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Assessment of Monocyte Chemo-Attractant Protein-1 (MCP-1) and Other Biochemical Parameters in Iraqi Pregnant Women

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Abstract

The monocyte chemo-attractant protein-1 (MCP-1) is one of the pro-inflammatory cytokines. It controls the passage and infiltration of monocytes, macrophages, natural killers, and T cells into the sites of inflammation. The aim of this study is to inspect the role of MCP-1 in maternal metabolic, physiological changes and pregnancy complications like gestational diabetes mellitus, dyslipidemia, and hypertension to develop pharmaceutical strategies for these complications. This study included ninety Iraqi women divided into three groups: thirty pregnant women in their first trimester as the P1 group; thirty pregnant women in their third trimester as the P2 group; and thirty healthy non-pregnant women as the control or C group. Serum concentrations of MCP-1 were analyzed by the ELISA technique (sandwich principle). Fasting plasma glucose (FPG), C-reactive protein (CRP), fasting serum insulin (FSI), glycosylated hemoglobin (HbA1c), lipid profile, systolic, diastolic blood pressure, liver function enzymes ALT, AST and anthropometric parameters were measured. Our results revealed that serum MCP-1 significantly declined in the first trimester (P1) compared to the C group (p<0.05) and non-significantly declined in the third trimester (P2) compared to that in the C group, while there was a significant difference in serum MCP-1 between the P1 and P2 groups (p<0.05). Serum CRP showed a highly significant increase in the P1 and P2 groups compared to the C group at (p<0.01). There is a highly significant difference between the P1 and P2 groups (p<0.01). Serum MCP-1 had a significant positive correlation with body mass index (BMI), body fat percentage (BF %), systolic blood pressure (SBP) and C-reactive protein (CRP) in the P2 group (p<0.05). No significant differences in FPG or HbA1C were found between all the studied groups. Lipid parameters: TC, TG, LDL, and VLDL showed a highly significant increase in the P2 group compared to the C and P1 groups (p<0.01). HDL showed a highly significant decrease in the P2 group compared to the C group (p<0.01), while it was only significantly decreased in the P2 group compared to the P1 group (p<0.05). Depending on these results, we found that serum MCP-1 declines in pregnancy, the BMI, BF%, and the contractile arterial blood pressure (SBP) have a positive correlation with MCP-1 in late pregnancy, and the inflammation marker (CRP) has an independent association with MCP-1 in early gestation.

Keywords: Monocyte chemo-attractant protein-1, gestation diabetic mellitus, dyslipidemia, CRP. monotantcyte chemoatractant protein MCP-1

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تقييم و عوامل كيموحيويه اخرى عند النساء الحوامل العراقيات

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الخلاصة

يعتبر monocyte chemoattractant protein (Mcp-1) احد الحركيات الكيميائية الجاذبة التي تسبق الالتهاب، وهو يسيطر على المرور عبر الاغشية لكل من monocytes, macrophages, natural killer cells , T cells للوصول لموضع الالتهاب. تهدف هذه الدراسة الى تحري دور ال MCP-1 في التمثيل الغذائي للام ، التغيرات الفسيولوجية ومضاعفات الحمل كسكر الحمل، تراكم الدهون وارتفاع ضغط الدم من اجل تطوير ستراتيجية دوائية لهذه المضاعفات شملت الدراسة تسعين امرأة عراقيه قسمن لثلاث مجموعات: ثلاثون امرأة في المرحلة الاولى من الحمل (P1)، ثلاثون امرأة في المرحلة الثالثة من الحمل (P2)و ثلاثون امرأة غير حامل كمجموعه تحكم (C). تم قياس كل من مصل Mcp-1 باستخدام تقنية ال ELISA (sandwich principle)، و قيس السكر الصائم (FPG) و مصل الانسولين الصائم C-reactive protein (CRP), (FSI) و السكر التراكمي (HbA1C) و مستوى الدهون lipid profile و ضغط الدم الانقباضي SBP و الانبساطي DBP و انزيمات وظائف الكبد AST, ALT وعوامل انثروبومترية. اظهرت النتائج ان مستوى MCP-1 انخفض بشكل ملحوظ بفترة الحمل الاولى (P1) مقارنة بالمجموعة C ($p<0.05$) و انخفض بشكل غير ملحوظ بفترة الحمل الثالثة (P2) مقارنة مع مجموعة (C) في حين ان هنالك فرق معنوي في مستوى الMcp-1 بين المجموعة P1 والمجموعة P2 ($p<0.05$) اظهر مصل ال CRPزيادة معنوية عالية في المجموعة P1 و المجموعة P2 مقارنة مع المجموعة C عند $p<0.01$ و ايضا هناك فرق كبير بين المجموعتين P1 وP2 عند $P<0.01$ و ان مستوى MCP-1 يرتبط معنويا بشكل ايجابي مع مؤشر كتلة الجسم BMI و نسبة الدهون BF% و ضغط الدم الانقباضي SBP و مؤشر الالتهاب CRPعند $p<0.05$ بمرحلة الحمل الاخيرة. لم يوجد فرق معنوي بقيمة FPG, HbA1C بين مجاميع الدراسة. عوامل مخطط الدهون TC, TG, LDL, VLDL: اظهرت ارتفاع ملحوظ بالمجموعة P2 مقارنة بالمجموعة C و المجموعة P1 عند ($P<0.01$). اظهر ال HDL انخفاض ملحوظ في المجموعة P2 مقارنة بالمجموعة C عند $p<0.01$ في حين كان هنالك انخفاض معنوي في المجموعة P2 مقارنة بالمجموعة P1 عند $p<0.05$. بالاعتماد على هذه النتائج وجد انخفاض بمصل ال MCP-1 بالحمل، BF% , BMI ضغط الدم الشرياني الانقباضي SBP له علاقه ايجابية مع ال MCP-1 بمرحلة الحمل الاخيرة وان مؤشر الالتهاب CRP مرتبط بشكل مستقل مع قيمة البروتين موضع الدراسة بمرحلة الحمل الاولى.

1. Introduction

Pregnancy is a state in which the maternal system witnesses metabolic and immunological changes to meet fetal needs for glucose. Cytokines, as messengers of immune cells, play a vital role in these changes; among them is MCP-1. It is involved in the maintenance of early multiple cellular division and in placentation in the first trimester as an inflammatory mediator that recruits monocytes to the placentation site to repair the endothelium layer and peel dead cells. The third trimester ends with a cytokine influx into the uterus to promote contraction during birth [1]. Normally, MCP-1 has highly regulated, short-lived action. Any disorder in MCP-1 expression or action will complicate gestation [2]. Maternal cytokine disruption occurs when pro-inflammatory cytokines interfere with the insulin signaling pathway, resulting in insulin resistance, which is the main feature of gestational diabetes

mellitus (GDM). GDM or glucose intolerance that is first diagnosed in pregnancy might persist into T2DM after birth [3]. The other consequence of MCP-1 disturbance is adipose tissue-monocytes infiltration that leads to endothelial dysfunction [4], which is an atherosclerosis-initial marker [5]. Many studies have linked elevated maternal serum MCP-1 levels to insulin resistance, obesity, systemic inflammation, and dyslipidemia [6,7]. CRP is another inflammatory marker that mediates maternal metabolic disturbance. Both the increasing amount of adipose tissue and placental secretion will increase inflammatory markers [8]. The aim of this paper is to investigate the correlation between serum MCP-1 and CRP with other biochemical and anthropometric parameters in the first and third trimesters of Iraqi pregnant women.

Subjects

The ninety subjects were divided into three groups: the first group included thirty pregnant women in their first trimester (P1); the second group included thirty pregnant women in their third trimester (P2); and the third group included thirty healthy non-pregnant women (C or control group). All subjects had been fasting for 10-12 hours. The subjects diagnosed with diabetes mellitus, hypertension, or thyroid disorders were excluded.

2. Methods

Age, weight, height, age, body mass index (BMI) (Equation 1), and body fat percentage (BF%) (Equation 2) are among the anthropometric and clinical data for subjects [9,10].

$$BMI = w / squared\ l \quad (1)$$

Where w = body weight, l = height.

$$BF\ \% = (1.2\ BMI) + (0.23\ age) - (1.8\ gender) - 5.4 \quad (2)$$

Where gender is 1 for male, and 0 for female

Clinical parameters of all blood samples were performed using the same analytical devices. The systolic blood pressure (SBP) and the diastolic blood pressure (DBP) were taken as the average of three consecutive readings, using the right arm and in a sitting position. The medical history of the control group was checked and new clinical examinations were done to ensure their property for the study.

Sampling

The blood samples were drawn from fasting subjects and then divided into two groups of tubes: one with an anti-coagulant substance to get plasma, and the other without anti-coagulant (gel tube). After clotting; they were centrifuged at 3000 *xg* for 10 minutes, then poured into (250 µl) Eppendorff tubes, and stored at -20 °C until used.

Laboratory measurements

Serum total cholesterol (TC) and triglycerides (TG) were analyzed by the colorimetric method using a linear kit (Spanish). High density lipoprotein (HDL-cholesterol) was analyzed by a colorimetric method using a spinreact kit (Spanish). The Friedewald formula was used to calculate low density lipoprotein (LDL) [10]. Fasting plasma glucose was measured by the hexokinase method using a Spinreact kit (Spanish). Serum insulin was analyzed by ELISA (Demidtech kit, Germany), while serum MCP-1 was analyzed by ELISA (Mybiosource kit, USA). ALT and AST were analyzed by an enzymatic method using (Linear kit, Spain). The index of homeostasis model assessment (HOMA2-IR) used for insulin resistance and (HOMA2-S) used for insulin sensitivity were calculated by using equations on the professional website http://www.dtu.ox.ac.uk

Statistical analyses

All statistics were surveyed using the Statistical Package for the Social Sciences program (SPSS) version 24, considering a p-value less than 0.01 is a statistically significant difference and a p-value less than 0.05 is a statistically significant difference. An analysis of variance (ANOVA) was used to compare the mean values of the three groups in the study. The Bivariate Pearson correlation was performed in the P1 and P2 groups, with the coefficient of correlation (r) used as an indicator for the strength of the relationship between MCP-1 and other parameters such as glycemic, lipid profile parameters, ALT, AST, SBP, DBP, and CRP.

3. Results

Table 1 summarizes the findings of all anthropometric, medical, and biochemical analyses conducted on the P1, P2, and C study groups. Results showed that age means were significantly decreased in the third trimester group (P2) compared to the non-pregnant group (C) ($p<0.05$), but the P1 group age means were not significantly different compared to the non-pregnant group (C). Also, there was no significant difference between the P1 and P2 groups. In addition, gestational BMI showed a highly significant increase in P2 compared to the C and P1 groups ($p<0.01$). While no significant difference was found between the P1 and C groups. BF% was significantly higher in the P2 group compared to the C and P1 groups ($p<0.01$), but there was no significant difference between the first trimester (P1) and the non-pregnant group (C). However, FSI was significantly lower in the non-pregnant group (C) compared to the third trimester group (P2) (9.61 *vs*. 15.07 µIU/ml) ($p<0.01$), but there is only a significant difference between the first trimester (P1) and non-pregnant group (C) (13.96 *vs*. 9.61 µIU/ml) ($p<0.05$), respectively. No significant difference was shown between the first (P1) and third trimester (P2) groups. Moreover, FPG and HbA1c were non-significantly different between all groups. HOMA-β showed a highly significant increase in pregnant groups (P1 and P2) compared to the non-pregnant group (C) (169.68 *vs*. 191.52 *vs*. 125.8) ($p<0.001$), but no significant difference between first trimester (P1) and third trimester (P2) groups. HOMA-IR was significantly lower in the P2 group compared to the non-pregnant group (C) (1.85 *vs*. 1.22) ($p<0.01$), respectively. However, there was only a significant difference between the first trimester group (P1) compared to the non-pregnant group (C) (1.75 *vs*. 1.22) ($p<0.05$), respectively. No significant differences were found between the P1 and P2 groups. HOMA-S was significantly decreased in the third trimester P2 group compared to the non-pregnant group (C) (65.58 *vs*. 85.31 µIU/ml) ($p<0.05$), respectively, but there was no significant difference between the first (P1) and non-pregnant group (C) (72.21 *vs*. 85.31 µIU/ml). In addition, there was no significant difference between the first P1 and third trimester P2 groups. Furthermore, SBP was a highly significant increase in the P2 group compared to the non-pregnant group (C) (128.23 *vs*. 122.7 mm Hg), respectively ($p<0.01$). Also, there was a significant difference between the first trimester (P1) and the non-pregnant group (C) (127.2 vs. 122.7 mm Hg), respectively ($p<0.05$), while there was no significant difference between the first trimester (P1) and third trimester (P2) groups. There was a highly significant increase in DBP in the third trimester (P2) compared to the non-pregnant group (C) (76.43 *vs*. 68.03 mmHg), respectively ($p<0.001$). Additionally, there was a highly significant difference between the first trimester group (P1) and the control group (C) ($p<0.01$). Between the first group (P1) and the third group (P2), there was no discernible change in DBP.

Table 1: Anthropometric, and biochemical analysis results of all studied groups

Parameter	Control (N = 30)	P1 group (N = 30)	P2 group (N = 30)	*p*-Value
Age(year)	29.77±5.45	29.6±6.27	25.53±7.34*b	<0.05
BMI(Kg/m^2)	25.01±3.97	25.03±2.8	29.93±6.46**b,**c	<0.01
BF %	31.46±5.28	31.44±4.44	36.58±8.21**b,**c	<0.01
FPG(mg/dl)	85.61±7.26	81.88±11.17	79.59±12.56	0.09
HbA1c %	5.86±0.3	5.46±0.72	5.41±1.07	0.05
FSI(µIU/ml)	9.61±2.49	13.97±6.17*a	15.08±7.14**b	<0.01
HOMA β	125.8±24.62	169.68±36.97**a	191.52±51.54**b	<0.01
HOMA S	85.31±17.62	72.21±24.1	65.58±31.3*b	<0.05
HOMA IR	1.23±0.31	1.75±0.8*a	1.85±0.9**b	<0.01
SBP(mmHg)	122.7±6.78	127.2±7.15*a	128.23±6.94**b	<0.01
DBP(mmHg)	68.03±3.19	73.27±5.78**a	76.43±6.4**b	<0.01
MCP-1(pg/ml)	116.12±40.54	86.81±26.83*a	111.92±44.83*c	<0.05
CRP(mg/L)	2.31±0.23	3.43±0.97**a	6.46±2.44**b,**c	<0.01
TC(mg/dl)	165.13±27.98	167.56±28.4	234.79±43.04**b,**c	<0.01
TG(mg/dl)	147.48±17.89	154.18±56.15	218.79±70.27**b,**c	<0.01
HDL(mg/dl)	46.62±11.46	44.85±8.33	38.27±6.77**b,*c	<0.01
LDL(mg/dl)	89.02±26.94	93.13±30.11	154.11±40.15**b,**c	<0.01
VLDL(mg/dl)	29.5±3.58	30.77±11.31	43.73±14.07**b,**c	<0.01
AST(IU/L)	18.28±3.54	17.56±7.1	14.56±4.03*b	<0.05
ALT(IU/L)	15.07±5.25	19.71±7.58*a	17.15±6.51	<0.05

The results are displayed as mean ± SD, *p<0.05 for a significant difference, and **p<0.01 for a highly significant difference. The symbol a refers to a significant difference between P1 and C groups; b refers to a significant difference between P2 and C groups; and C refers to a significant difference between P1 and P2 groups. MCP-1 was significantly decreased in the first trimester group (P1) compared to the non-pregnant group (C) (86.81 *vs*. 116.11 pgm/ml) (p<0.05), respectively, but it was non-significantly increased in the third trimester group (P2) compared to the non-pregnant group (C) (111.91 *vs*.116.11 pgm/ml), respectively. A significant difference in MCP-1 means was found between the first trimester (P1) and third trimester (P2) groups (86.81 *vs*. 11.91 pgm/ml) (p<0.05). The TC, TG, LDL and VLDL were highly significant increases in the third trimester group (P2) compared to the non-pregnant group (C) (p<0.001), while differences were not significant in the first trimester group (P1) compared to the non-pregnant group (C), as well as highly significant differences were found between the first trimester (P1) and third trimester (P2) groups (p<0.001). On the other hand, HDL showed a highly significant decrease in the third trimester group (P2) compared to the non-pregnant group (C) (38.26 *vs*. 46.61 mg/dl) (p<0.01), respectively. While no significant difference was shown in the first trimester group (P1) compared to the non-pregnant group (C) (44.84 *vs*. 46.61 mg/dl), respectively. A significant difference was shown between the first trimester (P1) and third trimester (P2) groups (44.84 *vs*. 38.26 mg/dl) (p<0.05), respectively. CRP increased significantly in the P1 and P2 groups compared to the C group (3.430±97 *vs*. 6.46±2.44 *vs*. 2.31±0.23 mg/l) (p<0.01). There was also a highly significant difference between the P1 and P2 groups (3.43±0.97 *vs*. 6.46±2.44 mg/l) (p<0.001). The AST

was significantly different in the third trimester group (P2) compared to the non-pregnant group (C) (14.45 *vs*. 18.28 u/l) (p<0.05), respectively. No significant differences were found between the first trimester group (P1) and the non-pregnant group (C), nor between the first trimester P1 and third trimester P2 groups. In addition, ALT was significantly different between the first trimester (P1) group and the non-pregnant group (C) (19.71 *vs*. 15.06 u/l) (p<0.05), but there was no significant difference found between the third trimester (P2) and non-pregnant C groups (17.41 *vs*. 15.06 u/l), as well as no significant difference was shown between the first trimester (P1) and third trimester P2 groups. As shown in Figure 1, serum MCP-1 levels in the control group (C) were higher than in the pregnant groups (P1 and P2). Figure 2 shows that the mean serum CRP was higher in the P2 group than in the P1 and control C groups.

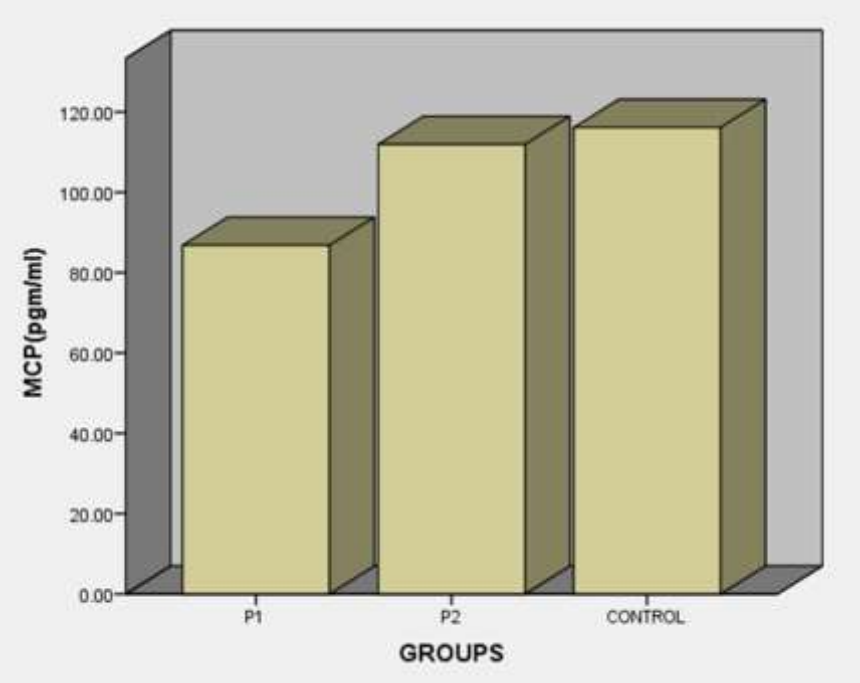

Figure 1: Serum MCP-1 level of all studied groups

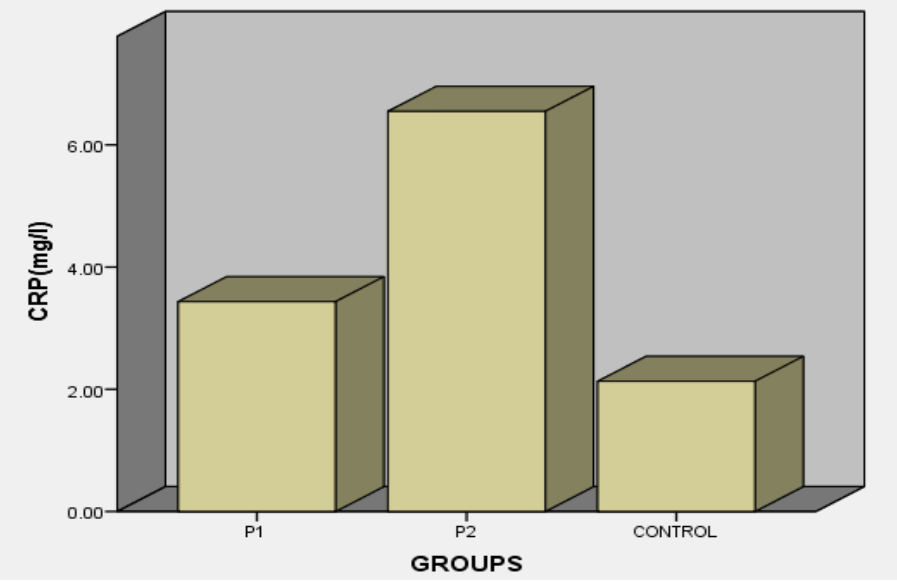

Figure 2: Serum CRP level of all studied groups

Table 2 exhibits the Pearson correlation coefficient (r) and the significance of correlation (p) between serum MCP-1 in pregnant groups and medical and biochemical aspects. According to the findings, serum MCP-1 was shown to have a significant positive connection with BMI and BF% in the third trimester group (P2) at (r = 0.426, *P* = 0.021 and r = 0.339, *P* = 0.032, respectively). In the P2 group, there was a substantial positive connection between serum MCP-1 and SBP and CRP (r = 0.433, *P* = 0.019, r = 0.452, *P* = 0.014, respectively). Additionally, the results showed that there was no significant association between serum MCP-1 and glycemic parameters, lipid profile, ALT, AST, or DBP in either the P1 or P2 group, but there was a significant positive correlation between serum MCP-1 and CRP in the P1 group (r = 0.457, *P* = 0.011).

Table 2: Analysis of Pearson correlation for serum MCP-1 with other parameters in P1 and P2 groups

Parameter	Serum MCP-1					
	P1 (N=30)			**P2(N=29)**		
	r	***P***	**Sig**	**R**	***P***	**sig**
BMI (Kg/m^2)	0.182	0.337	N.S.	0.426	0.021	S.
BF%	0.168	0.374	N.S.	0.339	0.032	S.
FPG (mg/dl)	0.024	0.901	N.S.	0.002	0.992	N.S.
HbA1c (%)	-0.107	0.573	N.S.	0.064	0.741	N.S.
FSI (µIU/ml)	0.133	0.482	N.S.	-0.043	0.826	N.S.
HOMA2-IR (%)	0.129	0.497	N.S.	0.007	0.969	N.S.
HOMA2-β (%)	0.157	0.406	N.S.	-0.045	0.818	N.S.
HOMA2-S (%)	-0.271	0.147	N.S.	+0.004	0.985	N.S.
TC (mg/dl)	-0.251	0.180	N.S.	-0.029	0.862	N.S.
TG (mg/dl)	0.007	0.972	N.S.	0.16	0.408	N.S.
HDL (mg/dl)	-0.12	0.529	N.S.	-0.018	0.926	N.S.
LDL (mg/dl)	-0.133	0.433	N.S.	-0.046	0.813	N.S.
VLDL (mg/dl)	0.01	0.959	N.S.	0.159	0.411	N.S.
AST (u/l)	0.301	0.105	N.S.	-0.016	0.934	N.S.
ALT (u/l)	0.031	0.873	N.S.	-0.305	0.101	N.S.
SBP (mmHg)	-0.007	0.969	N.S.	0.433	0.019	S.
DBP (mmHg)	-0.065	0.732	N.S.	0.329	0.081	N.S.
CRP (mg/l)	0.457	0.011	S.	0.452	0.014	S.

H.S. = High significant at $p < 0.01$, S. = significant for $p < 0.05$, N.S. = not significant for $p \geq 0.05$

Table 3 represents the regression analysis for the association of investigated parameters with serum MCP-1 concentration. The results showed that BMI, BF, SBP, and CRP have a positive significant correlation with maternal serum MCP-1 in the third trimester ($p<0.05$). In the first trimester, CRP is an independent predictor of maternal serum MCP-1 ($p<0.05$).

Table 3: The regression analysis for the association of investigated parameters with serum MCP-1 concentration

MCP-1 R^2=0.209, adjusted R^2=0.181

model 1	β	Coefficient of standard error	*p*-value
CRP	0.457	4.64	0.011

H.S. = High significant if $P < 0.01$, S. = significant if $p < 0.05$, N.S. = not significant if $p \geq 0.05$, SE: standard error

4. Discussion

The current study aimed to evaluate the serum level of MCP-1 in the first and third trimesters of pregnancy. Another aim of this study is to assess the relationships between the

adipokine and other anthropometric, glycemic, lipid, liver function, blood pressure, and inflammation parameters. The results of this study showed that serum MCP-1 declined in the first trimester and then returned to increase in the third trimester. However, serum MCP-1 in non-pregnant women was higher than that in pregnancy. The early decline in MCP-1 levels may be required for successful placentation, whereas the late elevation in MCP-1 levels may be required to prepare the pregnancy for delivery and uterine contractions [1]. The statistical analysis revealed that serum MCP-1 was significantly correlated with BMI, BF%, SBP, and CRP. Previous research found a significant decrease in serum MCP-1 levels between the first and third trimesters in non-obese pregnant women (BMI <30 kg/m^2), whereas serum MCP-1 was up-regulated and considered an additional risk factor in obese pregnant women [11]. Naruse *et al*., found that serum MCP-1 was lower in complicated pregnancy with hypertension than in non-pregnant healthy women [12]. Maternal serum MCP-1 levels were observed to be lower in late pregnancy with GDM compared to healthy women who were not pregnant by Telejko *et al*. [13]. The Pearson correlation results showed a significant positive correlation between serum MCP-1 concentrations and BMI in the third trimester. These findings somewhat agreed with those of Powell and co-workers [11], who discovered a substantial positive connection between maternal BMI and MCP-1 in maternal plasma. Previous studies attributed the correlation between obesity and the concentrations of MCP-1 to the considerable maternal adipose tissue enlargement in the obesity state, which is a considerable source of this cytokine [14]. Additionally, there was a distinct increase in MCP-1 mRNA expression in the adipose tissue of obese pregnant women compared to normal-weight pregnant women [15], but this finding differs from that of Kirk *et al*., who discovered in an *in vitro* study on mice that MCP-1 might be involved in the restriction of lipid accumulation in adipocytes if the weight gain persists [16]. The findings revealed a significant positive correlation between MCP-1 and SBP, which is consistent with the findings of Taylor and co-workers in 1997, who discovered that "cultured aortic vascular smooth muscle cells when ~~were~~ strained mechanically showed **a** significant rise in MCP-1 expression. This suggested that hemodynamic strain applied onto arterial cells in hypertension was a vital stimuli for MCP-1 expression" [17]. This positive correlation is also partially consistent with previous studies, which stated that up-regulating of CCL2 expression results in systemic inflammation like preeclampsia or hypertensive disorders in pregnancy (PE/HDP) [18]. Naruse *et al*. found that "MCP-1 concentrations were considerably higher in pregnant women with hypertension than in normal pregnant women" [12]. The results exhibited a positive correlation between serum MCP-1 and serum CRP levels. This finding is in agreement with Han *et al*., who found that CRP stimuli induce the up-regulation of MCP-1 receptor (CCR2) expression in human monocytes, which enhances monocyte chemotactic movements in response to MCP-1 [19]. The regression analysis aimed to detect parameters that are independently associated with MCP-1 in the third trimester. It showed that serum CRP met that association. According to a prior study, there is a significant correlation between BMI and obesity. Adipose tissue and immunological response have been linked in previous studies [20]. The ANOVA results stated that FPG did not significantly decline in the first and third trimesters compared with the non-pregnant group. This finding is in agreement with previous studies that this decrease is due to placental and fetus-glucose uptake, which was independent of insulin and blood volume increase [21]. The current study results declared that HbA1c was non-significantly decreased in pregnancy compared with the non-pregnant group. This finding is in agreement with previous studies [22,23]. The decline in HbA1c in late pregnancy was related to a decrease in the life span of erythrocytes, which was accompanied by physiological gestational anemia [24]. The results of this study declared that there is no correlation between the serum MCP-1 and insulin resistance or that it is reciprocal (insulin sensitivity), which is in partial consistency with the findings of a previous study [25]. The results of the current study

are in agreement with those of a previous study, which found a decrease in MCP-1 in normal non-obese pregnant women (BMI <30 Kg/m^2), preventing the shift from homeostatic insulin resistance to a pathologic state [26]. The ANOVA analysis of the current study declares a non-significant increase in TC, TG, LDL, and VLD levels in early pregnancy. In late pregnancy, those parameters are significantly increased due to the shifting from TG, fatty acid deposition in adipose tissue, to a fat catabolic state that releases them into circulation and promotes inflammation (as a response to fat deposition in early pregnancy). The pro-inflammatory MCP-1 down-regulates lipoprotein lipase activity (LPL), resulting in elevated TG and VLDL blood levels [27-30]. The ANOVA results of the current study stated a significant increase in ALT in early pregnancy, which is consistent with the results of a previous study [31]. Previous studies declared that there was no agreement on the effect of gestation on ALT and AST levels and that their levels remained within the reference normal range for non-pregnant women [32]. Other studies linked deletion of MCP-1 to reduced ALT and AST due to MCP-1-delete activation of hepatic lipase that accumulates lipids in the liver [33,34].

5. Conclusion

The findings of the current study suggest that the early decline in maternal serum MCP-1 levels may be a physiological adaptation mechanism to safeguard the maternal system from prolonged exposure to pathological effects, minimizing the synergistic effects of MCP-1 with naturally rising insulin resistance, lipid parameters, CRP, BMI, BF%, and SBP. CRP has a significant positive correlation with maternal serum MCP-1. Serum CRP levels are a significant independent predictor of maternal serum MCP-1 in early pregnancy.

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