Medication Compliance in Type 2 Diabetes Patients: HbA1c and Lipid Profile at Aulia Jombang Clinic 2020

Kepatuhan Minum Obat pada Pasien Diabetes Melitus Tipe 2: Profil HbA1c dan Lipid di Klinik Aulia Jombang 2020

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ABSTRACT
Diabetes Mellitus (DM) is a chronic metabolic disease characterized by high blood sugar levels due to insulin secretion or work defects. Poor treatment adherence leads to uncontrolled glycemic levels and complications. Therefore, ensuring patient adherence to therapy and reducing HbA1c and lipid profiles is essential. This research employs an observational, cross-sectional design, using non-probability purposive sampling to select 55 respondents via the Slovin formula. The study examines medication adherence as the independent variable, HbA1c levels, and lipid profile as the dependent variables. Data analysis involves SPSS, utilizing univariate and bivariate methods for ordinal and nominal scales. MMAS-8 questionnaire assesses the knowledge, while data comes from questionnaires and medical records of type 2 DM patients at Aulia Jombang Clinic. Study findings showed notable adherence to treatment, with 38 respondents (60.9%) complying and 17 (30.1%) not. Chi-square tests yielded significance, p values: HbA1c 0.012, LDL 0.035, total cholesterol 0.008, triacylglycerides 0.011, and HDL 0.002, based on MMAS-8 questionnaire data. In conclusion, the results indicate statistical significance (p-value < 0.05), so there is a positive correlation coefficient, indicating that higher levels of treatment adherence are associated with more optimal HbA1c control and lipid profiles.

Keywords: Diabetes Mellitus; Lipid Profile; HbA1c; Compliance with taking medication; Refer Back Program

ABSTRAK
Diabetes Melitus (DM) adalah penyakit metabolik menahun yang ditandai dengan tingginya kadar gula darah akibat sekresi insulin atau defek kerja. Kepatuhan pengobatan yang buruk menyebabkan tingkat glikemik yang tidak terkontrol dan komplikasi. Oleh karena itu, dianggap penting untuk memastikan kepatuhan pasien terhadap terapi dan untuk mencapai tujuan pengurangan profil HbA1c dan lipid. Penelitian ini menggunakan desain observasional, cross-sectional, dengan menggunakan non-probability purposive sampling untuk memilih 55 responden melalui rumus Slovin. Penelitian ini menilai kepatuhan minum obat sebagai variabel bebas, serta kadar HbA1c dan profil lipid sebagai variabel terikat. Analisis data menggunakan SPSS, dengan menggunakan
INTRODUCTION

According to the Ministry of Health Research, in 2018, Diabetes Mellitus (DM) patients in Indonesia reached 2%. In East Java, the prevalence in 2013 increased from 2.1% to 2.6% (Direktorat P2PTM, 2018). Diabetes Mellitus is a metabolic disease characterized by hyperglycemia resulting from impaired insulin secretion, insulin action, or both. Chronic hyperglycemia in DM patients can cause damage, dysfunction, and failure of several organs, including the kidneys, heart, blood vessels, and nerves (Fahrial Syam, Alwi, & Setiati, 2015). DM is also the most significant cause of death in America and was the seventh leading cause of death in 2007 and is the top five leading cause of death worldwide, which caused nearly 4 million deaths in 2010 (Kasper et al., 2015).

Monitoring treatment and control of DM patients by checking HbA1c levels is highly recommended by the American Diabetic Association (ADA). This is because HbA1c describes the patient's average blood glucose for the last 2-3 months so that it can be used as a basis for treatment planning. Research conducted by the United Kingdom Prospective DM Study (UKPDS) stated that the higher the HbA1c value in DM patients, the greater the potential for complications. A 1% decrease in HbA1c will reduce the risk of cardiovascular vascular disorders by 35%, complications due to DM will decrease by 21%, and the risk of death will decrease by 21%. Average HbA1c values can be achieved by controlling blood sugar levels over time (Ramadhan & Marissa, 2015).

Measurement of HbA1c as an indicator of adherence of DM patients in treatment is better than measuring blood glucose and urine glucose. HbA1c is an accurate biomarker for testing diabetic and prediabetic individuals. This glycated hemoglobin analysis provides evidence about a patient's average blood glucose level over the previous 2-3 months. HbA1c is recommended as a standard for controlling DM patients, especially type 2 DM, and can be used as a specific biomarker for cardiovascular complications, neuropathy, and retinopathy (Kartono et al., 2020). When the blood sugar of DM patients is high, there will also be disturbances in fat metabolism with increased lipolysis, which causes fat levels in the blood (Puspitasari & Aliviameita, 2018).

Blood sugar control is measured by patient medication adherence and other factors such as physical exercise. Physical exercise can provide benefits and positive results in glycemic control, reducing fasting blood sugar, BMI, and blood pressure, and is highly recommended for people with diabetes mellitus (Mannucci et al., 2021). In addition, diet is also very influential in blood glucose control. A low-carbohydrate diet can reduce blood sugar levels, lipid profile, and BMI and produce better glycemic control. Better than a low-fat diet (Mannucci et al., 2021; Wang et al., 2018). However, in this study, researchers wanted to measure patients' glycemic control and lipid profile from medication adherence patients because it is easy to monitor and evaluate when patients control every 3 months in a referral program for chronic diseases.

This is supported by the opinion of Sun Jae Moon, who explained in his research entitled: A systematic review and meta-analysis of the Morisky Medication Adherence Scale-8 that to determine the control of chronic disease, it is highly recommended to assess patient adherence in taking medication, this is because patients with asymptomatic or asymptomatic chronic illness usually have poor drug adherence rates. Meanwhile, patient adherence to therapy is essential to control chronic diseases, where they have to take drugs for a long time. And...
this is what makes many people with chronic illnesses have poor adherence rates.

According to research conducted by Iloh et al. (2012) in their study with 120 diabetic patients, blood sugar control in diabetic patients significantly correlates with adherence to medication (p=0.025) because other subjects' non-adherence is due to cost. Another study was also conducted by Sendekie et al. (2022), who concluded that 76.9% of the sample was diabetic mellitus with a total of 403 pieces, had low medication adherence, and this correlated with poor blood sugar control in patients, namely 74.7% of samples had poor blood sugar control.

Poor glycemic control in patients with diabetes mellitus can affect the patient's lipid profile, which was stated by Artha et al. (2019) in their research, which says that the LDL lipid profile and total cholesterol will be higher in respondents with poor glycemic control and lower in respondents with reasonable glycemic control. This is also supported by Prasetyorini et al. (2021), who said that when diabetes mellitus patients have poor glycemic control, it will cause insulin resistance, which causes lipoprotein metabolism abnormalities. This insulin can cause lipolysis and the release of free fatty acids in the bloodstream, causing the concentration of free fatty acids in the blood to increase.

Referral Program services are aimed at BPJS participants with chronic diseases such as DM, heart disease, hypertension, asthma, chronic obstructive pulmonary disease (COPD), epilepsy, stroke, schizophrenia, systemic lupus erythematosus (SLE) whose condition is stable but still requires treatment and care long-term (Rokom, 2012). DRR services are carried out at the FKTP upon referral from the specialist doctor at the FKRTL who treats them (Rokom, 2012). However, after 3 months, the participant can be referred by the FKTP to be evaluated at the FKRTL by a specialist doctor. When the patient's condition is unstable, the patient can be referred to a specialist before 3 months by notifying the FKTP doctor's examination results, which state that the patient's condition has worsened until it needs treatment by a specialist (Rokom, 2012).

Based on the background that has been presented above, with the Health Insurance program from BPJS Health for people with chronic diseases such as diabetes mellitus in the form of the Refer Back Program, it is hoped that it can increase compliance and ease of access for DM patients to get medication and improve adherence to therapy to control their chronic disease. It also enhances the quality of life and prevents complications due to worsening conditions. Therefore, the researcher wanted to find out whether it is true that the level of adherence to taking medication in patients with type 2 Diabetes Mellitus has a relationship to control or control of HbA1c levels and lipid profiles, with the respondent being a Referral Program Patient with a diagnosis of Type 2 Diabetes Mellitus in 2020 at the Aulia Jombang Clinic.

MATERIALS AND METHODS

The research method used in writing this journal is observational with an analytic design and uses a cross-sectional research approach. The sampling used in this study is non-probability sampling with a purposive sampling technique. The sample size in this study was calculated using the Slovin formula, and the sample size was 55 DM patients. The independent variable in this study was medication adherence, while the dependent variable was Hba1c level and lipid profile, which consisted of LDL, total cholesterol, HDL, and triacylglycerides.

The inclusion criteria in this study were patients from the referral program diagnosed with DM at the Aulia Jombang Clinic for the 2020 period and willing to fill out the research questionnaire. Exclusion criteria in this study were patients who withdrew from the study, never controlled or took PRB drugs at the Aulia Clinic, patients who died, and incomplete laboratory data.

The data analysis used was univariate analysis and bivariate analysis. The variable scale used is ordinal and nominal and uses cross-tabulation SPSS. The research data consists of primary data and secondary data sources. The primary data source is data obtained directly from the research respondents, so in this study, the preliminary data is the answers to the questionnaire of 55 respondents who met the inclusion and exclusion criteria. At the same time, secondary data is not directly obtained from the source. This study's secondary data was medical record data of type 2 DM patients registered with PRB at the Aulia Jombang Clinic. The ethical eligibility of the research was obtained from the Health Research Ethics Committee of FK UHT, with the certificate number of research moral eligibility No. I/180/UHT.KEPK.03/VIII/2021.
RESULTS AND DISCUSSIONS

Based on Table 1, regarding the distribution of medication adherence among patients, it can be seen that most PRB patients diagnosed with diabetes mellitus were compliant with taking medication, with 38 adherent respondents (69.1%). Then, for the non-compliant respondents, there were 17 people (30.9%). This is by research conducted by Jannah (2018), which wrote that the % of patients who adhere to taking medication in type 2 Diabetes Mellitus patients in RSUD Dr. Haryanto Lumajang is 60%. Another 35% have moderate compliance, and the remaining 5% have low compliance. The type of patient treatment also influences it, where patients undergoing monotherapy (one kind of drug) will more easily remember when to take medication than patients undergoing combination therapy.

Based on Table 2 regarding the distribution of HbA1c levels in PRB patients, it can be seen that most PRB patients diagnosed with diabetes mellitus had controlled HbA1c levels. Namely, 33 people (60%), and the remaining 22 had uncontrolled HbA1c levels. This is by research conducted by Arini (2020) at Sanglah General Hospital in Bali for people with diabetes mellitus with high adherence to therapy (80%). Most respondents had HbA1C levels < 7%, as much as 64.47% of all respondents.

OAD combination therapy and combination OAD plus insulin are strongly associated with decreased HbA1c. At the Aulia clinic, PRB patients are constantly monitored for their treatment every 2 weeks through the PROLANIS program, where education, morning exercises, blood sugar checks, and examinations by a doctor are carried out. This powerfully supports decreased HbA1c levels in PRB patients at the Aulia Jombang clinic.

Based on Table 3 about the cross-tabulation test between Medication Adherence Level and HbA1c Control, researchers divided the level of medication adherence into 2, namely adherent and non-adherent respondents as measured by the MMAS-8 questionnaire (Morisky Medication 8 - Adherence Scale item). Of the respondents who adhered to taking medication, the majority had controlled HbA1c levels. Namely, 27 respondents (71.1%), and those who were not arrested were 11 people (35.5%). The majority of respondents who did not comply with taking medication had uncontrolled HbA1c levels, namely 11 people (64.7%), and those who were controlled were 6 people (35.5%).

With this, it can be concluded that the higher the level of medication adherence in patients, the more controlled the HbA1c level will be. This is consistent with a study conducted by (Kartono et al., 2020), which stated that there was an effect of medication adherence on fasting blood sugar levels.
and HbA1c values in PROLANIS participants with a diagnosis of type 2 diabetes mellitus. The results of this study are also in line with other studies conducted by Usnaini et al. (2020), which stated that there was a significant relationship between the level of adherence to consumption of anti-diabetic drugs and HbA1c levels in Diabetes Mellitus patients at NTB Hospital.

Anti-diabetic therapy is a treatment given to patients diagnosed with diabetes mellitus whose function is to assess the benefits of treatment, adjust diet, and prevent patients from hyperglycemia or hypoglycemia. The effectiveness of the therapy given can be seen from the HbA1c examination. Anti-diabetic drugs work differently, from triggering insulin sensitivity to inhibiting gluconeogenesis and glucose absorption. If the patient does not comply with the medication, it will interfere with the drug's efficacy, so blood sugar is uncontrolled. If blood sugar levels are not controlled, it can cause an increase in the bond between blood sugar and hemoglobin through a post-translational glycation process where glycated hemoglobin has the essential component, namely HbA1c, where HbA1c is used as a benchmark for controlling Diabetes Mellitus because it can describe blood glucose levels for 1 to 3 months (Usnaini et al., 2020).

In this study, an analysis of the results was also carried out using the chi-square test and the contingency coefficient. The chi-square test obtained a p-value of 0.012, and the contingency coefficient test obtained a p-value of 0.012, which, from these results, it is known that \( p < \alpha \). This proves that there is a relationship between medication adherence in PRB patients diagnosed with Diabetes Mellitus and HbA1c control.

Based on Table 5 regarding the cross-tabulation test between Medication Compliance and LDL Lipid Profile Levels, the researchers divided LDL levels into 3 based on Perkeni (2019): Optimal, Borderline (Slightly High), and High. Meanwhile, compliance is divided into 2, namely Compliant and Non-Compliant. Based on Table 5.7, it is known that the majority of obedient respondents have optimal LDL levels, namely 22 respondents (57.9%). Borderline levels were 5 people (13.2%), and high levels were 11 (28.9%). For non-adherent respondents, the majority of them had high LDL levels, namely 11 respondents (64.7%). Borderline levels were 2 people (11.8%), and the optimal level was 4 (23.5%).

In the chi-square test that was carried out, the result was a "p-value" of 0.035 and a correlation coefficient test value of 0.035. From these results, it was known that the "p-value" < \( \alpha \) based on the results could be concluded that there was a significant relationship between adherence to medication in diagnosed PRB patients with diabetes mellitus LDL Lipid Profile levels. From the correlation coefficient test, the results are positive, which means that the more a person adheres to medication, the more optimal the LDL level will be.

The results of this study are also by research conducted by Artha et al. (2019), which said that the LDL lipid profile and total cholesterol would be higher in respondents with poor glycemic control and lower in respondents with reasonable glycemic control. A study conducted by Adikusuma & Qiyaam (2017) said that reasonable glycemic control can be achieved with high medication adherence. This was also supported by research conducted by Wahab (2015), which said that there was a significant relationship between HbA1c control and LDL levels. Then, according to Prasetyorini et al. (2021), the relationship between HbA1c and LDL control is that when diabetes mellitus patients have poor glycemic control, it will cause insulin resistance, which causes lipoprotein metabolism abnormalities where this insulin disorder can cause lipolysis and the release of free fatty acids in the bloodstream causes the concentration of free fatty acids in the blood increases. This increase in free fatty acids causes a change in fatty acids in the liver into phospholipids and cholesterol. The increase in free fatty acids also triggers the liver to produce phospholipids, cholesterol, and triglycerides, which are then released from the liver into lipoproteins, namely LDL, so that in poor glycemic control, there is an increase in LDL. The research concluded that glycemic control can be achieved with high medication adherence; if a patient adheres to medication, glycemic control can be achieved so that the LDL lipid profile can reach optimal levels.

Based on Table 7 of the cross-tabulation test between medication adherence and total cholesterol lipid profile levels, with guidelines from Perkeni (2019), the researchers divided total cholesterol levels into Optimum, borderline (Slightly high), and high. The story of compliance is divided into Compliant and non-compliant. In the Compliant category of Respondents, the majority had total cholesterol levels at the Borderline level, namely 19 respondents (50%). Then, the respondents obeyed
with optimal total cholesterol levels of 9 people (23.7%) and high total cholesterol levels of 10 respondents (26.3%).

For respondents in the non-compliance category, the majority had high cholesterol levels, namely 12 respondents (70.6%). Then 3 respondents (17.6%) did not comply with borderline cholesterol levels and 2 respondents (11.8%) optimal cholesterol levels.

Chi-square test was performed, a "p-value" of 0.008 was obtained where the "p-value" < α, and for the correlation coefficient test a value of 0.008 was obtained. Based on these results, it can be concluded that there is a relationship between the level of medication adherence in PRB patients diagnosed with diabetes mellitus and Total Cholesterol Lipid Profile levels.

This is supported by research conducted by Rdeliani et al. (2021) which said that the higher the level of adherence of a patient to treatment, the better glycemic control would be also supported by research Wang (S. Wang, Ji, Zhang, & Xue, 2020) which says that glycemic control of HbA1c has a positive correlation with total cholesterol. So, if the glycemic control is reasonable, the whole cholesterol level will also be more optimal. If the patient's adherence to treatment is poor, it will cause glycemic control on HbA1c levels in these patients to become uncontrollable (Rdeliani et al., 2021). Poor glycemic control can cause an increase in blood glucose levels due to the inability to store sugar in the muscles and as glycogen in the liver. So, to meet energy sources, the body metabolizes fat through lipolysis, which increases free fatty acids. Excess free fatty acids will be taken to the liver to be metabolized into phospholipids, cholesterol, and triglycerides, increasing total cholesterol levels (Adinda Putri, 2021).

From the exposure and some of the research results above, the researchers concluded that high adherence to medication would improve glycemic control to produce optimal total cholesterol levels.

Based on Table 9 regarding the cross-tabulation test between the level of medication adherence and triglyceride levels, with guidance from Perkeni (2019), the researchers divided triglyceride levels into 3 groups, namely Optimal, Borderline (Slightly High), and High, for adherence to taking medication is divided into 2, namely Compliant and Non-Adherent. For compliant respondents, the majority had optimal triglyceride levels, namely 20 respondents (52.2%), then 11 respondents (28.9%) were compliant respondents with borderline levels, and 7 people (18.4%) had high triacylglyceride levels. Respondents in the Non-Compliant category had the majority of high triacylglyceride levels, namely 10 respondents (58.8%), then optimal triacylglyceride levels were 4 respondents (23.5%), and at Borderline levels (Slightly High) were 3 people (17.6%).
Table 10 Chi-Square Test of Medication Adherence and Total Cholesterol.

<table>
<thead>
<tr>
<th>Total Cholesterol Level</th>
<th>Good</th>
<th>Borderline</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good medication Adherence</td>
<td>9</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Frequency (n)</td>
<td>(23.7%)</td>
<td>(50%)</td>
<td>(26.3%)</td>
</tr>
<tr>
<td>Poor Medication Adherence</td>
<td>4</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Frequency (n)</td>
<td>(20.0%)</td>
<td>(40.0%)</td>
<td>(40.0%)</td>
</tr>
</tbody>
</table>

P Value 0.008

Table 11 Contingency Test Coefficient of Medication Compliance and Total Cholesterol.

<table>
<thead>
<tr>
<th>Value</th>
<th>Approx. Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.387</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Table 12 Chi-Square Test of Medication Compliance and Triacylglycerides.

<table>
<thead>
<tr>
<th>Triacylglycerides Level</th>
<th>Good</th>
<th>Borderline</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good Medication Adherence</td>
<td>20</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Frequency (n)</td>
<td>(52.6%)</td>
<td>(28.9%)</td>
<td>(18.4%)</td>
</tr>
<tr>
<td>Poor Medication Adherence</td>
<td>4</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Frequency (n)</td>
<td>(23.5%)</td>
<td>(17.6%)</td>
<td>(58.8%)</td>
</tr>
</tbody>
</table>

P Value 0.011

Table 13 Contingency Test Coefficient of Compliance with Taking Medication with Triacylglycerides.

<table>
<thead>
<tr>
<th>Value</th>
<th>Approx. Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.376</td>
<td>0.011</td>
</tr>
</tbody>
</table>

After the chi-square test, the result was a "p-value" of 0.011. After testing the correlation coefficient, the resulting p-value is 0.011, so it is known that the value of p < α. It can be concluded that there is a relationship between the Compliance Level of Taking Medication in PRB Patients diagnosed with Diabetes Mellitus and Triglyceride Levels. This is supported by research conducted by Puspiya et al. (2018), which states that DM disease that is not controlled by medication can cause changes in the metabolism of lipid profiles in the blood, thereby increasing levels, especially cholesterol and triglycerides. Other research also stated that there was a correlation between glycemic control based on HbA1c levels and triglycerides (Sumampou & Halim, 2019). If the HbA1c level is controlled, the triglyceride level will also be held. Ayu18 explains that reasonable glycemic control is positively correlated with high treatment adherence, so it can be concluded that good treatment adherence can produce controlled glycemic control so that triglyceride levels can also be controlled.

Table 14 Chi-Square Test of Medication Compliance and HDL.

<table>
<thead>
<tr>
<th>HDL Level</th>
<th>Good</th>
<th>Borderline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good Medication Adherence</td>
<td>8</td>
<td>30</td>
</tr>
<tr>
<td>Frequency (n)</td>
<td>(21.1%)</td>
<td>(78.9%)</td>
</tr>
<tr>
<td>Poor Medication Adherence</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Frequency (n)</td>
<td>(64.7%)</td>
<td>(35.3%)</td>
</tr>
</tbody>
</table>

p-value 0.002

Table 15 Medication Adherence Coefficient Contingency Test and HDL

<table>
<thead>
<tr>
<th>Value</th>
<th>Approx. Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.391</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Artini et al. explained in their research that poor glycemic control increases blood glucose, activating the lipoprotein lipase enzyme and causing the lipolysis of triglycerides in adipose tissue (Zulfian et al., 2020). This lipolysis will result in an excess of free fatty acids, where later the excess free fatty acids will be taken to the liver and formed into triglycerides again; this causes triglyceride and VLDL levels, which are rich in triglycerides, to increase.

Based on Table 11 regarding the cross-tabulation test between the Compliance Level with Taking Medication and HDL Levels, the results are as follows. Based on the guidelines from Perkeni17, the researchers divided the respondents' HDL levels into high and low. Meanwhile, the level of compliance is divided into Compliant and Non-Compliant. After the chi-square test was carried out, the results showed that most respondents who adhered to taking medication had high HDL levels, namely 30.
respondents (78.9%), then 8 (21.1%) adherent respondents with low HDL levels.

Most non-compliant respondents had low HDL levels, namely 11 respondents (64.7%), and those with high HDL levels were 6 respondents (35.3%). After the chi-square test was carried out, it was found that the p-value was 0.002, so the p-value < α means that the chi-square test has a significant value. After that, a correlation coefficient test was carried out, and a p-value of 0.002 was obtained where the p-value < α so that the correlation coefficient test value was significant. Thus, the researchers concluded that there was a relationship between the level of medication adherence in PRB patients diagnosed with Diabetes Mellitus and the HDL Lipid Profile levels.

This finding is supported by research from Driyah et al. (2019), who say glycemic control has a significant relationship with HDL levels. His research also says that high medication adherence can achieve controlled glycemic levels. Based on this, the researchers concluded that high adherence to medication can improve glycemic control in patients, where HDL levels will be increased if glycemic levels are controlled.

CONCLUSION

After conducting research, data analysis, and discussion, it can be concluded that:
1. Most respondents, namely PRB patients diagnosed with Diabetes Mellitus at the Aulia Jombang Clinic, had a high level of medication adherence.
2. There is a significant relationship between medication adherence and HbA1c levels, LDL lipid profile levels, total cholesterol levels, triacylglyceride levels, and HDL cholesterol levels.

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REFERENSI


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