# ASSOCIATION OF GLOMERULAR FILTRATION RATE AND DIABETES PARAMETERS WITH SYMPTOMATIC GERD IN THE ELDERLY POPULATION

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#### ABSTRAK

Latar Belakang: Penyakit refluks gastroesofageal (GERD) umum terjadi pada lansia, dengan diabetes dan gangguan fungsi ginjal sebagai faktor yang mungkin berkontribusi. Kontrol glukosa darah yang buruk dan penurunan laju filtrasi glomerulus (GFR) dapat memengaruhi gejala GERD melalui gangguan metabolik, perlambatan pengosongan lambung, dan disfungsi esofagus. Tujuan: Penelitian ini bertujuan untuk menganalisis hubungan antara GFR, parameter diabetes, dan GERD simptomatik pada populasi lansia guna memberikan wawasan mengenai signifikansi klinisnya. Metode: Studi potong lintang dilakukan pada tahun 2024 dengan 93 lansia penghuni Panti Wreda Bina Bhakti yang direkrut melalui total sampling. GERD simptomatik dinilai menggunakan kuesioner GERD-Q, sedangkan GFR diperkirakan menggunakan rumus CKD-EPI. Parameter diabetes, termasuk glukosa darah puasa, HbA1c, dan insulin puasa, diukur melalui pengambilan darah vena. Uji korelasi Spearman digunakan untuk menentukan hubungan antara variabel-variabel tersebut. Hasil: Glukosa darah puasa menunjukkan korelasi signifikan dengan skor GERD-Q (r = 0.223, p = 0.031), yang mengindikasikan bahwa kadar glukosa yang lebih tinggi berkaitan dengan gejala GERD yang lebih berat. Namun, eGFR (r = 0,034, p = 0,750), HbA1c (r = 0,106, p = 0,310), dan insulin puasa (r = -0,075, p = 0,475) menunjukkan korelasi yang lemah dan tidak signifikan secara statistik dengan tingkat keparahan GERD. Usia juga tidak memiliki hubungan yang signifikan dengan skor GERD-Q (r = 0.015, p = 0.884). Kesimpulan: Kontrol glukosa darah yang buruk berhubungan signifikan dengan tingkat keparahan GERD pada lansia, sedangkan fungsi ginjal dan parameter diabetes lainnya menunjukkan korelasi yang lebih lemah. Optimalisasi kontrol glikemik dapat membantu mengurangi gejala GERD dan meningkatkan hasil kesehatan secara keseluruhan pada populasi lansia.

Kata Kunci : GERD, Glukosa Darah, Laju Filtrasi Glomerulus, Lansia

#### ABSTRACT

**Background:** Gastroesophageal reflux disease (GERD) is common in the elderly, with diabetes and impaired kidney function being potential contributing factors. Poor blood glucose control and declining glomerular filtration rate (GFR) may influence GERD symptoms through metabolic disturbances, delayed gastric emptying, and esophageal dysfunction. **Purpose:** This study aims to analyze the relationship between GFR, diabetes parameters, and symptomatic GERD in the elderly population to provide insights into their clinical significance. **Methods:** A crosssectional study was conducted in 2024 with 93 elderly residents of Bina Bhakti Nursing Home, recruited through total sampling. Symptomatic GERD was assessed using the GERD-Q questionnaire, while GFR was estimated using the CKD-EPI equation. diabetes parameters, including fasting blood glucose, HbA1c, and fasting insulin, were measured via venous blood sampling. Spearman's correlation test was used to determine associations between these variables. **Results:** Fasting blood glucose significantly correlated with GERD-Q scores (r = 0.223, p = 0.031), indicating that higher glucose levels were associated with more severe GERD symptoms. However, eGFR (r = 0.034, p = 0.750), HbA1c (r = 0.106, p = 0.310), and fasting insulin (r = -0.075, p = 0.475) demonstrated weak and

statistically insignificant correlations with GERD severity. Age also had no significant relationship with GERD-Q scores (r = 0.015, p = 0.884). **Conclusion:** Poor blood glucose control is significantly associated with GERD severity in the elderly, whereas kidney function and other diabetes parameters show weaker correlations. Optimizing glycemic control may help reduce GERD symptoms and improve overall health outcomes in the elderly population.

Keywords: Blood Glucose, Elderly, GERD, Glomerular Filtration Rate

### 1. INTRODUCTION

Gastroesophageal reflux disease (GERD) is a long-term digestive condition where stomach acids or food move back up into the esophagus, resulting in symptoms and/or complications (Tack et al., 2012; Vakil et al., 2006). The global prevalence of GERD is estimated at around 13.98%, but it varies widely across regions. In Saudi Arabia, rates are significantly higher, ranging from 15% to 45.4%. Western Asia sees rates between 10% and 20%, while the Middle East has a broader range of 8.7% to 33.1%. Eastern Asia reports the lowest prevalence, with less than 10% of people affected (Alshammari et al., 2020; Alsuwat et al., 2018; Nirwan et al., 2020). GERD is more common in individuals aged 50 and above compared to younger people. Age-related changes, such as reduced esophageal motility and decreased saliva production, impair acid clearance in older adults, increasing their susceptibility to GERD (Chait, 2010; Notariza et al., 2021). In Indonesia, the prevalence of GERD has reached 27.4%. Most of those affected are women, accounting for 53.66% of cases. The condition is most common among individuals aged 26 to 35, accounting for 29.26% of cases (Suherman et al., 2021).

The pathogenesis of GERD in CKD patients is rather complex and multifactorial, with all the details not elucidated yet. Researchers have hypothesized that uremia and an electrolyte imbalance could lead to esophageal malfunction. According to Clovis et al., people with ESRD who were on hemodialysis tended to have higher resting pressure in the lower esophageal sphincter (LES) but shorter LES relaxation times (Kuwahara, 2011; Wang et al., 2023). Research has demonstrated that GERD can occur when the renin-angiotensin-aldosterone system (RAAS), associated with CKD, remains active.

The GERD Questionnaire (GERD-Q) is a tool that scores the severity of symptoms and how those symptoms impact an individual's daily life (Tandarto et al., 2020). Chronic conditions such as diabetes mellitus (DM) and kidney disease are now recognized as major contributors to GERD, ranking higher than many other known influences. GERD was found to be more prevalent among patients with chronic kidney disease (CKD) (23.5%) compared to those without CKD (14.8%) (Wang et al., 2023).

Diabetes is a widespread disorder and affects a huge population worldwide, resulting in complications involving impaired digestion and increased inflammation, which might worsen the symptoms of GERD. One of the reasons diabetes mellitus (DM) could contribute to gastroesophageal reflux disease (GERD) is obesity, which is a common affliction among people suffering from DM, especially those with type 2 DM. Esophageal dysfunction is one of the common complications in diabetic patients, mainly due to autonomic neuropathy with predominant damage to the vagus nerve (Sun, 2015; Verne & Sninsky, 1998). The clinical presentation includes impaired esophageal contractions, decreased peristaltic waves, slowed peristalsis, reduced lower esophageal sphincter pressure, and abnormal gastroesophageal reflux (Loke, 2013; Sun, 2015). The co-existence of kidney dysfunction further exacerbates systemic inflammation and metabolic imbalances due to shared etiological factors with diabetes, thereby worsening the condition. However, the combined effects of diabetes and kidney dysfunction on GERD, particularly symptom severity as measured by GERD-Q scores, remain poorly understood. The gut and the kidneys are metabolically linked systems. Several studies have

suggested metabolic and inflammatory factors may mediate this link, predisposing to worsening symptoms in GERD. For example, elevated blood sugar in diabetes and the accumulation of toxins from kidney malfunction create an imbalance in the gut-kidney axis and exacerbate symptoms of GERD. These relationships are important for better management of GERD to improve patients' quality of life (Yang et al., 2018).

Understanding the relationship between glomerular filtration rate (GFR) and diabetes-related parameters is crucial, as these factors provide valuable insights into the health status of the elderly population. This study examines the association between GFR and diabetes parameters with symptomatic gastroesophageal reflux disease (GERD) in older adults. By investigating these connections, It enables healthcare professionals to implement effective interventions and ultimately enhance the quality of life in the elderly population.

## 2. METHODS

This cross-sectional study was conducted in 2024 and involved 93 elderly residents of Bina Bhakti Nursing Home, selected through total sampling. Participants were eligible if they were aged 60 or older and had the cognitive ability to comprehend the study procedures, provide informed consent, and undergo blood sampling. Exclusion criteria included a history of significant upper gastrointestinal bleeding or a diagnosis of active gastric or duodenal ulcers within the past six months. Additionally, the study did not include individuals with kidney disease undergoing hemodialysis.

This study examines symptomatic GERD, estimated glomerular filtration rate (e-GFR), and diabetes mellitus parameters. Symptomatic GERD was assessed using the GERD-Q questionnaire, which consists of six questions evaluating the frequency of GERD-related symptoms over the past seven days. These symptoms include heartburn, regurgitation, epigastric or chest pain, bloating, difficulty swallowing, and coughing. Responses indicate how often each symptom was experienced. The estimated glomerular filtration rate is determined using serum creatinine levels and calculated based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Further, diabetes mellitus panels are quantified and obtained through meticulously conducted venous blood tests, with strict adherence to all normal protocols. The diabetes parameter includes fasting insulin ( $\mu$ U/mL), fasting glucose (mg/dL), and HbA1c (%), which provides a detailed evaluation of the metabolic profile.

In this study on the association between glomerular filtration rate, diabetes parameters, and symptomatic GERD in the elderly population, data analysis was conducted using SPSS version 26 to process both univariate and bivariate data quantitatively. The Kolmogorov-Smirnov test was applied to assess data normality. Spearman's Rho test was utilized to examine relationships among variables, as it is a non-parametric correlation test with a significance level set at p < 0.05. Correlation strength was categorized as negligible (0.00–0.10), weak (0.10–0.39), moderate (0.40–0.69), strong (0.70–0.89), or very strong (0.90–1.00). Respondent characteristics were presented using means and standard deviations.

## 3. RESULTS AND DISCUSSION

The study involved 93 respondents, whose characteristics are summarized in Table 1. Most were female (79.6%), while males accounted for 20.4%. The average age of the participants was 74.19 years. The mean estimated glomerular filtration rate (eGFR) was 62.89, while the average fasting blood glucose level was 86.54 mg/dL. The mean HbA1c level was recorded at 7.59%, and the average fasting insulin level was 4.83  $\mu$ U/mL. Based on the GERD-Q questionnaire, the respondents had an average score of 5.46.

Table 1. Respondent Characteristics		
Parameter	N (%)	Mean (SD)
Gender		
• Male	19 (20.4%)	
• Female	74 (79.6%)	
Age (years)		74.19 (7.95)
e- Glomerular Filtration Rate		62.89 (20.21)
Fasting Blood Glucose (mg/dL)		86.54 (16.06)
Hbalc (%)		7.59 (1.41)
Fasting Insuline (µU/mL)		4.83 (1.8)
GERD-Q		5.46 (3.59)

The findings revealed significant correlations between several parameters and GERD-Q scores, highlighting the impact of diabetes-related factors on symptomatic GERD in the elderly. Fasting blood glucose positively correlated with GERD-Q scores (r = 0.223, p = 0.031), indicating that higher glucose levels were associated with more severe GERD symptoms. HbA1c also showed a positive correlation (r = 0.106, p = 0.310), although the association was not statistically significant. The estimated glomerular filtration rate (eGFR) demonstrated a weak positive correlation (r = 0.034, p = 0.750), suggesting a limited relationship with GERD symptoms. Age showed a minimal correlation with GERD-Q scores (r = 0.015, p = 0.884), implying no significant influence. Additionally, fasting insulin levels were negatively correlated with GERD-Q scores (r = -0.075, p = 0.475), but this relationship was not statistically significant. These results suggest that fasting blood glucose is the most relevant factor associated with GERD severity among the examined parameters in the elderly population (Table 2).

Parameter — N = 93 Respondent	GERD-Q	
	r-correlation (spearman)	p-value
Age	0,015	0,884
-Glomerular Filtration Rate	0,034	0,750
Fasting Blood Glucose	0,223	0,031
HbA1c (%)	0,106	0,310
Fasting Insuline	-0,075	0,475

 Table 2. Correlation between Glomerular Filtration Rate and Diabetes Parameters with

 Symptomatic GERD in the Elderly Population

Poorly controlled diabetes mellitus has widespread effects on multiple organ systems, including the gastrointestinal tract. Chronic hyperglycemia is a well-established risk factor for autonomic neuropathy, which disrupts the physiological functions of the esophagus and stomach. A primary consequence of diabetic autonomic dysfunction is delayed gastric emptying, or gastroparesis, which predisposes individuals to gastroesophageal reflux by prolonging gastric retention and increasing the likelihood of acid regurgitation into the esophagus. This pathophysiological mechanism exacerbates GERD symptoms, resulting in more frequent and severe episodes of heartburn and regurgitation, ultimately contributing to a decline in patient quality of life (Krishnan, 2013; Rayner et al., 2001).

Another critical consequence of poor glycemic control is esophageal motility dysfunction. In healthy individuals, the lower esophageal sphincter (LES) is a protective barrier, preventing gastric contents from refluxing into the esophagus. However, in patients with diabetes, particularly those with prolonged hyperglycemia, autonomic neuropathy can compromise LES function due to progressive neuronal damage. This dysfunction reduces sphincter tone, increasing the propensity for acid reflux and chronic mucosal irritation. Persistent exposure to gastric acid can lead to esophageal inflammation, exacerbating GERD symptoms and contributing to complications such as erosive esophagitis and Barrett's esophagus (Kase et al., 2008; Krishnan, 2013; Rayner et al., 2001).

Furthermore, Glomerular filtration rate (GFR) is a fundamental marker of renal function, and its decline is prevalent among elderly individuals, particularly those with diabetes mellitus. Impaired kidney function has been associated with an increased incidence of acid-related gastrointestinal disorders, including gastroesophageal reflux disease (GERD). The pathophysiological mechanisms linking renal dysfunction to GERD involve disruptions in fluid balance, acid-base homeostasis, and gastrointestinal motility. As kidney function deteriorates, the body's ability to regulate acid-base equilibrium becomes compromised, potentially leading to increased gastric acid production and exacerbation of GERD symptoms (Kase et al., 2008; Rayner et al., 2001).

These findings highlight the intricate relationship between glomerular filtration rate, diabetes parameters, and symptomatic GERD in the elderly population. However, several limitations must be considered when interpreting the results. The cross-sectional design of this study prevents the establishment of causal relationships, as it captures associations at a single point in time. Additionally, the study was conducted exclusively among elderly residents of Bina Bhakti Nursing Home, limiting the generalizability of the findings to other populations or settings. Furthermore, potential confounding variables, such as variations in dietary habits, medication use, and other comorbid conditions, were not extensively controlled, which may have influenced the observed associations. Future research with a larger and more diverse sample and longitudinal or interventional studies is needed to confirm these findings and explore underlying mechanisms in greater detail.

### 4. CONCLUSION

Assessing glomerular filtration rate, diabetes parameters, and symptomatic GERD provides valuable insights into the complex interactions between metabolic and gastrointestinal health in the elderly population. This study underscores the association between poor glycemic control, reduced kidney function, and GERD symptoms, emphasizing the importance of early detection and comprehensive management. Optimizing blood glucose levels and maintaining kidney function may reduce GERD severity and improve overall health outcomes in older adults. Future research should explore interventional approaches, including dietary modifications, pharmacological treatments, and lifestyle changes, to understand better the mechanisms underlying these associations and develop targeted strategies for prevention and management.

### REFERENCES

- Alshammari, S. A., Alabdulkareem, A. M., Aloqeely, K. M., Alhumud, M. I., Alghufaily, S. A., Al-Dossare, Y. I., & Alrashdan, N. O. (2020). The Determinants of the Quality of Life of Gastroesophageal Reflux Disease Patients Attending King Saud University Medical City. *Cureus*. https://doi.org/10.7759/cureus.9505
- Alsuwat, O. B., Alzahrani, A. A., Alzhrani, M. A., Alkhathami, A. M., & Mahfouz, M. E. M. (2018). Prevalence of Gastroesophageal Reflux Disease in Saudi Arabia. *Journal of Clinical Medicine Research*, 10(3), 221–225. https://doi.org/10.14740/jocmr3292w
- Chait, M. M. (2010). Gastroesophageal reflux disease: Important considerations for the older patients. *World Journal of Gastrointestinal Endoscopy*, 2(12), 388. <u>https://doi.org/10.4253/wjge.v2.i12.388</u>

- Kase, H., Hattori, Y., Sato, N., Banba, N., & Kasai, K. (2008). Symptoms of gastroesophageal reflux in diabetes patients. *Diabetes Research and Clinical Practice*, 79(2), e6–e7. https://doi.org/10.1016/j.diabres.2007.08.019
- Krishnan, B. (2013). Gastrointestinal complications of diabetes mellitus. *World Journal of Diabetes*, 4(3), 51. https://doi.org/10.4239/wjd.v4.i3.51
- Kuwahara. (2011). Esophageal Dysmotility in Chronic Hemodialysis Patients After Ingestion of Liquids With Different Viscosities. *Gastroenterology Research*. https://doi.org/10.4021/gr300w
- Loke, S.-S. (2013). Erosive esophagitis associated with metabolic syndrome, impaired liver function, and dyslipidemia. *World Journal of Gastroenterology*, 19(35), 5883. https://doi.org/10.3748/wjg.v19.i35.5883
- Nirwan, J. S., Hasan, S. S., Babar, Z.-U.-D., Conway, B. R., & Ghori, M. U. (2020). Global Prevalence and Risk Factors of Gastro-oesophageal Reflux Disease (GORD): Systematic Review with Meta-analysis. *Scientific Reports*, 10(1), 5814. https://doi.org/10.1038/s41598-020-62795-1
- Notariza, K. R., Nurcholis, N., Yusaryahya, H., Karimah, N. S., Mansur, A. Y., Adhiguna, G., & Tarigan, T. J. E. (2021). Gastroesophageal Reflux Disease among Elderly Type 2 Diabetes Mellitus in a Rural Area of Central Sulawesi: A Cross-sectional Study. *Acta Medica Indonesiana*, *53*(1), 42–51. <u>http://www.ncbi.nlm.nih.gov/pubmed/33818406</u>
- Promberger, R., Lenglinger, J., Riedl, O., Seebacher, G., Eilenberg, W. H., Ott, J., Riegler, F. M., Gadenstätter, M., & Neumayer, C. (2013). Gastro-oesophageal reflux disease in type 2 diabetics: symptom load and pathophysiologic aspects a retro-pro study. BMC Gastroenterology, 13(1), 132. https://doi.org/10.1186/1471-230X-13-132
- Rayner, C. K., Samsom, M., Jones, K. L., & Horowitz, M. (2001). Relationships of Upper Gastrointestinal Motor and Sensory Function With Glycemic Control. *Diabetes Care*, 24(2), 371–381. <u>https://doi.org/10.2337/diacare.24.2.371</u>
- Suherman, L., Ramdani, R., Septiani, V., Indrayani, W., Islamiyah, A. N., & Hasyim, P. (2021). POLA PENGGUNAAN OBAT PADA PASIEN GASTROESOPHAGEAL REFLUX DISEASE (GERD) DI SALAH SATU RUMAH SAKIT DI BANDUNG. *Pharmacoscript*, 4(2), 222–233. https://doi.org/10.36423/pharmacoscript.v4i2.713
- Sun, X.-M. (2015). Association between diabetes mellitus and gastroesophageal reflux disease: A meta-analysis. *World Journal of Gastroenterology*, 21(10), 3085. https://doi.org/10.3748/wjg.v21.i10.3085
- Syam, A. F., Hapsari, P. F. C., & Makmun, D. (2016). The Prevalence and Risk Factors of GERD among Indonesian Medical Doctors. *Makara Journal of Health Research*, 20(2). https://doi.org/10.7454/msk.v20i2.5740
- Tack, J., Becher, A., Mulligan, C., & Johnson, D. A. (2012). Systematic review: the burden of disruptive gastro-oesophageal reflux disease on health-related quality of life. *Alimentary Pharmacology & Therapeutics*, 35(11), 1257–1266. https://doi.org/10.1111/j.1365-2036.2012.05086.x
- Tandarto, K., Tenggara, R., Chriestya, F., & Steffanus, M. (2020). Correlation between Quality of Life and Gastroesophageal Reflux Disease. *Majalah Kedokteran Bandung*, 52(2), 81–86. https://doi.org/10.15395/mkb.v52n2.2003
- Vakil, N., van Zanten, S. V, Kahrilas, P., Dent, J., & Jones, R. (2006). The Montreal Definition and Classification of Gastroesophageal Reflux Disease: A Global Evidence-Based Consensus. *The American Journal of Gastroenterology*, 101(8), 1900–1920. https://doi.org/10.1111/j.1572-0241.2006.00630.x

- Verne, G. N., & Sninsky, C. A. (1998). DIABETES AND THE GASTROINTESTINAL TRACT. Gastroenterology Clinics of North America, 27(4), 861–874. https://doi.org/10.1016/S0889-8553(05)70035-2
- Wang, X., Wright, Z., Patton-Tackett, E. D., & Song, G. (2023). The Relationship between Gastroesophageal Reflux Disease and Chronic Kidney Disease. *Journal of Personalized Medicine*, 13(5), 827. https://doi.org/10.3390/jpm13050827
- Yang, T., Richards, E. M., Pepine, C. J., & Raizada, M. K. (2018). The gut microbiota and the brain-gut-kidney axis in hypertension and chronic kidney disease. *Nature Reviews Nephrology*, 14(7), 442–456. <u>https://doi.org/10.1038/s41581-018-0018-2</u>

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