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Original article

A Study of Interleukin-6 Gene Polymorphism in Egyptian Obese Subjects

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ABSTRACT

Background: Polymorphisms in the interleukin 6 gene have been studied in various chronic diseases. Increased levels of IL-6 in humans have been associated with visceral fat accumulation and obesity. The aim of the work was to study interleukin-6 gene polymorphism in Egyptian obese patients.
Methods: A total of 100 people were enrolled in the study. They were divided into: Group A included 35 subjects of simple obesity, group B included 35 patients of complicated obesity, and group C included 30 healthy subjects. Laboratory investigations were done for all subjects including IL-6 gene snp rs1800796 polymorphism, uric acid, amylase, lipase, C reactive protein and lipid profile. Abdominal ultrasound was done to assess presence of fatty liver and/or fatty pancreas.
Results: Regarding the IL-6 gene polymorphism, there was no significant difference statistically between both obese groups, however there was a significant difference statistically among obese groups and healthy people. Employing a univariate regression; waist circumference, hip circumference, waist/hip ratio, uric acid, cholesterol, C reactive protein, GG allele of IL-6 ($p<0.001$), fatty liver and/or fatty pancreas ($p<0.001$) were statistically significant parameters for obesity. In multivariate analytical regression, uric acid ($p=0.041$), and the GG allele of IL-6 polymorphism ($p=0.028$) were statistically significant risk factors for obesity.
Conclusions: IL-6 gene snp rs1800796 polymorphism was associated with increased risk of obesity. The obesity traits were linked to G allele. Future studies on gene-environment interactions should be carried out to clarify the connection between the IL-6 polymorphism and obesity.
Key words: obesity; interleukin 6; polymorphism.

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INTRODUCTION

Obesity is considered as a chronic disease accompanied with respiratory, cardiovascular, metabolic, psychological and social related co-morbidities. The causes are multiple and interwoven, related to diet, sedentary lifestyles, psychological, socio-economic, biological and genetic factors [1].

The notion of metabolically healthy obesity (MHO) was born out of observations that a section of obese people had a much-decreased risk of cardio-metabolic disorders. Normal glucose and lipid metabolism indices, as well as the absence of hypertension, are generally used to identify MHO, despite the lack of a defined description. Individuals with MHO, unlike those with metabolic unhealthy obesity (MUO), have no metabolic problems such as insulin resistance, hypertension, or dyslipidemia. MHO has a reduced level of systemic inflammation

and a better immunological and hepatic function profile, although having a similar total fat mass [2,3].

One of the main characteristics of obesity is the build-up of pro-inflammatory macrophages in adipose tissues; as a chronic inflammatory disease, obesity is known for its cytokine release. Pleiotropic inflammatory cytokine IL-6 has been linked to obesity and is regarded as a "metabolic hormone" that influences the metabolism of fats, proteins, and carbohydrates.

Increased levels of IL-6 in humans have been associated with visceral fat accumulation and obesity [4-6], type 2 diabetes mellitus (T2DM), increased impaired glucose tolerance risk [7-9], and hypertension [10,11].

Pro-inflammatory cytokines like IL-6 have an impact on insulin sensitivity, blood pressure, homeostasis, adipocyte activity, and lipid metabolism. As a result, IL-6 is crucial in the emergence of atherosclerosis, diabetes, and cardiovascular disorder [12].

Accordingly, the available data shows that cytokine and metabolic regulation are linked to polymorphisms in the IL-6 gene. It may thus have a significant impact on poor lipid and glucose homeostasis, cardiometabolic risk, and how people react to dietary fat. Further research on this subject is required because the results are still debatable [13].

Much research have looked into the links between polymorphisms in the IL-6 gene and obesity. The IL-6 gene is found on chromosome 7's short arm (7p21). In recent years, several unique SNPs have been identified in the promoter region of this gene, including 174G/C (rs1800795), 597G/A (rs10242595), 373A(n)T(n), and 572G/C. The latter is the most prevalent and biologically relevant of the group. Additionally, the rs1800796 SNP, which is in the IL-6 gene's promoter region, has been connected to obesity [14].

The rs1800796 polymorphism may influence the IL-6 gene's transcriptional effectiveness. The aim of the work was to study interleukin-6 gene polymorphism in Egyptian obese patients.

METHODS

This work had been approved from the ethical committee of the internal medicine department of faculty of medicine, Alexandria University on 16th of July 2020, serial number: 0106466. All patients involved in the study provided informed consent, and the principles of the Helsinki Declaration were observed. A consent for publication was taken from the participants.

A hundred people between the ages of 15 and 60 participated in the study, all were enrolled from those attending the Endocrinology clinic or the inpatient departments at the Alexandria Main University Hospital. They were sub-divided into three groups; Group A involved 35 individuals of simple obesity who were classified as metabolically healthy obese (MHO) due to their BMI of ≥30 kg/m2 and fulfilling all the requirements: serum triglycerides ≤150 mg/dl, serum concentrations of HDL cholesterol >40 mg/dl (for men) or >50 mg/dl (for women), systolic blood pressure (SBP) ≤130 mmHg, diastolic blood pressure (SBP) ≤85 mmHg, absence of antihypertensive medication, fasting blood glucose ≤100 mg/dl, and absence of glucose lowering medication treatment [15]. Group B included 35 patients of complicated obesity defined as metabolically unhealthy obese (MUHO) including obese persons with presence of any metabolic disorder and cardiovascular disease, including type 2 diabetes, dyslipidemia, hypertension, or atherosclerotic cardiovascular disease (ASCVD) [3] Group C included 30 healthy subjects. Patients with chronic renal, liver, or respiratory diseases, adrenal and thyroid disorders, pregnant women were excluded from the study.

History taking and complete physical examination including measurement of the waist circumference (WC), hip circumference (HC), calculation of the body mass index (BMI) and waist to hip ratio (WHR) were done. All subjects were subjected to the following investigations: complete blood count, urea, creatinine, aspartate aminotransferase (AST), alanine transaminase (ALT), serum albumin, total serum bilirubin (TSB), total cholesterol, triglycerides (TGs), low density lipoproteins (LDL), very low-density lipoproteins (VLDL), high density lipoproteins (HDL) and fasting blood glucose. All were done using RXL dimension automated chemistry analyzer. Serum amylase, lipase was done by manual kit. Hemoglobin A1c (HbA1c) by Glycohemoglobin analyzer HIS-G8. Thyroid stimulating hormone (TSH), free thyroxine (FT4) levels were done using chemiluminescence by centaur. Five ml of blood were used to extract DNA using DNA mini kit of QIAamp according to manufacturer's instructions. The DNA concentration and purity were determined using nanodrop at wavelength 260/280. Measurement of IL-6 gene polymorphism (snp rs1800796) by Realtime pcr

tackmann assay technique using Biorad instrument. We used abdominal ultrasonography to examine the abdomen for the existence of fatty liver and/or fatty pancreas. The following parameters were employed in conventional B-mode ultrasonography to determine the presence of fatty liver: parenchymal brightness, liver-to-kidney contrast, bright vessel walls, and gallbladder wall definition [16]. Fatty pancreas was described as a hyperechoic pancreas with higher echogenicity in comparison to that of the liver or renal cortex [17].

STATISTICAL ANALYSIS:

The IBM SPSS software application, version 20.0 (IBM Corp., New York's Armonk), was used to analyze the computer-supplied data. Numbers and percentages were used to express qualitative data. The distribution's normality was checked using the Shapiro-Wilk test. The range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR) have all been used to represent quantitative data. Quantitative variables with non-normal distribution were compared using the Mann-Whitney test, and categorical data were compared using the Chi-square test, in order to compare two groups. The data significance that was acquired was evaluated using the 5% level.

RESULTS:

The study included 35 patients (11 males and 24 females) with simple obesity (mean BM
35.31b ± 4.65) at the mean age of 35.26 ± 9.71 years and 35 patients (8 males and 27 females) with complicated obesity (mean BMI 39.39 ± 7.87) at the mean age of 37.40 ± 11.45 in addition to 30 healthy individuals (8 males and 22 females) had a mean BMI of 22.13 ± 1.62.

A significant increase in the WC, HC, WHR, HbA1c, fasting blood glucose, TC, TG, LDL and VLDL was detected among obese patients either of simple or complicated obesity in relation to normal subjects. Clinical and laboratory characteristics of the participants are shown in tables (1) and(2.)

All patients with complicated obesity (Group B) had co-morbidities beside obesity; four of them were diabetic (11.4%), eighteen of them were hypertensive (51.4%), and 14 had dyslipidemia (40%).

Twenty-four patients with simple obesity (68.6%) were homozygous (allele GG), 26 patients in the complicated obesity group 26 (74.3%) were homozygous (allele GG), while for the healthy subjects' group; 7 individuals (23.3) were homozygous (allele GG). So, there was statistical insignificant difference among both obese groups A and B as regards to IL-6 gene snp rs1800796 polymorphism (p=0.836), but there was difference with statistical significance between both the obese groups versus the control group involving healthy subjects (p<0.001) (see table 3 and figures 1-3).

Abdominal ultrasound findings are shown in table 2 where there was a statistically significant difference between the control group versus the cases regarding the presence of fatty liver and fatty pancreas (p<0.001), while there was no statistically significant difference between groups A and B (p=0.091).

In the univariate regression analysis; waist circumference (p=0.006), hip circumference (p=0.002), waist/hip ratio (p=0.002), uric acid (p=0.004), HbA1c (p<0.001), total cholesterol (p<0.001), TGs (p<0.001), LDL (p=0.005), VLDL (p<0.001), CRP (p=0.018), GG allele of IL-6 snp rs1800796 polymorphism (p<0.001), fatty liver +/- fatty pancreas (p<0.001) were statistically significant parameters for obesity. In the analysis employing multivariate regression, uric acid (p=0.041), and the GG allele of IL-6 snp rs1800796 polymorphism (p=0.028) were statistically significant risk factors for obesity (Table 5).

Table 1: Comparison among the three study involved groups based on their anthropometric measurements, glycemic parameters and lipid profile

	Group A (n = 35)	Group B (n = 35)	Group C (n = 30)	Test of Sig.	p
BMI (km/m^2)					
Mean ± SD.	35.31^b ± 4.65	39.39^a ± 7.87	22.13^c ± 1.62	F= 5.704*	<0.001*
Median (Min. – Max.)	34 (30 – 48.7)	38 (31 – 70.6)	22 (19 – 24.8)		
Waist circumference (cm)				F= 80.471*	<0.001*
Mean ± SD.	97.6^a ± 6.29	99.2^a ± 5.41	83.93^b ± 3.39		
Median (Min. – Max.)	96 (90 – 110)	98 (90 – 110)	83 (80 – 92)		
Hip circumference (cm)					

	Group A (n = 35)	Group B (n = 35)	Group C (n = 30)	Test of Sig.	p
Mean ± SD.	106.5[a] ± 5.44	108.1[a] ± 5.31	94.77[b] ± 2.65	F= 75.026*	<0.001*
Median (Min. – Max.)	105 (98 – 116)	108 (96 – 116)	95 (88 – 99)		
Waist /Hip ratio					
Mean ± SD.	0.91[a] ± 0.03	0.91[a] ± 0.04	0.89[b] ± 0.03	F= 5.995*	0.004*
Median (Min. – Max.)	0.92 (0.84 – 0.98)	0.92 (0.84 – 0.98)	0.88 (0.83 – 0.98)		
FBS					
Mean ± SD.	83.46[a] ± 10.3	91.2[a] ± 21.37	84[a] ± 1.89	F= 3.231	0.051
Median (Min. – Max.)	85 (58 – 99)	91 (60 – 169)	84.5 (80 – 86)		
HBA1c (%)					
Mean ± SD.	5.48[b] ± 0.32	6.19[a] ± 0.88	5.23[b] ± 0.12	F= 26.010*	<0.001*
Median (Min. – Max.)	5.4 (5 – 5.6)	6 (5.1 – 9.5)	5.2 (5.1 – 5.4)		
Total cholesterol					
Mean ± SD.	177.09[a] ± 30.5	195.77[a] ± 44.88	153[b] ± 21.13	F= 12.687*	<0.001*
Median (Min. – Max.)	173 (121 – 200)	195 (75 – 299)	146.5 (126 – 196)		
Triglycerides					
Mean ± SD.	108.80 ± 55.39	154.26 ± 70.68	61.67 ± 7.27	H= 45.636*	<0.001*
Median (Min. – Max.)	99[b] (34 – 145)	153[a] (36 – 355)	60.5[c] (52 – 73)		
LDL					
Mean ± SD.	103.17[ab] ± 26.33	114.89[a] ± 39.76	89.33[b] ± 15.37	F= 6.077*	0.003*
Median (Min. – Max.)	105 (40 – 168)	107 (26 – 206)	88.5 (65 – 127)		
VLDL					
Mean ± SD.	22.46[b] ± 11.12	31.03[a] ± 14.01	12.33[c] ± 1.92	F= 24.925*	<0.001*
Median (Min. – Max.)	21 (7 – 47)	31 (7 – 71)	12 (10 – 15)		
HDL					
Mean ± SD.	52.43[a] ± 13.38	49.4[a] ± 11.68	51.33[a] ± 3.54	F= 0.719	0.490
Median (Min. – Max.)	51 (42 – 92)	48 (34 – 76)	51 (46 – 57)		

SD: Standard deviation, $\chi 2$: Chi square test, F: ANOVA test, as Post Hoc Test (Tukey) was employed for comparing Pairwise Each of the two study involved study groups, H: Kruskal Wallis test, as Post Hoc Test (Dunn's for multiple comparisons test) was employed for pairwise comparing both two involved study groups, p: p value for the study involved groups comparison, *: Statistically significant at $p \leq 0.05$

Table 2: Comparison of the 3 involved study groups based on their laboratory investigations and imaging

	Group A (n = 35)	Group B (n = 35)	Group C (n = 30)	Test of Sig.	p
TSH					
Mean ± SD.	1.78 ± 0.82	1.97 ± 1.03	1.54 ± 0.19	H= 4.643	0.098
Median (Min. – Max.)	1.64[a] (0.58 – 3.9)	1.72[a] (0.67 – 4.1)	1.56[a] (1.23 – 1.8)		
FT4					
Mean ± SD.	1.14[a] ± 0.19	1.21[a] ± 0.22	1.21[a] ± 0.08	F= 1.743	0.180
Median (Min. – Max.)	1.1 (0.9 – 1.74)	1.24 (0.89 – 1.6)	1.21 (1.1 – 1.34)		
CRP					
Mean ± SD.	7.83 ± 8.65	11.65 ± 22.55	3.87 ± 0.47	H= 4.028	0.133
Median (Min. – Max.)	4.1[a] (0.5 – 39.3)	5.5[a] (1 – 134.5)	3.84[a] (3.1 – 4.5)		
Hemoglobin					
Mean ± SD.	12.56[a] ± 1.37	12.55[a] ± 1.42	12.43[a] ± 0.42	F= 0.112	0.894
Median (Min. – Max.)	12.2 (10.9 – 16)	12.4 (11.7 – 13.35)	12.45 (11.8 – 13)		
WBCs					
Mean ± SD.	6.49 ± 1.72	6.96 ± 2.07	6.23 ± 0.78	F= 1.656	0.196
Median (Min. – Max.)	6.7 (4 – 10.8)	6.5 (4.3 – 12.3)	6.1 (5 – 7.5)		
Urea					
Mean ± SD.	26.29[a] ± 6.64	27.48[ab] ± 7.69	31.33[b] ± 5.11	F= 5.005*	0.009*
Median (Min. – Max.)	27 (15 – 45)	28 (12.8 – 44)	31.5 (25 – 41)		
Creatinine					
Mean ± SD.	0.71[b] ± 0.18	0.74[b] ± 0.19	0.89[a] ± 0.1	F= 11.226*	<0.001*
Median (Min. – Max.)	0.7 (0.33 – 1.14)	0.7 (0.47 – 1.2)	0.9 (0.7 – 1)		
Uric Acid					
Mean ± SD.	4.73[ab] ± 1.18	5.02±1.1	4.13[b] ± 1.05	F= 5.353*	0.006*
Median (Min. – Max.)	4.70 (2.8 – 7.6)	5 (3.2-7.6)	4.35 (2.5 – 6)		
AST					
Mean ± SD.	22.2 ± 8.85	22.29 ± 10.93	19 ± 6.96	H= 1.710	0.425
Median (Min. – Max.)	21[a] (10 – 45)	20[a] (8 – 59)	18.5[a] (7 – 33)		
ALT					
Mean ± SD.	25.54 ± 10.74	24.46 ± 13.36	22.7 ± 7.47	H= 1.328	0.515
Median (Min. – Max.)	26[a] (5 – 52)	22[a] (5 – 66)	21.5[a] (13 – 39)		
Albumin					
Mean ± SD.	3.75[a] ± 0.36	3.79[a] ± 0.45	3.87[a] ± 0.11	F= 0.862	0.425
Median (Min. – Max.)	3.80 (3 – 4.4)	3.9 (2.9 – 4.5)	3.9 (3.7 – 4)		
Total serum bilirubin					
Mean ± SD.	0.41[a] ± 0.17	0.48[a] ± 0.17	0.43[a] ± 0.21	F= 1.285	0.281
Median (Min. – Max.)	0.36 (0.21 – 0.91)	0.44 (0.22 – 0.92)	0.36 (0.2 – 0.9)		
Amylase					
Mean ± SD.	57.74[a] ± 18.97	57.91[a] ± 30.14	64.67[a] ± 11.56	F= 1.014	0.367
Median (Min. – Max.)	53 (27 – 101)	51 (17 – 137)	64 (48 – 84)		
Lipase					
Mean ± SD.	28.54[a] ± 8.88	31.11[a] ± 12.14	29.67[a] ± 2.88	F= 0.711	0.494
Median (Min. – Max.)	27 (17 – 50)	30 (15 – 81)	30 (26 – 35)		
Ultrasound Abdomen No Fatty liver Fatty liver and pancreas	13(37.1%) 19(54.3%) 3(8.6%)	5(14.3%) 26(74.2%) 4(11.4%)	30(100%) 0 0	X^2=36.72	<0.001

SD: Standard deviation, F: F for ANOVA test, H: H for Kruskal Wallis test, $\chi 2$: Chi square test, MC: Monte Carlo, p: p value for study involved groups comparison, *: Statistical significance at $p \leq 0.05$

Table 3: Comparison of the three study involved groups based on the IL-6 SNP

	Group A (n = 35)	Group B (n = 35)	Group C (n = 30)	Sig. bet. Grps.		
				P_1	p_2	p_3
IL-6 SNP						
CC	2 (5.7%)	1 (2.9%)	4 (13.3%)	$^{MC}p_1$= 0.836	$^{MC}p_2$= 0.001*	$^{MC}p_3$ <0.001*
CG	9 (25.7%)	8 (22.9%)	19 (63.3%)			
GG	24 (68.6%)	26 (74.3%)	7 (23.3%)			
HWE	**0.376**	**0.693**	**0.126**			
Allele						
C	13 (18.6%)	10 (14.3%)	27 (45.0%)	0.494	0.001*	<0.001*
G	57 (81.4%)	60 (85.7%)	33 (55.0%)			

MC: Monte Carlo, HWE: p value for Hardy-Weinberg, p1: p value for Group A and Group B comparison, p2: p value for Group A and Group C comparison, p3: p value for Group B and Group C comparison, *: Statistical significance at $p \leq 0.05$

Table 4: Univariate and multivariate logistic regression analysis for obesity patients (group A + group B) regarding to different factors (n = 70 vs. 30).

	Obesity patients (n = 70)	Control group (n = 30)	Univariate		Multivariate	
			OR (95%C. I)	p	OR (95%C. I)	p
Waist circumference (cm)	98.40 ± 5.88	83.93 ± 3.39	3.228 (1.392 – 7.489)	0.006*		
Hip circumference (cm)	107.3 ± 5.40	94.77 ± 2.65	3.822 (1.627 – 8.980)	0.002*		
Waist /Hip ratio	0.91 ± 0.03	0.89 ± 0.03	9.389$ (2.329 –37.844)	0.002*		
Uric Acid	4.88 ± 1.14	4.13 ± 1.05	1.875 (1.220 – 2.880)	0.004*	2.767 (1.043 – 7.342)	0.041*
SGOT	22.24 ± 9.87	19.0 ± 6.96	1.045 (0.990 – 1.103)	0.109		
SGPT	25.0 ± 12.05	22.70 ± 7.47	1.021 (0.979 – 1.064)	0.333		
Albumin	3.77 ± 0.41	3.87 ± 0.11	0.443 (0.120 – 1.640)	0.223		
TSB	0.44 ± 0.17	0.43 ± 0.21	1.545 (0.142 – 16.752)	0.721		
Amylase	57.83 ± 25.0	64.67 ± 11.56	0.986 (0.967 – 1.005)	0.159		
Lipase	29.83 ± 10.64	29.67 ± 2.88	1.002 (0.955 – 1.051)	0.934		
FBS	87.33 ± 17.10	84.0 ± 1.89	1.019 (0.984 – 1.055)	0.292		
HBA1c	5.83 ± 0.75	5.23 ± 0.12	1.631$ (1.304 – 2.040)	<0.001*		

	Obesity patients (n = 70)	Control group (n = 30)	Univariate		Multivariate	
			OR (95%C. I)	p	OR (95%C. I)	p
Total cholesterol	186.4 ± 39.24	153.0 ± 21.13	1.033 (1.015 – 1.050)	<0.001*	1.032 (0.974 – 1.094)	0.282
Triglycerides	131.5 ± 67.06	61.67 ± 7.27	1.077 (1.034 – 1.122)	<0.001*		
LDL	109.0 ± 33.99	89.33 ± 15.37	1.026 (1.008 – 1.045)	0.005*	1.030 (0.956 – 1.110)	0.433
VLDL	26.74 ± 13.28	12.33 ± 1.92	1.391 (1.167 – 1.658)	<0.001*		
HDL	50.91 ± 12.56	51.33 ± 3.54	0.996 (0.957 – 1.037)	0.856		
TSH	1.87 ± 0.93	1.54 ± 0.19	1.879 (0.958 – 3.688)	0.067		
FT4	1.18 ± 0.21	1.21 ± 0.08	0.337 (0.032 – 3.556)	0.365		
CRP	9.74 ± 17.06	3.87 ± 0.47	1.249 (1.040 – 1.500)	0.018*	1.380 (0.892 – 2.134)	0.148
GG	50 (71.4%)	7 (23.3%)	8.214 (3.045 – 22.158)	<0.001*	6.908 (1.237 – 38.572)	0.028*
Fatty liver with/ without pancreas	52 (74.3%)	4 (13.3%)	18.778 (5.763 –61.188)	<0.001*	2.992 (0.426 – 21.040)	0.271

Quantitative data was expressed using Mean ± SD, Qualitative data was expressed using Number (%), OR: **Odd`s ratio**, C.I: Confidence interval, LL: Lower limit, UL: Upper Limit, p: p value for **Odd`s ratio** for comparing between the studied groups, *: Statistically significant at $p \leq 0.05$ $: for each 0.1

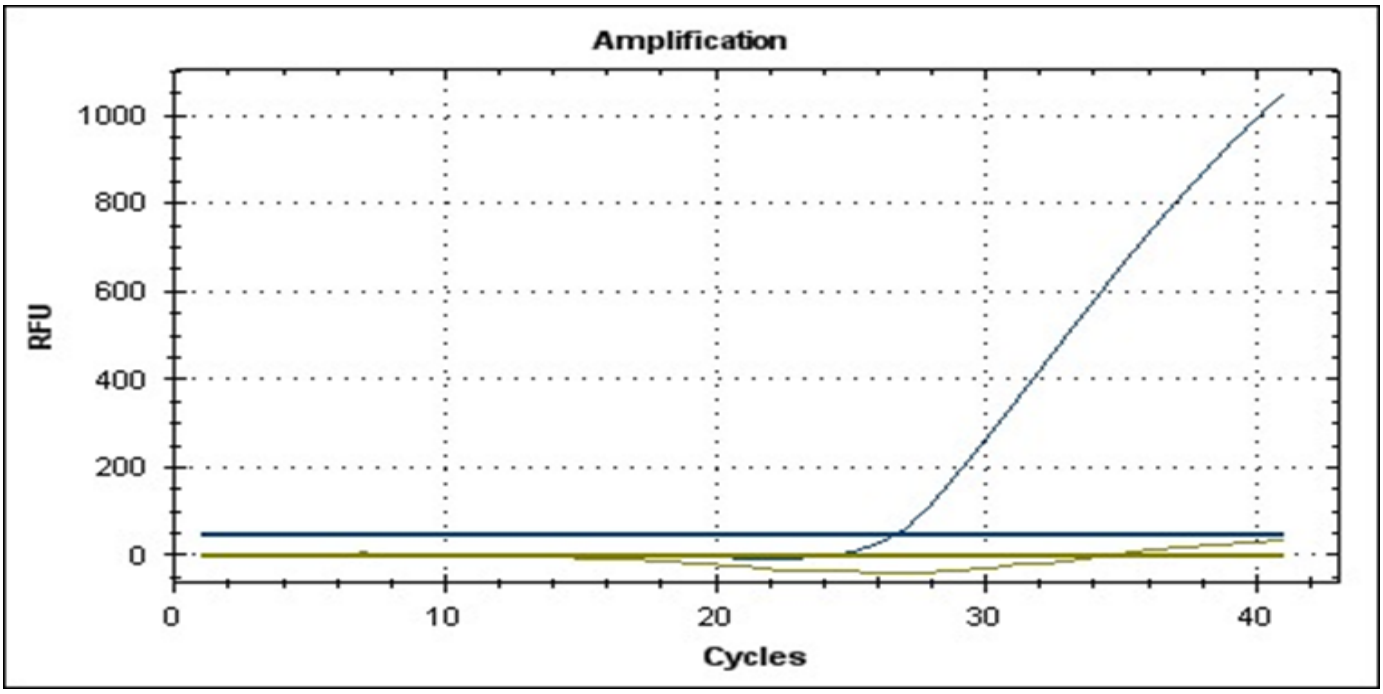

Figure 1: Homozygous allele (GG)

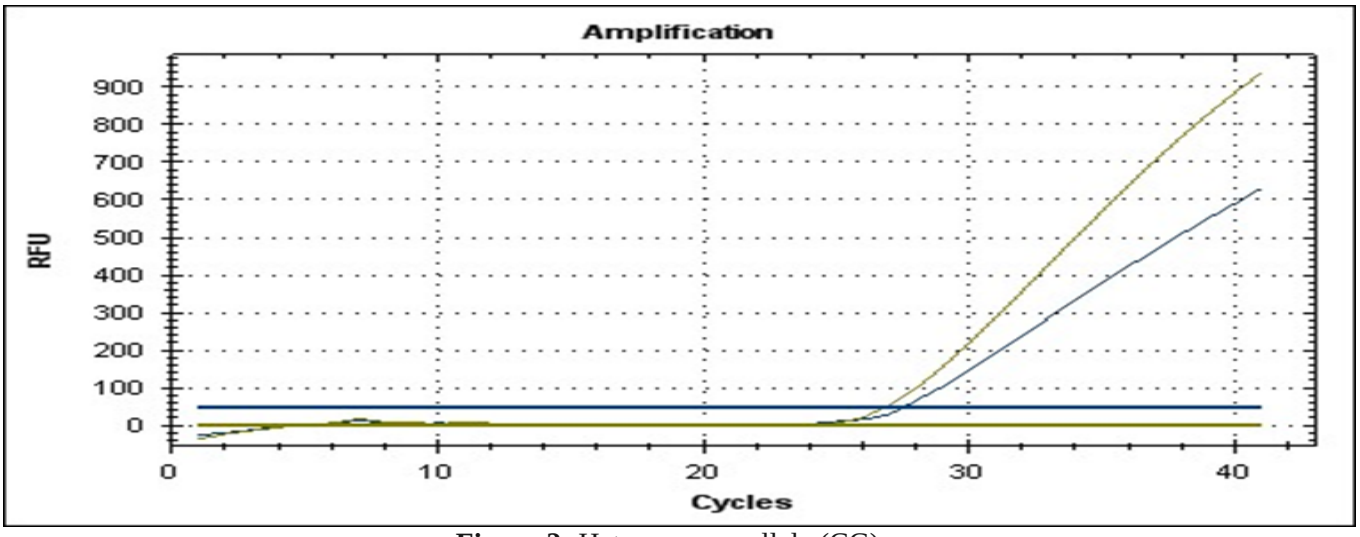

Figure 2: Heterozygous allele (CG)

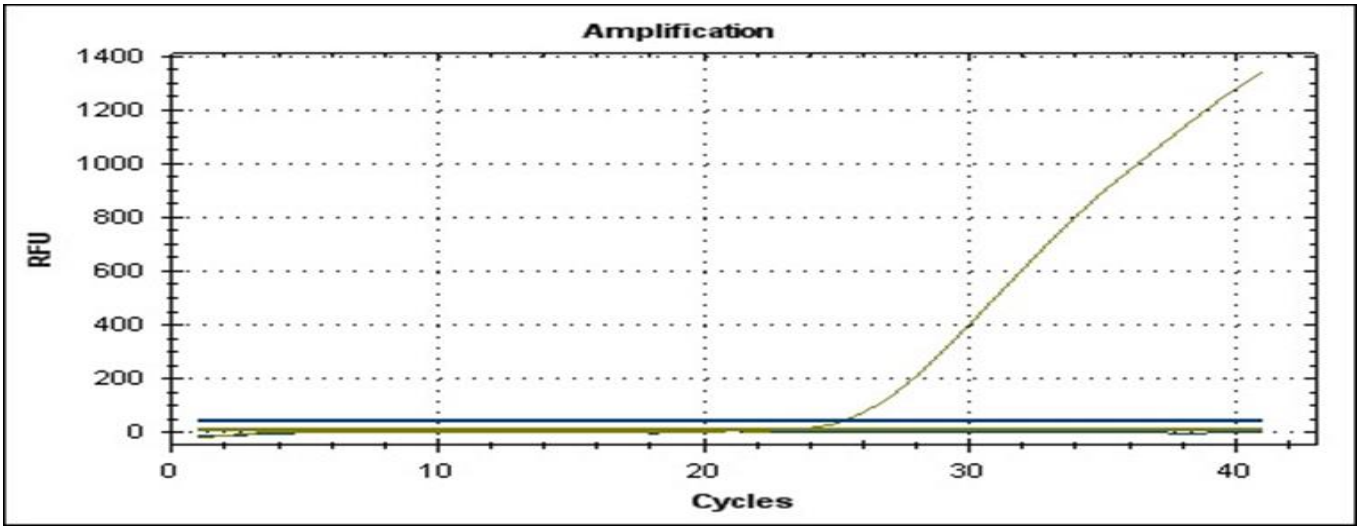

Figure 3: Homozygous allele (CC)

DISCUSSION:

A chronic inflammation in the adipose tissue induced by imbalance of inflammatory factors can promote obesity. It is known that the IL-6 gene has a role in the metabolism of fat and energy, yet it is unknown how this gene is related to obesity.

In this paper, we investigated the potential association between the IL6 gene snp rs1800796 polymorphism and the risk of obesity in Egyptian population and its relation to simple and complicated obesity. The findings showed that the obese groups had a higher prevalence of the GG homozygote genotype than the controls, with a statistically significant difference. This study showed a prevalence 81.4 % of this G allele among the simple obese group and 85.7% among complicated obese patients as compared with 55 % in the normal weight people. According to these aspects, the results of this study seem to confirm the hypothetical relation between the *IL6 G* genotype and the risk of developing obesity among Egyptian population.

Numerous investigations revealed a strong correlation between the IL-6 gene polymorphism and the metabolic syndrome, fatty liver, obesity, and insulin resistance. Meanwhile, several investigations discovered a strong correlation between the IL-6–174G/C polymorphism and an increased risk of obesity. Nonetheless, certain research has indicated that there is no noteworthy correlation between obesity and the IL-6–174G/C genotypes [14].

Consistent with our results, data from an Iranian study with 242 participants showed that obesity was associated with more common G alleles, but the difference was not statistically significant [18]. A further meta-analysis failed to show a function for the IL6 (174G/C) polymorphism in adiposity and found no significant relationships between the genotype and the waist-to-hip ratio, waist circumference, or central obesity [19].

Gulsah Koc et al study, between the control and obese groups, there was a significant difference in the IL-6 rs1800795 and rs1800796 variations ($p = 0.027$; $p = 0.013$). The SNPs rs1800795(G/C) and rs1800796(G/C) in IL-6 seemed to be associated with an increased risk of obesity in their investigation. The characteristics associated with obesity were linked to the C allele. [20].

In a study of Ibrahim et al, children who were obese exhibited notably elevated serum levels of IL-6 in contrast to their control counterparts ($P = 0.003$). Obese participants showed a high prevalence of IL-6 gene polymorphism GC (93.7%), whereas IL-6 polymorphism GG (70.6 %) was more common in the control group [21].

On the other hand, a substantial connection between the rs1800796 polymorphism and higher body mass index was shown in prior research by Barati et al. although only for the CC genotype of the polymorphism, not the GG [22].

Different research by Teixeira et al. included 314 patients with metabolic syndrome (MetS)and 298 patients without it, respectively. In both groups, the G/G carriers were more common than the GC and C/C genotypes. The GG genotype accounted for 39.1% of the population under study when divided into two different IL-6 genotype groups, C carriers (including G/C and C/C genotypes), and GG genotype. When compared to the GG group, the C carriers' group had a higher MetS prevalence. When comparing among groups, there were significant differences statistically for each MetS component. The BMI, waist circumference, and VLDL-C levels were greater among the C carrier group whereas HDL-C and Apo-A levels were lower [23].

Like this, significant relationships between the rs1800796 variation and greater waist circumference, insulin resistance, lower IL-6 levels, and higher CRP levels were discovered in an investigation for Boeta-Lopez, et al. The rs1800797 variation was linked to increased IL-6 levels and reduced CRP levels but not metabolic characteristics [24].

In a study by Suazo et al. to examine the association among IL-6 genetic polymorphisms (rs1800795, rs1800796 and rs1800797), IL-6R, IL18 and metabolic syndrome and/or its components in an obese children sample; IL-6, IL-6R and IL18 displayed no relation with metabolic syndrome [25]. Interleukin -6 is secreted from multiple tissue cells, including the hypothalamus, adipose tissue and muscles. Furthermore, cytokines, hormones and the transcription factors all influence the expression of the IL-6 gene. As a result, lifestyle and environmental factors, such as food consumption, which may have an impact on the IL-6 polymorphism, and the equilibrium between energy intake and energy expenditure, may be related to the variations in study findings. Second, because different studies have varied inclusion and exclusion criteria, confounding variables like age, family history, and smoking may have an impact on the outcome. Lastly, there is ongoing debate concerning the relationship between the IL-6 polymorphism and the predisposition to obesity.

In our study, we found that the presence of fatty liver and/ or fatty pancreas was more frequent in obese groups in comparison to controls, but they ($p<0.001$) were statistically significant parameters for obesity.

In a study done by Lee et al, they demonstrated that fatty pancreases were associated with insulin resistance, visceral adipose tissue, triglyceride and alanine transferase levels in 293 individuals. They concluded that fatty pancreas is strongly correlated with metabolic syndrome [26].

Additionally, in research to assess the risk variables linked to the development of fatty pancreas using endoscopic ultrasound; Increasing BMI, fatty liver, hyperlipidemia, and metabolic syndrome were factors linked to fatty pancreas on univariate analysis. The prevalence of fatty pancreatic was found to be 27.8%. The incidence of fatty pancreas increased by 37% in the presence of any of the metabolic syndrome components, specifically BMI ≥30, hyperlipidemia, diabetes, or hypertension [27].

The study has some drawbacks, including a limited size of sample. The patients investigated were discovered through a referral center, therefore they may differ from the general community.

Conclusion:

In conclusion, our study revealed a link between the IL-6 gene snp rs1800796 polymorphism and an increased risk of obesity. Future studies focusing on gene-environment interactions should be carried out to

clarify the connection between the IL-6 polymorphism and the likelihood of developing obesity, considering the range of interfering factors.

Disclosure of potential conflicts of interest

The authors declare that they have no conflict of interest. The authors did not receive support from any organization for the submitted work.

Contributors

MA and IM designed the study. MA and PI acquired the data. MA, PI, ME and EN analyzed and interpreted the data. MA drafted the manuscript. All authors revised the manuscript, approved the final manuscript and took responsibility for the integrity of the data analysis. The authors confirm that the manuscript is original and has not been published before but it has been presented as poster in Alexmed e posters. Each author acknowledges that he/she has contributed in a substantial way to the work described in the manuscript and its preparation.

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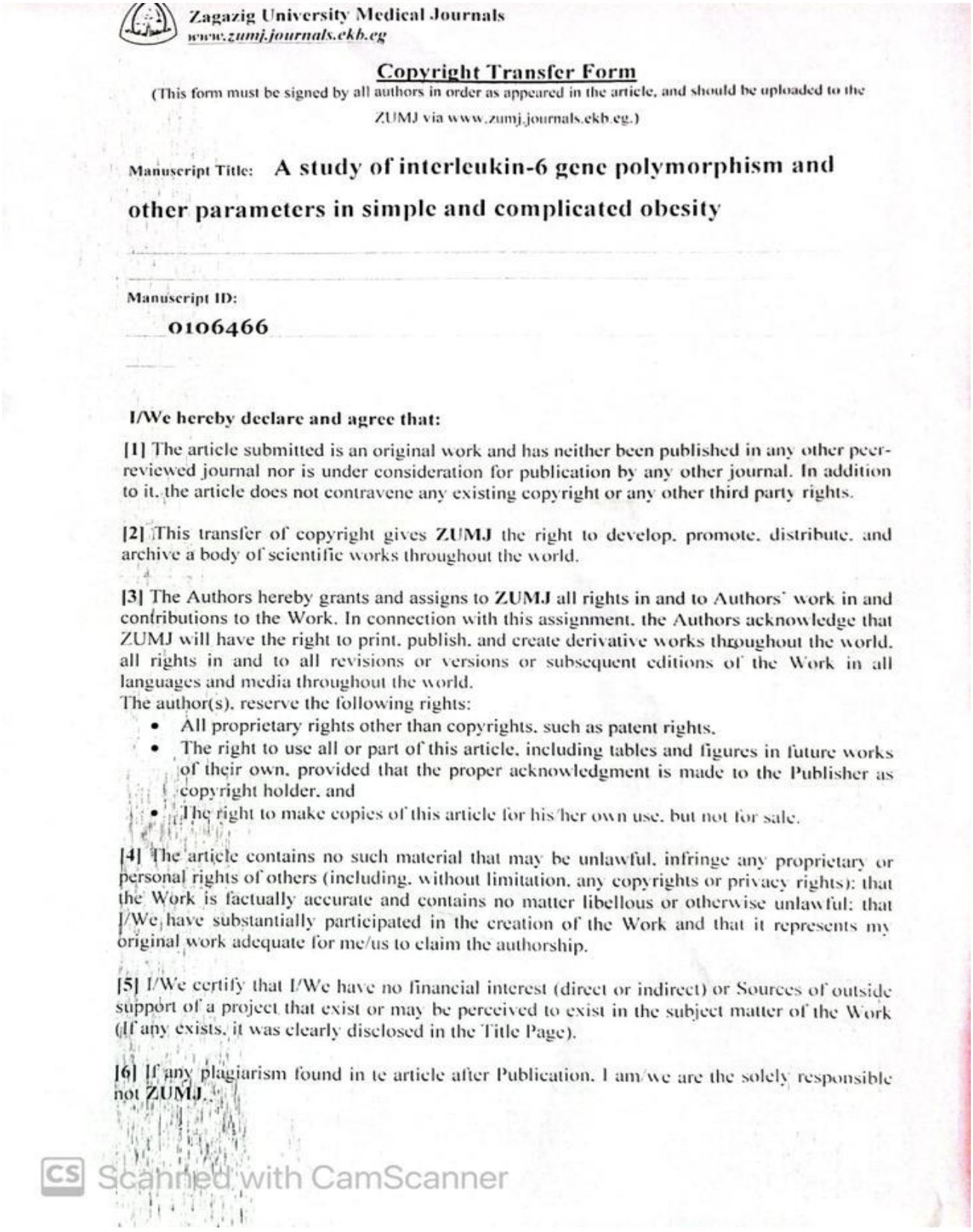

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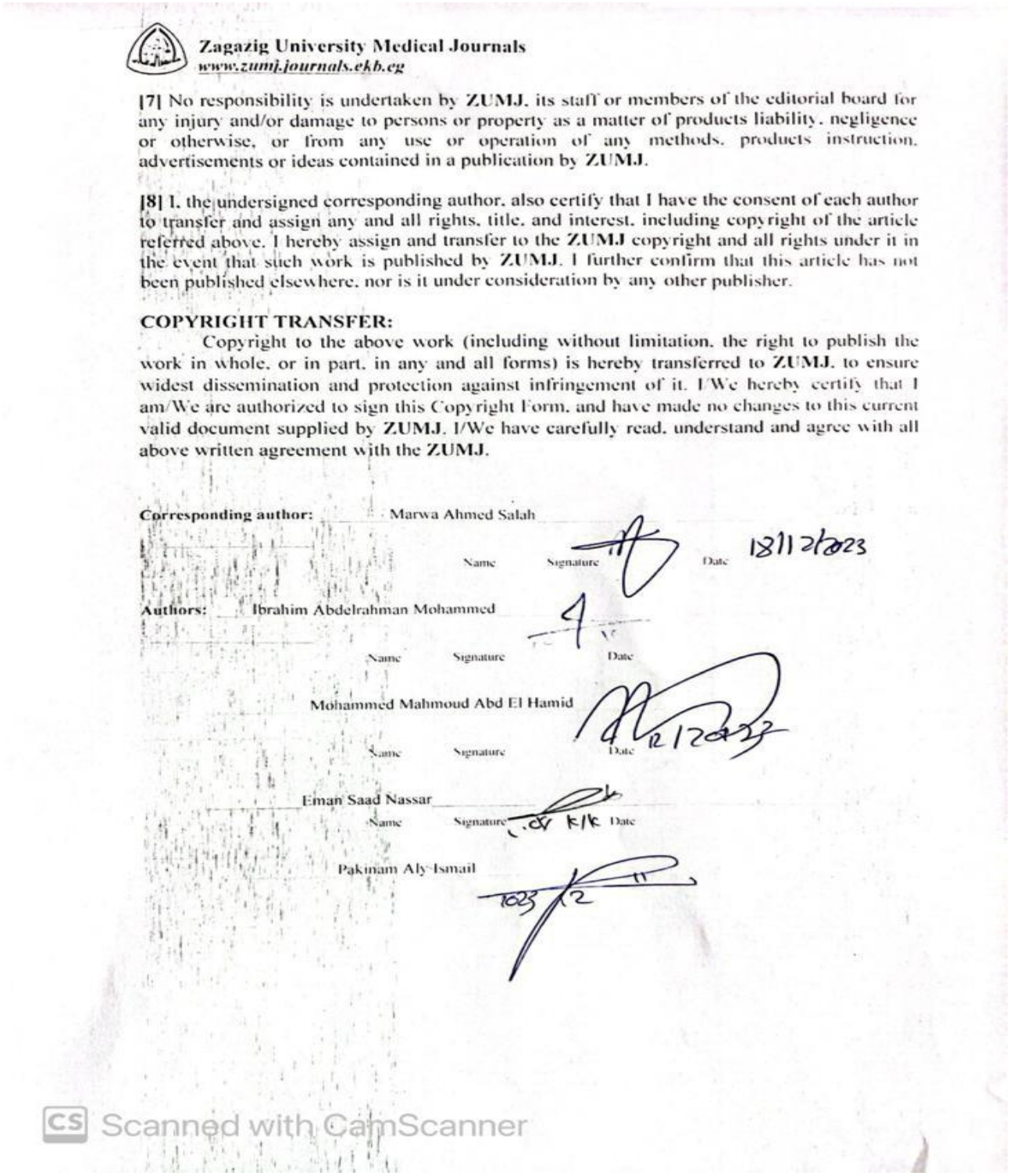

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