dan Informasi Kementerian Kesehatan RI Tetap Produktif, Cegah dan Atasi Diabetes Melitus* (Jakarta : Kementerian Kesehatan RI, ed.). Jakarta : Kementerian Kesehatan RI. Retrieved from [https://www.kemkes.go.id/downloads/resources/download/pusdatin/infodatin/Infodatin 2020 Diabetes Melitus.pdf](https://www.kemkes.go.id/downloads/resources/download/pusdatin/infodatin/Infodatin%2020%20Diabetes%20Melitus.pdf)
- Li, Y.-S., Li, X.-T., Yu, L.-G., Wang, L., Shi, Z.-Y., & Guo, X.-L. (2020). Roles of galectin-3 in metabolic disorders and tumor cell metabolism. *International Journal of Biological Macromolecules*, 142(1), 463–473. <https://doi.org/https://doi.org/10.1016/j.ijbiomac.2019.09.118>
- Li, Y., Li, T., Zhou, Z., & Xiao, Y. (2022). Emerging roles of Galectin-3 in diabetes and diabetes complications: A snapshot. *Reviews in Endocrine and Metabolic Disorders*, 23(3), 569–577. <https://doi.org/10.1007/s11154-021-09704-7>
- Lin, D., Hong, X., Sun, K., Zhang, X., Lian, H., Wang, J., ... You, L. (2021). Galectin-3 / adiponectin as a new biological indicator for assessing the risk of type 2 diabetes : a cross-sectional study in a community population. *Aging (Albany NY)*, 13(11), 15433–15443. <https://doi.org/https://doi.org/10.18632/aging.203101>
- Lok, D. J. A., Van Der Meer, P., de la Porte, P. W., Lipsic, E., Van Wijngaarden, J., Hillege, H. L., & van Veldhuisen, D. J. (2010). Prognostic value of galectin-3, a novel marker of fibrosis, in patients with chronic heart failure: data from the DEAL-HF study. *Clinical Research in Cardiology*, 99(5), 323–328.
- Ma, S., Li, S., Lv, R., Hou, X., Nie, S., & Yin, Q. (2020). Prevalence of mild cognitive impairment in type 2 diabetes mellitus is associated with serum galectin-3 level. *Journal*

- of *Diabetes Investigation*, 11(5), 1295–1302. <https://doi.org/10.1111/jdi.13256>
- Owora, A. H. (2018). Diagnostic validity and clinical utility of HbA1c tests for type 2 diabetes mellitus. *Current Diabetes Reviews*, 14(2), 196.
- Ozturk, D., Celik, O., Satilmis, S., Aslan, S., Erturk, M., Cakmak, H. A., ... Gul, M. (2015). Association between serum galectin-3 levels and coronary atherosclerosis and plaque burden/structure in patients with type 2 diabetes mellitus. *Coronary Artery Disease*, 26(5), 396–401.
- Powers, A. (2005). No Title. *Diabetes Mellitus in Harrison's Principles of Internal Medicine*, 2 MCGraw-H(2152-63.).
- Punthakee, Z., Goldenberg, R., & Katz, P. (2018). Definition, classification and diagnosis of Diabetes, prediabetes and metabolic syndrome. *Canadian Journal of Diabetes*, 42, S10–S15.
- Que, A., Yasa, I. W. P. S., & Lestari, A. A. W. (2015). Gambaran Hasil Pemeriksaan Kadar HbA1c Pada Penderita Diabetes Mellitus di Laboratorium Rumah Sakit Umum Surya Husadha Tahun 2013. *E-Jurnal Medika Udayana*, pp. 1395–2303. dec.
- Rahmawati, C., Aini, & Ramadani. (2019). Pengaruh Dosis Antikoagulan Edta 10% Dan Natrium Sitrat 3,8% Pada Pemeriksaan Laju Endap Darah. *Jurnal Penelitian Dan Kajian Ilmiah Kesehatan Volume*, 5(1), 79–85. <https://doi.org/https://doi.org/10.33651/jpkik.v5i1.25>
- Sa'diyah, I. F., Abidin, F. P., Purba, L. A., & Yuniasari, H. (2018). Efek Anti-Angiogenesis Ekstrak Kayu Secang Sebagai Terapi Adjuvant pada Diabetes Retinopati. *Saintika Medika*, 14(2), 114–118. <https://doi.org/10.22219/sm.vol14.smumm2.7160>
- Vora, A., De Lemos, J. A., Ayers, C., Grodin, J. L., & Lingvay, I. (2019). Association of galectin-3 with Diabetes mellitus in the dallas heart study. *The Journal of Clinical Endocrinology & Metabolism*, 104(10), 4449–4458.
- Wang, J., Luo, X., Jin, X., Lv, M., Li, X., Dou, J., ... Mu, Y. (2020). Effects of Preoperative HbA1c Levels on the Postoperative Outcomes of Coronary Artery Disease Surgical Treatment in Patients with Diabetes Mellitus and Nondiabetic Patients: A Systematic Review and Meta-Analysis. *Journal of Diabetes Research*, 2020, 1–14. <https://doi.org/10.1155/2020/3547491>
- Weigert, J., Neumeier, M., Wanninger, J., Bauer, S., Farkas, S., Scherer, M. N., ... Scha, A. (2010). Serum Galectin-3 Is Elevated in Obesity and Negatively Correlates with Glycosylated Hemoglobin in Type 2 Diabetes. *J Clin Endocrinol Metab*, 95(March), 1404–1411. <https://doi.org/10.1210/jc.2009-1619>
- WHO. (2016). *Global report on Diabetes*. World Health Organization. Retrieved from https://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf;jsessionid=F543DBAEA2B8AF04D952A160303A76B5?sequence=1
- Widowati, W. (2007). *Peran antioksidan sebagai agen hipokolesterolemia, pencegah oksidasi lipid dan ateroskeloris*. Widowati, W. 2007. Peran antioksidan *Majalah Kedokteran Damianus* 6: 227-232.
- Zheng, Y., Ley, S. H., & Hu, F. B. (2018). Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews Endocrinology*, 14(2), 88–98. <https://doi.org/10.1038/nrendo.2017.151>
- Zulfian, Anggunan, Sukma, V., & Syuhada. (2022). Hubungan Kadar HbA1c dengan Kadar Kreatinin Serum Pada Penderita Diabetes Melitus Tipe 2 di Rumah Sakit Pertamina Bintang Amin Husada, Bandar Lampung Tahun 2022. *Medula (Medical Profession Journal of Lampung)*, 12(2), 224–230. <https://doi.org/https://doi.org/10.53089/medula.v12i2.362>