

The Effects of Preeclampsia On The Enzymatic Activity Of Full Term Placentae:Histochemical Study

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Summary:

Background: This study is concerned with the effects of preeclampsia on the availability of the important enzymes in the full term placenta. For this purpose 2 groups of placentae were taken from the full term pregnant women immediately after labour, each group consists of 10 placentae, the first group are those placentae obtained from pregnant women having uneventful pregnancy with no history of any disease or complication (as a control group) while the second group includes those pregnant women having a history of preeclampsia, the results showed significant histochemical changes in the placentae of the second group when compared with the first group, such changes result from syncytial damage and destruction affecting the preeclamptic placentae of the second group, thus loss of alkaline phosphatase enzyme with increase in the amount of the degenerating acid phosphatase enzyme were observed in the placentae obtained from the preeclamptic group. the placentae have been implicated in the pathophysiology of preeclampsia.

Patients & Methods: The specimens were obtained from Al-Batool & Al-Khansaa Teaching Hospital in Mosul between February and July (2006) and studied in the Department of Anatomy, College of Medicine, University of Mosul. Two groups of placentae were taken from the full term pregnant women immediately after labour, each group consists of 10 placentae, the first group was obtained from healthy pregnant women (control group) while the second group was obtained from pregnant women with history of preeclampsia (10 patients).

Results: the placental alkaline phosphatase enzyme is very important in trophoblastic transfer mechanism, this enzyme is abundant at term normal placenta. The human placenta contains this enzyme which is produced mainly by syncytiotrophoblast cells thus destruction of these cells which occurs in preeclampsia will lead to decrease in this enzyme activity and increase in degenerating acid phosphatase enzyme activity.

Conclusion: there is a disturbance in the level of acid and alkaline phosphatase enzymes in the preeclamptic full term placentae.

Key Words: Enzyme, Placenta.

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Introduction:

The placenta has been implicated in the pathophysiology of preeclampsia. Preeclampsia is more common in multifetal gestation which has an increased placental mass compared to singleton pregnancies¹⁵. An initiating event in preeclampsia has been postulated to be a reduction in the placental perfusion and destruction of the placental tissue both lead to widespread dysfunction of the maternal vascular endothelium by mechanisms that remain unknown⁵, removal of the placenta in preeclampsia is regarded as the main step in the treatment⁹. Normally there is an invasion of the uterine spiral vessels by cytotrophoblasts and with the end of the second trimester of the pregnancy, the uterine spiral arteries are lined exclusively by the cytotrophoblasts and the endothelial cells are no longer present in the endometrial and superficial myometrial region of the uterus⁴. This remodeling of the uterine spiral arteries was referred to as physiological changes and it changes the spiral arteries from thick walled muscular vessels to sac-like flaccid vessels¹⁴.

Failure of the spiral arteries to remodel has been postulated to be the morphological basis for decreased placental perfusion in preeclampsia⁸. Particular attention has been paid to the alkaline and acid phosphatase enzymes largely because they are thought to play an important role in the function of the placenta. There is an inverse relationship between the amount of acid and alkaline phosphatase enzymes. Normally the alkaline phosphatase enzyme is produced from the basement membrane of the syncytiotrophoblast and the microvilli on their surfaces. This enzyme is formed in small amount during the first and second trimester, increases in amount towards the third trimester and become maximum quantity in the full term placentae¹. The acid phosphatase enzyme is dominating during the first half of pregnancy due to a remodeling process occurred normally in the vasculature of the placentae during the first trimester while it is absent in normal full term placentae⁶. In this study histochemical techniques were used to demonstrate alkaline phosphatase and acid phosphatase in the placentae of preeclamptic women.

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Patients, Materials, and Methods:

Histochemical study was carried out on the placentae obtained from full term pregnant women. The specimens were obtained from Al-Batool and Al-Khansaa Teaching Hospitals in Mosul, between February (2006) and July (2006) and studied in the Department of Anatomy, College of Medicine, University of Mosul. Twenty placentae were used in this study, 10 placentae were collected from pregnant women who had normal range of antenatal blood pressure and normal general urine examination and had no other complication throughout their pregnancy (as a control group) and other 10 placentae were collected from pregnant women who were diagnosed to have a history of preeclampsia (more than 140/90 mmHg) & their urine examination for proteinuria (more than 300 mg of protein in a 24 hr. specimen correlated with +1 or +2 reading on dipstick) in addition to their history of generalized edema during pregnancy (particularly edema of the hand and face). A complete record for every pregnant woman was reported including: name, age, parity, gestational age (estimated by taking into account the menstrual history, early ultrasound and clinical examination), serial measurements of the blood pressure, any medication taken, history of generalized edema and edema of the hand and/or face, review of the past medical history, obstetric history (abortion, dead babies), investigations including ultrasound, urine examination for proteinuria, in addition to any antepartum complications such as preterm labour, diabetes mellitus, placenta praevia, fetal anomalies and abruptio placentae. Following delivery of the fetus and the placenta. Two pieces were chosen from each placenta, one from the fetal surface and the other from the maternal surface. The specimens were put in a fixative solution (10% neutral formalin) for 24 hours then each specimen was cut into 1 cm thick slices and dehydrated in graded alcohol solutions (70% alcohol for overnight, two changes in 90% alcohol one hour for each and two changes in 100% alcohol for two hours). Then the specimens were immersed in xylene using three changes with one-hour interval for each. Complete removal of the clearing solution was made by immersing the tissue specimens into three successive paraffin baths in oven, one hour for each. Finally paraffin blocks were prepared by embedding the tissue specimens using paraffin wax (melting point is 55-60°C) and these paraffin blocks were now ready for sectioning using Reichert Rotary Microtome, serial paraffin sections of (4 micrometers thick sections) were cut from each block, the sections were collected and mounted (using DPX) on glass slides then the slides were put for one hour at room temperature then stained to detect the alkaline and acid phosphatase enzymes activities in full term placentae using Gomori's alkaline phosphatase at pH (9) and Gomori's acid phosphatase at pH (3.5) respectively

11. Sections of positive and negative control were used for the assurance of accurate reactions of these enzymes. A positive control for alkaline phosphatase enzyme was a rat kidney processed in the same method and treated by Gomori's method while positive control for acid phosphatase enzyme was a small part of the human prostate obtained from Al-Jumhuri Teaching Hospital and processed in the same method and treated by Gomori's method. Negative control for both alkaline and acid phosphatase enzymes reactions were a placental sections processed in the same method and treated by Gomori's reaction but incubated without using substrate solution.

Results:

The full term placentae obtained from the pregnant women having no history of preeclampsia or any other maternal complications (i.e. the control group) showed very strong reaction to the alkaline phosphatase enzyme (Fig. 1). The villous stroma showed moderate reaction to the alkaline phosphatase enzyme while the cytotrophoblasts showed negative reaction to alkaline phosphatase enzyme. Maternal decidua showed moderate reaction to the same enzyme (Fig. 2). The full term placenta obtained from the control group showed negative reaction to the acid phosphatase enzyme in syncytiotrophoblast, villous stroma and in the maternal decidua. The full term placentae obtained from the preeclamptic women showed diminished alkaline phosphatase activity in the syncytiotrophoblast, villous stroma and in the maternal decidua (Fig. 3). Full term placentae of the control group showed negative reaction to acid phosphatase in the maternal decidua and chorionic villi (Fig. 4) while there is a considerable increase in the activity of acid phosphatase enzyme in the villi of the placentae obtained from the preeclamptic women (Fig. 5).

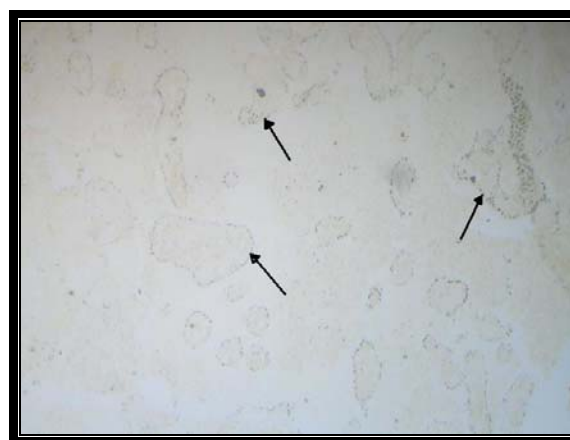


Figure (1): Light microscopical appearance of the normal full term placenta obtained from the control group showing very strong reaction to alkaline phosphatase enzyme (arrows) (Alk. Ph. X100).

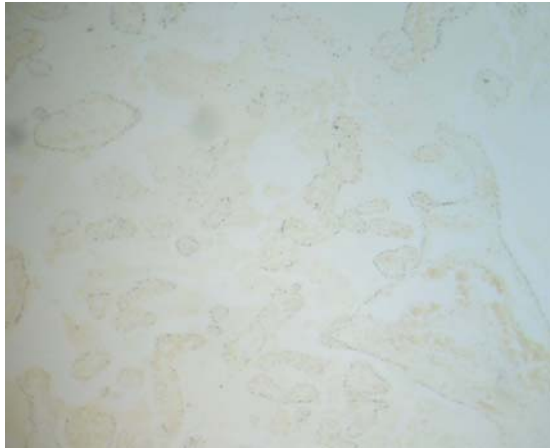


Figure (2): Light microscopical appearance of maternal decidua of the normal full term placenta obtained from the control group showing moderate reaction to the alkaline phosphatase enzyme (Alk. Ph. X100).



Figure (3): Light microscopical appearance of the normal full term placenta obtained from the control group showing negative reaction to the alkaline phosphatase enzyme in the syncytiotrophoblasts (Alk. Ph. X100).

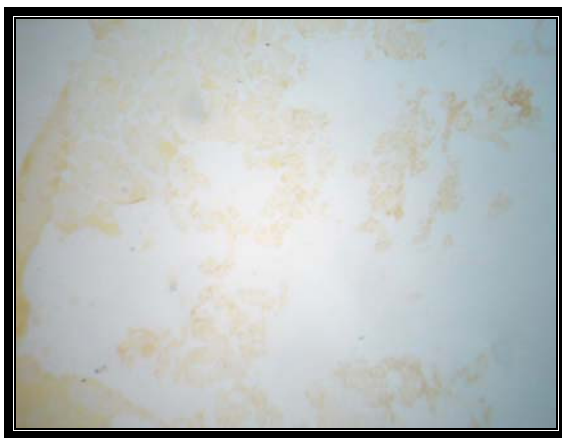


Figure (4): Light microscopical appearance of the normal full term placenta obtained from the control group showing negative reaction to the acid phosphatase enzyme (Acid. Ph. X100).



Figure (5): Light microscopical appearance of the full term placenta obtained from the preeclamptic group showing positive reaction to the acid phosphatase enzyme (arrows) (Acid. Ph. X100).

Discussion:

Our finding in regard to the distribution of alkaline phosphatase and acid phosphatase enzymes in the placentae obtained from the full term pregnant women with no history of preeclampsia or any other maternal complications (i.e. the control group) were similar to those noted by other workers 12. The alkaline phosphatase is an important enzyme for the trophoblastic transfer thus the full term placenta is adequately equipped with this enzyme 7, it has a vital role in the endocytosis process occurred within the placentae and this function is indicated by the abundant alkaline phosphatase content of the syncytiotrophoblastic basement membrane and their microvilli. The trophoblasts have two important phosphatase-linked transfer systems, one depends principally upon acid phosphatase enzyme being utilized mainly during the first half of pregnancy and the other depends on alkaline phosphatase enzyme and it dominates during the second half of pregnancy 13. The alkaline phosphatase of the placentae obtained from full term preeclamptic women appeared to be affected by the placental ischemia and reduced uteroplacental perfusion leading to a progressive decline in the availability of this enzyme. This is presumably considered as a response to tissue hypoxia which alters the tissue PH of the trophoblast 7. In this study it is clear that destruction of the syncytiotrophoblasts due to placental ischemia is the most important factor in decreasing the availability of this enzyme largely because it is formed from the basement membrane of the syncytiotrophoblasts and their microvilli 1. It is also appeared that syncytial damage and destruction in the placentae obtained from the preeclamptic women is responsible for the increased activity of acid phosphatase which is normally a degenerating enzyme and it is absent in the normal

full term placentae. In normal full term placentae, alkaline phosphatase enzyme gradually increases and it become abundant in full term, while acid phosphatase enzyme decreases progressively as gestation proceeds and it become absent at full term. In the placentae obtained from preeclamptic women, this trend is reversed thus alkaline phosphatase enzyme progressively decreases until it disappears, this is usually accompanied by a marked gradual increase in the acid phosphatase activity, such observation is attributed to the continued destructive process within the placentae resulted from reduced uteroplacental perfusion, endothelial cell damage and placental ischemia 2. This finding differs from the observation of previous workers 10, 3 who found that alkaline phosphatase activity is not lost in the syncytium of the preeclamptic placentae but only there is increase in the activity of acid phosphatase enzyme.

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