Original Article

Levels of Tumor necrosis factor - alpha in pre- eclampsia

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Abstract

Background : Preeclampsia is a severe complication of pregnancy characterized by an excessive maternal systemic inflammatory response with activation of the immune system.

Material and Method: 25 of preeclampsia (i.e., high blood pressure [BP] and proteinuria) and 15 of normal pregnancy were enrolled for the study. The blood samples were analysed for tumor necrosis factor-alpha.

Result: Significantly increased values of TNF-α were found in preclampsia when compared to normal pregnant females.

Discussion : TNF- α, is a potential mediator of endothelial dysfunction, which is a hall mark of the maternal syndrome of preclampsia.

Key Words : Pre- eclampsia, TNF-alpha

Introduction

Pre-eclampsia is a pregnancy-specific condition characterized by hypertension and proteinuria that remits after delivery. It is amongst the leading causes of foetomaternal morbidity and mortality worldwide(1). The exact etiology remains obscure, however maternal symptoms are thought to be secondary to vascular damage in the maternal uteroplacental and foetal umbilical placental circulation is supposed to be the central feature(2).

The maternal immune system has been proposed to have an influence on both the placentation and the subsequent systemic reactions. Several studies (3, 4)have indicated variations in the levels of cytokines in preeclamptic females, however there possible role in disease pathogenesis and expression in disease is still controversial. Amongst the cytokines, tumor necrosis factor (TNF)-α elicits the widest spectrum of biological activities and has a major role in cytokine network. The placental trophoblast cells and fetoplacental macrophages normally produce TNF-α which upregulates the endothelial expression of platelet derived growth factor, endothelin -1 and plasminogen activator inhibitor. All these cofactors are responsible for vasoconstriction and are capable of producing endothelial cell activation and dysfunction. Hence, with this in mind it was thought worthwhile to assess the levels of these cytokines in pre-eclamptic patients.

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Material and Method

Females in the third trimester of their pregnancy attending the antenatal clinic or admitted to the maternity ward of NKP Salve Institute of Medical Sciences, Nagpur were enrolled in this case control study. The ethical institutional committee approved the study and all participants gave written informed consent. 25 of preeclampsia (i.e., high blood pressure [BP] and proteinuria) and 15 of normal pregnancy were enrolled for the study. Pre-eclampsia was defined as systolic and diastolic BP greater than 140 mm Hg and 90 mm Hg, respectively, with significant proteinuria (N300 mg per 24 h); mild pre-eclampsia was defined as diastolic BP less than 110 mm Hg,with significant proteinuria; and severe preeclampsia as diastolic BP greater than 110mm Hg, or massive proteinuria (N2 g/24 h), or serum creatinine level greater than 1.2 mg/dL, or when other signs and symptoms of severe pre-eclampsia such as persistent headache, visual disturbances, persistent epigastric pain, and/or thrombocytopenia were present [5]. Detailed patient history was taken and a physical

examination performed. Blood pressure was measured in the left arm with a syphygomanometer. Urinalysis was done for proteinuria. A total of 2 mL of venous blood was taken from all women. All blood samples were drawn into tubes free of endotoxins and containing heparin. TNF α was measured by Microplate enzyme linked immunoassay kit method .Statistical significance of difference was estimated using students `t` test.

Results and Discussion

Our study demonstrates that the levels of TNF-α are significantly higher ($p<0.001$) in preeclamptic females as compared to normal pregnant females in relation to age and parity. This is in accordance to the study of Sharma A(3) and Muzammil S(6). However, there is no significant difference in the levels of TNF alpha when the preeclamptic patients are compared in relationship to age and parity. However, Roudsari FV (4) demonstrated that the increase in the levels of TNF-α was not significant in the patients of preeclampsia. TNF- alpha is a cytokine derived from macrophages, lymphocytes, vascular endothelial cells, trophoblasts and Hofbauer cells in the placenta; it induces functional alterations in the endothelial cells. TNF- α being a proinflammatory cytokine, its biological activity is inflammation and endothelial cell activation. Inflammation in preeclampsia may cause increased cytokine levels sufficient to change the vascular endothelial function. The inflammatory response by cytokines may be due to oxidative stress(7) or due to inhibition of nitric oxide and the stimulatory action on endothelin -1 and prostaglandins(8).

Though our study demonstrates a significant increase in the levels of TNF-α, the small number of patient size taken suggests that it would be necessary to undertake further studies with more samples. Also, since the half life of TNF-α is only a few minutes in circulation a single blood sample might fail to detect the periodic decline or elevation in the levels in its levels. In our study due to the budgetary constraints only a single sample was withdrawn from the patients. Hence, in conclusion our study and previous findings demonstrate an increase in the levels of TNF α in preeclampsia. However, further studies in a large volume from different population are required to find whether treatment of the immune responses may be possibility in the future for patients with preclampsia

TABLE I
Levels of TNF-α in patients with preeclampsia compared with normal pregnancy.

	Normal pregnant females		Pre- eclamptic females	
	No of subjects	TNF-α (pg/ml)	No of subjects	TNF-α (pg/ml)
Total subjects	20	9.27 ± 0.19	25	80.58 ± 28.73*
<25 yrs age	5	9.18 ± 0.06	5	79.14 ± 19.43*
>25 yrs age	15	9.3 ± 0.21	15	80.94 ± 31.02*
Primipara	3	9.14 ± 0.06	2	72.32 ± 9.41*
multipara	17	9.29 ± 0.02	18	81.29 ± 29.82*

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