

EFFECT ON FETAL BIRTH WEIGHT OF EARLY VERSUS LATE ONSET ECLAMPSIA

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ABSTRACT

Objective: To compare the effect on fetal birth weight of early onset versus late onset eclampsia.

Material and Methods: This descriptive study was conducted in the Gynae C unit of Department of Obstetrics and Gynecology, Khyber Teaching Hospital, Peshawar from January 2009 to December 2009. Patients who presented with eclampsia were included in the study. A detailed history was taken and examination done and a proforma was filled. Forty-one live singleton infants were born after eclamptic pregnancies. We compared the weight of those with a sample of 41 infants born during the same period to normotensive patients with a similar period of gestation.

Result: Among primigravida early onset eclampsia was associated with significant reduction in fetal weight. However babies of those who developed late onset eclampsia were of comparable weight to the babies of non-eclamptics. In cases of multiparas, eclampsia of both early and late onset was associated with significant reduction in fetal weight.

Conclusion: Pre-eclampsia is an etiologically heterogeneous disorder that occurs in at least two subsets, one with normal or enhanced placental function and the other involving placental dysfunction. It is unlikely that a single treatment or preventive measure will be effective. In further studies it may be important to study the two subtypes separately.

Keyword: Eclampsia, fetus, birth weight.

INTRODUCTION

Hypertensive disorders of pregnancy are the second leading cause of maternal mortality after embolism and are responsible for significant maternal and perinatal morbidity. Pre-eclampsia has been known as the disease of theories as the exact course of events that lead to the clinical syndrome has not been elucidated. However there is increasing understanding of these events. In normal human pregnancy the spiral arteries in the placental bed progressively lose their musculoelastic tissue by migration of trophoblasts into their wall. These trophoblast induced changes involve the entire length of the spiral artery from the intervillous space to its origin in the inner third of the myometrium. This process widens the spiral arteries and creates a low resistance, low pressure high flow system that allows the increased blood supply to reach the pregnant uterus. The first stage of the change may involve the decidual parts of the spiral arteries and occurs in the first trimester. The second stage starts at sixteen weeks gestation and the process progresses to the

myometrium. In women with gestational hypertension, small for gestational age fetuses, trophoblast induced stages are restricted to the decidual arteries. The myometrial segment of the spiral arteries are left with their musculoelastic architecture, which makes them sensitive to vasomotor influences. This process may account for the two to three fold decrease in the uteroplacental perfusion seen in hypertensive patients compared with normotensive women¹.

Placental microfragmentation results from ischemia due to abnormal trophoblast invasion. Debris enters the circulation and one or more chemical agents promote a microangiopathy with wide spread damage to the maternal vascular endothelium and small infarcts. There is increased sensitivity to natural pressor agents such as angiotensin, catecholamines and arginine vasopressin. The two primary consequences are vasoconstriction and increased capillary permeability. The loss of protein through kidney and of fluid into interstitial space reduces the circulating blood volume which probably increases the placental ischemia². The current theory proposes a two stage model in the development of this condition. The first stage appears to involve the defective trophoblastic invasion of the placental bed which results in hypoperfusion and an ischemic placenta. The second stage appears to involve the release of unknown factors into the maternal circulation from the

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placenta in response to the first stage that then causes the multi system disorder, that includes generalized endothelial cell dysfunction which gives rise to the characteristic symptoms of hypertension, proteinuria and sudden edema^{3,4,5}.

Fetal growth restriction shares features of the pathophysiology of preeclamptic toxemia. Failure of spiral artery remodeling has been reported in cases of both pure preeclamptic toxemia and fetal growth restriction and fetal vascular development and ultimately villous morphology is now known to be different in both preeclamptic toxemia and fetal growth restriction compared with normal pregnancy^{6,7}. Although the basic pathophysiology is known to be similar however casual observations reveal that not all preeclamptic women deliver small babies. The maternal syndrome of pre-eclampsia must be related to additional factors as inadequate trophoblast invasion is also seen in pregnancies complicated by fetal growth restriction without maternal disease. Maternal disease and fetal involvement do not always co-relate. Some studies in Europe have shown that some cases of late onset preeclampsia (more than 37 weeks) may be associated with normal birth weights or large for gestational age babies^{8,9}. The large for gestational age infants can be explained by demonstration of increased cardiac output in late onset pre-eclamptic pregnancies¹⁰.

MATERIAL AND METHODS

This was a descriptive study done in Gynae C Unit of Department of Obstetrics and Gynecology, Khyber Teaching Hospital, Peshawar. Patients with severe pre-eclampsia (Eclampsia and Hellp syndrome), carrying a singleton pregnancy were included in the study. The study period was from January 2009 – December 2009. Most of the patients were critical and were admitted to the labor room of Khyber Teaching Hospital, Peshawar through emergency and referred from other hospitals in critical condition. A total of 41 cases of eclampsia were admitted during the study period. Forty-one normal subjects were taken as control (Gestational age and parity matched with no evidence of pre-eclampsia). The onset of severe pre-eclampsia was divided into two periods, less than 37 weeks period of gestation, and more than 37 weeks period of gestation.

The data was collected through a proforma. The salient features of proforma included name, age, parity, obstetrical history (recurrent pre-eclampsia), last menstrual period, detailed medical history of present illness including nature and number of fits, findings of general physical examination, abdominal and pelvic examination, notes on labor and delivery, fetal weight and maternal complications. Gestational age was based on the first day of the last menstrual period or from the earliest ultrasound available. Exclusion criteria were women with chronic hypertension,

diabetes mellitus or gestational diabetes, chronic renal disease, connective tissue disorders, hyperthyroidism, hypo-thyroidism, cardiac disease, BMI of less than 30. The data collected was analyzed using SPSS-10. P-value of less than 0.05 was interpreted as statistically significant.

RESULTS

Eclamptic patients were initially divided into primigravida and multigravida. Each were further subdivided into 2 groups based on the period of gestation of less than 37 weeks, and more than 37 weeks Table 1. Nulliparous women who develop late onset eclampsia delivered babies whose birth weight were comparable to those of non-eclamptic patients.

Table 1: Number of Cases = 41

Parity	Period of Gestation	
	< 37 weeks	> 37 weeks
Primigravida	12	18
Multigravida	2	9

Table 2: Mean birth weight of babies in Kg

	Parity	Period of Gestation	
		<37 wks	>37 wks
Eclamptic	Primigravida	2.1 kg	2.94 kg
	Multigravida	2.05 kg	2.96 kg
Control	Primigravida	2.86 kg	3.05 kg
	Multigravida	2.7 kg	3.42 kg

Table 3: Difference in mean fetal weight between cases (eclamptic patients) and controls (normotensive)

Gravidity	Mean birth wt ±SD		P-Value
	Cases	Controls	
Primigravida POG <37 wks n = 12 POG > 37 wks n = 18	2.1 ± 0.382	2.86 ± 0.155	0.005
	2.94 ± 0.347	3.05 ± 0.266	0.313
Multigravida POG <37 wks n = 2 POG > 37 wks n = 9	2.05 ± 0.071	2.7 ± 0.141	0.028
	2.96 ± 0.260	3.42 ± 0.474	0.020

n = Number of patients

POG = Period of gestation

P-Value < 0.005 (Significant)

There was a statistically significant difference in birth weight of babies delivered to patients with early onset eclampsia. Mean birth weight of babies in kg are shown in Table 2. The difference in mean fetal weight between cases (eclamptic patient) and controls along with P values are shown in Table 3.

DISCUSSION

Pre-eclampsia is an etiologically heterogeneous disorder that occurs in at least two subsets, late onset with normal or enhanced placental function and fetal weight. Early onset, involving placental dysfunction and fetal growth restriction, often with asymmetrical fetal body proportions¹¹. The objective of this prospective study was to evaluate the effect of early onset and late onset severe pre-eclampsia on fetal weight. Studies on the effect of pre-eclampsia on fetal weight have all been observational with the patient being monitored throughout pregnancy, so that the exact onset of pre-eclampsia can be known. In this study, due to lack of regular antenatal visits, the follow up of patients throughout pregnancy was not possible. In most cases, medical consultation is related to pathological episodes and not by compliance with the established program to follow the normal development of pregnancy. Pre-eclampsia is seen after the development of the condition, making it difficult to date the exact onset and thus classify the patients according to the onset of pre-eclampsia. It was however possible to time the onset of eclampsia, one of the complications of pre-eclamptic toxemia and thus divide the cases into early and late onset and compare its effect on fetal weight.

The etiology of pre-eclamptic toxemia and fetal growth restriction remains controversial, and their prevention continues to elude us, but it is now accepted that both are associated with alteration in the growth and development of placental villi and their underlying vasculature¹⁶. The pathophysiology of both pre-eclamptic toxemia and fetal growth restriction was thought to be at the placental level, involving defective spiral artery remodeling in early pregnancy, decreased intervillous space expansion and ultimately reduced fetal blood supply. However recent studies have shown that, all patients with pre-eclamptic toxemia do not have small for date babies and morphometric placental villous and vascular abnormalities in early and late onset pre-eclampsia with and without fetal growth restriction are different¹⁷.

Recent evidence shows that isolated early onset pre-eclamptic toxemia is associated with abnormal placental morphology but placentas from late onset pre-eclamptic toxemia are morphologically similar to placentas from gestational age matched controls. Early onset pre-eclamptic toxemia and fetal growth restriction in general might share common pathophysiologic mechanisms¹⁸. Based on these observations it is now believed that pre-eclamptic toxemia exists in two subsets; early onset cases, where

there is evidence of abnormal fetoplacental angiogenesis leading to abnormal placental development and small for date fetuses and late onset pre-eclamptic toxemia, in which placental dysfunction is not necessary (with normal placental morphology) and it may be an abnormal maternal vascular response to a number of circulating antigens (different profile of angiogenic factors and adipocytokines between women who develop early and late onset pre-eclampsia)¹⁹. Supporting the hypothesis that late onset pre-eclamptic toxemia is a maternal disorder and not a placental disease, associated with normal birth weight, which supports the hypothesis of placental hypoperfusion caused by shallow invasion of fetal trophoblast in early pregnancy leading to fetal growth restriction in pre-eclampsia.^{13,14} In cases of multiparous women, there is a statistically significant difference in birth weight, both in early and late onset eclampsia. A study from Abbottabad showed mean \pm SD of birth weight 2.9 ± 0.63 kg, where as in control mean \pm SD of weight was 3.0 ± 0.49 kg (Statistically not significant). However all case of pre-eclampsia were grouped together regardless of the period of gestation¹⁵.

Eclampsia, one of the complications of pre-eclamptic toxemia, also has early and late onset. The objective of this prospective study was to evaluate the effects of early and late onset eclampsia on fetal weight and to confirm whether this distinction of early and late onset pre-eclamptic toxemia also applies to its complications. Similar studies on patients with eclampsia and its effect on fetal weight have not been done. The questions arise 1. Does eclampsia in primigravidas have a different etiology and pathophysiology from eclampsia in multigravidas? It is needed to know whether eclampsia in primigravida and multigravida are different phenomena with different developmental pathways. In future studies distinguishing between the two subtypes maybe important.

CONCLUSION

The effect of eclampsia on fetal weight depends upon the period of gestation at which it develops. Early onset eclampsia was associated with significant reduction in fetal weight, whereas patients with late onset eclampsia had babies with birth weight comparable to normotensive patients delivered during the same period. This supports the hypothesis that pre-eclampsia is an etiologically heterogeneous disorder that occurs in at least two subsets, one with normal or enhanced placental function and the other involving placental dysfunction.

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