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Potential Role of Serum Neutrophil Gelatinase-Associated Lipocalin and Legume Based Dietary Therapy in Alleviation of Obesity-Associated Metabolic and Renal Disorders

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Abstract

Background: Lipocalin-2 (LCN-2) or Neutrophil Gelatinase Associated Lipocan (NGAL) is a biomarker for acute, chronic renal damage, and metabolic diseases. **Aim:** to evaluate the relation of serum NGAL with glycolipid metabolism and the inflammatory status among a sample of obese Egyptian women, and to study it as a sensitive biomarker to predict early changes in renal functions. Assess the role of specific dietary therapy in improving such conditions. **Methods**. The dietary therapy intervention study ran for 8 weeks and was divided into 2 sessions, 57 obese women with varying degrees of obesity and associated comorbidities took part as volunteers, their mean age and BMI were 50.84±1.48 ys, 34.99±0.64 kg/m^2. Patients were monitored clinically, anthropometrically, dietary 24 h recall for three successive days and biochemically. In the first session all, participants followed a low caloric balanced regimen with a specific nutritional supplement that was omitted in the second phase. **Results:** All of the recorded anthropometric values improved after the intervention. Significant reductions in the mean concentrations of sNGAL, tumor necrosis factor-alpha (TNFα), and the other biochemical parameters were found in the first session, increasing after the omission of the supplement. Data revealed constant significant correlations between sNGAL and age, FBG and TNFα along the study and with BMI, %BF, non-HDL-C and SBP at the different sessions. **Conclusion:** Data indicate that including chickpea in dietary therapy plus sNGAL up-regulation are involved in counteract obesity, glycolipid metabolism, chronic inflammation and the associated kidney disease.

Keywords: Obesity; Women, Obesity, Glycolipid metabolism, Biomarker of early AKI, Chickpea

Introduction:

The 198 amino acid adipocytokine lipocalin-2 (LCN-2) is also known as neutrophil gelatinase-associated lipocalin (NGAL). LCN-2 transports tiny, hydrophobic molecules (steroid, free fatty acids, prostaglandins, and hormones) to target organs after binding to megalin/glycoprotein and GP330 SLC22A17 or 24p3R LCN-2 receptors. LCN-2 is considered a biomarker for both acute and chronic renal damage. Recent studies suggest a connection between LCN-2 and insulin sensitivity and glucose homeostasis since metabolic diseases including obesity and type 2 diabetes are associated with elevated tissue levels of LCN-2. LCN-2 modulates insulin sensitivity, glucose, and lipid metabolism, but its exact function in these processes is uncertain. [1].

Al-Absi et al. (2021) [2] reported that diabetes did not affect plasma LCN2 and adiponectin, implying the observed changes in LCN2 and adiponectin in type 2 DM are due to obesity rather than the diabetic condition. This complexity can be explained by common pathophysiological pathways (chronic inflammation, increased oxidative stress, hyperinsulinemia, etc.), a range of risk factors and associated diseases (insulin resistance, hypertension, dyslipidemia, etc [3].

Adipose tissue, in addition to its traditional role as an energy storehouse depot, is a major endocrine organ that secretes various hormones, the concentrations of which are affected by the degree of obesity. Obesity causes macrophage infiltration of the expanded adipose tissue and increased concentrations of proinflammatory cytokines. The increased expression of a proinflammatory cytokine

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tumor necrosis factor- alpha (TNF- α), in the adipose tissue of obese mice in the early 1990s handed the first suggestion for increased cytokine release in obesity, [4]. Tumor necrosis factor receptors (TNFRs) have been intertwined in the development of the early and late renal failure (diabetic nephropathy, nephroangiosclerosis, acute kidney transplant rejection, renal cell carcinoma,, glomerulonephritis, sepsis, and obstructive renal injury) in several studies [5].

The 2015-2020 Dietary Guidelines for Americans [6] advocate increasing vegetable consumption and replacing high-energy foods with nutrient-dense foods. Hummus consumers have higher nutritional intakes of fiber, polyunsaturated fats, vitamin A, E, vitamin C, folic acid, magnesium, potassium, and iron. It also performed well on the Healthy Dietary Index (HEI-2005). Hummus may have higher NNR (Naturally Nutrient Rich) score than other dips and spreads. According to new research, chickpeas and hummus may help with weight management, regulate glucose and insulin and even improve some cardiovascular disease (CVD) markers. Raw or cooked chickpeas and hummus also contain dietary bioactive ingredients such as phytic acid, sterols, tannins, carotenoids, and other polyphenols that provide benefits such as isoflavones, [7].

Herbal medicine has received much attention in recent years and is increasingly being used as an alternative to chemical drugs. Several lines of evidence point to the beneficial effects of medicinal plants in the prevention and treatment of a wide range of diseases. Thymus plants are marketed for various purposes due to their pleasant odour, high nutritional value, and abundance of health-promoting phytochemicals. Thyme is known for its nutrients and phenolic compounds, as well as its antioxidant and antibacterial properties. The plants stood out for having high levels of polyunsaturated fatty acids, a low ratio of omega-6 to omega-3 fatty acids, and a high K/Na ratio, all of which are crucial for maintaining a balanced diet [8].

The aim: The aim of the study was to evaluate the role of serum NGAL in the glucose and lipid (glycolipid) metabolism and the inflammatory status among sample of obese Egyptian women. Also to study it as sensitive biomarker to predict early changes in renal functions. In addition to assess the role of specific dietary strategies including low calories dietary regimen and supplement with antioxidative and anti-inflammatory properties and potential glucose and lipid-lowering effects.

Subjects and Methods

A: Subjects

Study design

In a dietary therapy interventional two-phase assessment study that lasted 8 weeks, 57 women with various degrees of obesity and associated comorbidities participated as volunteers from the National Research Center's employees and their families, Giza Governorate. The individuals' mean age was 50.84± 1.48, ranging from 32 to 64 years, and their BMI was 34.99± 0.64 kg/m2. They ate a balanced, low-calorie diet of between 1000 and 1200 Kcal per day, plus the pies supplement, two pies (50 g) to supply 210.19 Calories were eaten with breakfast and two pies with dinner. In the second phase, the tradition bread was used in place of the supplements to provide the same number of calories, and the subjects continued to consume just this low-calorie well-balanced diet.

Written consent was obtained from each participant after they had been informed of the study's objectives.

The study was complied with the International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS/WHO, 1993) [15].The "Ethical Committee" of the "National Research Centre" with Registration Number 19-180 gave its approval to the protocol

At the start of the study (Basal visit), 4 weeks after completion of the supplement and at the end of the study the following investigations were performed.

B: Supplement composition

The basic formula was prepared by mixing 50% of the wheat flour (72%) with Chickpea flour at the levels of 30%, thyme 3%, and then combined with the remaining ingredients as shown in the table (1). According to (AOAC, 2000) [9], the appropriate amount of water and 14.7 ml of dextrose solution (5.93%) were added to make pies that each weighed between 20 and 25 grammars. For about 15 minutes, the formulae were baked at 200 °C in the oven.

Table (1): Formula composition of the chickpea Pie (100 g dry weight)

Ingredients	Formula%
Wheat flour (72%)	50%
Chickpea flour	30%
Milk	10%
Corn oil	7%
Thyme	3%
Yeast	0.1%

C: Methods

Chemical analysis of the pies:

Functional products' protein, fat, ash, fiber, and moisture levels were evaluated in accordance with AOAC (2000) [9], while carbohydrate content was determined using the method described by Tadrus (1989) [10].The KazuyoShi and Yuuko (1992) [11] technique was used to determine the amounts of important elements in the tested samples. The AOCS (1998} [12] method was used to estimate fatty acids. The Ijarotimi and Olopade {2009} [13] method assessed amino acids.

Sensory Evaluation of the Pies:

A panel of 15 experts assessed sensory qualities of the pies. Color, smell, taste, texture, look, and general acceptability were all put to the test. All panelists were asked to give ratings of 0 to 20 for the qualities of taste, texture, color, and appearance, and a score of 100 for total acceptance [14].

Anthropometric and Blood Pressure Measurements

Pertinent anthropometric data was reported [16], weight, height, mid waist, hip and neck circumferences. Waist to hip ratio (WH/R) and body mass index (BMI) were calculated using height in meters squared and weight in kilogrammes. Using the German body fitness scale Geratherm (B-5010), body fat (BF) was measured as a percentage of total body weight. Each patient's blood pressure was checked three times, with the mean reading being recorded. To ensure accuracy, all measurements were made by the same researcher.

Blood Sampling and Biochemical Analysis

The patients' blood sample was drawn while they had been fasting for 12 hours. The sera were separated after centrifuging the samples after allowing them to clot at room temperature. Fresh samples were utilized to assess fasting blood glucose (FBG) using the glucose oxidase method [17]; fasting sera were used for other biochemical markers were kept at -70 C until needed. Total serum cholesterol (TC) was estimated according to Allain et al. (2011) [18], triglycerides (TG) were enzymatically deduced according to Seidel et al. (1993) [19] determined and high-density lipoprotein cholesterol (HDL-C) estimated according to Wornick et al. (1978) [20]. Friedewald equation [21] was used to calculate Low density lipoprotein cholesterol (LDL-C):

LDL-C (mg/dl) = TC− HDL-C−TG/5 (Friedewald et al. 1972), while non-HDL-C was calculated as: Non-HDL-C = (TC) − (HDL-C).

By utilizing the kit provided by Erba Lachemas.r.o., Karásek 1d, 621 00 Brno, CZ. REF/BLT00020, serum creatinine was analyzed using the kinetic technique deduced by Chromy et al. (2008) [22].The Cockcroft-Gault Equation was used to determine creatinine clearance:

[140 age (yr)*weight (kg)] / [72*serum Cr (mg/dL)] (multiply by 0.85 for women) (Cockcroft and Gault, 1976) [23].

Urea was estimated by colorimetric method (Tietz 1990) [24]. Blood urea nitrogen (BUN) was calculated, where BUN (mg/dL) = Serum urea (mg/dL)*0.467.Conversion factor derived by 28/60=0.467 [MW of urea=60, MW of urea nitrogen=28 (14*2)] [24]. Neutrophil gelatinase associated lipocalin and Tumor necrosis factor alpha were determined_using ELISA assay kits, according to Stejskal et al. (2004) and (Intiso et al. (2004)[26, 27].

Dietary recalls

The 24-hour dietary intake recall for three successive days, and consumption frequency were used to collect data on food intake. The total dietary intake was analyzed using the (Nutrisurvey, 2007) computer program [28].

Statistical Analysis

All values were expressed as mean ± SE. A paired-samples t-test was used to compare data before and after nutritional therapy. A P-value ≤ 0.05 was considered statistically significant. Correlation coefficients (r) were calculated to find correlations between different variables. p ≤ 0.05 was considered statistically significant. SPSS Windows software version 17.0 (SPSS Inc. Chicago, IL, USA, 2008) was used.

Results

Table (2) showed the organoleptic characteristics of the chickpea pies. All the sensory parameters ranged from 17.39-18.62/20, with overall acceptability 90.1%.

Sample	Sensory parameters					
	Crust color (20)	Texture (20)	Taste (20)	Odor (20)	Appearance (20)	Overall acceptability (100)
Pie	17.66	18.51	17.92	18.62	17.39	90.1

Tables (3 &4) showed the proximate composition of the macronutrients and micronutrients of the chickpea pies supplement. The Chickpea pie contains a good amount of carbohydrate, protein, fiber and low fat contents. The pie characterized by high content of minerals especially the potassium, calcium, iron and zinc, low in sodium. Women consumed two pies a day (100 gm) get 19.11, 22.44, 27.35, and 7.51% of their DRA for calories, protein, carbohydrate, and fat, respectively, and 36.50, 10.36, 272.4, and 70% of their DRA for potassium, calcium, iron, and zinc, respectively.

Table (3): Proximate macronutrients contents of the supplement (g/100g in dry basis)

Components (%)	Moisture	Ash	Protein	Fiber	Fat	CHO	Total calories
Chickpea Pie	26.44	0.85	11.22	0.63	5.26	82.04	420.38

Table (4): Minerals content (μ g/ 100g in dry basis) of the supplement

Iron	Zinc	Magnesium	Potassium	Sodium	Calcium
40.86	8.402	227.659	729.923	326.710	124.35

The important fatty acids content of pie were linolenic acid n-3, 8% and linoleic acid n- 6, 77.06 % (Fig.1).

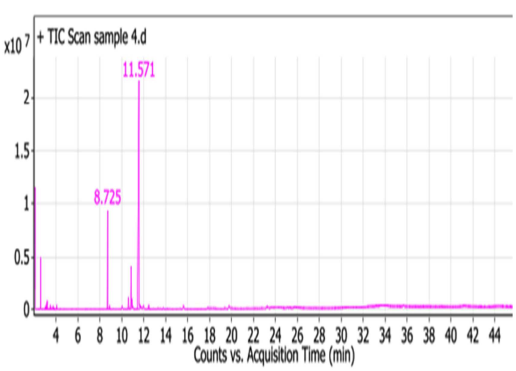

Figure (1) : Fatty acids percentage in tested sample :Palmitic acid (8.725min),9.52 %, palmitoleic acid(8.905min) n-7, 0.32%, linolenic acid (10.869min) n-3, 8% and linoleic acid (11.571min) n- 6, 77.06 %

Table (5) every day consumption results revealed the highest percentage of the participants 68.16% and 35.18% consumed carbohydrate foods such as bread and bakery products. In comparison participants only 19.38% of them consumed milk and milk products. For the two types of protein, 8.15% consumed animal protein such as meat, chicken, fish and egg, while 52.44% consumed plant protein. Consumption rates for fresh and cooked vegetables, fresh fruit and fresh fruit juice were very low at 10.08% and 8.62%, respectively.

Table (5): The percent of the participants according to the frequency of consumption of different food items of the traditional diet

Items	frequency of consumption				
	Didn't eat	Every day	Twice / week	Every/ Week	More
Carbohydrate Foods					
Bread	0.00	68.16	27.52	4.32	0.00
Bakery products	1.59	35.18	33.26	18.54	11.43
Pasta	1.36	1.84	30.97	57.12	8.71
Total	**0.98**	**35.06**	**11.03**	**26.66**	**6.71**
Milk & Milk Products					
Milk	2.37	12.37	34.72	23.14	27.40
Cheese	1.36	22.38	29.18	30.17	16.91
Yoghurt	7.87	23.41	29.43	18.97	20.32
Total	**3.86**	**19.38**	**31.11**	**24.09**	**21.54**
Animal protein foods					
Chicken	**0.0**	**0.0**	**51.30**	**38.20**	**10.50**
Meat	0.0	0.0	26.40	34.70	38.90
Fish	18.93	0.0	12.67	19.49	48.91
Egg	3.71	32.60	39.84	20.50	3.32
Total	**5.66**	**8.15**	**32.55**	**28.22**	**25.41**
Plant protein food					
Legumes	**0.0**	**52.44**	**28.01**	**18.30**	**1.25**
Fresh& Cooked Vegetables					
Fresh Vegetables	0.0	11.45	42.25	26.72	19.58
Cooked vegetable	0.0	8.72	44.72	31.61	14.95
Total	**0.0**	**10.08**	**43.48**	**29.16**	**17.26**
Fruits					
Fresh Fruits	0.0	10.13	32.67	47.22	9.98
Fruit Juices	2.31	7.12	13.24	28.71	48.62
Total	**1.15**	**8.62**	**22.95**	**37.96**	**29.30**
Sweet					
Sweet	**3.64**	**22.36**	**29.74**	**38.62**	**5.64**
Others					
Tea	4.30	17.83	42.45	32.41	3.01
Carbonated drink	6.30	14.23	36.31	39.65	3.51
Total	**5.30**	**16.03**	**39.38**	**36.03**	**3.26**

Data of this study showed that the traditional diet of the participants contained the highest values of calories, carbohydrates, total fats, saturated and unsaturated fats and cholesterol, with a low level of dietary fiber. On the contrary, the levels of these nutrients were significantly lower in the dietary therapy with and without the supplement with $p \leq 0.012-0.001$ (Table 6).

Table (6): Nutritional levels of the traditional diet and the different 2 dietary therapies consumed by the studied subjects

Nutrient intake	**Traditional diet**	**Low caloric regimen (with chickpea Pie)**	**Low caloric regimen (with bread)**	**RDAs**	P-Value
	Mean value± SE (%RDAs)				
Energy (kcal)	1979.86±9.21 89.99%	1042.55±13.18 47.38	1074.29±15.34 48.83	2200	0.**001****
Protein (g)	68.51±5.26 137.02%	46.23±2.17 92.46	44.19±5.90 88.38	50	0.012*
Carbohydrates (g)	242.93±8.87 80.98%	119.03±4.15 39.67	124.46±6.29 41.48	300	0.015*
Fat (g)	81.57±6.12 116.52%	42.39±3.12 60.55	44.41±2.31 63.44	70	0.000**
SFAs (g)	32.18±2.13 13.16%	8.62±1.20 7.44	9.03±1.10 7.56	No more than 7%	0.000**
MUFAs (g)	20.41±2.04 8.35%	13.44±1.07 11.60	15.72±2.13 13.16	12%-14% Total Calories	0.003*
PUFAs (g)	12.81±1.01 5.24%	10.30±1.15 8.89	11.71±1.17 9.81	6%-8% Total Calories	0.010*
Cholesterol (mg)	192.63±4.50 96.32%	103.40±6.71 51.70	105.33±5.47 52.66	200	0.000**
Dietary fiber (g)	16.04±7.10 64.16%	22.79±0.31 91.16	21.76±0.27 87.04	25	0.012*

Significant; *p≤0.05, **p≤0.01

Table (7) displayed the anthropometric measurements and blood pressure of the obese women under study at the start of the study and at the end of the each of the two sessions for nutritional therapy. The results showed that the volunteers suffered from different degrees of obesity as indicated by the high values of their anthropometric parameters especially the body mass index (BMI) and the mid waist circumference (MWC). After the intervention all the anthropometric parameters decreased significantly and simultaneously both the systolic and diastolic blood pressure, at the range p≤0.05-0.01.

Table (7): Characteristic anthropometric and blood pressure parameters of the studied sample at the basal and at the end of the 2 dietary therapies intervention

Parameters	**Basal (1st visit)**	**Mid (2nd visit)**	**Last (3nd visit)**
	Mean± SEM (no:57) (Minimum-Maximum)		
Age (year)	50.84±1.48 (32-64)		
Height (cm)	156.63±0.77 (146-168)		
Weight (Kg)	85.90±1.78 (67-113)	83.61±1.77^{**a} (66-108.5)	79.92±1.75^{**b,**c} (66-102)
BMI (Kg/m^2)	34.99±0.64 (28.3-44.7)	34.02± 0.62^{**a} (27.6-42.9)	32.97±0.65^{**b,**c} (27.6-40.9)
%BF	47.51±0.51 (40.60-53.90)	47.05±0.52^{**a} (70.0-105.0)	46.15±0.58^{**b,**c} (38.80-51.90)
MWC (cm)	89.03±1.14 72,0-106.0	86,68±119^{**a} 70.0-105.0	83.19±1.15^{**a,**c} 69.0-98.0
WH/R (cm/cm)	0.77±0.01 (0.67-0.87)	0.76±0.01^{**a} (0.66-0.85)	0.75±0.01*$^{b\ **c}$ (0.66-0.83)
Neck Circum. (cm)	33.76±0.33 (30.0-40.0)	33.14±0.26^{**a} (30.0-38.0)	32.62±0.26$^{**b\ **c}$ (30.0-36.0)
SBP (mmHg)	121.58±1.64 (100-140)	125.26±2.08^{*a} (100-156)	120.38±2.51^{**b} (100-150)
DBP (mmHg)	79.47±0.97 (70-90)	76.00±1.28^{**a} (60-92)	75.92±1.85^{**c} (56-93)

BMI: Body Mass Index, %BF: Percent body fat, MWC: Mid waist circumference, WHR: Waist hip ratio, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure. Significant; *p≤0.05, **p≤0.01 a: Basal vs. Mid, b: Mid vs. Last, c: Basal vs. Last

Biochemical results in the research samples before intervention showed modest high concentrations in fasting blood glucose (FBG), total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C), non-HDL-C and the urea among the participants, when compared to standard values. After the dietary intervention, these parameters significantly decreased at p≤0.05-0.01, and the decrease was most pronounced during the period in which the patients consumed the chickpea pies with the hypocaloric regimen. After omitting the supplement the values of these parameters increased with numerical or significant different compared to the results at the basal and at the first phase. The two cytokines NGAC and TNFα revealed the same results. The mean values of creatinine, urea and BUN were within the normal range; significant decrease was reported in the value of the creatinine at the end of the study while that for urea and BUN significant decreases were found in both phases, (Table 8).

Table (8): Mean ±SE of Biochemical Parameters among the studied sample before and after intervention

Parameters	**Basal (1st visit)**	**Mid (2nd visit)**	**Last (3nd visit)**
	Mean± SEM (no:57) (Minimum-Maximum)		
FBG (mg/dl)	109±4.66 82.0-237.0	103.05±2.41 76.0-146.0	133.23±5.09 **b 90.0-207.0
T. Cholesterol (mg/dl)	217.85±3.69 179.20-286.40	200.0±2.63 ** a 157.60- 233.60	213.17±3.53 **b 164.80-247.20
LDL-C (mg/dl)	140.52±3.68 103.91-199.85	124.58±2.89 **a 78.89-165.88	136.18±4.29 **bc 74.39-181.32
HDL-C (mg/dl)	54.78±1.76 30.21-74.10	59.88±1.61 ** a 39.90-79.23	61.69±1.72 **b **c 37.62-74.67
Non HDL-C (mg/dl)	163.07±4.02 118.21-227.64	140.12±3.07 **a 93.19-186.86	151.48±4.18 **b **c 94.12-195.98
TG (mg/dl)	82.78±3.22 53.39-145.70	77.68±2.89 50.68-128.51	76.50±2.77 48.87-106.79
Creatinine (mg/dl)	0.59±.0.02 0.36-0.93	0..58±.0.02 0.40-0.93	0.51±0.03 **b **c 0.23-0.76
Creatinine clearance (ml/min)	163.43±7.03 88.67-260.83	160.98±6.52 66.19-255.66	175.29±11.23 **b *c 80.99-361.25
Urea (mg/dl)	33.71± 1.10 21.10-50.21	30.75±1.05 ** a 22.26-47.89	31.88±1.37 **c 20.04-45.36
BUN (mg/dl)	15.74±0,52 9.85-23.45	14.36±0.49** a 10.39-22.36	14.88±0.64 **c 9.36-21.18
NGAL (pg/ml)	98.46 ±4.69 68.20-204.51	76.014 ±2.13 **a 55.05- 123.33	79.585 ±5.06 **c 51.25-168.91
TNF-alpha (ng/L)	262.9 ±31.28 140.48-1224.68	213.65 ±27.14**a 131.51-1067.69	249.66 ±36.38**c 138.28-986.86

NGAL: Neurophilgelatinase associated lipocalin, TNF-alpha: Tumor necrosis factor alpha
Significant; *p≤0.05, **p≤0.01 a: Basal vs. Mid, b: Mid vs. Last, c: Basal vs. Last

Table (9) showed the correlation coefficient between NGAL and age, TNFα and MetS criteria in the basal and the first and second sessions. Data revealed constant significant correlations between NGAL and age, FBG and TNFα at the basal and at the end of both sessions. At the end of the first session correlation found with %BF, while at the end of session 2 the correlation detected with BMI, %BF, non-HDL-C and SBP, significant differences ranged at p≤0.05 and ≤0.01.

Table (9): Correlation coefficient between NGAL and age, TNFα and MetS criteria in the basal and the first and second sessions

Parameters	Basal (no:57)		1st phase (no:57)		2end phase(n0:39)	
	NGAL Correlation coefficient					
	r	P	r	P	r	P
Age	0.342**	0.003**	0.379**	0.004**	0.331*	0.040*
BMI	0.043	0.752	0.236	0.077	0.322*	0.046*
%BF	0.188	0.242	0.265*	0.048*	0.386*	0.015*
MWC	-0.212	0.114	-0.136	0.314	-0.013	0.939
WHR	-0.159	0.238	-0.262*	0.049*	0.298	0.066
FBG	0.640**	0.000**	0.315*	0.017*	0.480**	0.003**
HDL-C	0.161	0.233	0.106	0.433	0.117	0.480
Non-HDL-C	0.013	0.922	-0.114	0.399	0.329*	0.041*
SBP	0.051	0.707	0.222	0.098	0.454**	0.004**
DBP	0.069	0.608	-0.049	0.487	0.163	0.322
Creatinine	0.091	0.418	0.109	0.418	0.150	0.362
Cr. CL	0.132	0.256	-0.028	0.836	-0.184	0.263
TNFα	0.755**	0.000**	0.730**	0.000**	0.929**	0.000**

*p≤0.05, **p≤0.01

Discussion

Obesity is significant risk factor for glycolipid metabolism disorders and chronic kidney disease. Early disease detection and diagnosis are helpful for risk reduction and treatment.

Data from this study revealed that at the start of the study, the participants' anthropometric parameters showed high BMI, percent BF, MWC, and other anthropometric parameters. Following intervention, the results demonstrated a healthy beneficial effect of the dietary therapy on BMI and central obesity, namely MWC, as well as a decrease in blood pressure values. Chickpea/hummus consumers were 53% less likely to be obese and 51% less likely to have an elevated glucose level in the National Health and Nutrition Examination Survey (NHANES) 2003-2010 dataset. Similarly, consumers had a lower BMI (26.4 0.5 vs. 28.6 0.1) and waist circumference (92.2 1.3 vs. 97.9 0.3 cm) than non-consumers [29]. Consumption of pulses, either alone [30] or as part of a dietary pattern [31], has also been linked in epidemiologic studies to risk of overweight and obesity, lower body weight and waist circumference.

According to Kovesdy et al. (2017) [32], obesity is one of the most significant risk factors for new-onset chronic kidney disease. Obese people experience compensatory hyperfiltration to meet the increased metabolic demands of their increased body weight to fulfill their increased metabolic needs. Increased intraglomerular pressure can increase the chance of developing chronic kidney disease which can injure the kidneys. In this context the results of this study showed that women had relatively high creatinine clearance when compared to the normal standard for women.

Glomerular or tubular enlargement, localized segmental glomerulosclerosis, and bulbous sclerosis are all symptoms of obesity-induced renal damage. Additionally, Wang et al. (2022) [33] discovered that insulin resistance, lipid metabolism issues, renal hemodynamic abnormalities, and inflammation all contribute to the onset and progression of obesity-induced nephropathy.

As previously mentioned, glucose hemostasis, and lipid profile disorder is one of the most important reasons for the deterioration of kidney function. According to this study, the basal biochemical data of the obese participants revealed high mean concentrations of FBG, TC, LDL-C and non-HDL-C, which mean that they were suffering from some grades of glycolipid disorder. Good improvement was detected after intervention especially with supplement consumption Li et al.(2021) [34] investigated the role of chickpea extract in metabolomics and gut microbiota, providing evidence for chickpea as a prebiotic to prevent diabetes. At the same time, Han et al.(2021) [35] reported that chickpea dietary fiber may have a positive effect on serum lipids and the gut bacterial ecosystem. Despite their well-established health benefits (6), the participants' traditional diet recorded in this study did not include enough legumes and vegetables.

For both primary and secondary CKD prevention, plant-based diets should be promoted, in terms of lowering hypertension, weight, hyperphosphatemia, hyperfiltration, and perhaps mortality, the adoption of plant-based diets in CKD may also be advantageous. The risk of excessive potassium intake from plant-based diets seems overblown, primary based on opinion, and supported by research. Plant-based diets often offer sufficient protein consumption, including necessary amino acids, and are generally well tolerated as long as the diet is appropriately followed [36].

Neutrophil gelatinase-associated lipocalin (NGAL), discovered to be released by circulating neutrophils, has been validated as an inflammatory marker {37]. A member of the lipocalin family is NGAL, it is abundantly expressed in tissues during metabolic diseases as a new adipokine. More and more studies point to NGAL as a possible marker for several lipid-related disorders. NGAL is most likely implicated in the metabolic syndrome caused by obesity and inflammation, endothelial dysfunction, insulin resistance, glucose and lipid metabolism, and the atherosclerosis pathway [38]. According to Bolignano et al. (2010) [39], NGAL is one of the most promising biomarkers of impending acute kidney injury. It is a tiny 25 kDa stress- a protein secreted from damaged tubular cells in response to various harmful stimuli. Additionally, numerous studies seem to support a potential involvement for this component in the beginning and progression of the condition. The kidney function parameter in this study showed significant decrease in the level of serum creatinine at the end of the study, whereas urea and BUN levels decreased significantly after dietary therapy with the supplement but increased numerically when the supplement was omitted. As for the mean serum concentration of NGAL and TNFα, significant decreases in their levels were verified after the patients consumed the supplemented nutritional therapy. This was followed by a significant increase when the participants followed only the low caloric regimen.

It has been reported that eating legumes as part of a varied Mediterranean diet can help prevent and control a various diseases, including chronic kidney disease (CKD). Martnez-Pineda et al. (2018) [40] demonstrated that cooking beans can reduce their potassium and phosphorus content to levels that renal patients can consume, and enable them to consume them more frequently. Furthermore, the nutritional supplement's role as an antioxidant and anti-inflammatory in kidney tissue protection is confirmed.

The correlation coefficient between NGAL and the MetS syndrome criteria revealed an association of the adipocytokine with the age and the fasting blood glucose concentration in the same time revealed a high significant correlation with TNF-alpha, a proinflammatory cytokine. These associations were consistent and were found during the basal and in the study's two phases. The relationship between body adiposity and sNGAL was detected at the end of the first session, where a correlation was found between it and per cent BF, then more with BMI, non-HDL-C, and SBP at the end of the second session.

Recent research has highlighted the role of inflammation and inflammatory mediators, such as tumour necrosis factor (TNF)-related biomarkers, in the development/progression of diabetic kidney disease (DKD) [41] .Furthermore, Gong et al. (2017) [42] stated that sNGAL is important not only in regulating energy metabolism, glucose metabolism, and lipid metabolism, but also in regulating inflammation which is important in diabetes and metabolic syndrome.

Conclusion

Data of this study indicate that serum neutrophil gelatinize associated lipocalin up-regulation is involved in the protective mechanism to counteract obesity, glycolipid disorder and the harmful inflammatory consequences of obesity and the expected associated kidney disease, In the meantime , including legume as chickpea in dietary therapy also had a role in improving fasting glucose level, lipid profile, and the proinflammatory marker tumor necrosis factor-α (TNF-α) and the serum neutrophil gelatinase-associated lipocalin (sNGAL) condition that accompanied obesity.

Abbreviation

%BF: Percent Body Fat
AKI: Acute kidney injury
BMI: Body Mass Index
BUN: Blood Urea Nitrogen
Cr/Cl: Creatinine/ Clearance
CVD: Cardiovascular Disease
DBP: Diastolic Blood Pressure
FBG: Fasting Blood Glucose
HDL-C: High Density Lipoprotein -Cholesterol
LCN-2: Lipocalin-2
LDL-C: Low Density Lipoprotein- Cholesterol
MWC: Mid Waist Circumference
NGAL: Neutrophil Gelatinase-Associated Lipocalin
NNR: Naturally Nutrient Rich
SBP: Systolic Blood Pressure

TC: Total Cholesterol
TG: Triglyceride
TNFα: Tumor Necrosis Factor alpha
WH/R: Waist Hip Ratio

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H.A.E: had responsibility for biochemical analysis and laboratory investigations.

M.I.A: was responsible for clinical examination and anthropometric measurements.

N.H was responsible for preparation of the supplement and analysis of nutritional intake and dietary habit and also in subject's selections and consent signature by the subjects

A.M and M.M were responsible for the chemical analysis of the supplement. .

H.A.E, M.I.A and N.H were responsible about statistical analysis

ST revised the final manuscript

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