

THE SIGNIFICANCE OF LIPOPROTEIN DEPOSITION IN THE RETINA OF PREGNANT WOMEN AS A MARKER OF PREECLAMPSIA, IUGR AND OTHER RELATED MATERNAL AND FETAL COMPLICATIONS

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Abstract

Background: Preeclampsia is a disorder characterized by three main clinical features, these are hypertension, edema and proteinuria. Fibrin deposition in various tissues can be easily demonstrated by microscopical examination, however this requires a biopsy. Fortunately, the eye is the mirror of the body.

Objective: To detect the deposition of fibrin in the eyes of pregnant women within the first two weeks of the third trimester before the women become preeclamptic, through simple ophthalmoscopy

Methods: 42 primigravida pregnant women were chosen as a study group, which include those women in whom hard exudate (Lipoprotein deposition) was detected at 28-30 weeks of gestation in their retina through simple ophthalmoscopy examination. While another control group of 46 women were selected in whom examination of the eye for hard exudate was negative. Both groups were followed routinely in the

third trimester and screened for any complication, which may develop.

Results: The incidence of preeclampsia, oligohydramnios, placenta abruption was significantly higher in the study group than in the control group, 45.23% vs 13.04, 28.57% vs 2.17 % and 16.66 % vs 2.17 % respectively. While the incidence of IUGR and perinatal death was still higher in the study group than in the control group 28.57 % vs 2.17 % and 9.52 % vs 0.00 %.

Conclusion: Simple ophthalmoscopic examination of the pregnant women eyes for the presence of hard exudate (Lipoprotein deposition) may be useful in sorting high-risk women for preeclampsia and its related complications.

Key words ; Preeclampsia, hard exudate, retina, lipoprotein

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Introduction

Preeclampsia is a human pregnancy specific disorder characterized by three main clinical features these are hypertension, edema and proteinuria^[1-3]. In the last twenty years, much work has been done to elucidate its precise etiological factors. Nowadays it is well established that preeclampsia is a disease of the placenta itself.

The placenta of those women liable to develop preeclampsia differ from those with normal pregnancy by two aspects from

biochemical point of view, they produce higher ratio of PG F2@ to that of PG E2. Also, they produce higher amount of placental renin, which is physiologically indistinguishable from the renal renin. The increased production of placental PG F2@ is responsible for the wide spread but low grade activation of the coagulation cascade, ultimately leading to wide spread deposition of fibrin in almost every organ in the body like the liver, spleen and kidneys.

While the increased production of placental renin is responsible for the development of hypertension, through the mechanism of angiotensin^[3,4]. The entire above finding is mediated by defective placentation and occurs as early as 12-14 weeks of gestation, and probably mediated by defective immune response^[6,7]. Fibrin deposition in various tissues can be easily demonstrated by microscopical examination

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of tissues stained with hematoxylin-eosin stains^[8-10].

However, this requires a biopsy has to be taken from specific organs. Fortunately, the eye is the mirror of the body. That is why we have adopted the principle of examining the pregnant women's eyes for the sake of early detection of lipoprotein deposition in the form of hard exudate, before the signs and symptoms of preeclampsia have yet developed. That is the pivotal idea that we have adopted in committing this paper. To assess whether lipoprotein deposition in the eye of pregnant women can be useful as a screening test for the development of pregnancy induced hypertension.

Preeclampsia and the eye

Actually, most of the studies that have been found in the literature, which describe the retinal changes with preeclampsia have been conducted among women with already established disease. Few if any have been found which describe the early changes in the retina of pregnant women shortly before the onset of preeclampsia. The most prominent findings in the eyes of preeclamptic women include retinal detachment, thrombosis of retinal vessels and retinal hemorrhage^[11-14]. In this study, we have tried to detect the deposition of fibrin in the eyes of pregnant women within the first two weeks of the third trimester before the women become preeclamptic, through simple ophthalmoscopy. In addition, to give more accurate assessment about the presence of fibrin deposition in the eye, further confirmation was done by a colleague ophthalmologist. As will be detailed further detailed in the section of methods and patients. Lipoprotein deposition in the retina was described as a lesion indistinguishable from typical hard exudate.

Patients and Methods

1. Population and patients' collection

The study was conducted in Baghdad City at two major maternity

hospitals, al-Elwyia maternity hospital and AL-Habibya maternity hospital. All the patients enrolled in this study were taken from the antenatal clinics from the above-mentioned hospitals. It has included a wide spectrum from Baghdad's inhabitants with different social status and educational degrees.

All the women who have been enrolled in this study have accepted to participate through their verbal consent and supplied with pre-printed data collection sheet to record exactly the events in the third trimester and the outcome of their pregnancy. All the women who have been enrolled in this study were primigravida to make their statistical analysis more conclusive. The study lasted about three years from June 2001 up to March 2004.

2. Follow up protocol

Starting as early as booking all the women were assessed initially by taking full history and meticulous physical examination especially for the blood pressure and uterine size. In addition, all the women were further assessed by the routine antenatal investigation, which include hemoglobin level, random blood sugar, general urine examination, blood urea, serum creatinine, serum uric acid, ABO- Rh blood group, VDRL, as well as Coomb's test for Rh -ve women.

In addition routine ultrasound scan was taken at 16 weeks of gestation. Those women who have been found hypertensive, proteinuric, multiple gestation and low-lying placenta were excluded from the study. The remaining women were followed in the routine way throughout the second trimester up to 28 weeks of gestation. Should as woman remain normotensive she is scheduled for simple outpatient ophthalmoscopic examination to assess the presence of hard exudate in the retina.

In addition, a colleague Ophthalmologist at AL-Jarah private hospital was sent those with positive hard exudate in their retina for further examination and confirmation. Fibrin deposition was described as a grayish

circular lesion, which are arranged in circular or radial arrangement. Accordingly all the women who have accepted to participate in the study were allocated either to the study group (N=42) which include those women in whom hard exudate was detected and confirmed at 28-30 weeks of gestation while they are normotensive.

While the control group (N=46) included normotensive women in whom hard exudate in the retina was absent as assessed by the dual examination. In addition to the above-mentioned screening test, rollover test and serum creatinine samples were assessed for each woman after being assigned to the group mentioned above. The aim is to find any correlation between the presence of hard exudate in the eye and positive roll over test and elevated serum uric acid. After assigning the women to their groups, they were followed up to delivery with the same way.

Those women in whom hypertension did not develop, where secluded to have spontaneous vaginal delivery unless guided by other obstetrical indication like cephalopelvic disproportion or malpresentation, in such cases elective cesarean section was done. Those women in whom hypertension and/ or preeclampsia has developed, were further assessed for the severity of hypertension and the fetal well being test. Those women with preeclampsia has developed in the absence of IUGR, were scheduled for planned delivery at 36 weeks of gestation. While those women with preeclampsia and IUGR, were scheduled to have planned delivery at 34 weeks of gestation or even earlier as guided by the

severity of hypertension or the fetal well being tests.

The following parameters were recorded and expressed for each woman in the study, hypertension, preeclampsia, IUGR, oligohydramnios, placental abruption, development of late and variable intrapartum deceleration, number of cesarean sections for fetal distress, Apgar score at 1-5 minutes and the number of infants with neonatal jaundice. Unfortunately Doppler indices and fetal pH estimation could not be collected from all the patients, so skipped from the results. Tanner Thompson's standards were used to assess fetal birth weight percentile.

3. Statistical analysis

The results were expressed as mean and standard deviation for the continuous data and number and percent for the discrete data. Student t test was used to compare the continuous data while Chi square test was used to compare the numerical data. P values less than 0.05 were considered as significant.

Results

After the analysis of the data, the following tables were constructed to show the results and their statistical comparisons. In table number one the overall epidemiological characteristics were presented for both study and control groups. It is interesting to note that the only significant difference between the study group and control groups at 28 weeks of gestation was the significantly higher mean serum uric acid and number of women with positive rollover test.

Table 1: Shows the overall epidemiological characteristics among both study groups

Characteristics	Study group (N=42)	Control group (N=46)	P-value
No. of women who's age is less than 20 years	6 (14.28%)	3 (6.52%)	NS
No. of women who's age is between 20-30 years	33 (78.575)	41 (89.1350)	NS
No. of women who's age is more than 30 years	3 (7.14%)	2 (4.34%)	NS
Mean age	23.19+4.41	24.19+3.78	NS
Mean systolic blood pressure at 28 weeks of gestation	111.66+14.51	109.35+14.49	NS
Mean diastolic blood pressure at 28 weeks of gestation	63.78+7.22	62.06+7.19	NS
Mean serum uric acid at 28 weeks of gestation	3.77+0.47	1.72+0.68	<0.05
No. of women with positive rollover test	24 (57.14%)	3 (6.525%)	<0.05

NS = Not significant statistically

Table 2: Shows the overall maternal outcome in women among both groups with their statistical analysis

Characteristics	Study group (N=42)	Control group (N=46)	P value
No. of women who have developed preeclampsia	19 (45.23%)	6 (13.04%)	P<0.05
No. of women who have developed oligohydramnios	12 (28.57%)	1 (2.17%)	P<0.05
No. of women with meconium stained liquor	7 (16.66%)	1 (2.17%)	P<0.05
No. of women with late dceleration	7 16.66%	2 (4.34%)	NS
No. of women with late and variable deceleration	9 (21.42%)	2 (4.34%)	NS
No. of cesarean section foe fetal distress	7 (16.66%)	1 (2.17%)	P<0.05P
Mean gestational age at delivery in weeks	34.1+1.3	37.12+1.8	<0.05

NS; Not significant statistically

The overall maternal outcome for both groups can be summarized as bellow

1. Number of women who developed preeclampsia was significantly higher in the study group than in the control group {nine (45.23%) vs. six (13.04%): P<0.05}.
2. The number of women who developed oligohydramnios was significantly higher in the study group than in the control group {12 (28.57%) vs. 1(2.17%): P<0.05}
3. The number of women who developed placental abruption was significantly higher in the study group {seven (16.66%) vs. one (2.17%): P<0.05}.
4. The number of women with meconium stained liquor was higher in the study group, yet the difference was not significant {7 (16.66% vs. 2 (4.34%): P<0.05}
5. The number of women who have developed late and variable deceleration was higher in the study group than in the control group {9 (21.425 vs. 2(4.34%); P<0.05}

6. The number of cesarean sections for fetal distress was higher among women in the study group than in the control group {7 (16.66%) vs. 1 (2.17%): P<0.05}

7. The mean gestational age at delivery was lower among women in the study group than in the control group {34.1+1.3 vs. 37.12+1.8: P<0.05}

It is worth mentioning in this regard that among women in the study group who have developed placental abruption two were complete with intrauterine death, while the remaining 5 were partial as confirmed at time of cesarean section by the presence of retroplacental clot. While the only woman in the control group who has developed placental abruption was diagnosed as a case of fetal distress upon developing variable deceleration in the first stage of labor, upon doing cesarean section retroplacental clot was found.

Table 3: Shows the overall neonatal outcome among both study groups

Characteristics	Study group (N=42)	Control group (N=46)	P value
Mean birth weight at delivery	2.1+0.41	3.3+0.54	P<0.05
Number of infants with IUGR	12(28.57%)	1(2.17%)	P<0.05
Apgar score less than 5 at 1 minute	14(33.33%)	7(15.215%)	P<0.05
Apgar score less than 7 at 5 minutes	10(23.80%)	3(6.52%)	P<0.05
Number of infants who developed neonatal jaundice requiring phototherapy	8(19.04%)	1(2.17%)	P<0.05
Number of perinatal death	4(9.52%)	0(0%0)	P<0.05

Table three, summarizes the overall neonatal outcome among infants in both study groups as bellow:

1. The mean birth weight is significantly lower in the study group than in the control group {2.1+0.41 vs. 3.3 + 0.54: P<0.05}
2. Number of infants with IUGR is significantly higher in the study group than in the control group {12(28.57%) vs. 1(2.17%); P <0.05}
3. The number of infants who's Apgar score was lower than 5 at 1 minute was significantly higher in the study group{ 14(33.33%) vs. 3(6.52%):p<0.05}
4. Number of infants who's Apgar score was less than 7 at 5 minutes was significantly higher in the study group(10/23.80%) vs. 3(6.52%);P<0.05}
5. The number of infants with neonatal jaundice requiring phototherapy was higher

in the study group {8(19.04%) vs. 1(2.17%); P<0.05}

Among infants in the study group, there were four perinatal deaths. Two cases were associated with complete placental abruption while another two cases were diagnosed as septicemia.

Discussion

There is a direct relationship between positive rollover test at 28 weeks of gestation and the presence of hard exudate in the retina of pregnant women liable to develop hypertension according to the results obtained in this study. Figure 1 shows that up to 57.14% of women in the study group showed positive rollover test compared o 6.52% in the control group.

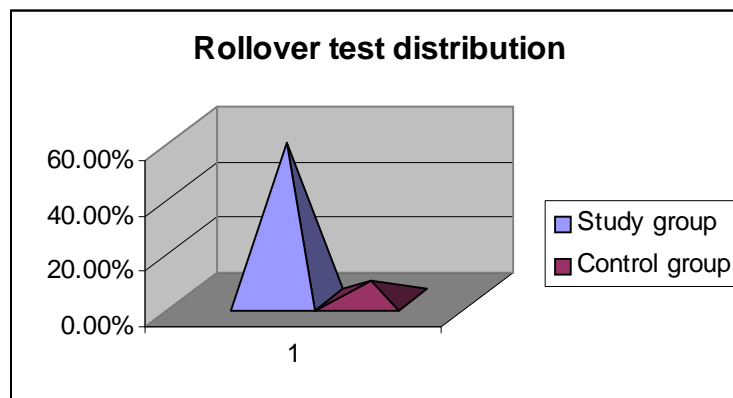


Figure 1: Shows the distribution of positive rollover test among the study groups

There is a direct relationship between elevated maternal serum uric acid and the presence of hard exudate in the retina of pregnant women at 28 weeks of

gestation according to the results obtained in this study. Figure 2 shows a histogram of the mean serum uric acid at 28 weeks of gestation between both study groups.

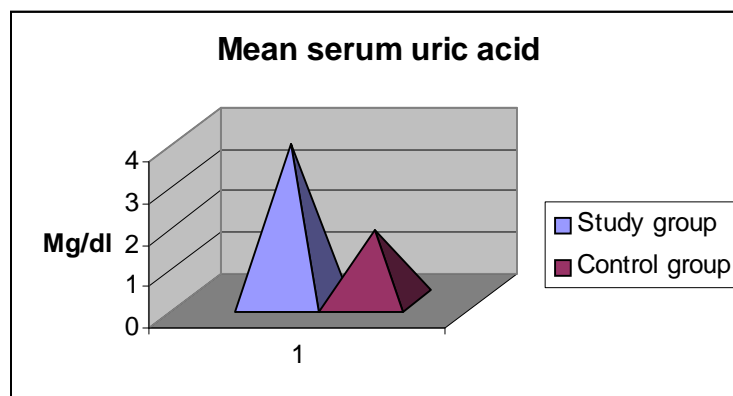


Figure 2: Shows mean serum uric acid at 28 weeks of gestation between both study groups

The idea behind showing increased maternal serum uric acid and the presence of positive rollover test between both study groups is that both are associated with increased incidence of preeclampsia, IUGR and other maternal and fetal complications. This is consistent with the results obtained by Christiansen et al, Yemini et al, Onuonga et al^[15-17] as all have stressed the importance of positive rollover test early in the third trimester and later liability to develop preeclampsia in pregnancy. While other researchers like Weasekera et al; Yoneyama et al and Garrone et al^[18-20] have stressed on the direct relationship between elevated maternal serum uric acid early in the third trimester and later liability to develop preeclampsia.

However despite the results we have reached in this study so far, other researchers like Capoor et al^[21], described another clinical course through the retinal changes which precedes the development of preeclampsia. In his paper, macular hemorrhage appeared rapidly and shortly before the patient develops preeclampsia. However in the original design of this paper we didn't include examination of the retina after the patient bypass 30 weeks of gestation of pregnancy or the patient already develop preeclampsia. Further researches are required to define the exact pathology, which commence in the eye as the earliest sign of preeclampsia.

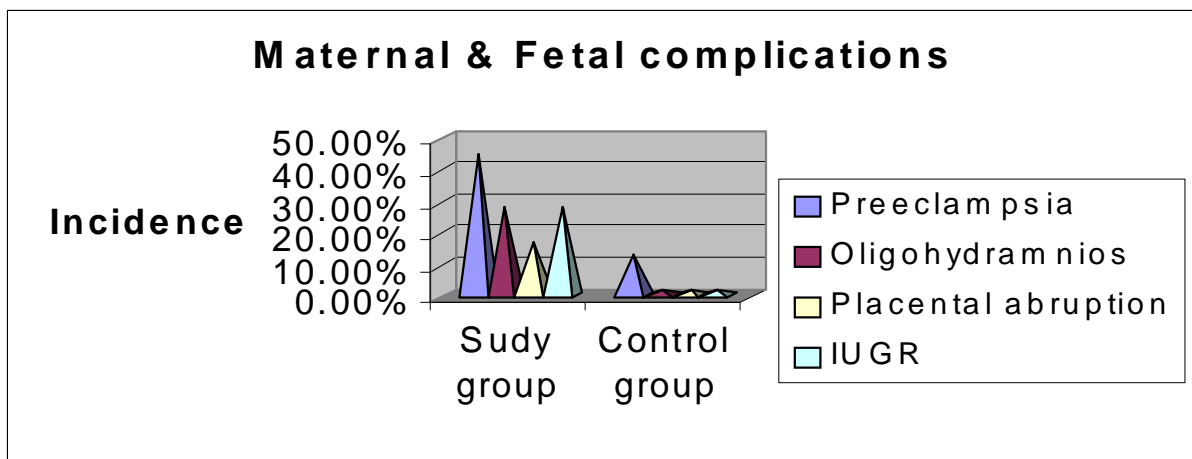


Figure 3: Show the distribution of various maternal and fetal complications between both study groups

The incidence of wide varieties of maternal and fetal complications was higher in the study group than in the control group as shown in figure number three. As it has been explained above that, there was a direct relationship between positive rollover test and elevated maternal serum uric acid with positive hard exudate in the retina of such women. In the same context the incidence of various maternal and fetal complications associated with those tests are expected to be higher among women with hard exudate in their eyes.

Actually, the incidence of preeclampsia placental abruption, IUGR and oligohydramnios were significantly higher in the study group than in the control group. These findings are consistent with results obtained from other researchers like Sanchez et al, Schiff et al; Tewari et al; Yemini et al and Verma et al^[22-26]. Among all the above-mentioned papers, the relationship between positive rollover test early in the third trimester and later liability for preeclampsia development has been well clarified.

Conclusion

Simple ophthalmoscopic examination of the retina for the presence of hard exudate in pregnant women early in the third trimester may be helpful in sorting out high-risk women for preeclampsia, IUGR and other related complications. However, it would be much better to follow conservative policy in interpreting the results obtained in this study. We would like to induce other colleagues to commit similar or related researchers to define the exact pathology in the eyes, which precede the development of preeclampsia, and to define the significance of such changes as a screening signs for this disorder.

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