RESEARCH ARTICLE

Expression of Vascular Endothelial Growth Factor in the Placenta of Iraqi Women Complicated with Hypertensive Disorder

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ABSTRACT

During pregnancy, high blood pressure disorder is the most common medical complication in pregnancy. It is the foremost cause of maternal mortality and perinatal diseases. Vascular endothelial growth factor (VEGF) affects the growth of vascular endothelial cells, existence, and multiplying, which are known to be expressed in the human placenta. This study aimed to identify the expression VEGF in the placenta of hypertension and normotensive women. In this study, a cross-sectional study from november 2019 to February 2020. A total of 100 placentae involved 50 hypertensive cases and 50 normotensive groups were assessed. VEGF-A expression in two placentas groups was evaluated by immunohistochemistry techniques. Strong and moderate VEGF expression was seen in syncytiotrophoblasts, stromal and endothelial cells of hypertensive cases, while not seen in hypertensive cases. There were statistically significant differences in VEGF-A expression between hypertensive cases and normotensive group. In conclusion, VEGF-A expression was significantly increased in each of syncytiotrophoblasts, stroma and endothelial cells in the placenta of hypertensive cases, and it could be used to predict the development of hypertension.

Keywords: Hypertensive, Placenta, Pregnancy, Vascular endothelial growth factor.

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INTRODUCTION

Hypertensive disorders characterize one of the most common problems of pregnant women, which affect about 10% of all pregnant women globally.[1] They cover a variety of conditions, containing gestational hypertension, preeclampsia, chronic hypertension and eclampsia are an essential cause of several cardiovascular diseases and a major cause of morbidity, long-term debility, and death in mothers and their neonates.[2]

Hypertensive disorder is elevated blood pressure (≥140/≥90 mmHg). Hypertensive disorder is one of the primary causes of maternal death.[3] Multiple organs dysfunction can occur, which may be a risk factor for mother and fetus life.[4] A tissue affected by pregnancies problematical like hypertension is the placenta; considering early placental vascular damage in hypertensive pregnancies and cause a decreasing of and cause a decreasing of oxygen amount.[5]

A possibly main procedure in the pathogenesis of hypertensive women is an inequity between placenta-derived pro-angiogenic and anti-angiogenic proteins. The pro-angiogenic proteins VEGF is included in regulating placental vascular growth and maternal endothelium cells function during the pregnancy.[6] Inadequate spreading of the maternal placental arteries results in deficient blood supply to the developing fetus.[7] The consequential decrease uteroplacental blood flow products placental hypoxia and ischemia.[8] The last is associated with maternal circulation containing decreased angiogenic factors and raised levels of anti-angiogenic reasons.[9] VEGF stimulates neovascularization, decreases blood pressure, and is essential in the construction and care of the glomerular filtration barrier. Consequently, its absence could well clarify the main clinical appearances of hypertension. In the human placenta, this factor has chiefly been identified in the villous cytotrophoblasts in the first trimester of pregnancy and in the syncytiotrophoblasts and extravillous trophoblast in the end of pregnancy.[10]

This study aims to determine the expression of vascular endothelium growth factor-A in the placenta of Iraqi women with hypertension disorders in compression to normotensive pregnant woman.

MATERIALS AND METHODS

One hundred placental tissue were obtained from women included in this study during their presence at Baghdad Medical City Hospital in Baghdad from November 2019 to

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Table 1: VEGF reactivity in placenta of hypertensive cases and normotensive group by using microscopic analysis.

VEGF reactive	*Normotensive group N =50 n(%)*	*Hypertensive cases N =50 n(%)*	*p-value between two groups*
Syncytiotrophoblast			
Non-expression	46(92)	0	0.000*
Low	4(8)	0	0.001*
Moderate	0	26(52)	0.000*
Strong	0	24(48)	0.000*
Stromal cells			
Non-expression	36(72)	0	0.000*
Low	14(28)	0	0.001*
Moderate	0	32(64)	0.000*
Strong	0	18(36)	0.001*
Endothelial cells			
Non-expression	32(64)	0	0.000*
Low	18(36)	0	0.001*
Moderate	0	38(76)	0.000*
Strong	0	12(24)	0.001*

Persons chi-square;* highly significant at $p \leq 0.001$.

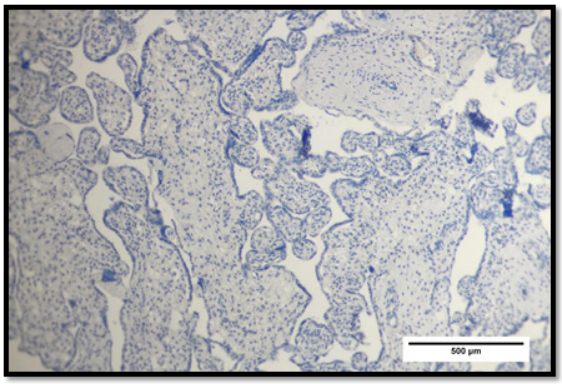

Figure 1: Section in the normotensive placenta with immunohistochemical of VEGF showing no-expression Syncytiotrophoblast (S), stromal cell (Sc), and endothelial cell (Ec), IHC, 10x.

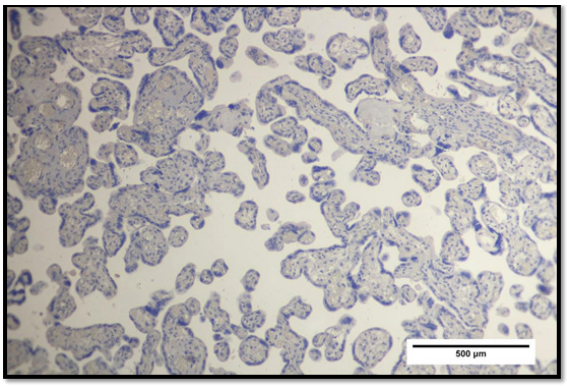

Figure 2: Section in the normotensive placenta with immunohistochemical of VEGF showing weak expression Syncytiotrophoblast (S), stromal cell (Sc), and endothelial cell (Ec), IHC, 10x.

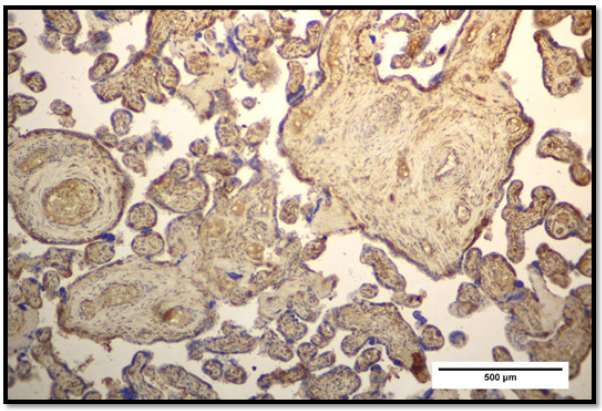

Figure 3: Section in the hypertensive placenta with immunohistochemical of VEGF showing moderate expression in Syncytiotrophoblast (S), stromal cell (Sc), and endothelial cell (Ec), IHC, 10x.

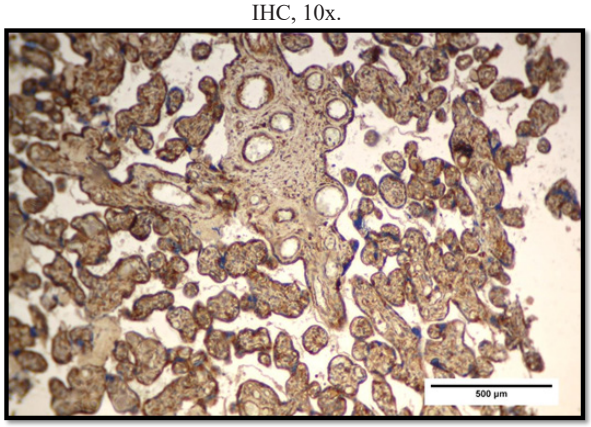

Figure 4: Section in the hypertensive placenta with immunohistochemical of VEGF showing strong expression in syncytiotrophoblast (S), stromal cell (Sc), and endothelial cell (Ec), IHC, 10x.

February 2020. Placental women tissues were designated as follows: 50 complicated with hypertension as a patient group and 50 normotensive pregnant women as a control. Through immunochemistry techniques, VEGF-A was estimated using sections embedded in paraffin, which were re-hydrated and incubated for 55 minutes at 20°C in methanol containing 10% H_2O_2 to prevent endogenous peroxidase. Pre-treatment of the section was carried out in the same kit to assist antigen retrieval and increase membrane penetrability on antibodies; after this step, the sections were then incubated with primary antibodies. A positive expression was conceived by 3.3-diaminobenzidine peroxidation according to usual methods. The sections were stained with Harris' hematoxylin as counterstain then dehydrated, and the cover slid, then the sections were examined under an optical microscope. Two perinatal blind pathologists assessed expression, prevalence discrimination (0, 30, 30%–60, 60%) density of four grades: non-expression, low, moderate and strong.[11]

Concerning statistical methodology, persons chi-squared test was used to estimate differences in VEGF-A expression between the two groups.

RESULTS

This study showed that VEGF-A expression in cases of high blood pressure was higher than those in the normotensive group, and that more severe cases of hypertension were related with higher VEGF-A levels. Immunohistochemical techniques showed very variable activity between VEGF-A and placenta cells. VEGF-A expression is examined within types of the following cells: syncytiotrophoblasts, stromal cells, and endothelial cells of placental vessels in high blood pressure cases and the normotensive group. VEGF-A displays less positivity in the placenta of normal women. In this group, the highest activity was appared in syncytiotrophoblasts cells, although the density was low, and there were few cells. Stromal placental cells also showed poor expression. A few positive cases showed positive expression (Table 1 and Figures 1 and 2).

VEGF-A immunohistochemistry was also approved in the hypertensive cases, where it was expressed. Its expression was strong in must of cases (24(48%)) in the syncytiotrophoblasts; it was also strong positive expression in endothelial cells (12(24%)) and stromal cells (18(36%)) (Table 1 and Figures 3 and 4). Statistical analysis displayed an alteration upon relating hypertensive cases with the normotensive group, where the VEGF-A expression in hypertensive cases. An strong or moderate VEGF-A expression in the syncytiotrophoblast is associated with higher risk of hypertension, but in the normotensive group, there was no or weak VEGF-A expression. Stromal cells had moderate and strong expression in hypertensive cases, and this expression appears to be a protective factor against hypertension. Endothelial cells in villous vessels had common expression in hypertensive cases.

DISCUSSION

Data obtained in cases of high blood pressure were compared with those gotten in a control group. In high blood pressure cases, results of immunochemical expression showed that VEGF-A was expressed in different placental components as observed in previous studies.[12-14] Furthermore, in this study, VEGF-A expression was also identified in the syncytiotrophoblast, stromal and endothelial cells observed previously in hypertensive cases. The VEGF-A expression in the hypertensive cases showed a significant increase with deference to those of the normotensive group. These findings might be related to clinical severity of hypertensive disorders.

Some previous studies that resemble the placental expression of VEGF-A, known as organized in response mostly to placental hypoxia, have indicated an increase in VEGF-A in high blood pressure pregnancies[15-17]. Stimulation and up-regulation of VEGF system through chronic hypoxia and endothelial cells activation were proposed as probable mechanisms for this increase. VEGF-A is an essential regulatory factor for angiogenesis and a highly conserved glycoprotein protein in pregnant women's bodies. VEGF-A can increase angiogenesis and promote endothelial cell division, playing an important role in vessels' physiological or pathological angiogenesis.[18]

Additionally, dis-regulation was proposed in the VEGF family and two possible mechanisms for interpreting defective vascular formation: one was the down-regulation of membrane-restricted VEGF-1 receptors (VEGFR-1) in the placenta leading to the development of the defective uteroplacental development, and the second was the over-production of inexpensive soluble VEGF-1, which could suppress the effects of VEGF and PIGF.[19,20]

The hypoxia environment that stimulates VEGF production may have different advantages in terms of severity and enhanced factors in cases of high blood pressure. However, despite high levels, the dis-regulation occurred at the receptor level leading to a defect in VEGF-A and the generation of defective vessels.[21]

Therefore, the expression VEGF-A, which was current in the syncytiotrophoblasts, stromal and epithelial cells of the villous vessels, is due to the binding of its receptors together and the synthesis of this factor the above mentioned cells.

CONCLUSIONS

In conclusion, the data demonstrated that low expression of VEGF-A combined with high risk of hypertension, therefor VEGF-A may be used to predict the development of hypertension.

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