DISCUSSION
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This study "Haematological and physical growth effects of toxaemia of pregnancy on newborns" was carried out in the department of Paediatrics in collaboration with the departments of Obstetrics & Gynaecology and Pathology, M.L.B. Medical College, Hospital, Jhansi.

Toxaemia of pregnancy is a fascinating and unique serious obstetrics condition which is associated with increased perinatal morbidity and mortality. Most perinatal deaths are related to prematurity, intrauterine growth retardation and abruptio placentae. To know its effects as disease per se or due to other factors like drugs, this study was planned, and total 39 study group newborns of toxaemia of pregnancy were compared with 39 control group newborns from March, 1991 to Feb., 1992.

The toxaemia of pregnancy mothers were divided into two groups i.e. mild and severe according to indicators of severity of pregnancy induced hypertension as mentioned in William's Obstetrics (18th edition, 1980) by MacDonal and Gaut.

As shown in figure I, out of 39 cases, 10 (25.64%) cases were of mild type and remaining 29 (74.36%) cases of severe type (Table 1).

In contrary to our observations, Jain (1982) reported the 66.8% incidence of mild type and 25.9% of
severe type. However, Kapoor et al (1991) reported incidence of mild type - 43.14% and 56.86% of severe type in their study. Thus incidence of severe type of toxaemia of pregnancy was higher in this study as compared to other studies, which may be because of missing of mild cases more in our set up due to referral nature of this hospital and poor antenatal follow up at periphery. Only severe type attracted attention thereby concentrating the incidence of severe type of toxaemia of pregnancy in the present study.

Various observers noticed that incidence of toxaemia of pregnancy is more common in primigravida than second and multigravida. Derham and Hawkin (1989) found 57.64% incidence in primigravida and 42.35% incidence in multigravida. Sharda Jain (1982) also found 53% incidences but Dr. Datta noted 70% incidence of this disease in primigravida. Our study also showed comparable results as of Dutta's (1987) i.e. 74.35% incidence in primigravida, and 25.63% in multigravida. Primigravidity is one of high risk factor in this disease. Its etiology is not clear but it is explained on the immunological basis of pregnancy as mentioned in 15th recent advances of Obstetrics and Gynaecology (1987). Failure of normal trophoblast invasion of spiral arteries could be due to immunological factors. Maternal immune response to trophoblast needs to be down regulated to permit normal invasiveness. The down
regulation may depend directly on immune response generating 'blocking antibodies' or suppressor cells (Redman et al, 1984). The protective effect of first pregnancy, the possible but unconfirmed protective effect of previous abortion, and of blood transfusion, increased incidence in multigravida who changes parterns or hence donor examination pregnancies are difficult to explain except on an immune basis.

Incidence of family history in toxaemia of pregnancy cases are very less in this study (7.69%). Dutta (1987) also stated the similar incidence suggesting it is not a familial disorder but Cooper and Leston (1979) explained severe pre-eclampsia by assuming that the affected women must be homozygous for a single recessive gene.

As defined earlier pre-eclampsia is a syndrome complex developed after 20th week of pregnancy but it may appear earlier in case of vascicular mole and hydramnios. In our study there were no case reported in first trimester, 3 cases in 2nd trimester and 36 cases in last trimester. But with this data we should not conclude that this syndrome develops mostly in last months, actually patient came here for check up when they developed severe symptoms and it is possible that mild symptoms like oedema in mid trimester were taken as a manifestation due to pregnancy and bothered when they developed severe symptoms and came for admission.
Eclampsia is defined as presence of convulsion or coma in cases of pre-eclampsia. In our study we noticed that 22(56.14%) cases developed convulsions. Brazy et al (1982) noticed 29% incidence of seizure in toxoaemia of pregnancy and these were the patients not receiving magnesium sulfate therapy. They noticed that seizure were usually associated with late entry into the health care system. Similar observation was noticed in this study that only one case among the 6 cases of pre-eclampsia who had taken antenatal care in early pregnancy, later on developed visual disturbance but not convulsion. It can be emphasized here that antenatal care is very necessary to prevent eclampsia among pre-eclampsia group.

HEMATOLOGICAL EFFECT OF TOXAEMIA OF PREGNANCY ON NEWBORNS.

The outstanding feature of foetal haemoglobin is its greater affinity for oxygen which is supplied at low tension in the placenta. Anoxic condition of the foetus might induce increased production of foetal Hb or delay the appearance of the adult form. Anoxia in the foetus may arise in condition which interfere with oxygenation of the foetal blood in the placenta, and with the passage of blood from placenta to foetus.

Observations of this study demonstrated significantly high foetal Hb% levels in newborns delivered of toxaeamic mothers in comparison to control group.
The mean total haemoglobin content of the cord blood showed a gradual fall in both the groups except in the newborns of toxaemic group with advancement of maturity of newborns. Foetal haemoglobin value showed a significantly fall with advancing gestational age in both the normal and toxaemic groups. But when this fall in total haemoglobin percentage and foetal haemoglobin percentage was compared in both group, newborn of toxaemic mothers showed higher haemoglobin and foetal haemoglobin percentage comparatively when appropriate for gestational age babies were compared with small for date group. Foetal Hb and total haemoglobin was reduced in small for date group indicating they had suffered from more intrauterine hypoxia.

Similar results were observed by Walber et al (1955), Bomberg et al (1955), Cook et al (1957), Balkrishnan et al (1972) and Gupta et al (1973).

Walkeer and Turnbull (1953) suggested this increase in haemoglobin is probably a response of the foetus to a falling oxygen supply. They also showed decreased level of oxygen in pre-eclamptic cases.

Several investigators have described neonatal thrombocytopenia i.e. platelet counts less than 1.5 lakh/mm$^3$ in newborns of mothers with pre-eclampsia and eclampsia. Thiagaraiah and co-workers (1984) reported severe thrombocytopenia in two of 10 neonates (20%)
those mothers had pre-eclampsia and emphasized that these findings should be a consideration in selecting the mode of delivery. They found no correlation between maternal and fetal platelet counts. Coeinstein (1985) later reported initial platelet count to have been less than 1.5 lakh/mm³ in 11(23.91%) of the 46 infants whose mothers were thrombocytopenic as the consequence of pre-eclampsia and eclampsia. Brazy et al (1982) reported 36% incidence of thrombocytopenia in infants of hypertensive mother and 11% incidence in control infants. Niels Chr Nielson (1968) noticed relatively low platelet count in the pre-eclamptics and explained it on the basis of consumption due to slightly increased activation of the coagulation system. He also noticed considerably changes in the parameters of coagulation including reduction in platelet count.

Contrary to these findings Paulette Mehta et al (1980) observed 13 cases of newborns of toxaemia of pregnancy with thrombocytopenia but when they were compared with control groups, 10 of them also had thrombocytopenia. (count ≤1.5 lakh) though cases were asymptomatic. No significant difference was observed by them in cases of maternal administration of thiazide diuretics, prostaglandin induction, steroid ingestion, hypertension, diabetes. They observed that 60% of infants studied had no recognizable cause of thrombocytopenia. But they concluded that hypoxia has been shown in laboratory rats, depressed platelet production by altering megabaryocyte structural and
functional characteristics.

Sibai et al (1983) also noticed no significant difference in incidence of thrombocytopenia and leucopenia in the control and eclamptic mothers. They stated that the frequent occurrence of these abnormal finding in these patients suggests that a factor other than eclampsia (sepsis, hypoxia, acidosis) might be responsible for these abnormalities. All of these factors may either suppress bone marrow production or increase peripheral sequestration. Does this hypoxia is responsible for thrombocytopenia? Birks et al (1975) produced thrombocytopenia in rats by keeping them in hypoxic condition and observed thrombocytopenia.

In our study we observed 30.76 (12) cases in study group and 12.8% (5) cases in control group showing platelet count less than 1.5 lakh/cumm but none of them developed rashes. The p value was 0.05. Similar finding was observed by Brazy et al (1982)-36%, Thiagariach et al (1984)-20% and Weinstein (1985)-23.91% incidence of thrombocytopenia in neonates. While Pritchard and colleagues (1987) observed no case of thrombocytopenia in newborns of eclamptic mothers.

In this study we also observed leucocytopenia in 13 (33.33%) cases in study group and 2 (5.13%) cases in control group. p value was <0.01. Same observations was observed by Brazy et al (1982) in 43% cases of newborns
of toxaemia of pregnancy while Sibai et al (1983) found no significant difference in control and study group. Manore et al previously noted an association between maternal hypertension and neutropenia but did not relate it to the severity or duration of the maternal disease process.

In toxaemia of pregnancy reduced uteroplacental blood and oxygen flow is a well known fact and it is suggested that this lead to reduced placental weight and foetal weight but in our study there was no significant difference (p 0.05) in weight of placenta of control and study group.

Chakraborty (1967) also observed no statistically significant difference in placental weight of study and control groups. He studied placental and foetal weights from 200 cases of pre-eclamptic toxaemia in which placental insufficiency was expected. Although there was a wide variability in both foetal weight and placental weight in normal cases as well as in pre-eclamptic cases. There was significant relationship in mean foetal weight in pre-eclampsia group as compared to normal group. No such difference was noticeable in the case of placental weight. Nebin and Das (1991) in their study also observed that no definite variation of placental weight in the hypertensive and control groups. De Souza (1976) also concluded that there was no significant difference in weight of placenta of between both study and control groups.
Marked placental changes were noted in the study of toxaemic group of pregnancy than normal pregnancy. Reduced uteroplacental blood flow and oxygen supply are blamed for these changes. There are lot of controversy about relation of these changes with toxaemia of pregnancy. We noted 7(15.78%) cases of significant infarction, 22 (56.67%) cases of multiple retroplacental clots, 2(5.13%) placentae with significant calcification in study group in comparison to 2(5.13%) placentae with infarction, 7(18.42%) with multiple retroplacental clots, 1(2.56%) with significant calcification. Fox (1970) observed 44.7% incidence of infarction and 6.2% incidence of retroplacental clot in pre-eclampsia group.

Several cord abnormalities are also noted in toxaemic groups as thick cord (4), Turtuous cord (4), multiple knots in cord (3), haemorrhage in cord (4) while in control group - thick cord (2), turtuous cord (1), multiple knots (10) are recorded. No abnormal attachment of cord were recorded in control group while 2 cases were recorded in study group. No pathognomic lesion was detected in study group.

Dr. Taylor published two classic paper on foetal loss in hypertension and pre-eclampsia. He demonstrated that the foetal outcome is directly related to the severity of maternal disease process and birth weight tend to be significantly low in toxaemia of pregnancy than normal
foetus in same gestation. Placenta also fails to achieve much weight in the toxaemia group. Difference of significance, for both the foetus of toxaemia of pregnancy and its placenta, fail to achieve the mean weight of infants of non toxaemic pregnancies.

The mean placental weight is not 5% less among the toxaemic group as compared to non toxaemic group.

Toxaemic patient has tendency to deliver earlier and premature birth increase more or less in direct proportion to the severity of maternal process.

BIRTH WEIGHT AND INTRAUTERINE GROWTH RETARDATION IN TOXAEMIA OF PREGNANCY

The contribution of placental pathology to the outcome of pregnancies complicated by pre-eclampsia small for date and essential hypertension babies remain controversial. Comparison of placenta from complicated pregnancies has produced contradictory findings. Chesley (1978) stated that the vascular lesion can explain the reduction in placental blood flow, the placental lesion, low birth weight and the hazards incurred by the foetus in the presence of maternal pre-eclampsia. Thus a picture is built up of the cause and effect of the reduced uteroplacental blood flow leading to reduced fetal growth. However, along with the aetiology of pre-eclampsia the mechanism of the effect of a poor uteroplacental circulation producing a small fetus remain obscure, for not
all babies born to mothers with pre-eclampsia are small for
size even in the presence of lesions in the spiral arteries
(Over Dh Veen and Fox, 1983). Keirse (1981) concluded
that the increased size of some growth retarded infants
relative to the size of their placentae may indicate a
narrower margin of fetal safety and explain their high
incidence of foetal distress.

Patrica A. Boyd et al (1985) stated that
placenta is rarely responsible for the poor growth of the
fetus but the growth and development of the placenta,
being a fetal organ, share in any depression of fetal
growth. Gruenwald (1975), Assali et al (1975) and Fox
(1978) have deprecated the use of term placental insuffi-
ciency. Numerous factors, maternal foetal and placental
are associated with poor fetal growth.

Ludlow (1933), Morris et al, (1955), Fitzzgerald
and Clift (1958) and Chakraborty (1967) have suggested that
pre-eclamptic toxaemic can retard fetal growth since birth
weight for gestational age was reduced in infants of
toxaemic mothers. On the other hand Brash (1949) and
Beaudry and Sutherland (1960) concluded from their studies
that toxaemia of pregnancy did not retard birth weight.
Further more Bailey et al (1957) and Butler et al (1969)
found no reduction in birth weight at different gestational
ages among infants, whose mothers had either mild or
moderate pre-eclamptic toxaemia though severe pre-eclamptic
Toxaemia was associated with reduced birth weight. But De Souza et al (1976) concluded reduced birth weight for gestational age was a frequent finding among infants whose mothers had severe toxaemia compared with those infants whose mothers had either mild or moderate toxaemia. De Souza also concluded that there were no significant difference in the distribution of mean birth weight, head size, placental weight between toxaemia and non toxaemic groups.

In our study there was significant difference in birth weight of control and study group. Mean birth weight in study group was 2.3 kg while in control group it was 2.6 kg (p < 0.05).

As stated earlier, in study group more low birth weight babies were recorded in comparison to control group. Control group had 40% incidence and study group had 69.23% incidence which is statistically significant.

When birth weight of both study and control group was compared, significant difference was observed between both the groups. Mean weight of study group was 2.3 kg while control group - 2.6 kg.

Brazy et al (1982), Sinha and Mukharjee (1973) Roy Choudhary (1979), Jyotsna Ojha (1979) also found significant difference in weight of newborns of toxaemic mothers and control groups but Sibai et al observed no significant difference in both groups.

Various workers have reported and suggested
Diet foetus depends on the supply of carbohydrate from the mother and in toxæmia of pregnancy the carbohydrate metabolism is grossly disturbed resulting in low birth weight and premature babies.

Some observers concluded low carbohydrate diet, low socio-economic status and faulty utilization of glucose in toxæmia of pregnancy probably results in low cord blood sugar levels and placental insufficiency leading to intrauterine growth retarded and low birth weight babies.

Effect of toxæmia of pregnancy on gestational age is a debatable topic. There were total 29(74.36%) premature cases, 2(5.13%) between 29-32 weeks gestational age group and 27(69.23%) between 33-36 weeks gestational age group showing no extreme prematurity in toxæmia of pregnancy. Kapoor M (1991) found 60% and Sibai et al (1983) found 56% incidence of prematurity. Most of the premature cases in our study were 34-36 weeks of gestational age. Only single postterm baby (2.56%) was there and 9(23.07%) cases were full term.

The problem of low birth weight cannot be over emphasized as this small group is the major cause of perinatal mortality. Moreover such a baby is a high risk neonate and more prone to morbidity and mortality. In our study among all the 39 cases, 29(74.36%) were appropriate for gestational age, while 8(20.51%) cases were small for gestational age and remaining 2.56% (1) case
As large for gestational age. When compared with controls we noticed incidence of low birth weight babies, 69.23% in study group and appropriate for gestational age, were 71.79% in same group i.e. the newborns of toxaemic mothers were low birth weight but most of them were appropriate for gestational age and incidence of IUGR was only 20.51%, in 1981 Lin reported almost similar results. S. Jain (1982) also recorded similar incidence as 26.3%.

In our study 8(20.51%) cases were intrauterine growth retarded babies. Six (75%) out of 8 were among the preterm infants and 2(25%) among the full term infants. Kapoor M (1991) recorded 11.6% incidence of IUGR in untreated group. Our untreated group (35 cases, 89.75%) has 7(20%) IUGR. Data are slightly higher but comparable. Sibai et al (1982) recorded 30% incidence of intrauterine growth retardation while Brazy et al (1982) recorded 39% babies of less than 10 percentile weight about two times more value as compared to our findings. Derham (1989) observed very high incidence (70%). Helen Wigidman observed 46.8% incidence of intrauterine growth retardation.

Microcephaly defined as a head circumference <10th percentile occurrence in our study was in 23% of cases. Similar 29% and 18.9% incidences were reported by Brazy et al (1982) and Sibai et al (1983) respectively. In our study there were 23.07% cases showing head circumference between 10-25 percentile as compared to Sibai et al (1983) who reported 29.7% and Brazy et al (1982) reported 24.1%
cases of head circumference between 10-25 percentile.

Newborns, falling between 25-50 percentile and 750 percentile of head circumference were 25.64% and 48.71% in the present study. Brazy et al (1982) showed 41.37% and 6.39% results respectively while Sibai et al (1982) showed 37.85% cases in 25-50 percentile and 21.6% cases in more than 50 percentile group. We found significant difference in head circumference of study group and control group in ≤10 and 10-25 percentile group as evident from table 12 (p ≤0.05 and 0.05).

According to Chase (1971) intrauterine undernutrition is more responsible for intrauterine growth retardation microcephaly and low head circumference percentile. The etiology of the poor intrauterine nutrition is complex, but is likely related to factors altering placental passage of nutrition, including poor placental blood supply to the foetus, maternal undernutrition, multiple births, maternal disease, genetic disturbances and intrauterine infections.

The human brain initiate the period of rapid weight gain during the last half of fetal life with a peak near the time of birth as stated by Deirson (1966). Approximately two third of the human brain cells, as represented by D.N.A. Accumulate prior to birth and one third between birth and age of 5 months.

Previous experiments in rats, have shown lower neonatal brain weight following intra uterine vasculature
ligature (Wiglesworth J, 1966) and lower newborn baby and
brain weights and DNA following a maternal low protein
diet.

Chase (1971) observed reduction in body and
brain weight and brain cellularity, protein and lipid
content are described in newborns guinea pigs under-
nourished in utero.

Schuttle (1971) also observed in his study of
small for gestational age newborns that biochemical
results of malnutrition during intrauterine development
have shown defective myelination as well as neuro-
cellular growths retardation.

In statistical analysis of percentile of Crown
heel length of newborn, we found 17.9% cases in \( \leq 10 
\)
percentile, 20.51% cases in 10-25 percentile and 30.76%
cases in 26-50 percentile group. Comparable findings
were observed by Sibai et al (1983) as 24.32% in \( \leq 10 
\)
percentile group, 27.02% in 25-50 percentile group. But
in 10-25 and 750 percentile group they observed higher
percentage i.e. 40.54% and 13.5% respectively.