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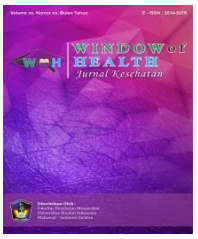

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Glomerular Filtration Rate in Prediabetic Subjects in Kendari City

[C]Theosobia Grace Orno[1], Ratih Feraritra Danu Atmaja[2], Supiati[3], Aswiro Hasan[4]
[c,1,2,3,4]Department of Medical Laboratory Technology, Health Polytechnics of Health Ministry Kendari, Indonesia
Correspondence author email([C]): theosobiagraceorno@gmail.com

ABSTRACT

Prediabetes is a condition of impaired blood glucose metabolism. However, it does not yet meet the criteria for diabetes mellitus, characterized by impaired fasting blood glucose (FBG) levels and the Oral Glucose Tolerance Test (OGTT). Chronic glucose intolerance can increase the workload of the kidney glomerulus in the filtration process and the tubules in the reabsorption process. The research aims to assess the Glomerular Filtration Rate (GFR) in prediabetic subjects in Kendari. This type of analytical observational research with a case-control design. The total sample was 90 samples consisting of 45 non-diabetic samples as the control group and 45 prediabetic samples as the case group. Characteristic data is presented as a frequency distribution and test data for differences between the control group and cases using an independent t-test with statistical test results said to be significant if $p<0.05$. The research results showed that the frequency distribution of subjects in the control group and cases based on gender was dominated by women, with the largest age range being 36-55 years. The FBG variable in the control group had a mean of 94 ± 5.31 mg/dL, and in the case group, 110 ± 8.09 mg/dL. The OGTT value in the control group was 118 ± 12.78 mg/dL, and the case group was 139 ± 23.90 mg/dL. The results of the calculation of the GFR showed a mean of 98.63 ± 14.28 mL/min/1.73 m2 in the control group and
50.10 ± 16.34 mL/min/1.73 m2 in the case group, different significant ($p=0.000$). There was a significant difference between GFR in the control group and the prediabetes case group. The results of the GFR assessment in the prediabetes group showed a mild decrease in renal function.

Keywords: Fasting blood glucose; Glomerular filtration rate; Prediabetic; Oral glucose tolerance test

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Email :
jurnal.fkm@umi.ac.id
Phone:
+6282188474721

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INTRODUCTION

Prediabetes is a global health problem. Prediabetes is referred to as the development of glucose tolerance to type 2 diabetes mellitus (T2DM) through the intermediate stage (Intermediate hyperglycaemia).[1,2] Criteria for diagnosing prediabetes currently vary between professional organizations, taking into account predisposing factors in an area that indirectly play a role in the status metabolism of each individual. In Indonesia, there are two criteria for prediabetes according to the Association of Endocrinology Indonesia (PERKENI) in 2021: (1) including the Impaired Fasting Blood Glucose (IFBG) category if the Fasting Blood Glucose (FBG) level is 100-125 mg/dL and the Oral Glucose Tolerance Test (OGTT) 2 hour plasma <140 mg/dL, (2) included in the Impaired Glucose Tolerance (IGT) category if the FBG level is <100 mg/dL and the 2 hour plasma OGTT level is 140-199 mg/dL. The diagnosis of prediabetes can also be confirmed by examining glycated hemoglobin (HbA1c) with a value of 5.7-6.4%.[3]

IFBG and IGT, which originate from uncontrolled hyperglycemia, will cause an increase in the workload of the kidneys, especially the tubules, in reabsorbing glucose.([4] The glomerulus filters around 163 mg of glucose in 24 hours; 90% of the glucose filtered in the glomerulus will be reabsorbed in the tubules through the role of the enzyme sodium glucose co-transporter-2 (SGLT-2) in the proximal tubule. The remaining 10% will be absorbed through the role of sodium-glucose co-transporter-1 (SGLT-1) in the descending and ascending tubules so that, ultimately, there is no glucose in the urine.[5,6] Chronic hyperglycemia that leads to T2DM can be complicated by kidney function failure called diabetic nephropathy (DN).[7] Diabetic nephropathy is the most common microvascular complication found in T2DM sufferers.[8] The occurrence of DN is motivated by an imbalance in renal hemodynamics caused by chronic hyperglycemia, which causes a build-up of substances or advanced glycation end products (AGEs).[9]

The initial sign of DN is a significant decrease in glomerular filtration rate (GFR). Basundoro, P.A., & Adhipireno, P. (2017), in their research on the relationship between blood glucose levels and GFR in T2DM patients, it was found that the average FBG was 169 mg/dL and the average GFR was 45 ml/minute, and there was a weak relationship between FBG levels and GFR in T2DM patients (r=-0.302; p=0.042).[10] Similar research conducted by Driyah, S., & Pradono, J. (2020) concluded that there was a strong positive correlation between HbA1c and hemoglobin and hematocrit levels in T2DM patients with Chronic Kidney Disease (CKD) (r=0.67; p<.0.05) but a weak negative correlation with GFR in T2DM without CKD (r=-0.29; p<0.05).[11]

Research on GFR in prediabetes subjects in Indonesia, especially in the city of Kendari, has never been carried out before. In fact, prediabetes is a transitional condition between non-diabetes and diabetes, which can still be prevented early through various control efforts, one of which is by routinely monitoring blood glucose and GFR levels to prevent chronic hyperglycemia, which has

microvascular complications. Therefore, this study aimed to assess GFR in prediabetic subjects in Kendari city.

METHODS

The research method used was analytical observational with a case-control study design. The research was conducted from June to September 2022. The research population was adults working as office workers in the city of Kendari, aged between 20-65 years, men and women, willing to participate in the research by signing an informed consent.

Subjects were explained the procedures for fasting at night with a fasting duration of 8-12 hours. In the morning, FBG levels were measured using the point of care testing (POCT) method, followed by administering a load of 75 mg glucose solution in 100 ml of water according to PERKENI standards to measure glucose tolerance orally after 2 hours. A total of 104 subjects took part in stage 1 screening in the form of anthropometric measurements, including body weight (BW) and FBG. Only 90 subjects were declared to have met the criteria to proceed to OGTT. There were 14 subjects excluded, 10 of whom had FBG levels >125 mg/dL, and four samples experienced lysis. The 90 subjects who met the criteria consisted of 45 non-diabetic subjects as the control group and 45 prediabetic subjects as the case group. This research has received recommendations for the ethical feasibility of research published by the Health Research Ethics Commission (KEPK) of the Health Polytechnic of the Ministry of Health, Tanjung Karang, with registration number No.312/KEPK-TJK/XI/2022.

After measuring OGTT levels, 3 ml of venous blood was taken to measure serum creatinine levels. Measurement of creatinine levels is based on the Jaffe reaction using a spectrophotometric method at a wavelength of 490 nm. The results of the examination of serum creatinine levels are continued to calculate GFR using the Cocroft-Gault equation formula:

$$\frac{\text{GFR} = (140 - \text{ages}) \times \text{BW} \times 0.85 \text{ (if women)}}{\text{Serum creatinine levels} \times 72}$$

Data analysis used SPSS 22. Data normality test used Shapiro-Wilk, followed by a difference test between the case group and the control group using the independent t-test. Statistical test results are said to be significant if $p<0.05$ with a 95% confidence interval.

RESULTS

A total of 90 samples which were divided into 45 non-diabetic samples as the control group and 45 prediabetic samples as the case group. The characteristics of the research subjects can be seen in the table 1.

Table 1. Subjects Characteristics

Characteristics	Control (n=45) N (%)	Case (n=45) N (%)
Sex		
Male	9 (20)	10 (22)
Female	36 (80)	35 (78)
Age (years)		
Early adulthood (20-35)	8 (18)	6 (13)
Most late adulthood (36-45)	10 (22)	18 (40)
Most recent elderly (46-55)	23 (51)	11 (24)
Elderly (56-65)	4 (9)	10 (23)
Serum creatinine		
Male : > 1.2	0 (0)	0 (0)
Female : > 1.0	5 (11)	12 (27)
GFR (mL/min/1.73 m^2)		
Normal : >90	41 (91)	32 (71)
Abnormal: ≤90	4 (9)	13 (29)

Based on gender, both the control and case groups were dominated by women (80% of the control group and 78% of the case group). The age category in the control group was dominated by early elderly (46-55 years) with a percentage of 51%, while the case group was dominated by late adults (36-45 years) with a percentage of 40%. The results of the GFR calculation in the control group were 91% normal and 9% abnormal, and in the case group, it was 71% normal and 29% abnormal.

Table 2. Variable Differences Between Groups

Variable	Control (n=45)	Case (n=45)	*P*
FBG (mg/dL)	94 ± 5,31	110 ± 8.09	0.000*
OGTT (mg/dL)	118 ± 12,78	139 ± 23.90	0.000*
GFR (mL/min/1.73 m^2)	98.63 ± 14.28	68.10 ± 16.34	0.000*

The FBG variable in the control group had a mean of 94 ± 5.31 mg/dL, and in the case group, 110 ± 8.09 mg/dL. The OGTT value in the control group was 118 ± 12.78 mg/dL, and the case group was 139 ± 23.90 mg/dL. The results of the GFR calculation showed a mean of 98.63 ± 14.28 mL/min/1.73 m2 in the control group and 50.10 ± 16.34 mL/min/1.73 m2 in the case group.

DISCUSSION

Prediabetes is a transitional condition between normal glucose metabolism and diabetes mellitus. Prediabetes can return to normal if blood glucose levels are monitored properly. Besides that, monitoring kidney function, including creatinine levels and GFR, is considered quite good in preventing a decrease in kidney function due to chronic hyperglycemia. The results of the research show that based on gender, more women experience metabolic syndrome, including prediabetes.

(78%). This is in line with research conducted by Driyah S. et al. (2019), which states that women are four times more at risk of experiencing metabolic syndrome than men.[12] Likewise, based on age, the largest group that experiences prediabetes is aged 36-45 years (40%), followed by age 46-55 (24%). This study's results align with a cohort study conducted by Driyah, S. et al. (2019), which found that the peak of metabolic syndrome occurred at the age of 45-54 years.[12]

FBG and OGTT levels were found to be significantly different between the control group and the prediabetes group (p=0.000). Elendu et al. (2023) stated that the GFR value for normal people is >90 mL/min/1.73 m2, the GFR category 60-89 mL/min/1.73 m2 indicates a mild decrease in kidney function.[13] The study results showed that in the control group, there were four people (9%), and in the prediabetes group, there were 13 people (29%) who experienced a decrease in GFR with the interpretation of a mild decrease in kidney function. The results of the difference test (table 2) show that there is a significant difference between GFR in the control group and the prediabetes group (p=0.000). The decrease in GFR, which indicates a mild decline in kidney function in the prediabetes group, reflects a disturbance in glucose metabolism, including glucose reabsorption in the renal tubules. In normal people, almost all of the filtered glucose is reabsorbed in the renal tubules. However, if the glucose filtration load exceeds the threshold for glucose reabsorption capacity (maximum tubular glucose reabsorption capacity of around 375 mg/minute or 425 g/day), the excess glucose will be excreted in the urine.[13,14] Several studies have shown an association with an increased risk of disease. chronic renal and early nephropathy with prediabetes. The causal nature of this association is still unclear because this association may be caused by an increased incidence of diabetes or the presence of other factors associated with hyperglycemia.[15-16]

Studies show that 20% of prediabetics suffer from nephropathy in the form of a mild decrease in kidney function. In nephropathy, activation of the local renin-angiotensin system occurs in proximal tubular epithelial cells, mesangial cells, and podocytes.[17] Prediabetic nephropathy is defined by a state of macroalbuminuria or urinary albumin excretion of more than 300 mg in 24 hours, an increase in serum creatinine levels that is consistent with an increase in creatinine clearance, or decreased glomerular filtration rate/GFR.[18] Clinically, prediabetic nephropathy is characterized by progressively increasing proteinuria and decreasing GFR, hypertension, and a high risk of cardiovascular morbidity and mortality. An increase in glomerular permeability will allow plasma proteins to escape into the glomerular filtrate.[19,20] However, in this study, microalbuminuria levels were not measured so that the cause of decreased kidney function in cases of prediabetes cannot yet be fully established.

CONCLUSIONS AND SUGGESTIONS

There was a significant difference between GFR in the control group and the prediabetes case group. The results of the GFR assessment in the prediabetes group showed a

mild decrease in kidney function. Further testing is needed regarding the relationship between GFR and HbA1c in prediabetic subjects.

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REFERENCES

1. World Health Organization, World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. Geneva: *World Health Organization*, 2018: 1-50
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care 2014; 37 Suppl* 1: S81-S90 [PMID: 24357215 DOI: 10.2337/dc14-S081]
3. Perkumpulan Endokriologi Indonesia. Pedoman Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 Dewasa di Indonesia, *PB Perkeni*, 2021
4. Centers for Disease Control and Prevention. National Diabetes Statitiscs Report: Estimates of Diabetes and Its Burden in the United States, Atlanta, GA: US *Department of Health and Human Services*, 2014
5. Rahmoune H, Thompson PW, Ward JM, Smith CD, Hong G, Brown J: Glucose transporters in human renal proximal tubular cells isolated from the urine of patients with non-insulin-dependent diabetes. *Diabetes*. 2015: 3427–3434
6. Monobe, K., Noso, S., Babaya, N., Hiromine, Y., Taketomo, Y., Niwano, F., Yoshida, S., Yasutake, S., Minohara, T., Kawabata, Y., & Ikegami, H. Clinical and genetic determinants of urinary glucose excretion in patients with diabetes mellitus. *Journal of diabetes investigation*, *12*(5), 2021: 728–737. https://doi.org/10.1111/jdi.13417
7. Sędzikowska, A., & Szablewski. Human Glucose Transporters in Renal Glucose Homeostasis. *International journal of molecular sciences*, *22*(24), 2021: 13522. https://doi.org/10.3390/ijms222413522
8. Girard J. Rôle des reins dans l'homéostasie du glucose. Implication du cotransporteur sodium–glucose SGLT2 dans le traitement du diabète [Role of the kidneys in glucose homeostasis. Implication of sodium-glucose cotransporter 2 (SGLT2) in diabetes mellitus treatment]. *Nephrologie & therapeutique*, *13 Suppl 1*, 2017: S35–S41. https://doi.org/10.1016/j.nephro.2017.01.006
9. Takenouchi, Akiko dkk. Direct Association of Visit to visit HbA1c Variation with Annual Decline in Estimated Glomerular Filtration Rate in Patients with Type 2 Diabetes. *Journal of Diabetes & Metabolic Disorders*: 14(69):1-7, 2015
10. Basundoro, P. A., & Adhipireno, P. Hubungan Kadar Glukosa Darah Terhadap Estimasi Laju Filtrasi Glomerulus Pada Pasien Diabetes Melitus. *Diponegoro Medical Journal. (Jurnal Kedokteran Diponegoro)*, *6*(2), 1027-1034, 2017, https://doi.org/10.14710/dmj.v6i2.18614
11. Driyah, S., & Pradono, J. Korelasi Hemoglobin A1c dengan Hemoglobin dan Laju Filtrasi Glomerulus Penderita Diabetes dengan dan Tanpa Komplikasi Gagal Ginjal Kronik di Bogor. Media Penelitian dan Pengembangan Kesehatan. *Litbangkes RI*. 2021. https://doi.org/10.22435/mpk.v30i4.3174
12. Driyah, S., dkk. Prediktor sindrom metabolik: Studi kohor perspektif selama enam tahun di Bogor, Indonesia. Media Litbangkes, Vol.29 No.3, September 2019: 215–224. https://doi.org/10.22435/mpk.v29i 3.654
13. Elendu, C., Elendu, R. C., Enyong, J. M, et al. Comprehensive review of current management guidelines of chronic kidney disease. Medicine, 102 (23), 2023: e33984. https://doi.org/10.1097/MD.0000000000033984

14. Li, X., Hao, W., & Yang, N. Inverse association of serum albumin levels with diabetic retinopathy in type 2 diabetic patients: a cross-sectional study. *Scientific reports*, *14*(1), 2024: 4016. https://doi.org/10.1038/s41598-024-54704-7
15. Accili, D., Du, W., Kitamoto, T., Kuo, T., McKimpson, W., Miyachi, Y., Mukhanova, M., Son, J., Wang, L., & Watanabe, H. Reflections on the state of diabetes research and prospects for treatment. *Diabetology international*, *14*(1), 2022: 21–31. https://doi.org/10.1007/s13340-022-00600-2
16. Samsu N. Diabetic Nephropathy: Challenges in Pathogenesis, Diagnosis, and Treatment. *BioMed research international*, *2021*, 1497449. https://doi.org/10.1155/2021/1497449
17. Yang, H., Kuang, M., Yang, R., Xie, G., Sheng, G., & Zou, Y. Evaluation of the role of atherogenic index of plasma in the reversion from Prediabetes to normoglycemia or progression to Diabetes: a multi-center retrospective cohort study. *Cardiovascular diabetology*, *23*(1), 2024: 17. https://doi.org/10.1186/s12933-023-02108-8
18. DeFronzo RA, Davidson JA, del Prato S: The role of the kidneys in glucose homeostasis: a new path towards normalizing glycaemia. Diabetes Obes Metab 14:5–14, 2012
19. Barutta, F., Bellini, S., & Gruden, G. Mechanisms of podocyte injury and implications for diabetic nephropathy. *Clinical science (London, England : 1979)*, *136*(7), 2022: 493–520. https://doi.org/10.1042/CS20210625
20. Heyman, S. N., Raz, I., Dwyer, J. P., Weinberg Sibony, R., Lewis, J. B., & Abassi, Z. (2022). Diabetic Proteinuria Revisited: Updated Physiologic Perspectives. *Cells*, *11*(18), 2917. https://doi.org/10.3390/cells11182917