

## Original Research Article

# **Evaluation of Nutritional Status of Haemodialysis Patients Using Malnutrition Inflammation Score**

### **Abstract**

**Background:** One of the common problems of maintenance dialysis patients is malnutrition especially Protein-Energy Malnutrition (PEM) and several studies have revealed that PEM is associated with increased morbidity, mortality, and impaired quality of life. The aim of this work was to evaluate the nutritional status in hemodialysis patients using malnutrition inflammation score (MIS).

**Methods:** This cross-sectional study was carried out on 100 patients on regular hemodialysis. Patients were classified in to two groups according to MIS status; group A which were well nourished and group B which were malnourished. Patients included were subjected to; through history taking, laboratory investigations [CBC, Blood glucose level, Kidney function, Liver function tests, Lipid profile (cholesterol- triglycerides-HDL-LDL), Sodium-Potassium-phosphorus, C-reactive protein, ESR, Iron study (serum iron-serum ferritin-total iron binding capacity)], malnutrition-inflammation questionnaire and malnutrition-inflammation score.

**Results:** There was a statistically significant difference regarding blood hemoglobin, TIBC, creatinine, sodium, HDL, ESR, and CRP between two groups as they all decreased in group B more than group A, except CRP and ESR, creatinine and HDL they increased in group B more than group A (P value <0.05).

**Conclusions:** It is important to incorporate MIS in the care of hemodialysis patients for early detection of malnutrition and for medical nutrition therapy to optimize patients' nutritional status for better outcomes.

**Keywords:** Nutritional Status, Haemodialysis, Malnutrition, Inflammation Score.

## **Introduction:**

Chronic kidney disease (CKD) is a major public health problem, and its incidence and prevalence are increasing worldwide(1).

CKD is defined as irreversible deterioration of kidney function that may eventually lead to end-stage renal disease (ESRD) and require renal replacement therapy such as renal transplantation or haemodialysis (HD)(2).

One of the common problems of maintenance dialysis patients is malnutrition especially Protein-Energy Malnutrition (PEM) and several studies have revealed that PEM is associated with increased morbidity, mortality, and impaired quality of life(3), and reports have suggested a strong association between nutrition and clinical outcome in hemodialysis patients(4).

Various factors involved in the aetiology of PEM may include poor food intake (due to anorexia, nausea and vomiting due to uraemia), endocrine disorders, metabolic acidosis and increased energy expenditure(5).

Moreover, restricted diet, loss of amino acids during dialysis, infection, gastrointestinal disorders, and the use of certain drugs may lead to PEM(6).

Therefore, in patients with chronic kidney disease and ESRD, a regular evaluation of nutritional status is required during both pre-dialysis and dialysis stages in order to detect PEM and its causes as early as possible, to treat and to prevent its worsening and its complications(7).

To assess the nutritional status of dialysis patients in various ways, including anthropometric measurements (body weight and height, body mass index), biochemical parameters, performance evaluation and a comprehensive evaluation of diet or the Subjective Global Assessment method (SGA) is used(8).

(SGA) was originally developed to identify poor nutrition status in subjects undergoing gastrointestinal surgery, but has since been adapted for use in patients with CKD and ESRD(9).

It has been used to quantify the prevalence of malnutrition in hemodialysis patients(10).

Which will be discussed later. This study aims to evaluate the nutritional status in haemodialysis patients using malnutrition inflammation score (MIS).

## **Patients and Methods:**

This Cross sectional study conducted in nephrology unit –internal medicine department at Tanta University hospital and El mahalla General hospital.

This study will be carried out on 100 patients who are on regular dialysis.

Inclusion criteria:

- All patients will be regularly treated for 4 h, thrice weekly.
- HD sessions using bicarbonate dialysate.
- At least 8 weeks of initiation of dialysis in the past.
- Able to interview and communicate.

Exclusion criteria:

Refuse of the procedure patients.

History of severe emotional disorders such as schizophrenia.

Every case will be subjected to the following:

1. History taking.
2. Complete clinical examination.
3. Lab. Investigations including :
  - Complete blood culture.
  - Blood glucose level(fasting-postprandial).
  - Kidney function tests (urea- creatinine).

- Liver function tests (direct bilirubin-indirect bilirubin-total bilirubin-SGOT-SGPT).
  - Lipid profile(cholesterol- triglycerids-HDL-LDL).
  - Sodium-Potassium- phosphorus.
  - C-reactive Protein(CRP)
  - Erythrocyte Sedimentation Rate(ESR) .
  - Iron study (serum iron-serum ferritin-total iron binding capacity).
4. Malnutrition-inflammation questionnaire:
- The questionnaire include: The patient's name, age, sex, ethnicity, occupation.
  - The etiology of the disease: History of dialysis time (referring to the patient's medical records). Weight (dry weight that will be measured after session) and height (anthropometric measurements).(11)
5. Demographic data that its reliability and validity had been examined previously in many studies, was completed)(12.(
- Malnutrition-inflammation score. Inflammation score has 10 questions including subjective global assessment (SGA) 7 questions and 3 other items that is body mass index, serum albumin and iron saturation capacity (TIBC) .
1. Weight loss during the previous 6 months.
  2. Symptoms of gastro-intestinal tract, such as anorexia, nausea, vomiting, diarrhea.
  3. Food intake.
  4. Functional capacity (related to power failure).
  5. The history of dialysis.
  6. Loss of subcutaneous fat in the mid arm muscle area and arm muscle area of the lateral line of the body.
  7. Loss of subcutaneous fat of the muscles in the shoulder and quadriceps muscle of the thigh.

8. Body mass index in four state ( $\geq 20\text{Kg/m}^2$ ) ( $18-19.9\text{ Kg/m}^2$ ) ( $16-17.99\text{Kg/m}^2$ ) ( $<16\text{Kg/m}^2$ ).
9. Serum albumin, in the four-state ( $\geq 4\text{ g/dl}$ ) ( $3.9-3.5\text{ g/dl}$ ) ( $3.4-3\text{ g/dl}$ ) ( $<3\text{ g/dl}$ ).
10. TIBC in four state ( $\geq 250\text{ g/dl}$ ) ( $200-249\text{ g/dl}$ ) ( $199-150\text{ g/dl}$ ) ( $<150\text{g/dl}$ ).

So the 10 questions MIS score, each with four status from 0 to 4 Score 0 (normal) to 3 (severe). (12)

### Statistical analysis

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation and chi-square test by SPSS V.22.

-1 Mean value : the sum of all observations divided by the number of observation :  

$$\bar{x} = \frac{\sum x}{n}$$

Where  $\sum$  = sum &  $n$  = number of observations .

-2 Standard Deviation [SD] :

It measures the degree of scatter of individual varieties around their mean :

-3 Standard student "t test", test of significance of the difference between two means:

$t =$

The calculated "t" was compared with tabulated one at different levels of significance at the degree of freedom (DF):

$DF = (D + n2) - 2$  Where:

$\bar{x}_1$  = The mean value of group L

$\bar{x}_2$  = The mean value of group II.

$SD_1$  = The standard deviation of group I.

$SD_2$  = The standard deviation of group II.

$n_1$  = The number of observations of group L

$n_2$  = The number of observations of group II.

-4 Chi-square test of significance was used in order to compare proportions between qualitative parameters.

Chi-square test:

For comparison between two groups as regards qualitative data.

$\chi^2 =$

Where:

$\sum$  = Summation .

O = Observed value .

E = Expected value =

### Results:

This study conducted on 100 patient aged from (18-70) on regular hemodialysis during the period from between October 2019 and March 2020 who were divided by using malnutrition inflammation score for nutritional assessment in to two groups group A and group B.

**Group A** which were well nourished

**Group B** which were malnourished

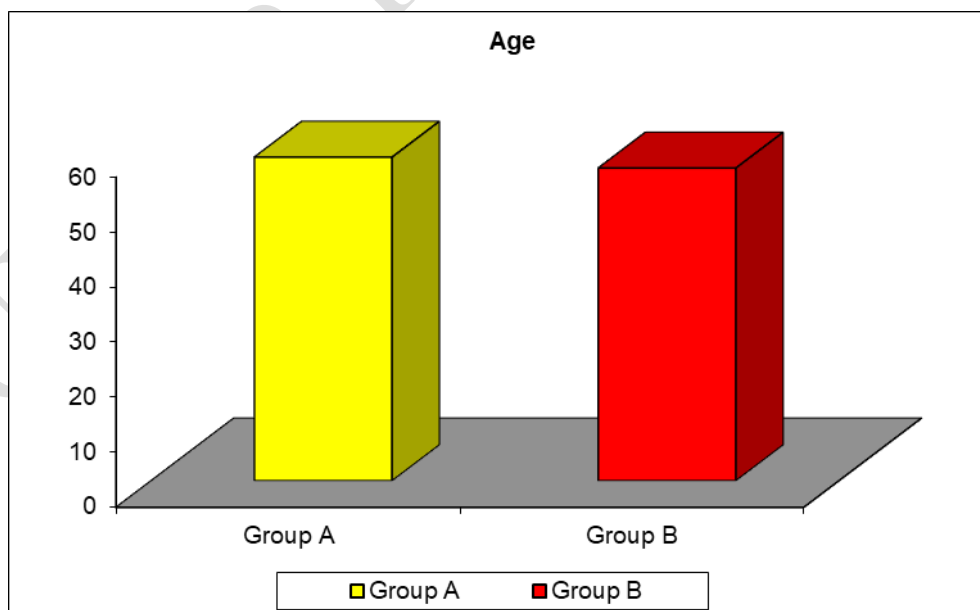
We compered between two groups by using demographic and anthropometric measurement data (age, sex, weight, height, body mass index).

Laboratory data (urea, creatinine, HB%, CRP, serum albumin, TIBC, serum ferretin, serum sodium, serum potassium, serum phosphate, ESR, direct bilirubin, indirect bilirubin, SGOT, SGPT, cholesterol, triglycerides, LDL, HDL).

**Table (1):** Comparison between group A and group B according to age

		Range			Mean	±	S. D	t. test	p. value
Age	Group A	23	–	70	58.77	±	8.67	0.937	0.335
	Group B	23	–	72	56.79	±	9.66		

**Table (1)** showed that; there was no statistically significant difference between two groups as regard age with p value 0.335



**Figure (1):** Comparison between group A and group B as regard age

**Table (2):** Comparison between group A and group B as regard sex

Sex		Group A	Group B	Total
Male	N	17	49	66
	%	56.7%	70.0%	66.0%
Female	N	13	21	34
	%	43.3%	30.0%	34.0%
Total	N	30	70	100
	%	100.0%	100.0%	100.0%
Chi-square	X <sup>2</sup>	1.664		
	P-value	0.197		

**Table 2** showed that; there was no statistically significant difference between two groups as regard to gender with p value 0.197

**Table (3):** Comparison between group A and group B as regard to weight,

		Range			Mean	±	S. D	t. test	p. value
Dry Weight	Group A	67	–	104	82.92	±	10.12	2.111	0.149
	Group B	46.5	–	142.5	78.20	±	16.46		

**Table 3** showed that; there was no statistically significant difference between two groups as regard to weight with p value 0.149

**Table (4):** Comparison between group A and group B as regard to height,

		Range			Mean	±	S. D	t. test	p. value
Height	Group A	1.5	–	1.8	1.65	±	0.10	1.872	0.174
	Group B	1.5	–	1.9	1.68	±	0.11		

**Table 4** showed that; there was no statistically significant difference between two groups as regard to weight with p value 0.174

**Table (5):** Comparison between group A and group B as regard to body mass index

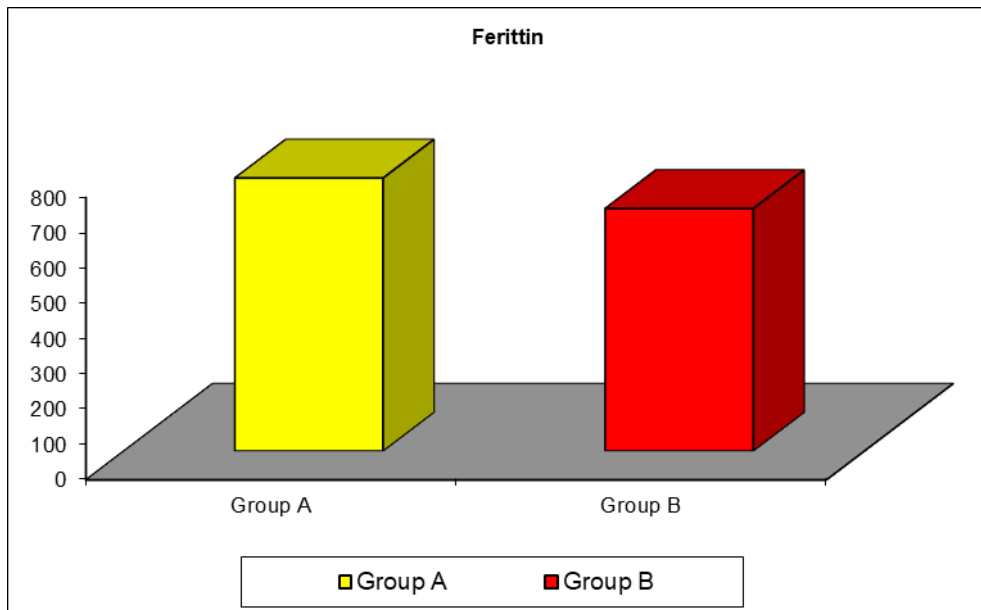
		Range			Mean	±	S. D	t. test	p. value
BMI	Group A	23.15	–	46.22	30.62	±	4.84	4.750	0.032*
	Group B	17.02	–	43.98	27.79	±	6.37		

**Table 5** showed that; there was statistically significant difference between two groups as regard to weight with p value 0.032

**Table (6):** Comparison between group A and group B as regard to S.ferittin

		Range			Mean	±	S. D	t. test	p. value
Ferittin	Group A	70	–	1510	773.37	±	410.42	0.420	0.519
	Group B	19	–	3235	687.02	±	677.62		

**Table 6** showed that; there was no statistically significant difference between two groups as regard to ferittin with p value 0.519

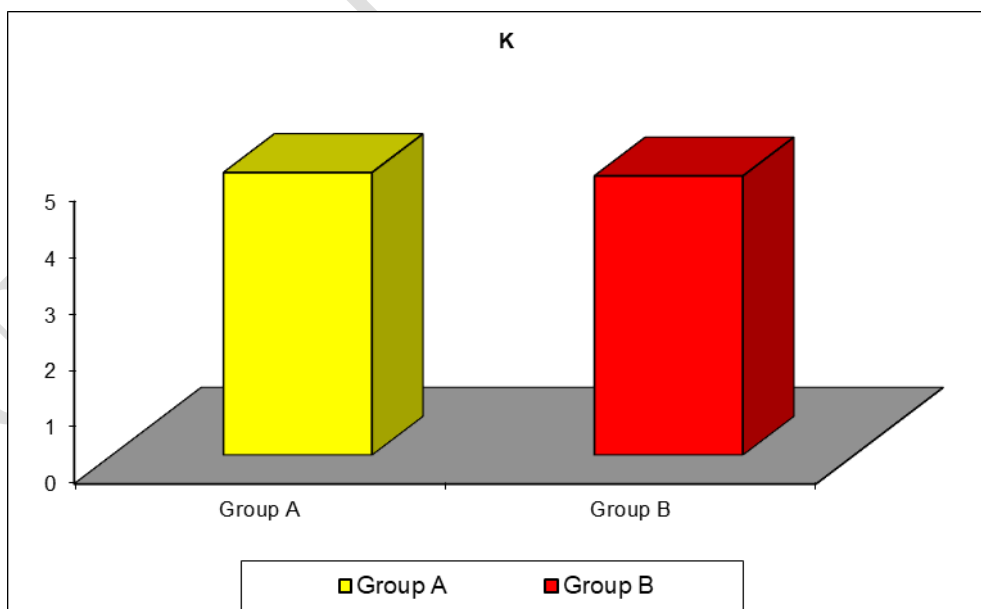


**Figure (2):** Comparison between group A and group B as regard to S. ferittin

**Table (7):** Comparison between group A and group B as regard to K

		Range			Mean	±	S. D	t. test	p. value
K	Group A	3.7	–	6.6	5.00	±	0.93	0.074	0.787
	Group B	3.1	–	8	4.94	±	0.98		

**Table 7** showed that; there was no statistically significant difference between two groups as regard to K with p value 0.787



**Figure (3):** Comparison between group A and group B as regard to K

**Table (8):** Comparison between group A and group B as regard to PO4

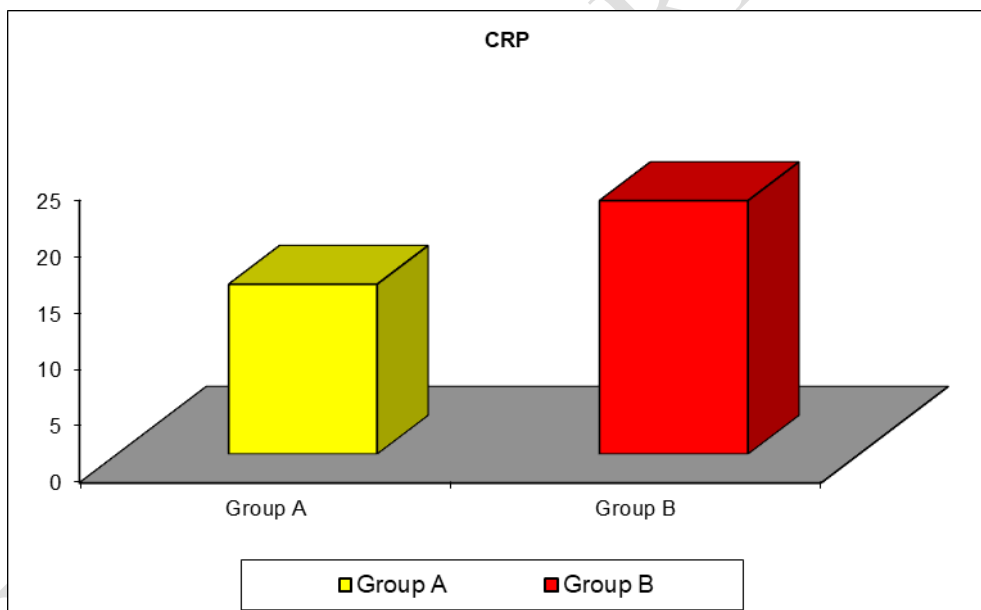
PO4	Group	Range			Mean	±	S. D	t. test	p. value
		Min	Max	Mean					
PO4	Group A	3.3	–	6.9	4.78	±	1.04	0.154	0.695
	Group B	2.6	–	7.8	4.70	±	0.96		

**Table 8** showed that; there was no statistically significant difference between two groups as regard to PO4 with p value 0.695

**Table (9):** Comparison between group A and group B as regard to CRP

CRP	Group	Range			Mean	±	S. D	t. test	p. value
		Min	Max	Mean					
CRP	Group A	3	–	48	15.03	±	10.77	5.761	0.018*
	Group B	3	–	64	22.43	±	15.31		

**Table 9** showed that; there was statistically significant difference between two groups as regard to CRP with p value 0.018



**Figure (4):** Comparison between group A and group B as regard to CRP

**Table (10):** Comparison between group A and group B as regard to ESR

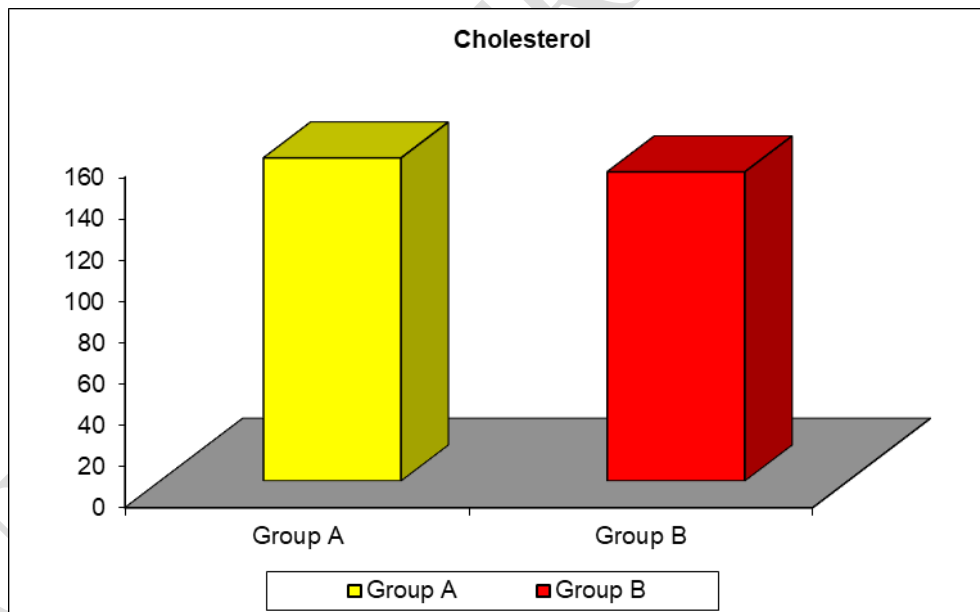
		Range			Mean	±	S. D	t. test	p. value
ESR 1	Group A	5	–	122	33.27	±	26.30	5.308	0.023*
	Group B	5	–	135	48.13	±	30.82		
ESR 2	Group A	10	–	135	59.23	±	33.04	6.985	0.010*
	Group B	10	–	140	78.61	±	33.84		

**Table 10** showed that; there was statistically significant difference between two groups as regard to ESR 1 with p value 0.023 and ESR 2 with p value 0.010

**Table (11):** Comparison between group A and group B as regard to Cholesterol

		Range			Mean	±	S. D	t. test	p. value
Cholesterol	Group A	99	–	200	156.27	±	28.58	1.195	0.277
	Group B	95	–	220	149.53	±	28.10		

**Table 11** showed that; there was no statistically significant difference between two groups as regard to Cholesterol with p value 0.277



**Figure (5):** Comparison between group A and group B as regard to Cholesterol

**Table (12):** Comparison between group A and group B as regard to liver function (SGOT,SGPT,DB,IDB)

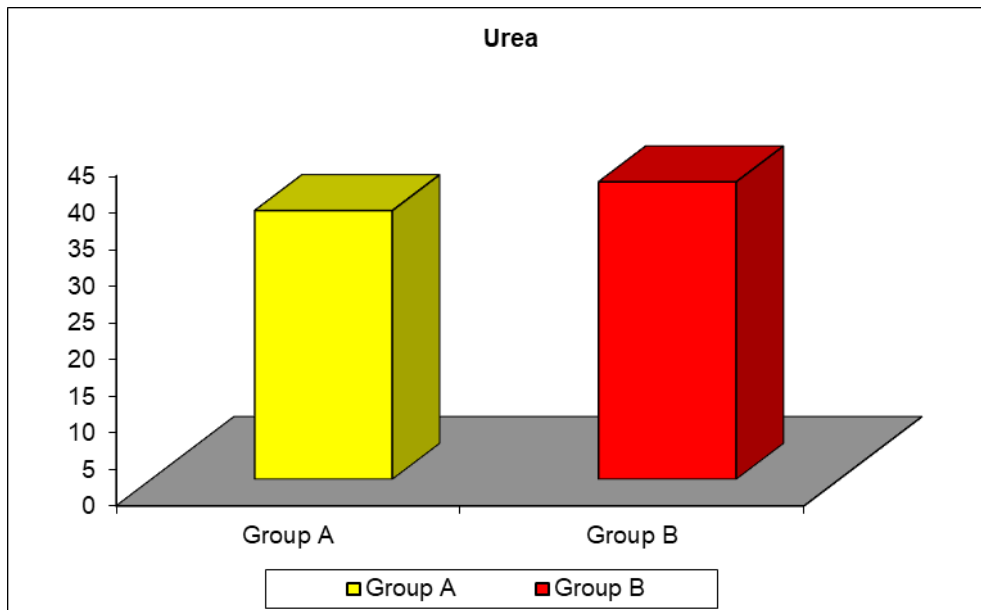
		Range			Mean	±	S. D	t. test	p. value
SGOT	Group A	7	–	90	20.73	±	16.50	0.034	0.854
	Group B	6	–	93	20.09	±	15.86		
SGPT	Group A	11	–	179	26.73	±	32.34	0.028	0.868
	Group B	11	–	181	25.53	±	33.38		
Direct bilirubin	Group A	0.1	–	0.2	0.15	±	0.05	0.918	0.340
	Group B	0.1	–	0.2	0.14	±	0.05		
Indirect bilirubin	Group A	0.8	–	0.9	0.85	±	0.05	0.047	0.829
	Group B	0.8	–	0.9	0.86	±	0.05		

**Table 12** showed that; there was no statistically significant difference between two groups as regard to SGOT with p value 0.854; SGPT with p value 0.868 ; DB with p value 0.340 and IDB with p value 0.829

**Table (13):** Comparison between group A and group B as regard to urea

		Range			Mean	±	S. D	t. test	p. value
Urea	Group A	15	–	63	36.60	±	11.79	1.040	0.310
	Group B	15	–	100	40.51	±	19.52		

**Table 13** showed that; there was no statistically significant difference between two groups as regard to urea with p value 0.310

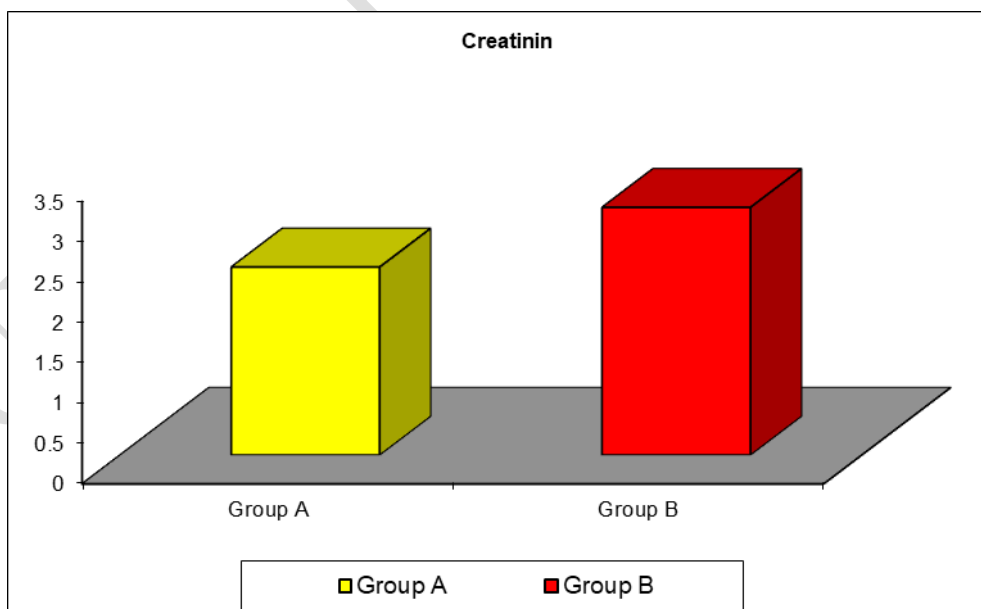


**Figure (6):** Comparison between group A and group B as regard to urea

**Table (14):** Comparison between group A and group B as regard to Creatinin

		Range			Mean	±	S. D	t. test	p. value
Creatinin	Group A	1	-	4.9	2.33	±	1.08	7.388	0.008*
	Group B	1.4	-	7.3	3.07	±	1.31		

**Table 14** showed that; there was statistically significant difference between two groups as regard to Creatinin with p value 0.008

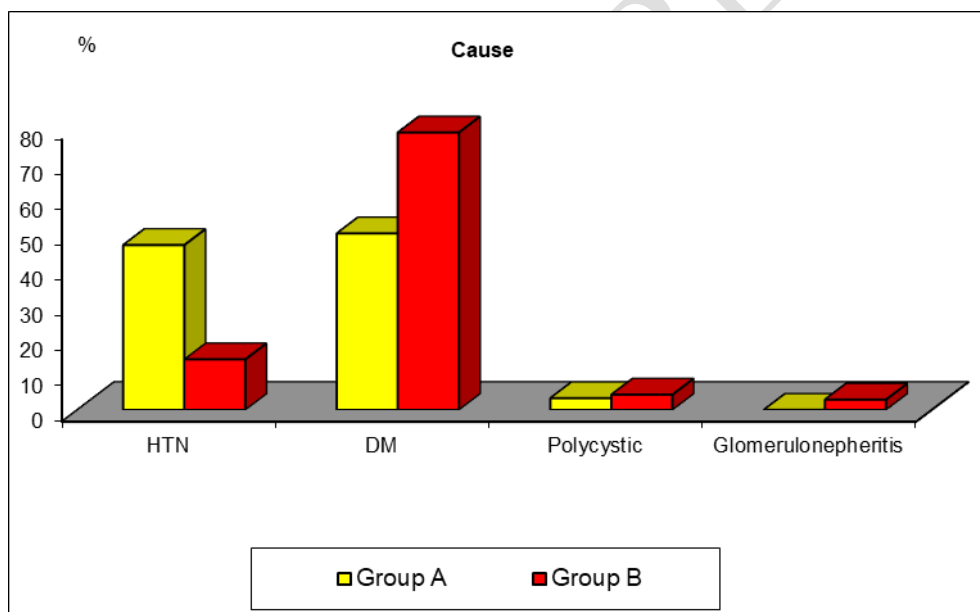


**Figure (7):** Comparison between group A and group B as regard to Creatinin

**Table (15):** Comparison between group A and group B as regard to cause of renal failure

Cause		Group A	Group B	Total
HTN	N	14	10	24
	%	46.7%	14.3%	24.0%
DM	N	15	55	70
	%	50.0%	78.6%	70.0%
Polycystic	N	1	3	4
	%	3.3%	4.3%	4.0%
Glomerulonephritis	N	0	2	2
	%	.0%	2.9%	2.0%
Total	N	30	70	100
	%	100.0%	100.0%	100.0%
Chi-square	X <sup>2</sup>	12.528		
	P-value	0.001*		

Table 15 showed that; there was high statistically significant difference between two groups as regard to cause of renal failure with p value 0.001



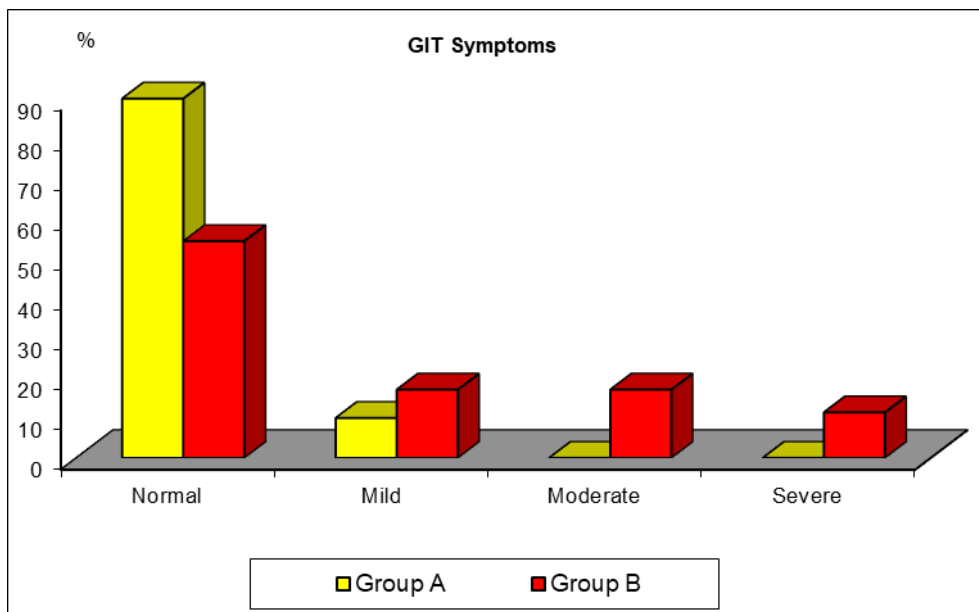
**Figure (8):** Comparison between group A and group B as regard to cause of renal failure

**Table (16):** Comparison between group A and group B as regard to GIT symptoms

GIT Symptoms		Group A	Group B	Total
Normal	N	27	38	65
	%	90.0%	54.3%	65.0%
Mild	N	3	12	15
	%	10.0%	17.1%	15.0%
Moderate	N	0	12	12
	%	.0%	17.1%	12.0%
Severe	N	0	8	8

	%	.0%	11.4%	8.0%
<b>Total</b>	<b>N</b>	30	70	100
	<b>%</b>	100.0%	100.0%	100.0%
<b>Chi-square</b>	<b>X<sup>2</sup></b>	<b>13.407</b>		
	<b>P-value</b>	<b>0.004*</b>		

**Table 16** showed that; there was high statistically significant difference between two groups as regard to GIT symptoms with p value 0.004

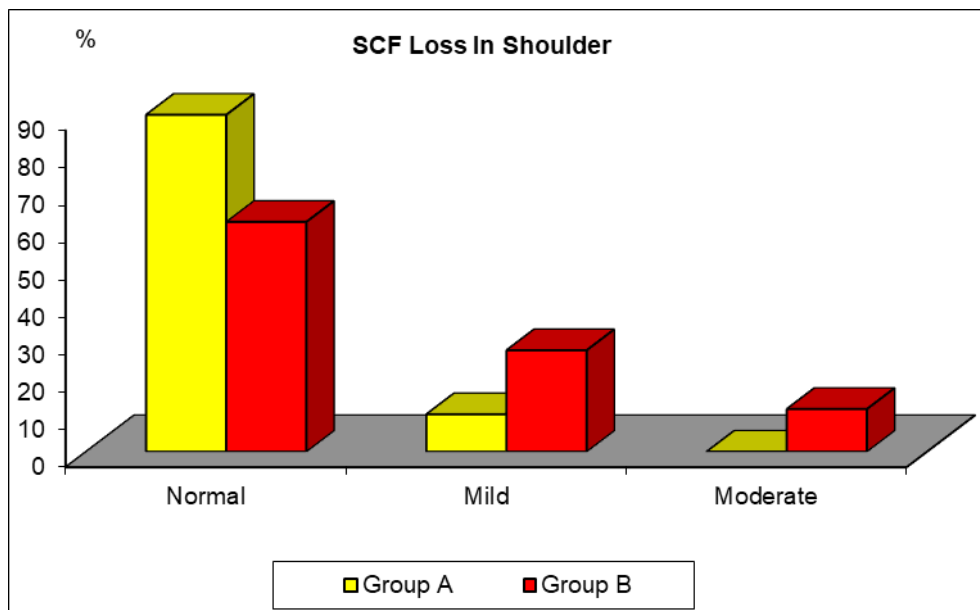


**Figure (9):** Comparison between group A and group B as regard to GIT symptoms

**Table (17):** Comparison between group A and group B as regard to subcutaneous fat loss in shoulder region

SCF Loss In Shoulder		Group A	Group B	Total
<b>Normal</b>	<b>N</b>	27	43	70
	<b>%</b>	90.0%	61.4%	70.0%
<b>Mild</b>	<b>N</b>	3	19	22
	<b>%</b>	10.0%	27.1%	22.0%
<b>Moderate</b>	<b>N</b>	0	8	8
	<b>%</b>	.0%	11.4%	8.0%
<b>Total</b>	<b>N</b>	30	70	100
	<b>%</b>	100.0%	100.0%	100.0%
<b>Chi-square</b>	<b>X<sup>2</sup></b>	<b>8.683</b>		
	<b>P-value</b>	<b>0.013*</b>		

**Table 17** showed that; there was statistically significant difference between two groups as regard to subcutaneous fat loss in shoulder region with p value 0.013



**Figure (10):** Comparison between group A and group B as regard to subcutaneous fat loss in shoulder region

## Discussion

Chronic kidney disease is a major public health issue, with a rising incidence and prevalence (13).

End-stage renal disease (ESRD) has a reported annual prevalence of 34 to 200 per million people worldwide, with an even higher proportion of individuals in the early stages of chronic kidney disease experiencing adverse outcomes such as kidney failure, cardiovascular disease, and premature mortality (14).

Malnutrition is frequent among ESRD patients. Inadequate nutritional intake is mostly attributed to uremia secondary to inadequate dialysis, which is regarded the single most common cause of malnutrition in dialysis patients. In maintenance hemodialysis patients, low protein and calorie intake is common (15). Several investigations found that supplementation of protein and energy improved outcome, such as reduction of mortality and hospitalization in malnourished patients with maintenance hemodialysis (16).

Malnutrition is linked to a longer recovery time, increased hospitalisation, infection susceptibility, mortality, and morbidity. Persistent diseases are frequently linked to chronic functional impairment and have a negative impact on one's quality of life (17)

One of the elements affecting one's quality of life is malnutrition. Early intervention improves the quality of life and lowers mortality in malnourished patients(18).The malnutrition-inflammation scale (MIS) score, developed by Kalantar-Zadeh et al., is a quantitative score that assesses nutritional status and severity (18). The MIS was found to be superior to conventional predictors such as serum levels of C-reactive protein (CRP) as well as to other scales used to assess malnutrition among HD patients such as subjective global assessment (19).

This study conducted on 100 patients on regular hemodialysis during the period from between October 2019 and March 2020 who were divided by using malnutrition inflammation score for nutritional assessment in to two groups group A (Well-nourished) and group B (malnourished).

In the current study, the incidence of malnutrition was 70%. This came in accordance with two studies from India. Janardhan et al. reported malnutrition in 91% and Tapiwala et al. in 68% in small cohorts of 66 and 28 HD patients, respectively (20).

These results were similar to the prevalence reported by similar study among HD patients in Egypt (Assuit city) which revealed about 85% malnourished patients (81.6% mild to moderate malnutrition and 3.6% severe malnutrition) (21).

In another study conducted in Cairo, Egypt, Zaki and his colleagues showed that the prevalence of malnutrition among HD patients (n=100) was 67% (50% were mild to moderate malnourished and 17% were severe malnourished) (22).

In comparison to the capital city, the south Egypt area has a lesser educational level, socioeconomic status, and health care facilities. However, our findings were similar to those

of another study in Jordan, which found a 61.8 percent malnutrition incidence among 178 patients undergoing HD treatment (23). According to SGA, 57 percent of HD patients were malnourished (49 percent were undernourished, and 18 percent were severely malnourished) in a research conducted in Saudi Arabia in 2018. (24).

These disparities in prevalence could be related to variances in environmental conditions and dietary habits in different parts of the Middle East. In other studies, moderate incidence of malnutrition was reported in other studies. Todd et al. reported 35% and 25% prevalence in Aboriginal and non-Aboriginal Australian HD patients, who had acceptable parameters of dialysis adequacy, respectively (25). Mazairac et al. in a multicenter study from the Netherlands reported malnutrition prevalence of 23% in large cohort of 560 patients (26).

This difference is probably due to several factors such as different sample size and the differences of adequate dialysis delivery.

Hemodialysis patients commonly have poor dietary habits, particularly with regard to the intake of foods with high concentrations of sugar and fats, and low levels of consumption of cereals, fruits and vegetables, an observation that is consistent with the findings of this study. Shortcomings in the intake of calories, proteins, saturated fats, cholesterol, vitamins and minerals, among other food components, are also found by other researchers (26), as was the case of the current study results.

**This finding was consistent with a cross-sectional study on malnutrition prediction using SGA-DMS, which found that the majority of patients (91%) were mild to moderately malnourished, and that there were no significant differences in malnutrition scores between men and women because both men and women had an equal tendency to malnutrition**

**(27)Conclusions:**

It is important to incorporate MIS in the care of hemodialysis patients for early detection of malnutrition and for medical nutrition therapy to optimize patients' nutritional status for better outcomes..

#### **Ethical Approval:**

As per international standard or university standard ethical approval has been collected and preserved by the authors.

#### **References:**

1. **Abd Elsalam WY, Mohammed EM, Safwat HI. Clomiphene citrate ‘stair-step’ protocol vs. traditional protocol in patients with polycystic ovary syndrome: a randomized controlled trial. J New York Scie. 2017 Jan ; 10 (1) :113-119**
2. **Abd-Elfattah AH, Hashish MA, Elomda FA , Megahed HI. Effect of Adding L-Carnitine to Clomiphene Resistant PCOs Women on the Ovulation and the Pregnancy Rate .The Egy J Hos Med. July 2019; 76 (5): 4138-4143 .**
3. **Abduljabbar HS.O., Hagrass M, Magadmy R. Effect of Aromatase Inhibitors versus Clomiphene Citrate for Ovulation Induction in Infertile Women with Ovulatory Dysfunction (PCO). In: Wang Z. Polycystic ovarian syndrome: 1st ed. London, PA: Intechopen limited; 2020: chapter3.**
4. **Abid KM, Hassan SI, Gousia S. Cutaneous manifestations of polycystic ovary syndrome: A cross-sectional clinical study. J Indian Dermatology Online. 2017 Mar; 8(2): 104-110.**
5. **Agrawal K, Gainer S, Dhaliwal L K , Suri V. Ovulation induction using clomiphene citrate using stair–Step regimen versus traditional regimen in polycystic**

ovary syndrome women—A randomized control trial. *Journal of human reproductive sciences*. 2017; 10(4): 261- 264.

6. Ali AAH, Khalaf SF, Farahat MM. Clomiphene Citrate and Metformin" Stair Step" Protocol Vs. Traditional Protocol in Patients with Polycystic Ovary Syndrome "PCOS". *The Egyptian Journal of Hospital Medicine*. 2018 Jul ; 72 (5): 4463-4468

7. Alsadi B, Zhengchao W: Clinical features of PCO. In:Polycystic ovarian syndrome. First edition.London,

8. Amer SA, Smith J, Mahran A, Fox P, Fakis A. Double-blind randomized controlled trial of letrozole versus clomiphene citrate in subfertile women with polycystic ovarian syndrome. *Hum Reprod*. 2017; 32(8):1631–1638.

9. American College of Obstetricians and Gynecologists ACOG (2019): Clinical management guidelines for obstetrician gynecologists number 768, December 2019. Screening and management of the hyperandrogenic adolescent. *Obstet Gynecol*, 134:106–14.

10. American College of Obstetricians and Gynecologists, ACOG Practice Bulletin (2002): Clinical management guidelines for obstetrician gynecologists number 34, February 2002. Management of infertility caused by ovulatory dysfunction. American College of Obstetricians and Gynecologists, *Obstet Gynecol*, 99:347–358.

11. American Society for Reproductive Medicine. Use of clomiphene citrate in infertile women: a committee opinion.*Fertil Steril*. 2013; 100 (2): 341-8.

12. Anitua E, Pino A, Martinez N, Orive G, Berridi D. The Effect of Plasma Rich in Growth Factors on Pattern Hair Loss: A Pilot Study. *Dermatol Surg*. 2017; 43(5):658-70.

13. Antonio L, Pauwels S, Laurent MR, Vanschoubroeck D, Jans I, Billen J, Claessens F, Decallonne B, De Neubourg D, Vermeersch P, Vanderschueren D. Free

**Testosterone Reflects Metabolic as well as Ovarian Disturbances in Subfertile Oligomenorrheic Women. Int J Endocrinol. 2018 Sep 10; 2018:7956951.**

**14. Arain F, Arif N, Halepota H. Frequency and outcome of treatment in polycystic ovaries related infertility. Pak J Med Sci. 2015; 31(3):694-699. doi:10.12669/pjms.313.8003**

**15. Ashraf S., Nabi M., Rasool S.u.A. et al. Hyperandrogenism in polycystic ovarian syndrome and role of CYP gene variants: a review. Egypt J Med Hum Genet. 2019 Nov.25.**

**16. Aswini R, Jayapalan S. Modified Ferriman-Gallwey Score in Hirsutism and its Association with Metabolic Syndrome. Int J Trichology. 2017; 9(1):7–13.**

**17. Azziz R, Kintziger K, Li R, et al. Recommendations for epidemiologic and phenotypic research in polycystic ovary syndrome: an androgen excess and PCOS society resource. Hum Reprod. 2019; 34(11):2254- 2265.**

**18. Bachanek M, Abdalla N, Cendrowski K, Sawicki W. Value of ultrasonography in the diagnosis of polycystic ovary syndrome - literature review. J Ultrason. 2015 Dec; 15(63):410-22.**

**19. Bani MM, Majdi SA. Polycystic Ovary Syndrome (PCOS), Diagnostic Criteria, and AMH. Asian Pac J Cancer Prev. 2017; 18(1):17–21. Published 2017 Jan 1.**

**20. BarBarbaric J, Abbott R, Posadzki P, Car M, Gunn LH, Layton AM,et al. Light therapies for acne: abridged Cochrane systemic review including GRADE assessments. Br J Dermatol.2018; 178(1):61-75.**

**21. Barber TM, Hanson P, Weickert MO, Franks S. Obesity and Polycystic Ovary Syndrome: Implications for Pathogenesis and Novel Management Strategies. Clin Med Insights Reprod Health. 2019; 13:1179558119874042. Published 2019 Sep 9.**

22. Baum C, Andino K, Wittbrodt E, Stewart S, Szymanski K, Turpin R. The Challenges and Opportunities Associated with Reimbursement for Obesity Pharmacotherapy in the USA. *Pharmacoeconomics*. 2015; 33(7):643–653.
23. Bellver J, Rodríguez-Tabernero L, Robles A, Muñoz E, Martínez F, Landeras J, García-Velasco J, Fontes J, Álvarez M, Álvarez C, Acevedo B; Group of interest in Reproductive Endocrinology (GIER) of the Spanish Fertility Society (SEF). Polycystic ovary syndrome throughout a woman's life. *J Assist Reprod Genet*. 2018 Jan; 35(1):25-39.
24. Blackshaw LCD, Chhour I, Stepto NK, Lim SS. Barriers and Facilitators to the Implementation of Evidence-Based Lifestyle Management in Polycystic Ovary Syndrome: A Narrative Review. *Med Sci (Basel)*. 2019 Jun 27; 7(7):76.
25. Brown J, Farquhar C. Clomiphene and other antioestrogens for ovulation induction in polycystic ovarian syndrome. *Cochrane Database Syst Rev*. 2016 Dec 15;12(12):CD002249.
26. Budinetz TH, Benadiva CA, Griffin DW, Engmann LL, Nulsen JC, DiLuigi AJ. Ovulation rate and cycle characteristics in a subsequent clomiphene citrate cycle after stair-step protocol. *Fertil Steril*. 2015;103(3):675-679.
27. Butterworth J, Deguara J, Borg CM. Bariatric Surgery, Polycystic Ovary Syndrome, and Infertility. *J Obes*. 2016; 2016:1871594.