Original Article

Soluble CD163, A Product of Monocyte/Macrophage Activation Is Significantly Lower In Maternal And Umblical Cord Serum In Women With Preeclampsia

Muneera Abdalziz Alsheeha[1], Abdelmarouf Hussan Moheldein[2]
Maamun Rgab[3], Eltuhami Abdel-Magied[1], Ishag Adam*[1]

ABSTRACT

Background: Although, the exact pathophysiology of preeclampsia is unknown, activation of monocytes and macrophages (monocyte/macrophage activation) is suggested to have a rolein the immunopathology of preeclampsia. Soluble CD163 (sCD163) is considered a specific marker of monocyte/macrophage activation. Nonetheless, investigations addressing sCD163 in cases preeclamptic women are needed.

Objectives: To investigate maternal and umbilical cord levels of sCD163 in women with preeclampsia.

Materials and Methods: A case – control study was conducted at the labour ward of Qassim Maternity Hospital, Kingdom of Saudi Arabia during the period of March -September 2015. Forty five cases of preeclamptic women and an equal number of healthy pregnant women were controls. Obstetrics and medical history was gathered using questionnaire. sCD163 levels were measured using ELISA.

Results: The two groups (45 in each arm of the study) were matched in their age and parity. Thirty- three of the 45 cases were patients with severe preeclampsia.

The median (interquartile) levels of both maternal [32.70(18.9 – 47.0) vs. 52.5(33.7–74.8)ng/ml, P= 0.001] and cord [12.30(10.9– 23.10) vs. 52.4(20.80 – 63.0) ng/ml, P< 0.001] sCD163 were significantly lower in the preeclamptic cases compared to the controls.

There was a significant direct correlation between the maternal and umbilical cord level of sCD163. Both maternal and umbilical cord sCD163 levels were inversely correlated with birth weight.

Conclusion: The current study showed significantly lower maternal and cord sCD163 levels in women with preeclampsia as compared to controls. Moreover, there was a significant direct correlation between the maternal and umbilical cord level of sCD163 on one hand and birth weight on the other.

Keywords: preeclampsia**,** Soluble CD163, macrophage, birth weight, Sudan.

Preeclampsia is big health problem where it complicates 3–8% of all pregnancies and manifests clinically after the 20 weeks of gestation[1]. Preeclampsia is a serious medical disorder; it can lead to convulsion and maternal death[2-5].

Although the exact pathophysiology of preeclampsia is not yet fully understood, certain factors have been attributed to. These include changes in placental perfusion, changes in the immune system, and endothelial dysfunction[6,7].

Macrophages which are antigen-presenting

1. College of Medicine, Qassim University, Kingdom of Saudi Arabia
2. College of Applied Medical Sciences, Qassim University, KSA
3. Maternity and Child Hospital, Qassim, KSA

*Correspondence to:Prof. Ishag Adam Department of Obstetrics and Gynaecology, Medical College, Qassim University, Kingdom of Saudi Arabia
Tel: +966537644287
E mails:ishagadam@qumed.edu.sa

cells, account for the second most numerous type of immune cellsin the human deciduas of pregnancy and act as immune-modulatory cells[8,9]. Involvement of different types of macrophages have recently been postulated in the pathogenesis of preeclampsia[10,11]. Soluble CD163 (sCD163) is a macrophage scavenging receptor. It is a mononuclear phagocyte–restricted cell surface glycoprotein antigen present on type 2 macrophages (M2 cells) which exerts an anti-inflammatory function[12]. Macrophages stimulated via Th1 cytokines/chemokiness polarize toward pro-inflammatory type 1 macrophages (M1 cells). These cells can defend against utero-placental infections, but they have no role in the tolerance of the fetus[11]. Recent research studies suggested a role for sCD163 in the pathogenesis of preeclampsia especially when it is associated with intrauterine growth restriction[13-17]. However, the results of these studies were not concordant. Thus, while some results showed low levels of expression of sCD163 in preeclampsia, others showed , the other showed no or high levels of expression. The current study was conducted to investigate maternal and umbilical cord level of s CD 163 in women with preeclampsia and the correlations (if any) between sCD163, maternal hemoglobin and birth weight.

MATERIALS AND METHODS:

A case control study was conducted at the labour ward of QassimMaternity Hospital, Kingdom of Saudi Arabia during the period of March-September 2015. Qassim.Qassim Maternity Hospital is a tertiary hospital for referring cases with high risk pregnancy. Cases were of women with preeclampsia which isdefined as the occurrence of hypertension (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥ 90 mm Hg) in the second half of pregnancy (after 20 weeks) and proteinuria (presence of 300 mg or more of protein in 24 h urine sample or ≥2+ on dipstick). Preeclampsia is considered mild or severe according to the diastolic blood pressure - mild if < 110 mmHg, or severe if ≥110 mmHg[18]. Healthy women were taken as controls. Thyroid disease, hypertension, renal disease, diabetes and liver disease were the exclusion criteria.

After signing an informed consent, medical and obstetrics history (age, parity, and gestational age) was gathered using a questionnaire.

Body mass index (BMI) was computed via weight in kilograms divided by the square of height in meters which were measured of each participant. Maternal hemoglobin was measured and the results recorded. The birth weight was measure and recorded following the delivery.

Then maternal and umbilical cord blood (5 mls) were taken from each woman (case or control), allowed to clot, centrifuged, and stored at −20°C until analyses was performed using Ultra-Sensitive sCD163 ELISA KIT, (bioactivadiagnostica GmbH - Bad Homburg, Germany). The manufacturers` instructions were followed.

A total sample size of 45 participants in each arm of the study was calculated to have the mean difference of the sCD163 and that would provide 80% power to detect a 5% difference at $\alpha = 0.05$, with an assumption that complete data might not be available for 10% of participants.

Statistics:

SPSS for Windows (version 20.0) was used for data analyses. Continuousvariables were checked for normality and their difference was compared between the cases and controls using T-test and Mann-Whitney U when the data were normally and not normally distributed, respectively. Spearman correlation was performed between maternal and umbilical cord sCD163 level, and birth weight andhaemoglobin level. P

< 0.05 was considered statistically significant.

RESULTS:

While there was no significant difference in the age, parity and BMI between the two groups (45 women in each arm), gestational age and birth weight were significantly lower in the cases, table1 .

Median (interquartile) levels of both maternal [32.70(18.9 – 47.0) vs. 52.5(33.7–74.8)ng/ml, P= 0.001] and cord [12.30(10.9– 23.10) vs. 52.4 (20.80 – 63.0)ng/ml, P< 0.001] sCD163 were significantly lower in the cases compared to the controls. While the sCD163 level in cord blood was significantly lower than that of maternal blood level in the preeclamptic cases, there was no such a significant difference between them in the controls (Table 2). There was a significant positive correlationbetween the maternal and umbilicalcord level of sCD163. Both maternaland umbilical cord sCD163 levelswere inversely correlated with birth weight (Table 3).

Table 1: Basic characteristics of the studied cases and controls

Variable	Cases (n=45)	Controls (n=45)	P
Age, years	27.5 (3.8)	28.1(4.2)	0.504
Parity	2.3(1.8)	2..6(1.4)	0.521
Gestational age, weeks	37.2(1.2)	38.1(1.1)	0.001
Body mass index, Kg/m^2	24.3(2.1)	24.4(2.4)	0.833
Birth weight, g	2346.6(2055.0)	2864.4(3747.0)	<0.001

Table 2: Median (interquartile range) of maternal and umbilical cord soluble CD 163 levels in the case and controls

Variable	Cases (n=45)	Controls (n=45)	P
Maternal s CD 163, ng/ml	32.70(18.9 – 47.0)	52.5(33.7–74.8)	0.001
Umbilical cord sCD163,ng/ml	12.30(10.9– 23.10)	52.4(20.80– 63.0)	<0.001
P	< 0.001	0.304	

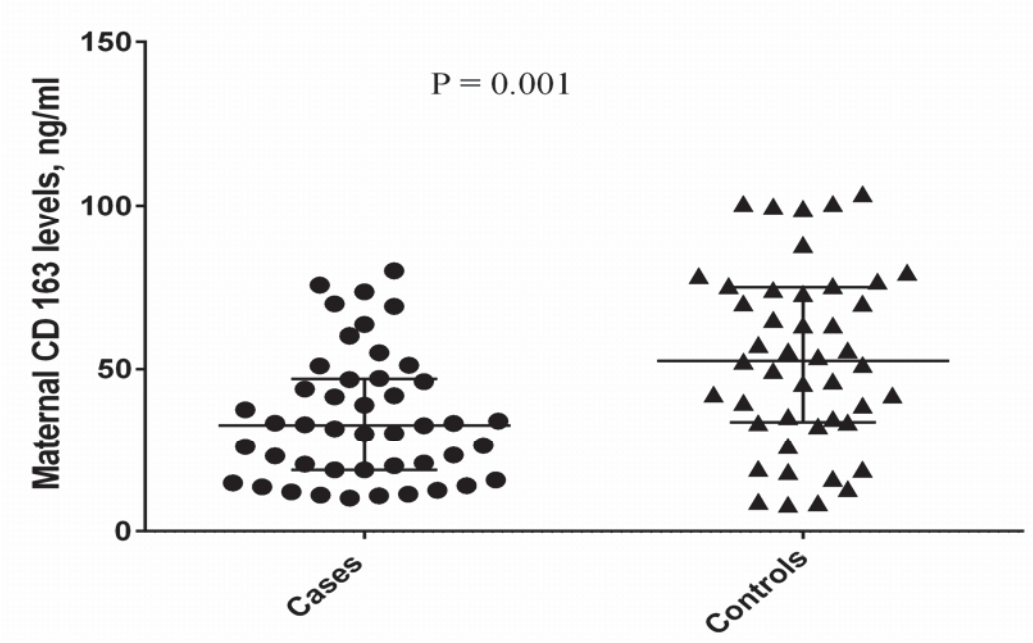

Figure 1: Median (interquartile range) of maternal soluble CD 163 levels in the case and controls**.**

DISCUSSION:

The main findings of the current study were; the significantly lower sCD163 in women with preeclampsia as compared to controls and an inverse correlation between sCD163 levels and birth weight. Our results are consistent with the previous finings where expression of CD163 was significantly lower in 58 women with preeclampsia compared with the 52 controls women that were matched for gestational age[4]. It has recently been reported that expression of CD163 was significantly lower in preeclamptic women compared with controls[13].

Table 3: Spearman correlation between the maternal, cord soluble 163 and birth weight

Variable	Maternal s 163		Cord s 163		Birth weight	
	r	P	*r*	P	*r*	P
Cord s 163	0.232	0.028	—	—	- 0.284	0.007
Birth weight	-0.333	0.001	- 0.284	0.007	—	—
Maternal hemoglobin	0.280	0.061	0.350	0.018	0.007	0.964

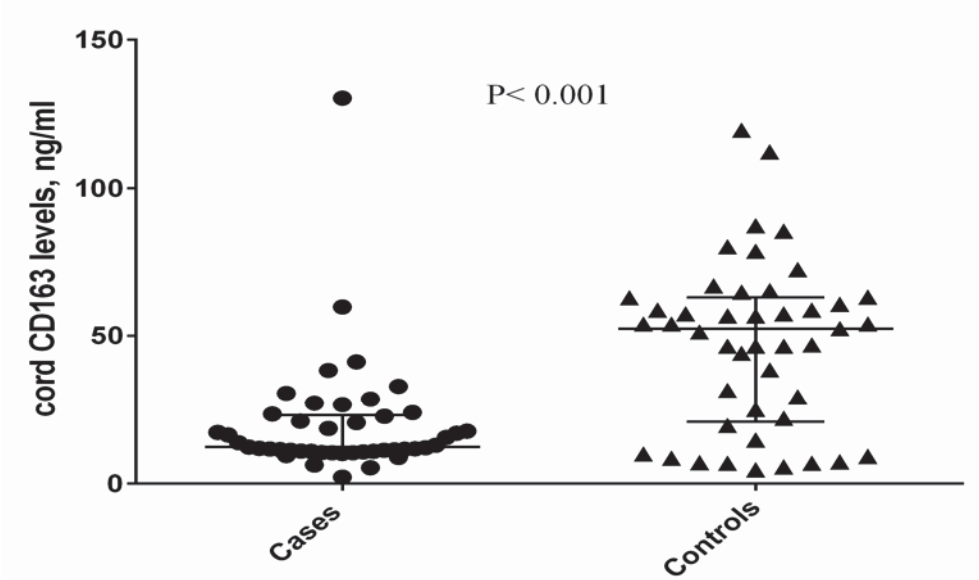

Figure 2: Median (interquartile range) of umbilical cord soluble CD 163 levels in the case and controls.

On the other hand there are reports that are discordant to ours. Thus Schonkeren et al. (2011) (Schonkeren *et al*. 2011) reported that CD163 expression increased significantly in preterm preeclamptic decidua basalis compared with preterm control pregnancies where as Kronborg *et al* (2007)observed that there was no significant difference in the serum level of sCD163 between pregnant and non-pregnant women, and that sCD163 level did not increase from week 18 to 38 and there was a tendency towards higher sCD163 in week 38 in preeclamptic women compared to healthy women. Likewise it has recently been observed that CD163 level showed a small but not statistically significant (p-value=0.37) increase in women with preeclampsia compared to controls[17].

The current study showed no significant correlation between maternal hemoglobin and sCD163 but showed a significant correlation between cord sCD163 and hemoglobin. Recently Chua et al., observed an inverse association of

sCD163, with haemoglobin levels in placental malaria., which is another disease charactreized by macrophage/monocyte infiltration[19]. CD163 is a key regulator of macrophage function and act in scavenging of free haemoglobin[20]. Free hemoglobin, a highly cytotoxic compound, has been reported to be elevated in preeclampsia[21,22].

CONCLUSION:

The current study showed significantly lower sCD163 levels (in both maternal and cord blood) in women with preeclampsia. There was a significant positive correlation between the maternal, umbilical cord level of sCD163 and birth weight

ETHICAL CONSIDERATIONS:

The study received ethical clearance from Regional Research Ethics Committee, Ministry of Health, Qassim, Kingdom Saudi Arabia.

COMPETING OF INTEREST:

Authors have no competing interest in this work.

AVAILABILITY OF THE DATA:

Data could be available upon request.

AUTHORS` CONTRIBUTIONS:

MAA and IA design the study, MAA, AHM and MR conducted the clinical work. AHM and EA conducted the laboratory work. AA and IA conducted the laboratory work. All the authors approved this version of the paper.

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