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Regulation of Fasting Blood Glucose, Insulin, and Homa-Ir in Relation to Malnutrition Among the Elderly: Mechanisms and Clinical Implications

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Abstract. *Malnutrition significantly disrupts metabolic processes like fasting blood glucose (FBG) regulation, insulin secretion, and insulin resistance (HOMA-IR), especially among the elderly. Aging amplifies these effects through declining β-cell function, reduced insulin sensitivity, and chronic inflammation, increasing the risk of type 2 diabetes and cardiovascular diseases. Globally, malnutrition affects 22% of the elderly, with prevalence reaching 28% in Indonesia due to food insecurity, limited healthcare access, and poor nutrition education. Malnutrition exacerbates glucose-insulin imbalances by causing muscle loss, increasing FBG levels, and inducing insulin resistance through chronic inflammation. Despite its impact, critical knowledge gaps remain, particularly in low- and middle-income countries like Indonesia. This study investigates how malnutrition affects FBG, insulin levels, and HOMA-IR in elderly individuals, focusing on mechanisms like inflammation and muscle loss to inform targeted interventions and improve metabolic health in resource-limited settings. This cross-sectional study evaluated fasting blood glucose, insulin, and HOMA-IR among 31 elderly participants at Panti Werdha Santa Anna. The study found no significant differences in fasting blood glucose, fasting insulin, HOMA-IR, or HbA1c levels across Mini Nutritional Assessment categories (normal, at risk, malnourished; $p > 0.05$). These results suggest no strong association between nutritional status and metabolic parameters, highlighting the need for further research with larger samples. This study finds no significant association between nutritional status and glycemic control in the elderly, suggesting malnutrition's indirect impact via mechanisms like inflammation and muscle loss. Comprehensive nutritional assessments remain essential to understanding its effects on metabolic health.*

Keywords: *Elderly, Fasting Blood Glucose, HOMA-IR, Insulin, Malnutrition*

1. INTRODUCTION

Malnutrition remains a significant global health issue, particularly among the elderly, as it disrupts key metabolic processes such as fasting blood glucose (FBG) regulation, insulin secretion, and insulin resistance, measured by the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). (Peng et al., 2019) Aging naturally predisposes individuals to metabolic imbalances due to declining β-cell function, reduced insulin sensitivity, and chronic inflammation. (Palmer & Jensen, 2022; Tamura et al., 2020) When malnutrition coexists with these age-related vulnerabilities, it exacerbates the disruption of glucose-insulin homeostasis, accelerating the risk of metabolic diseases like type 2 diabetes and cardiovascular disorders. (N. Ahmed et al., 2018)

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Globally, malnutrition affects an estimated 22% of the elderly population, with prevalence rates varying across regions due to differences in socioeconomic conditions, healthcare access, and dietary patterns. (O'Keeffe et al., 2019) In Indonesia, the issue is particularly concerning, with studies indicating that up to 28% of elderly individuals experience malnutrition or are at risk. (Dewiasty et al., 2022) This high prevalence reflects challenges such as food insecurity, limited access to healthcare, and inadequate nutrition education, compounded by Indonesia's rapidly aging population. (Norman et al., 2021) Malnutrition among the elderly in Indonesia is associated with poor health outcomes, increased hospitalizations, and higher mortality rates, underscoring the urgency of addressing this public health challenge. (Arjuna et al., 2017)

Malnutrition, characterized by inadequate nutrient intake and altered body composition, triggers physiological changes that significantly impact glucose-insulin regulation. (Rajamanickam et al., 2020) Muscle loss reduces the primary site for glucose uptake, impairing glucose utilization and increasing FBG levels. (Chia et al., 2018) Chronic inflammation caused by malnutrition disrupts insulin signaling pathways, leading to insulin resistance. These effects are particularly detrimental in the elderly, whose metabolic reserves are already compromised by age-related changes such as sarcopenia, altered fat distribution, and pro-inflammatory states. (de Luca & Olefsky, 2007)

Despite increasing recognition of the link between malnutrition and impaired glucose-insulin homeostasis, critical gaps remain in understanding the prevalence and mechanisms of this relationship, particularly in low- and middle-income countries like Indonesia. (Kurniawan et al., 2022) Addressing these gaps is essential for designing effective interventions to mitigate the metabolic and clinical consequences of malnutrition. (Grey et al., 2021)

This study aims to investigate the impact of malnutrition on FBG, insulin levels, and HOMA-IR in elderly individuals, focusing on mechanisms such as inflammation, muscle loss, and hepatic glucose metabolism. We hypothesize that malnutrition worsens insulin resistance and disrupts glucose regulation through these pathways. By examining these relationships in the context of global and Indonesian prevalence, we seek to provide actionable insights for improving metabolic health and reducing disease burdens in malnourished elderly populations. These findings could inform targeted nutritional, behavioral, and medical interventions, particularly in resource-limited settings.

2. LITERATURE REVIEW

Clinicians and researchers widely use HOMA-IR as a non-invasive and cost-effective tool to assess insulin resistance, a key factor in the pathogenesis of metabolic disorders such as T2DM, metabolic syndrome, and cardiovascular disease. Insulin resistance occurs when muscle, fat, and liver cells fail to respond effectively to insulin, leading to reduced glucose uptake and elevated blood glucose levels. High HOMA-IR values correlate with an increased risk of metabolic disorders, making it a crucial screening tool for early detection and metabolic health monitoring. (Vladu et al., 2022)

Blood sugar levels refer to the concentration of glucose in the bloodstream, which plays a crucial role in providing energy for body cells. Healthcare providers commonly use two blood sugar tests: fasting blood sugar and postprandial blood sugar. (Mathew et al., 2023)

Another commonly used routine glucose test is fasting blood glucose (FBG). A diagnosis of diabetes mellitus is confirmed if FBG levels reach ≥126 mg/dL. One advantage of this test is its relatively low cost. However, several factors can influence FBG results, including fasting duration, recent physical activity, and acute stress. The test's specificity and sensitivity tend to be lower in individuals over 65 years old. Glycolysis also poses a concern, as glucose concentrations may decrease if the sample is not properly stored and processed immediately. (Perkumpulan Endokrinologi Indonesia, 2021; Seclen et al., 2015; Tan et al., 2023)

Postprandial blood glucose (PPBG) refers to glucose levels measured 1–2 hours after a meal. This test assesses how efficiently the body responds to glucose intake from food. Normal PPBG levels typically remain below 140 mg/dL. Elevated PPBG levels indicate impaired glucose metabolism, which is a common characteristic of insulin resistance and type 2 diabetes mellitus (T2DM). (Ernawati et al., 2023; Moniaga et al., 2023)

Maintaining normal blood glucose levels is essential for metabolic health. Persistent elevations in fasting blood glucose (FBG) or postprandial blood glucose (PPBG) indicate poor glucose control, which is associated with several adverse health outcomes. High blood glucose levels cause endothelial dysfunction, increase oxidative stress, and trigger inflammation, all of which serve as risk factors for cardiovascular disease. Chronic hyperglycemia also contributes to the development of microvascular complications, such as diabetic retinopathy, nephropathy, and neuropathy, further worsening morbidity in diabetic patients. (Hendrawan et al., 2023)

Insulin, a hormone composed of 51 amino acids, is produced by the beta cells of the islets of Langerhans in the pancreas. Insulin plays a crucial role in glucose homeostasis, cell

growth, and metabolism. The body secretes insulin to regulate blood glucose levels and stimulate glucose storage in the liver, muscles, and adipose tissue, ensuring that blood glucose levels remain normal. (Munguia & Correa, 2024; Rahman et al., 2021; Thota & Akbar, 2024)

Fasting insulin concentration reflects the state of glucose metabolism. Clinicians use fasting insulin measurement to evaluate insulin resistance, which manifests as hyperinsulinemia, and to diagnose specific endocrine disorders such as insulinoma. Insulin resistance occurs when insulin fails to enhance glucose uptake and utilization by cells, leading to compensatory hyperglycemia. (Freeman et al., 2023; Wang et al., 2017)

The Mini Nutritional Assessment (MNA) serves as a validated and widely used tool to assess nutritional status in older adults. Researchers and clinicians designed this tool to identify individuals at risk of malnutrition or those already malnourished, enabling early intervention and management to prevent further health decline. Healthcare professionals recognize the MNA for its accuracy, simplicity, and utility across various healthcare settings, including hospitals, nursing homes, and community-based elderly care. (Holvoet et al., 2020)

3. METHODS

This cross-sectional observational study aimed to evaluate the regulation of fasting blood glucose, insulin, and HOMA-IR in relation to malnutrition among the elderly. Conducted at Panti Werdha Santa Anna, the study included participants aged 50 years and above, who were residents of the facility and provided informed consent. Individuals with severe systemic illnesses or infections, those on medications affecting glucose metabolism or insulin, and residents with incomplete data or inability to provide blood samples were excluded. A purposive sampling method yielded 31 eligible participants.

Key outcomes measured were fasting blood glucose, fasting insulin, and HOMA-IR. Nutritional status, assessed using the Mini Nutritional Assessment (MNA), served as the primary exposure. Blood biomarkers were obtained via venous blood samples following a minimum 10-hour fast. Fasting blood glucose was measured using an enzymatic assay, HbA1c levels were assessed with Fluorescence Immunoassay (FIA), and fasting insulin was measured using ELISA. Laboratory analyses adhered to accredited standards, and HOMA-IR was calculated using the formula.

Statistical analysis included descriptive statistics (mean ± SD, median [min–max] for continuous variables; frequencies and percentages for categorical variables). The Kruskal-Wallis test compared fasting blood glucose, fasting insulin, and HOMA-IR across MNA

categories, while Spearman's correlation assessed relationships between MNA scores and fasting glucose, insulin, HOMA-IR, and HbA1c levels. Ethical approval was obtained from the Tarumanagara University Human Research Ethics Committee.

4. RRESULT AND DISCUSSION

The study included a total of 31 participants, with a mean age of 73.06 years, ranging from 52 to 88 years. The majority of the participants were female, accounting for 71% of the sample, while males constituted 29%. The fasting blood glucose levels had a mean of 94 mg/dL, with a median of 85 mg/dL and a range from 72 to 270 mg/dL. Fasting insulin levels showed a mean of 12.55 µU/mL, with a median of 9.4 µU/mL and values ranging between 5.4 and 29.5 µU/mL. The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) demonstrated a mean value of 3.16, with a median of 1.98 and a range from 1.03 to 19.33, indicating some degree of insulin resistance in the sample. The Mini Nutritional Assessment (MNA) revealed that 32.3% of participants were classified as having normal nutritional status. However, 45.2% were at risk of malnutrition, and 22.6% were classified as malnourished. (Table 1)

Table 1. Characteristics of Research Results

Parameter	N (%)	Mean (SD)	Med (Min-Max)
Age	31 (100)	73.06 (1.73)	73 (52-88)
Gender			
Male	9 (29)		
Female	22 (71)		
Fasting Blood Glucose		94 (6.28)	85 (72-270)
Fasting Insulin		12.55 (1.27)	9.4 (5.4-29.5)
HOMA-IR		3.16 (0.61)	1.98 (1.03-19.33)
Mini Nutrition Assessment (MNA)			
Normal	10 (32.3)		
Risk	14 (45.2)		
Malnourished	7 (22.6)		

The study evaluated the relationship between Mini Nutritional Assessment (MNA) scores and various metabolic parameters, including fasting blood glucose, fasting insulin, HOMA-IR, and HbA1c. The correlation analysis showed a weak and non-significant positive association between MNA scores and fasting blood glucose levels ($r = 0.087$, $p = 0.640$). Similarly, fasting insulin levels demonstrated a moderate but non-significant positive correlation with MNA scores ($r = 0.300$, $p = 0.102$). For insulin resistance, as assessed by HOMA-IR, the analysis revealed a weak positive correlation with MNA scores ($r = 0.278$, $p = 0.130$). Lastly, HbA1c levels also showed a weak and non-significant positive correlation

with MNA scores (r = 0.123, p = 0.109). These results indicate no statistically significant relationship between nutritional status, as measured by the MNA, and the evaluated metabolic parameters. However, the moderate correlation observed with fasting insulin suggests a potential trend that may warrant further investigation in larger samples. (Table 2)

Table 2. Correlation of Fasting Blood Glucose, Insulin, HOMA-IR, and HbA1c with Mini Nutritional Assessment Scores

Parameter	***Mini Nutritional Assessment* Scores**	
	r-correlation	***p*-value**
Fasting Blood Glucose	0.087	0.640
Fasting Insulin	0.300	0.102
HOMA-IR	0.278	0.130
HbA1c	0.123	0.109

The study compared metabolic parameters, including fasting blood glucose, fasting insulin, HOMA-IR, and HbA1c, across different Mini Nutritional Assessment (MNA) classifications: normal nutritional status (scores 24–30), at risk of malnutrition (scores 17–23.5), and malnourished (scores <17). Fasting blood glucose levels showed no significant difference among the three MNA categories (p = 0.561). Similarly, fasting insulin levels did not differ significantly across the groups (p = 0.372). The HOMA-IR values also revealed no statistically significant difference among individuals with normal nutritional status, those at risk of malnutrition, and malnourished individuals (p = 0.389). While HbA1c levels appeared lower in the malnourished group compared to other groups, the difference did not reach statistical significance (p = 0.111). Overall, these findings indicate that nutritional status, as classified by the MNA, does not significantly associate with variations in these metabolic parameters in the study population. Further research with larger sample sizes is needed to explore potential trends. (Table 3 and Figure 1)

Table 3. Differences in Mean Fasting Blood Glucose, Insulin, and HOMA-IR Across Malnutrition Status

Type 2 Diabetes Mellitus Parameters	**MNA Classification**			**Mean Rank**	**p-value**
	Normal (24-30 score)	**At Risk of Malnutrition (17-23.5 score)**	**Malnourished (<17 score)**		
Fasting Blood Glucose	87.5 (73-270)	81.5 (72-122)	85 (75-109)	18.5 vs 14.54 vs 15.36	0.561
Fasting Insulin	10.1 (8.2-29)	9.35 (5.4-29.5)	7.6 (6.7-16.8)	19.25 vs 14.86 vs 13.64	0.372
HOMA-IR	2.17 (1.69-19.33)	1.91 (1.03-7.94)	1.80 (1.28-3.96)	19.25 vs 14.54 vs 14.29	0.389
HbA1c	6.05 (5.2-8.0)	6.05 (5.0-8.10)	5.5 (5.1-5.70)	17.5 vs 18.07 vs 9.71	0.111

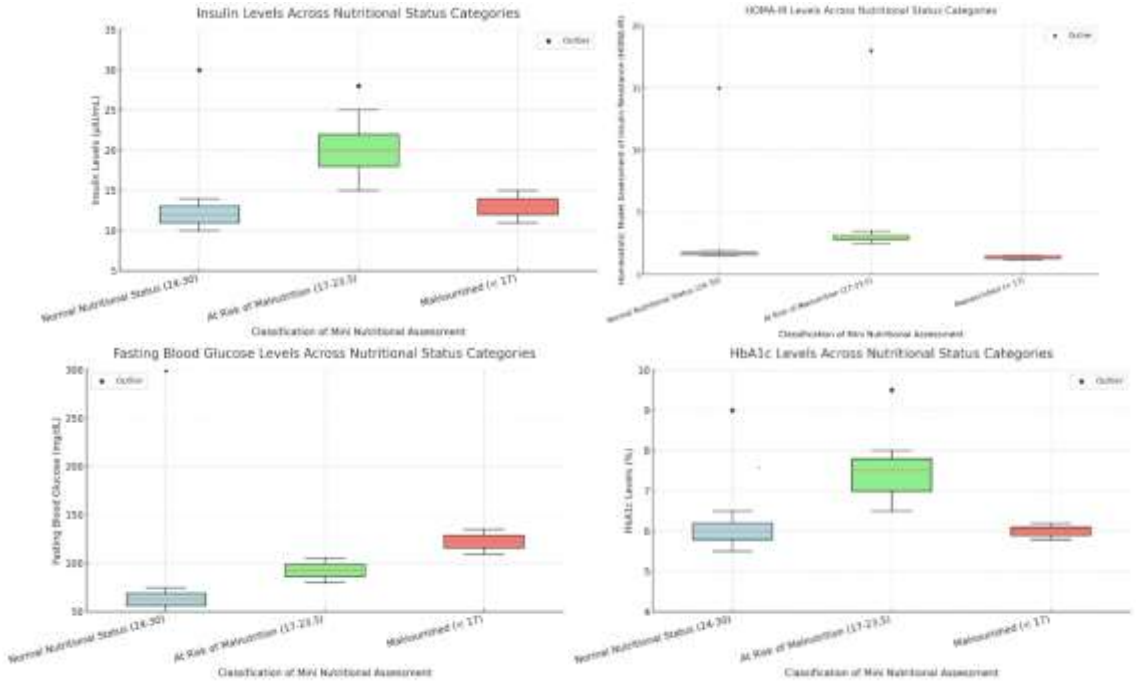

Figure 1. Fasting Blood Glucose, HbA1c, Insulin, and HOMA-IR Levels Across Nutritional Status Categories

The findings of this study reveal no statistically significant associations between nutritional status, as assessed by the Mini Nutritional Assessment (MNA), and fasting blood glucose, fasting insulin, HOMA-IR, or HbA1c levels in the elderly population. This suggests that malnutrition may not exert a direct or immediate effect on glycemic control or insulin resistance in this demographic.

Several mechanisms may explain these results. First, glucose regulation in the elderly is influenced by complex factors, including age-related insulin resistance, reduced pancreatic beta-cell function, and decreased physical activity. (De Tata et al., 2014) These physiological changes associated with aging may overshadow the impact of malnutrition on fasting glucose and insulin resistance. Additionally, malnutrition's metabolic effects, such as muscle wasting, reduced hepatic glucose production, or altered hormonal regulation, often require extended periods to manifest. (Longo et al., 2019)

Consequently, the cross-sectional design of this study may not capture the long-term consequences of malnutrition on metabolic parameters. Furthermore, adaptive mechanisms may play a role in maintaining glucose homeostasis in malnourished elderly individuals. Reduced caloric intake associated with malnutrition could lower the overall glucose load, stabilizing fasting blood glucose levels despite poor nutritional status. (Marroquí et al., 2012) At the same time, sarcopenia, commonly seen in malnourished individuals, may reduce

skeletal muscle mass and, consequently, glucose uptake, altering glucose metabolism without significantly affecting fasting glucose or HbA1c levels. (Nishikawa et al., 2021)

Chronic low-grade inflammation, frequently observed in malnourished elderly individuals, might also influence insulin resistance and glucose homeostasis, adding complexity to the interplay between malnutrition and metabolic health. (De Rekeneire et al., 2006) Another consideration is the limitations of the MNA, which provides a broad assessment of nutritional status but does not detail specific nutritional deficiencies, such as micronutrient imbalances or macronutrient insufficiencies, that might directly affect glucose metabolism. (Yen et al., 2024) The small sample size and potential heterogeneity of the study population, including differences in comorbidities, medication use, and lifestyle factors, could have introduced variability that masked significant associations. (Norman et al., 2021)

The lack of significant differences in fasting blood glucose and HOMA-IR among individuals with normal nutritional status, those at risk of malnutrition, and malnourished participants suggests that malnutrition may not acutely affect insulin sensitivity or fasting glucose levels in the short term. (Kobayashi et al., 2023) This finding aligns with previous studies indicating that chronic changes in nutritional intake may be required to induce measurable metabolic effects. (Cernea et al., 2018) Malnutrition might also indirectly impact glucose homeostasis through altered hepatic gluconeogenesis, peripheral insulin signaling, or inflammatory pathways. (Puigserver et al., 2003)

However, the observed weak correlations and lack of significance indicate that these effects may be subtle or modulated by other factors, such as age, physical activity, or comorbidities. The findings indicate that malnutrition does not acutely affect insulin sensitivity or fasting glucose levels in the short term, as evidenced by the lack of significant differences in fasting blood glucose and HOMA-IR among individuals with normal nutritional status, those at risk of malnutrition, and malnourished participants. This aligns with the theory that chronic nutritional deficiencies, rather than acute malnutrition, are necessary to induce measurable metabolic effects. Over time, prolonged malnutrition can alter key metabolic pathways, but the acute state may not be sufficient to trigger significant disruptions. (di Giovanni et al., 2016; Filteau et al., 2021)

Malnutrition may indirectly influence glucose homeostasis through several mechanisms. One potential mechanism is altered hepatic gluconeogenesis. In malnourished individuals, insufficient protein intake may reduce the availability of gluconeogenic substrates, such as alanine, thereby affecting hepatic glucose production. (Bhutta et al., 2017) This mechanism could stabilize fasting glucose levels despite malnutrition. However, the

degree of gluconeogenic impairment depends on the severity and duration of malnutrition. Peripheral insulin signaling might also be affected. Malnutrition can lead to a reduction in skeletal muscle mass, a primary site for glucose uptake in response to insulin. Muscle wasting, commonly seen in malnourished individuals, can decrease insulin-stimulated glucose disposal, potentially contributing to insulin resistance over time. (Emery, 2005)

However, this process may not be immediately apparent in fasting glucose or HOMA-IR values, as these measures primarily reflect basal, rather than postprandial, metabolic states. Inflammation serves as another key mechanism. (Lee et al., 2011) Chronic malnutrition often triggers low-grade systemic inflammation, which can interfere with insulin signaling pathways. Pro-inflammatory cytokines, such as TNF-α and IL-6, impair insulin receptor substrate (IRS) function and downstream signaling, contributing to insulin resistance. (Li et al., 2022) Despite these potential pathways, the weak correlations and lack of significant findings in this study suggest that the effects of malnutrition on glucose homeostasis may be subtle, requiring larger sample sizes or more sensitive measures to detect.

Additionally, age and comorbidities likely modulate these mechanisms. Aging is associated with physiological changes, such as reduced beta-cell function and increased insulin resistance, which may overshadow the specific effects of malnutrition. (Chang et al., 2006) Physical activity also influences glucose metabolism, as regular activity enhances insulin sensitivity and glucose uptake. (Röhling et al., 2016) Comorbid conditions, such as cardiovascular disease or chronic kidney disease, may further complicate the relationship between malnutrition and metabolic health. (Lopes & Raimundo, 2011)

Interestingly, the moderate yet non-significant positive correlation between fasting insulin and MNA scores hints at a possible trend. Participants with better nutritional status may exhibit higher fasting insulin levels, reflecting a compensatory mechanism to maintain glucose homeostasis. This trend underscores the complexity of glucose regulation in malnutrition, as both undernutrition and overnutrition can lead to disruptions in insulin secretion and action. (Ling et al., 2016; Wells et al., 2019)

The absence of significant differences in HbA1c levels across MNA classifications further supports the notion that malnutrition may not exert pronounced effects on long-term glycemic control in the elderly. (Thaenpramun et al., 2024) However, the slightly lower HbA1c levels observed in the malnourished group could result from reduced caloric intake and lower carbohydrate availability, leading to transient decreases in postprandial glucose levels. (Al-Adwi et al., 2023)

The lack of significant differences in HbA1c levels across MNA classifications suggests that malnutrition does not have a pronounced impact on long-term glycemic control in the elderly. (Thaenpramun et al., 2024) HbA1c, which reflects the average blood glucose levels over a two-to-three-month period, remains relatively stable despite variations in nutritional status. (Abdelhafiz et al., 2016) This stability indicates that acute or short-term nutritional deficits may not exert strong effects on long-term glucose regulation. However, the slightly lower HbA1c levels observed in malnourished individuals may stem from reduced caloric intake and limited carbohydrate availability. (Klein et al., 2021)

When caloric and carbohydrate intake are insufficient, the body's postprandial glucose responses are diminished due to a lower dietary glucose load. (Nishino et al., 2018) Postprandial glucose contributes significantly to overall glycemic exposure, and its reduction can lead to slightly lower HbA1c values. (Yamakawa et al., 2019) This is particularly relevant in malnutrition, where protein and fat metabolism may compensate for insufficient carbohydrate intake, altering the balance of glucose homeostasis. Additionally, malnutrition can influence glucose metabolism through hepatic and peripheral mechanisms. (Bandsma et al., 2010)

In the liver, reduced glycogen stores due to chronic undernutrition may impair gluconeogenesis and glycogenolysis, leading to lower fasting and postprandial glucose levels. (Sobotka et al., 2006) Peripherally, malnutrition may affect insulin sensitivity. On one hand, prolonged malnutrition might improve insulin sensitivity due to decreased adiposity and lower circulating free fatty acids. (Blaak, 2020) On the other hand, deficiencies in key micronutrients such as chromium, magnesium, or zinc, common in malnourished individuals—could impair insulin action and glucose uptake. (Via, 2012) The interplay between malnutrition and glycemic control also involves hormonal and inflammatory changes. (Tsalamandris et al., 2019)

Malnutrition often leads to reduced levels of insulin-like growth factor-1 (IGF-1) and altered cortisol dynamics, both of which can affect glucose metabolism. (Alto, 1986) Chronic inflammation, commonly observed in malnutrition, can further disrupt glucose homeostasis by impairing insulin signaling pathways. (Zhao et al., 2023) However, in elderly individuals, these mechanisms may be less pronounced due to age-related metabolic adaptations that prioritize glucose stability. The slightly lower HbA1c levels in malnourished individuals highlight the need for comprehensive nutritional assessments that go beyond caloric intake to include macronutrient composition and micronutrient status. (Thaenpramun et al., 2024) Evaluating the balance of carbohydrates, proteins, and fats, as well as specific nutrient

deficiencies, can help elucidate the subtle mechanisms underlying glucose regulation in malnourished elderly populations. (T. Ahmed & Haboubi, 2010)

5. CONCLUSION AND RECOMMENDATION

The absence of a significant association between the Mini Nutritional Assessment (MNA) classification and fasting glucose, fasting insulin, HOMA-IR, or HbA1c levels suggests that malnutrition may not directly impact glucose metabolism or insulin resistance. However, indirect mechanisms such as reduced muscle mass, low-grade chronic inflammation, and altered hepatic function may still play a role. The lower HbA1c levels observed in malnourished elderly individuals are more likely due to reduced caloric and carbohydrate intake rather than underlying metabolic dysfunction. This study has several limitations. The cross-sectional design prevents causal inference, the MNA tool does not capture specific micronutrient deficiencies, and the relatively small sample size may limit statistical power. Moreover, the metabolic parameters assessed did not include postprandial glucose dynamics or pancreatic beta-cell function. Age-related metabolic adaptations were also not accounted for. Further research using longitudinal designs and advanced technologies, such as metabolomics and continuous glucose monitoring (CGM) is recommended to better elucidate the relationship between malnutrition and metabolic dysregulation. Future studies should also explore the role of micronutrient deficiencies, including zinc, magnesium, and chromium. Targeted nutritional interventions may be key to mitigating the metabolic consequences of malnutrition in older adults. Additionally, age-related factors such as sarcopenia, chronic inflammation, and hormonal changes should be considered to provide a more comprehensive understanding.

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