Original Article

Link Between Malnutrition and Insulin Resistance in Patients Undergoing Maintenance Hemodialysis

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ABSTRACT

Introduction: *Over the past thirty years, chronic kidney disease (CKD) has significantly increased globally, with 77.5% of end-stage kidney disease (ESKD) patients requiring kidney replacement therapy (KRT) and 43.1% relying on dialysis. Hemodialysis (HD) constitutes 89% of treatments for ESKD, leading to high cardiovascular morbidity and mortality. Traditional risk factors do not fully explain cardiovascular mortality in CKD patients, with insulin resistance (IR) now recognized as a significant contributor.* ***Aim of the study:*** *This study aims to explore the relationship between malnutrition and insulin resistance in patients undergoing maintenance hemodialysis.* ***Methods & Materials:*** *This cross-sectional study, conducted in the Nephrology Department of Dhaka Medical College over 18 months (from May 2021 to October 2022), involved 120 patients on maintenance hemodialysis. Patients were chosen through purposive sampling based on inclusion criteria and excluding those under 18 with specific diseases, obesity, or pregnancy. Informed consent was obtained, and the Research Review Committee granted ethical approval.* ***Result:*** *The study involved 120 subjects; 86 were identified as insulin-resistant, and 34 were not. Among insulin-resistant patients, the majority were aged 41-50 (32.6%) and 51-60 (30.2%). In contrast, 41.2% of non-insulin-resistant patients were 41-50, and 26.5% were 51-60. Males comprised 53.5% of insulin-resistant and 58.8% of non-insulin-resistant subjects.* ***Conclusion:*** *Insulin resistance is closely linked to malnutrition in hemodialysis patients, with*

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higher malnutrition rates observed in insulin-resistant individuals, as evidenced by anthropometric measurements and SGA scores.

Keywords: *Malnutrition, Insulin Resistance, Maintenance Hemodialysis*

INTRODUCTION

Over the past thirty years, there has been a significant increase in the global burden of chronic kidney disease (CKD), with 77.5% of end-stage kidney disease (ESKD) patients requiring kidney replacement therapy (KRT) and 43.1% of these patients receiving dialysis alone[1]. Hemodialysis (HD) accounts for 89% of the worldwide treatment for patients with ESKD[2]. It is linked to substantial cardiovascular morbidity and mortality, including ischemic heart disease, stroke, peripheral artery disease, and sudden death[3,4]. Traditional risk factors like hypertension, smoking, hyperlipidemia, obesity, diabetes mellitus, or a family history of coronary artery disease cannot fully account for the elevated cardiovascular mortality in CKD patients. Insulin resistance is increasingly acknowledged as a 'nontraditional' risk factor contributing to cardiovascular disease through endothelial dysfunction, oxidative stress, dyslipidemia, systemic inflammation, and activation of the renin-angiotensin-aldosterone system[5].

Additionally, dialysis patients' insulin resistance (IR) has been associated with accelerated protein catabolism, resulting in protein energy wasting and malnutrition[6]. Malnutrition is common among hemodialysis patients, affecting 20% to 70% of those undergoing maintenance hemodialysis[7-9]. Hemodialysis patients have a high burden of malnutrition (20-61.8%)[10,11]. Mortality in HD patients has been associated with body size as well as the duration of dialysis[12]. Muscle mass and body fat are significantly associated with IR in dialysis patients. Other studies have also reported a significant positive correlation between BMI, body fat, and IR[13]. In CKD patients needing dialysis, skeletal muscle is the primary tissue responsible for IR. While IR increases with skeletal muscle mass, in sarcopenic patients, factors such as metabolic acidosis, inflammation, and oxidative stress may be the main contributors to IR[14]. Protein-energy malnutrition leads to insulin resistance, a metabolic condition marked by the loss of both somatic and visceral protein stores, which is not solely explained by insufficient nutrient intake. In the general population, insulin resistance is linked to increased protein catabolism. Among ESRD patients, those with Type II diabetes exhibit heightened muscle protein breakdown compared to those without diabetes.

Even in the absence of diabetes or severe obesity, insulin resistance is present in dialysis patients. It is strongly associated with elevated muscle protein breakdown due to activating a common proteolytic pathway[6]. Regular monitoring of nutritional status in dialysis patients is essential for preventing, diagnosing, and treating protein-energy malnutrition.

The Subjective Global Assessment (SGA) is a valuable and reliable tool for evaluating the nutritional status of these patients. Due to its effectiveness, the National Kidney Foundation Kidney Disease/Dialysis Outcome and Quality Initiative (NKF/KDOQI) recommends that the nutritional status of patients undergoing maintenance hemodialysis be assessed using SGA at least every six months[15]. Understanding the relationship between malnutrition and insulin resistance is crucial for developing targeted interventions to improve MHD patients' nutritional and metabolic status. This study aims to explore the relationship between malnutrition and insulin resistance in patients undergoing maintenance hemodialysis.

METHODOS & MATERIALS

This cross-sectional study was conducted in the Nephrology Department of Dhaka Medical College. Patients were selected by purposive sampling according to inclusion and exclusion criteria. One hundred twenty patients were enrolled in this study 18 months from May 2021 to October 2022. After informing each participant about the study's aim, objectives, and procedure, informed written consent was obtained. Meticulous history was taken, and a physical examination was performed to include and exclude each patient. The study obtained ethical approval from the Research Review Committee (RRC) of the Department of Nephrology DMC.

Inclusion criteria:

- Patients on maintenance hemodialysis.

Exclusion criteria:

- Age <18 years.
- Patients with Chronic liver disease and polycystic ovarian syndrome
- Obesity (>30 kg/m2)
- Hyperthyroid, Hypothyroid, and Malignancy.
- Pregnant women.

Operational definition:

ESRD patients are on regular hemodialysis for 8-12 hours/ week for at least three months[14]. Insulin resistance is when the hormone cannot bind to its receptors and signals the expected physiological responses, e.g., insufficient or defective insulin sensitivity [15]. Body mass index or BMI is a statistical index using a person's weight and height to estimate body fat in males and females of any age. It is calculated by taking a person's weight, in kilograms, divided by their height, in meters square. BMI defines a person as underweight, average weight, overweight, or obese instead of traditional height vs. weight charts. However, individual variations do exist. WHO recommends that ≥ 30.0 is obese, 25-29.9 is overweight, 18.5-24.9 is normal, and <18.5 is underweight[16].

Malnutrition:

Based on malnutrition score[17]:

- Patients were nourished with a score range of 7 to 10
- Mild to moderately malnourished with a score range of 11 to 20

- Moderate to severely malnourished with a score range of 21 to 35

Patient data on baseline characteristics (age, gender, BMI) associated with risk factors of CKD and hemodynamics, along with all other relevant socio-demographic particulars, were recorded in a predesigned data collection sheet. Then, the patients were assessed with investigations. Patients were instructed to attend the dialysis center on the scheduled day of dialysis with overnight (at least 8 hours) fasting state, and blood was taken from the peripheral vein before the start of dialysis for biochemical testing. Patient venous blood (5ml) was collected by sterile disposable syringe with aseptic precaution and immediately transferred to two dry clean test tubes. To estimate fasting blood glucose, 2cc blood was collected in a tube mixed with anticoagulant sodium chloride, and the rest of the blood was collected in another tube to analyze fasting insulin. After collection, samples were sent to the laboratory within thirty minutes and were measured by a fully automated biochemistry analyzer (Atellica, Siemens Germany, Capillar 3 Octa). Then, patients with insulin resistance will be diagnosed with the HOMA-IR index. All laboratory investigations were carried out in the biochemistry laboratory of Bangabandhu Sheikh Mujib Medical University (BSMMU).

BMI and anthropometry were measured after dry weight was achieved. For BMI, height and post-dialysis weight were taken. Then, BMI was calculated using the weight formula (in kilograms)/height (in meters)2. Anthropometry in patients on maintenance haemodialysis was assessed 10- 20 minutes after the termination of the dialysis session. According to the National Health and Nutrition Examination Survey, anthropometry of mid-arm circumference (MAC), mid-arm muscle circumference (MAMC), and triceps skin fold thickness (TST) was measured on the non-fistula arm. The midpoint was marked between the upper edge of the acromion process's posterior border and the olecranon process's tip. This was the site for measuring mid-arm circumference (MAC) and triceps skin fold thickness (TST). Mid-arm circumference was measured using a flexible, non-stretchable measuring tape. All skin folds were measured with the skinfold caliper. Nutritional status was assessed using a malnutrition score based on subjective global assessment. Detailed patient-related medical history was obtained regarding the end dialysis dry weight (overall change in the past six months), dietary intake, gastrointestinal symptoms, functional capacity, and co-morbidities. Physical examination was done to observe subcutaneous fat loss and signs of muscle wasting. The scoring sheet consists of two parts and seven elements. During each patient's evaluation, a questionnaire regarding the first five components or the patient's related medical history was obtained to facilitate the optimal evaluation.

Data Collection and Analysis:

Data was collected in a pre-tested questionnaire by taking history, conducting a clinical examination, determining laboratory findings, and determining patient outcomes. The researcher himself collected the data. Following data collection, the collected data was assessed for completeness, accuracy, and consistency before analysis was commenced. Data analysis was done using SPSS version 22 (IBM). Exploratory data analysis was conducted to describe the study population, where categorical variables were summarized using frequency tables. In contrast, continuous variables were summarized using measures of central tendency and dispersion such as mean, median, percentiles, and standard deviation. Qualitative or categorical variables were described as frequencies and proportions. The correlation was determined by Spearman's correlation coefficient (r). A level of P< 0.05 was considered statistically significant.

RESULT

The study comprised 120 subjects, of which 86 were insulin resistant, and 34 were not. Among the 120 patients, 86 were identified as insulin resistant, while 34 did not exhibit insulin resistance. Regarding age distribution, most insulin-resistant patients were between 41 and 50 years (32.6%), followed closely by those aged 51 to 60 years (30.2%). In contrast, among patients without insulin resistance, those aged 41 to 50 represented 41.2% of the group, while those aged 51 to 60 accounted for 26.5%. More than half (53.5%) of the insulin-resistant subjects were male, while 58.8% of those without insulin resistance were male (**Table I**).

Table – I: Distribution of the Study Subjects According to Demographic Profile (*n*=120)

Demographic Profile	Insulin Resistant			
	Present (n=86)		Absent (n=34)	
	n	**%**	***n***	**%**
Age (years)				
<30	2	2.3	1	2.9
31-40	22	25.6	6	17.6
41-50	28	32.6	14	41.2
51-60	27	30.2	9	26.5
>60	8	9.3	4	11.8
Sex				
Male	46	53.5	20	58.8
Female	40	46.5	14	41.2

TST measurements show that 33.7% of insulin-resistant patients had TST values indicative of malnutrition, whereas only 5.9% of patients without insulin resistance exhibited similar measurements. Similarly, for MAC, 53.5% of insulin-resistant patients had measurements suggestive of malnutrition, compared to 8.8% of those without insulin resistance. The MAMC also shows a marked difference, with 43% of insulin-resistant patients having MAMC values associated with malnutrition, while only 8.8% of non-insulin-resistant patients were similarly affected. The two groups had a statistically significant difference (**Table II**).

Table – II: Malnutrition Status in the Study Population According Anthropometric Measurement (*n*=120)

Anthropometric Measurement	Insulin resistant				*p*-value
	Present (n=86)		Absent (n=34)		
	n	%	*n*	%	
TST (mm)	29	33.7	2	5.9	0.001
MAC (cm)	46	53.5	3	8.8	
MAMC (cm)	37	43	3	8.8	

Table III shows that 32.6% were classified as well-nourished (SGA score of 7 to 10), in contrast to 88.2% of non-insulin-resistant patients. 67.4% of insulin-resistant patients were mild to moderately malnourished (SGA score of 11 to 20), compared to only 11.8% of non-insulin-resistant patients.

Table – III: Distribution of the Study Subjects According to Malnutrition Score Based on SGA (*n*=120)

Malnutrition Score	Insulin resistant				*p*-value
	Present (*n*=86)		Absent (*n*=34)		
	n	%	*n*	%	
Well nourished (7 to 10)	28	32.6	30	88.2	0.001
Mild to moderately malnourished (11 to 20)	58	67.4	4	11.8	
Severe malnourished (21 to 35)	0	0	0	0	

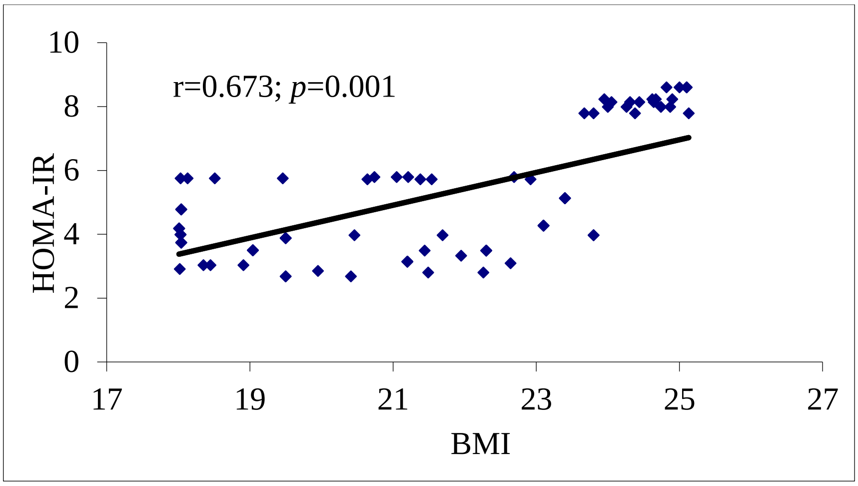

Figure – 1: Scatter Diagram Showing Correlation of HOMA-IR with BMI Among Study Subjects

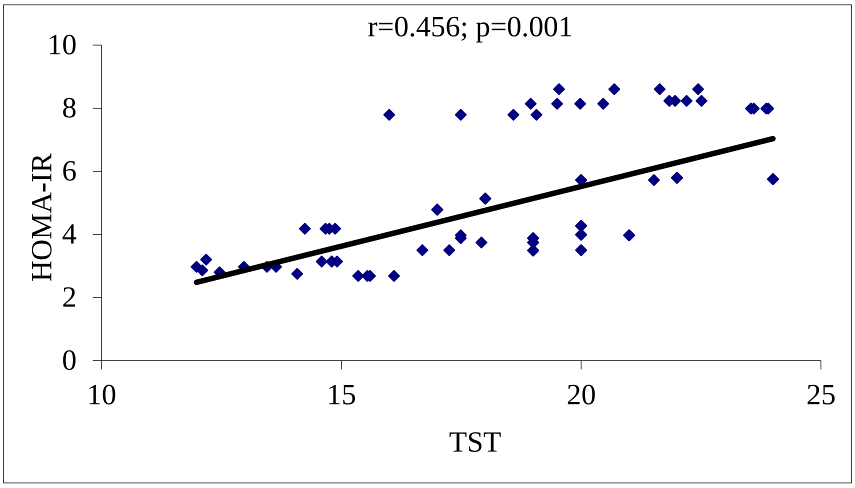

Figure – 2: Scatter Diagram Showing Correlation of HOMA-IR with Triceps Skin Fold Thickness (TST) Among Study Subjects

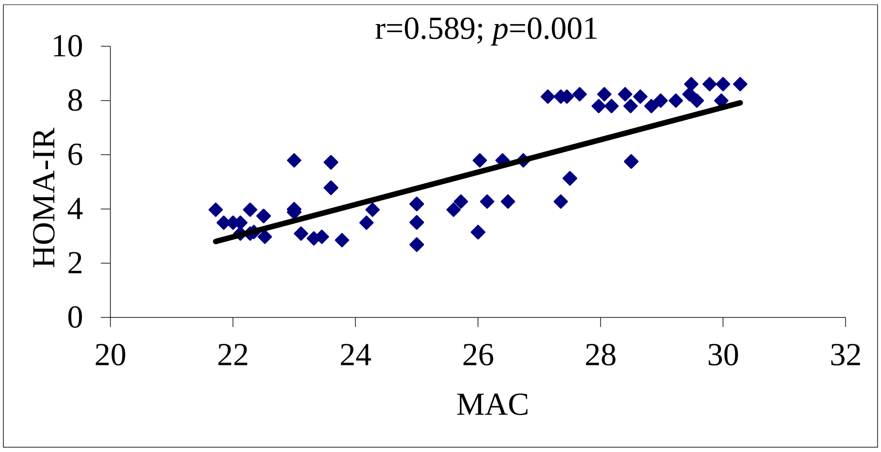

Figure – 3: Scatter Diagram Showing Correlation of HOMA-IR with Mid Arm Circumference (MAC) Among Study Subjects

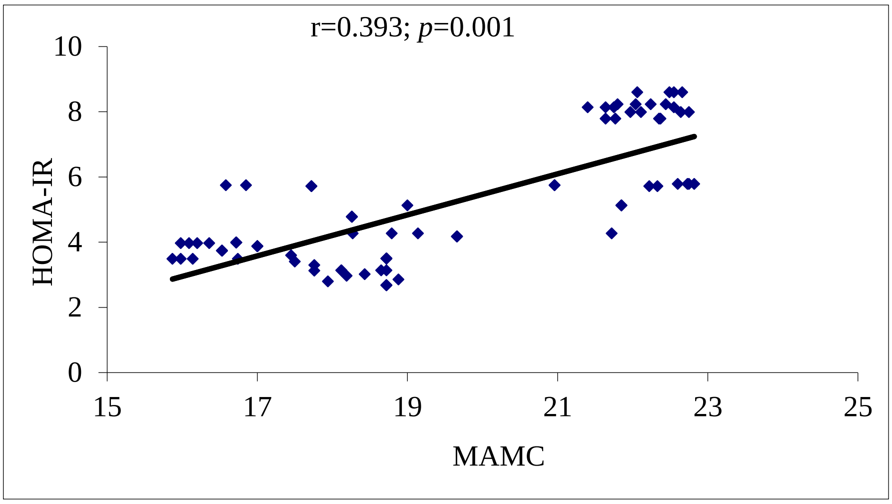

Figure – 4: Scatter Diagram Showing Correlation of HOMA-IR with Mid Arm Muscle Circumference (MAMC) Among Study Subjects

A noteworthy positive connection was seen between HOMA-IR and BMI (r=0.673, *p*=0.001), HOMA-IR and TST (r=0.456, p=0.001), HOMA-IR and MAC (r=0.589, *p*=0.001), and HOMA-IR and MAMC (r=0.393, *p*=0.001) (**Figure 1-4**).

DISCUSSION

Malnutrition is a significant concern for patients undergoing maintenance HD. This condition, often referred to as Protein Energy Wasting (PEW) or the Malnutrition Inflammation Atherosclerosis (MIA) syndrome, significantly contributes to increased morbidity and mortality rates in these patients[18-20]. The interplay between malnutrition and insulin resistance is particularly concerning, as both conditions can exacerbate each other, leading to a vicious cycle that complicates the management of chronic kidney disease (CKD) and its associated complications[21]. This study aims to investigate the relationship between malnutrition and insulin resistance in patients undergoing HD. The demographic profile of the study population highlights a higher prevalence of insulin resistance among patients aged between 41 and 50 years (32.6%) and those aged between 51 and 60 years (30.2%). Our study aligns with another similar study suggesting that aged individuals undergoing hemodialysis are more prone to insulin resistance[22].

Additionally, the male predominance in both insulin-resistant (53.5%) and non-insulin-resistant (58.8%) groups could suggest that gender may not play a significant role in insulin resistance within this population. This result closely resembled studies by ***Jhorawat et. al.*** and ***Nazzal et al.***[14,23]. The anthropometric measurements, including TST, MAC, and MAMC, clearly demonstrate the higher incidence of malnutrition among insulin-resistant patients. Specifically, 33.7% of insulin-resistant patients had TST values indicative of malnutrition, compared to only 5.9% of non-insulin-resistant patients. Similarly, MAC and MAMC measurements also showed a significant difference, with 53.5% and 43% of insulin-resistant patients exhibiting malnutrition compared to 8.8% in both categories among non-insulin-resistant patients. ***Esen et al.*** also showed the relationship between IR and anthropometric measurements in patients with kidney disease[24]. Similarly, other studies suggested that insulin resistance in hemodialysis patients is closely linked to a decline in nutritional status, potentially due to metabolic imbalances that affect nutrient absorption and utilization[22,25]. Our observations indicate that over two-thirds (67.4%) of the insulin-resistant subjects were mild to moderately malnourished, compared to only 11.8% of the non-insulin-resistant subjects. This difference between the two groups was statistically significant (p<0.05) and is consistent with the findings of the study by ***Jhorawat et al.***[14]. The study also highlights the positive correlations between HOMA-IR and various nutritional indicators. Specifically, significant positive correlations were observed between HOMA-IR and Body Mass Index (BMI) (r=0.673, p=0.001), HOMA-IR and TST (r=0.456, p=0.001), HOMA-IR and MAC (r=0.589, p=0.001), and HOMA-IR and MAMC (r=0.393, p=0.001). A similar correlation was found in the study of ***Jhorawat et. al.***, ***Han et. al.***, and Tucker[14,26,27]. These correlations suggest that higher insulin resistance is associated with poorer nutritional status, as lower BMI, TST, MAC, and MAMC values indicate. This relationship could be attributed to insulin resistance, often leading to a catabolic state, where the body's ability to build and maintain muscle mass and fat stores is impaired.

Limitations of the study:

It is important to note that conducting the study at a single center could introduce biases related to the specific practices, patient demographics, and socioeconomic factors unique to that center. This could potentially limit the external validity of the results, so caution is advised when interpreting the findings. The study was conducted with a relatively small sample size of 120 patients, which may limit the generalizability of the findings to the broader population of hemodialysis patients. The present study was conducted in a very short period.

Conclusion & Recommendation

A significant link exists between malnutrition and insulin resistance in patients undergoing maintenance hemodialysis. Insulin-resistant patients exhibited markedly higher malnutrition rates, as indicated by anthropometric measurements and SGA scores, than their non-insulin-resistant counterparts. The positive correlation between HOMA-IR and various nutritional indicators suggests that higher insulin resistance is associated with poorer nutritional status. These findings highlight the importance of addressing nutritional deficiencies in insulin-resistant hemodialysis patients to improve their overall health and quality of life. Further research is needed to develop targeted interventions for this population.

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Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

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