INSULIN LIKE GROWTH FACTOR 1 (IGF-1) AS ASSESSMENT TOOL FOR PROTEIN ENERGY WASTING IN DIFFERENT DIALYSIS MODALITIES

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INTRODUCTION

Protein-energy wasting (PEW) is a term refers to multiple nutritional & catabolic alterations that occur in chronic kidney disease; risk factors for its development include undernutrition, acidosis, inflammation, & dialysis procedure itself [1]. Malnutrition in end stage renal disease (ESRD) patients adversely affects morbidity, mortality, functional activity, & patients' quality of life [2].

Proper Nutritional assessment requires interpretation of a combination of clinical and biochemical parameters [3]. Clinical assessment of the nutritional status of chronic kidney disease (CKD) patients can be performed using of several scoring tools including Subjective Global Assessment (SGA), Malnutrition Inflammation Score (MIS), Geriatric Nutritional Risk Index (GNRI), and PEW diagnostic criteria [4]. Serum levels of albumin, prealbumin, total protein, creatinine, cholesterol, transferrin, and insulin-like growth factor-1 (IGF-1) are commonly used biochemical surrogate markers. Serum albumin level is a valid & clinically useful measure of protein-energy nutritional status in dialysis patients, and stabilized serum albumin is a measure of visceral protein pool size [5]. IGF-1 was suggested to be a good indicator that may reflect the initiation of a malnutritional state in patients with ESRD [6].

This study aimed to assess the use of serum Insulin like growth factor-1 (IGF-1) level as a laboratory marker of the nutritional status among dialysis patients in comparison to other malnutrition and inflammatory markers.

MATERIALS & METHODS

This study was conducted at Department of Nephrology, King Abdul-Aziz Specialist Hospital (Taif, Saudi Arabia). It included 60 ESRD patients between 18-60 years old stable on regular dialysis for >6 months, & they were categorized according to type of dialysis into 3 groups. Group 1 included 20 ESRD patients maintained on hemodialysis (HD) using high-flux dialyzers (HFHD), Group 2 included 20 ESRD patients maintained on HD using low-flux dialyzers (LFHD), Group 3 included 20 ESRD patients maintained on continuous ambulatory peritoneal dialysis (CAPD). Patients with history of malignancy, diabetes mellitus, active infections, and/or sepsis were excluded from the study; as well as patients undergoing dialysis through HD catheter or arteriovenous graft.

After approval of the study protocol by the Local Ethical Committee, patients gave written fully informed consent for study participation. Clinical assessment for patients was performed by history taking, clinical examination, body mass index (BMI) & Mid-arm circumference (MAC) [7].

Hemodialysis adequacy was determined using urea reduction ration (URR), single pool Kt/V (spKt/V), while peritoneal dialysis adequacy was determined using on Kt/V (pKt/V).

Subjective Global Assessment tool (SGA) was used for as an assessment for nutritional state in addition to serum albumin and anthropometric measures [8-10]. Score from 7-14 was categorized as well nourished, score from 15-35 was categorized as mild to moderate malnourished, and score 36-49 was categorized as severely malnourished.

Laboratory investigations included estimation serum creatinine, serum urea, serum albumin, estimation of serum high-sensitivity C-reactive protein (hsCRP) using ELISA Kit, estimation of IGF-1 in fasting venous blood sample using a two-site immunoradiometric assay (IRMA).

RESULTS

The studied groups were homogenous as regards age, gender, etiology of ESRD, duration of dialysis, height, and etiology of ESRD.

Comparison of dry weight & BMI among studied groups showed significant difference between HFHD and LFHD groups compared to CAPD group with non-significant difference between HFHD and LFHD groups. Furthermore, MAC showed significant difference between CAPD and HFHD groups, with no difference between LFHD and either CAPD or HFHD group. Additionally, Comparing BMI category among studied groups showed higher prevalence of overweight patients among HFHD (75%) than LFHD (50%) and CAPD (10%).

Furthermore, serum hsCRP levels showed significantly difference between the three studied groups, with the highest level in CAPD patients (23.2±6.08 mg/L) followed by HFHD patients (15.87±3.44 mg/L) then LFHD patients (10.11±1.55 mg/L). In addition, serum albumin showed significantly difference between the three studied groups, but it exhibits different pattern than hsCRP with the lowest in CAPD patients (2.89±0.24mg/L) followed by LFHD patients (3.21±0.20 mg/L) then HFHD (3.49±0.27 mg/L) patients.

Total SGA score was significantly higher in CAPD patients (24.3±6.14) compared to both HD groups, with no significant difference between LFHD patient (20.3±6.18) & HFHD patients (18.4±6.43). On the other hand, there was no statistical significant difference between the three groups as regard nutritional state based upon SGA score as percentage of malnutrition was 70% in HFHD patients, 75%in LFHD patients, and 85% in CAPD patients.

Serum IGF-1 showed significant difference between groups, as it was significantly high in HFHD patients (156.4±19.12 ng/ml) in comparison to CAPD patients (124.27±29.86 ng/ml) and LFHD patients (134.9±22.37 ng/ml), with no significant difference between CAPD and LFHD.

Serum levels of IGF-1 were significantly negatively correlated with age among all groups as well as all patients group together (r value = -0.548). On the other hand, it has positive significant correlation with serum albumin (r value = 0.415) in all patients grouped together despite having non-significant correlation in each group alone. Additionally, serum IGF-1 level did not show any significant correlation with BMI, MAC, serum urea, serum creatinine, hsCRP, or total SGA score.

These findings were confirmed when performing multivariate regression analysis testing IGF as dependent variable in the whole patients' population that showed negative significant standardized coefficient with age, but positive with serum albumin levels.

Comparison of studied parameters among 3 groups

		Group 1 (HFHD)	Group 2 (LFHD)	Group 3 (CAPD)	Sig
		52.40±5.96	51.95±7.30	51.90±5.66	0.963
Gender	Male	14 (70.0%)	13 (65.0%)	13 (65.0%)	0.928
	Female	6 (30.0%)	7 (35.0%)	7 (35.0%)	
Etiology of ESRD	Hypertension	12 (60.0%)	13 (65.0%)	10 (50.0%)	0.952
	Chronic GN	3 (15.0%)	2 (10.0%)	3 (15.0%)	
	Lupus nephritis	1 (5.0%)	3 (15.0%)	4 (20.0%)	
	ADPKD	2 (10.0%)	1 (5.0%)	1 (5.0%)	
	Analgesic nephropathy	1 (5.0%)	0 (0.0%)	1 (5.0%)	
	Unknown	1 (5.0%)	1 (5.0%)	1 (5.0%)	
Dialysis Duration [month]		22.00±4.84	23.70±6.85	22.70±7.23	0.701
Dry weight [Kg]		74.30±6.07	71.30±5.17	65.90±4.42	**0.000***
Height [cm]		171.70±2.89	170.45±2.63	171.30±3.34	0.402
BMI (Kg/m²)		25.21±2.10	24.57±2.12	22.50±1.95	**0.000***
BMI category	Normal	5 (25.0%)	10 (50.0%)	18 (90.0%)	0.000
	Over-weight	15 (75.0%)	10 (50.0%)	2 (10.0%)	
MAC [mm]		254.90±15.49	248.50±15.74	240.40±16.73	**0.021#**
S. Urea (Pre-dialysis) [mg/dl]		209.60±24.26	204.50±37.45	205.60±27.05	0.854
URR (%)		65.24±4.53	64.43±5.27		0.605
spKt/V		1.15±.20	1.11±0.14		0.443
pKt/V				1.95±0.11	
S. Creatinine [mg/dl]		7.36±1.96	7.52±1.51	7.44±1.66	0.958
S. Albumin [mg/dl]		3.49±0.27	3.21±0.20	2.89±0.24	**0.000****
IGF-1 [ng/ml]		156.40±19.12	134.90±22.37	124.27±29.86	**0.000†**
hsCRP (mg/L)		15.87±3.44	10.11±1.55	23.20±6.08	**0.000****
Total SGA score		18.40±6.43	20.30±6.18	24.30±6.14	**0.014***
SGA category	Well nourished (7-14)	6 (30%)	5 (25%)	3 (15%)	0.521
	Mild to Moderate Malnourished (15-35)	14 (70%)	15 (75%)	17 (85%)	
	Severely Malnourished (36-49)	0 (0%)	0 (0%)	0 (0%)	

** LSD post-hoc test showed significant difference between all groups.

* LSD post-hoc test showed significant difference between group 3 and both group 1 & 2, with non-significant difference between group 1&2.

LSD post-hoc test showed significant difference between group 1 and group 3, with non-significant difference between group 2 and both group 1& 3.

† LSD post-hoc test showed significant difference between group 1 and both group 2 & 3, with non-significant difference between group 2 & 3.

Comparison of different nutritional assessment tools

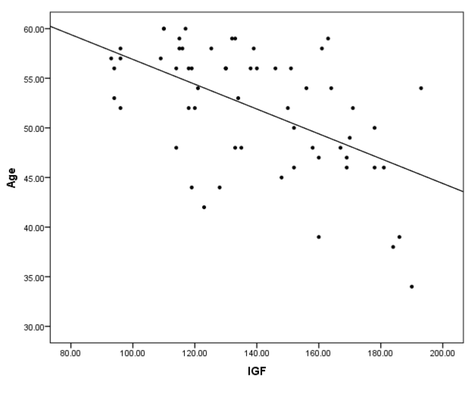
		MAC [mm]	S. Albumin [mg/dl]	IGF-1 [ng/ml]	Total SGA score
Gender	Male	278.78±16.87	3.21±0.34	140.58±27.46	21.53±6.56
	Female	246.25±17.03	3.17±0.35	134.40±27.33	19.95±6.79
	Sig	0.588	0.670	0.414	0.390
BMI category	Normal	243.52±14.91	3.08±0.32	131.75±29.31	22.52±6.42
	Over-weight	253.33±17.70	3.34±0.31	146.81±22.57	19.15±6.51
	Sig	**0.023**	**0.002**	**0.032**	**0.049**
SGA category	Well nourished	249.57±18.30	3.30±0.38	146.93±20.54	
	Mild to Moderate Malnourished	247.43±16.53	3.17±0.32	135.96±28.80	
	Sig	0.681	0.195	0.191	

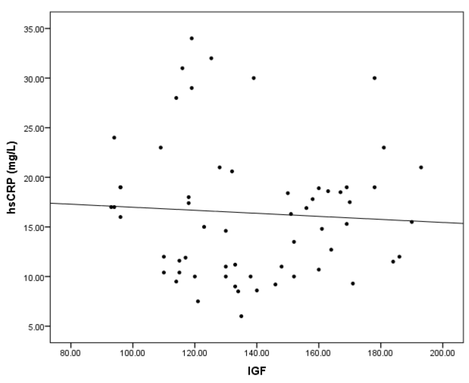
Correlation between IGF-1 and different study parameters

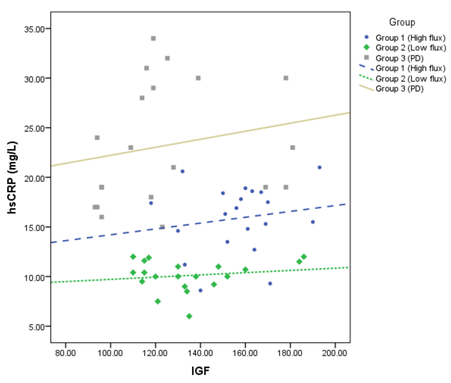
	IGF-1 (ng/ml)			
	Group 1 (HFHD)	Group 2 (LFHD)	Group 3 (CAPD)	All patients
Age	**-0.594***	**-0.889***	**-0.512***	**-0.548***
Dialysis duration	0.292	-0.126	0.041	-0.001
Dry weight	-0.030	-0.073	0.034	0.245
Height	0.044	0.039	-0.310	-0.061
BMI	-0.037	-0.075	0.171	0.242
MAC	-0.229	0.077	0.137	0.189
S. Urea (Pre-dialysis)	0.336	0.140	-0.150	0.092
URR	0.426	0.183		
spKt/V	0.248	0.088		
pKt/V			-0.164	
S. Creatinine	-0.152	0.097	-0.250	-0.116
S. Albumin	-0.182	0.270	0.227	**0.415***
hsCRP	0.164	0.163	-0.264	-0.062
Total SGA score	0.432	0.159	-0.264	-0.123

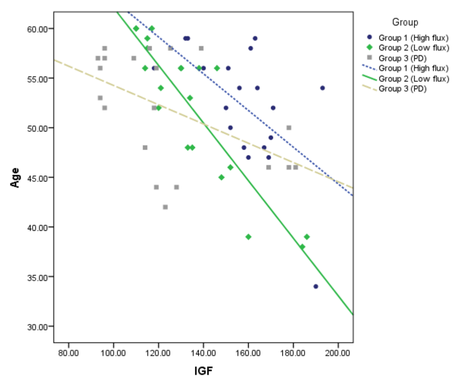
Regression analysis of studied parameters versus serum IGF as dependent variable

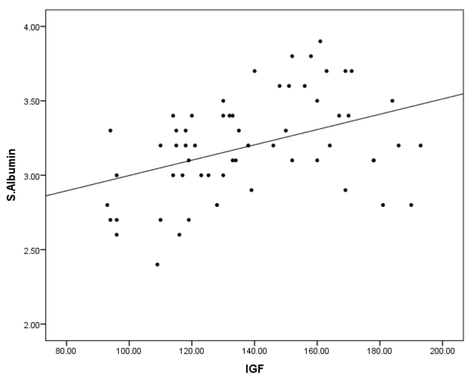
	Unstandardized Coefficients	Standardized Coefficients	Sig.
	B	Beta	
(Constant)	111.421		0.093
Age	-2.334	-0.533	**0.000**
Dialysis Duration	-0.213	-0.049	0.658
Dry weight	0.183	0.042	0.891
BMI	0.599	0.051	0.864
MAC	0.116	0.072	0.559
S. Urea (Pre-dialysis)	-9.675E-06	0.000	1.000
S. Creatinine	-0.123	-0.008	0.949
S. Albumin	29.540	0.366	0.012
hsCRP	0.541	0.134	0.266
Total SGA score	-0.243	-0.059	0.693

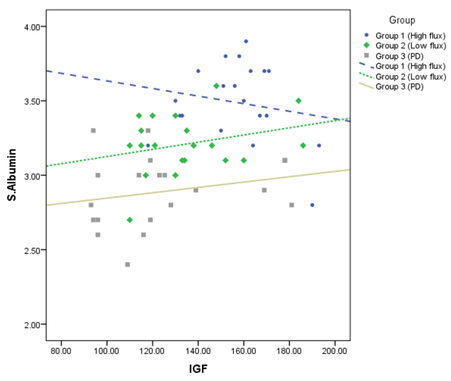


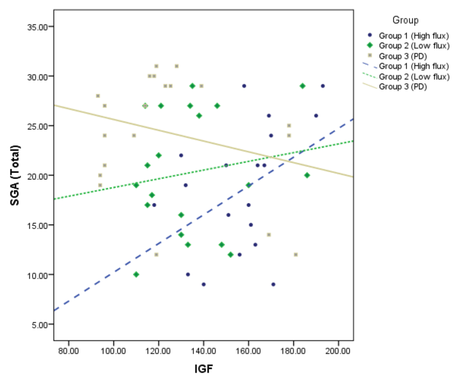


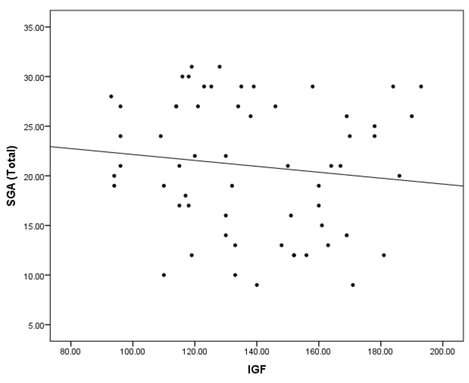












CONCLUSIONS

IGF-1 can be used as additional valuable marker in assessment of nutritional state in dialysis patients along with other nutritional & inflammatory markers.

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