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Original research article

Pathophysiological Changes in Cord Blood and Placenta in Hypertensive Pregnant Women

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Abstract

Background: Infant and maternal mortality has raised serious concerns since ages. Ongoing researches in this field aim to develop insights in successful maternal and infant care programmes.

Objective: A comparative study of haematological changes in cord blood and morphological changes in placenta in hypertensive pregnant women with normal pregnant women.

Method: This study was conducted in the department of Physiology in collaboration with the department of Obstetrics and Gynaecology and department of Pathology, after taking permission from the institutional Ethics Committee. Sample size included 100 third trimester pregnant women of 20-40 yrs. Study group included subjects (n=50) with Blood Pressure ≥ 140/90mmHg. Control group included subjects (n=50) with normal Blood Pressure (Systolic=100-139 mm Hg; Diastolic= 60-89 mm Hg). foetal details i.e. foetal weight, maturity, Apgar scores at the first and fifth minute, Haematological parameters (haemoglobin concentration, total RBC count, Blood Indices, total platelets count, total WBC count, differential leucocyte count in cord blood) and gross changes in placental morphology (weight, shape, surface area, thickness, no of cotyledons) and histopathological changes (syncytial knot formation, fibrinoid necrosis, syncytial trophoblastic proliferation, hyalinised villi, calcification in placenta) were duly studied.

Results: The gestational age was significantly lower in hypertensive group (37±1.3). Premature babies were delivered more to hypertensive mothers. Cesarean sections were more done in hypertensive mothers (n=33). The weight of newborn baby was found lower in hypertensive group (2408±413). Absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelets count were significantly lower in hypertensive mother's cord blood when compared with maternal blood ($p<.05$). The reduced placental weight was found in hypertensive group as compared to normal group. In hypertensive group, the less thickness and surface area were noted. The less mean number of cotyledons were observed in anaemic group. Calcified areas, Syncytial knot formation, Fibrinoid necrosis, hyalinised villi, perivillous fibrin deposition, intervillous space, hypovascular villi were seen significantly more in hypertensive group as compared to normal group. Calcified areas, Syncytial knot formation, Fibrinoid necrosis, hyalinised villi, perivillous fibrin deposition, intervillous space, hypovascular villi were seen significantly more in hypertensive group as compared to normal group.

Conclusion: Hypertension in pregnancy influence haematological changes in cord blood and morphology of placenta which in turn adversely affect the perinatal outcome.
Keywords: Pregnancy Induced Hypertension, Placenta, Cord blood, Third Trimester.

Introduction

The hypertensive disorders of pregnancy are responsible for 5-8% of all maternal deaths.[(1)] The basic classification for hypertension describes as first gestational hypertension, second Pre-eclampsia and eclampsia syndrome, third Chronic hypertension of any etiology and fourth Preeclampsia or chronic hypertension. Gestational hypertension is defined as new hypertension presenting after 20 weeks without significant proteinuria, this diagnosis is made in women whose blood pressures reach 140/90 mmHg or greater for the first time after 20 weeks of gestation, but in whom proteinuria is not identified.[(2)] The uteroplacental unit is one of the organs which is affected by capillary damage in hypertensive pregnant women. Early and long-term hypertension may lead to uteroplacental failure, foetal distress, intrauterine growth retardation and preterm delivery.[(3)]

The placenta is the interface between the foetus and the mother. The survival and growth of the foetus is essentially dependent on the formation and the full development of the placenta. It undergoes changes in weight, volume, structure, shape and function continuously throughout gestation to support the prenatal life.[(4)] Examination of the cord blood can be done as a tool for screening of the newborns of both hypertensive and normotensive mothers to detect vulnerability to diseases which can result in improving the health of their newborns. So, the purpose of this study was to examine the haematological parameters in maternal and cord blood along with morphological and histological changes in placenta of hypertensive mothers, which may affect the status of the mothers and their foetus of which an early diagnosis may allow prompt treatment or facilitate proper planning to improve quality of life in these mothers and their newborns.

Materials and Methods-

This study was conducted in the department of Physiology in collaboration with the department of Obstetrics and Gynaecology and department of Pathology after taking written informed consent from the subjects.

Inclusion Criteria-

- Pregnant women aged 20-40 years.
- Pregnant women in third trimester from the outpatient department (OPD) or on the day of delivery admitted in labour room or operation theatre.
- Women with primary and multiple pregnancies.
- Pregnant women with normal haemoglobin concentration and normal blood pressure (haemoglobin concentration>=11gm/dl, Blood Pressure- Systolic range 100-139mmHg, Diastolic 60-89mmHg) and not having any oedema and proteinuria in control group.
- Blood Pressure>=140/90mmHg on at least two occasions 6 hours apart after 20 weeks of gestation with or without having oedema and proteinuria.
- Non-smokers, non-alcoholic, non-diabetic mothers having perfect sense of physical, mental and psychological well being.

Exclusion criteria-

- Elderly women aged more than forty years.
- Pregnant women in 1st and 2nd trimester.

- Pregnant women with a known case of coronary artery disease/ischemic heart disease or congenital heart disease.
- Subjects having a history of neurological disorder, diabetes, with features of hypo- or hyperthyroidism, patients on any drug that alters the sinus node impulse generation and AV conduction, patients with fever and features suggestive of infections, patients with chronic obstructive pulmonary disease and other chronic lung disorders were excluded.

Sample size -100 pregnant women aged 20-40 years.

Patients were divided into two groups-

The subjects that satisfied the inclusion and exclusion criteria were divided into:

1. Group I- Normal healthy control (n=50)

2. Group II- Study group (n=50)

Group I- Healthy controls

In this group one hundred fifty subjects were included who had haemoglobin concentration > 11gm/dl, Systolic blood pressure ranging between 100-139 mmHg and Diastolic blood pressure ranging between 60-89 mmHg.

Group II-

Group II consisted of fifty subjects with Blood Pressure>= 140/90 mmHg.

Eligible participants were recruited from the outpatient department (OPD) and labour room in the third trimester based on the inclusion and exclusion criteria. The demographic data of the mothers (age, chronic disease, drug usage, parity, blood group, gestational week, history of past illness, history of previous childbirth, problems during pregnancy, mode of delivery, administration of anaesthesia, presence of meconium, foetal deceleration and presence of a nuchal cord), birth weight of the newborn, length of the newborn, gender, heart rate, body temperature, maturity of the newborn were recorded. APGAR scores at the first and fifth minutes were recorded. The placentas with cord and membrane were collected from labour room or operation theatre after delivery for gross and histopathological studies.

Observations and Results-

In the above study, no significant difference was found in parity, APGAR score, gender, shape of placenta and mode of delivery between the groups. The gestational age was found lower in hypertensive group (37±1.3) which was statistically significant. Premature babies were delivered more to hypertensive mothers(n=15). Cesarean sections were done more in hypertensive mothers (n=33). The weight of newborn babies was found to be lower in hypertensive group (2408±413). Absolute neutrophil count (ANC), absolute lymphocyte count (ALC) and platelet count were found lower in hypertensive mother's cord blood when compared with maternal blood ($p<0.05$) and this was found to be statistically significant. A reduced placental weight was found in hypertensive group as compared to normal group. Also, in hypertensive group, thickness and surface area of placenta noted were lesser. Apart from this, a lesser mean number of cotyledons were observed in anaemic group. Besides, calcified areas, syncytial knot formation, fibrinoid necrosis, hyalinized villi, perivillous fibrin deposition, intervillous space and hypovascular villi were seen significantly more in hypertensive group as compared to normal group.

Table 1: Basal Parameters in Pregnant Women-

Parameter	Control group (n=50)	Hypertensive group (n=50)	Statistical significance $p<0.05$
1. Maternal age (years)	27±4.7	28 ±4.6	Not significant
2. BMI(Kg/m^2)	22±1.7	23±0.7	Not significant
3. Blood Pressure (mmHg)	SBP-118±4.3 DBP-81±5.0	SBP-149±2.9 DBP-94±2.9	Significant

4. Parity	Primi-12 Multi-38	Primi-16 Multi-44	Not significant
5. Diet	Veg-40 Non-veg-10	Veg-42 Non-veg-8	Not significant
6. Education	Edu-35 Unedu-15	Edu-27 Unedu-13	Not significant

Student t-test applied. Variables are presented as mean ± SD. The * represents significant at p <0 .05

Table 2: Basal Parameters in newborn-

Parameter	Control group (n=50)	Hypertensive group (n=50)	Statistical significance p <0.05
1. Gestational age (weeks)	40± 0.4	37± 1.3	Significant
2. Premature (≤ 37 weeks)	12	15	Significant
3. Mature(>37weeks)	38	35	Significant
4. Mode of delivery (vaginal/cesarean)	NVD-44 LSCS-6	NVD-17 LSCS-33	Significant
5. Apgar score at 1st minute	7± 0.9	6± 1.1	Not Significant
6. Apgar score at 5th minute	8± 0.8	7 ±0.8	Not Significant
7. Birth weight (gm)	3175±210	2408±413	Significant
8. Gender	Male-33 Female-17	Male-28 Female-22	Not Significant

Student t-test applied. Variables are presented as mean ± SD. The * represents significant at p < 0.05

Table 3: Haematological Parameters in maternal Blood-

Parameter	Control group (n=50)	Hypertensive group (n=50)	Statistical significance p <0.05
Hb (gm%)	12±0.5	13±0.3	significant
Total RBC count (million/mm^3)	4± 0.2	4±2.3	Not significant
Haematocrit (%)	35± 1.7	33±0.9	Significant
MCV (fl)	96±2.4	91±5.2	significant
MCH (pg)	29 ±2.1	30±2.2	Not significant
MCHC (%)	35± 2.5	33±1.3	Significant
Total WBC count (thousands/ mm^3)	7696 ± 1173.4	5632±845.4	significant
ANC (thousands/ mm^3)	4415 ± 723.6	1984±271.4	Significant
ALC (thousands/ mm^3)	2928 ±569.9	1255±178.2	Significant
Platelets count (lacs/cc)	2 ±0.4	1±0.1	Significant

Student t-test applied. Variables are presented as mean ± SD. The * represents significant at p < .05.

Table 4: Haematological Parameters in cord blood-

Parameter	Control group (n=50)	Hypertensive group (n=150)	Statistical significance p<0.05
Hb (gm%)	12.6±0.7	13±0.4	Not significant
Total RBC count (million/mm^3)	4±0.3	4±0.2	Not significant
Haematocrit (%)	37±1.6	31±0.9	Significant
MCV (fl)	97±6.6	92±5.3	significant
MCH (pg)	29±2.3	32±2.4	Significant
MCHC (%)	33±1.9	33±1.3	Not significant
Total WBC count (thousands/ mm^3)	7556±1127.5	4653±863.9	Significant
ANC ((thousands/ mm^3)	4409±719.0	1998±277.4	Significant
ALC ((thousands/ mm^3)	2833±502.8	1232±165.9	Significant
Platelets count (lacs/cc)	3±0.3	1±0.1	Significant

Student t-test applied. Variables are presented as mean ± SD. The * represents significant at $p < 0.05$

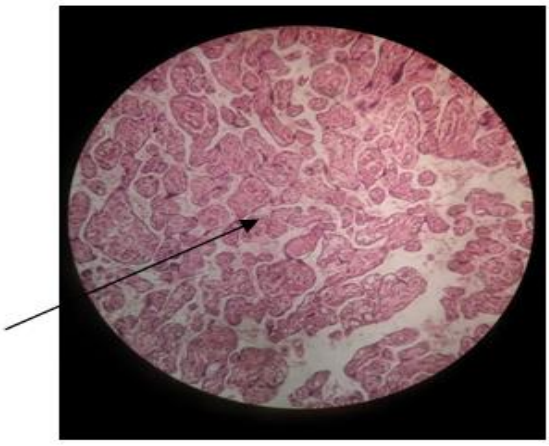

Fig 1: Microphotograph showing Placental Villi (H& E stain,100 x)

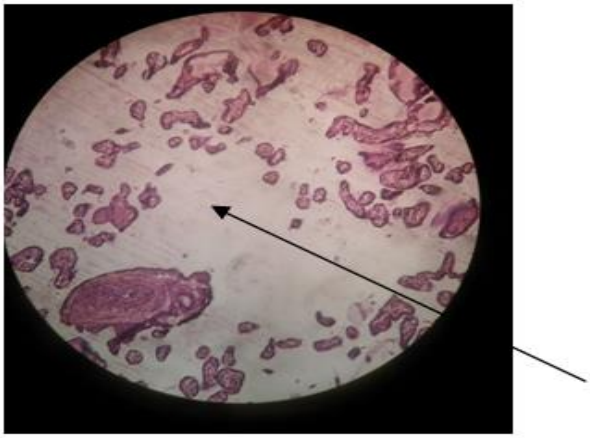

Fig 2: Microphotograph showing Increased Intervillous space (H& E

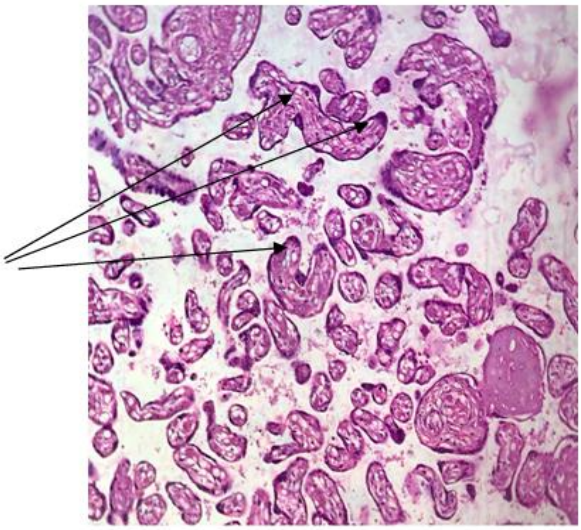

Fig 3: Microphotograph showing Syncytial Trophoblastic (H& E stain,100 x) proliferation

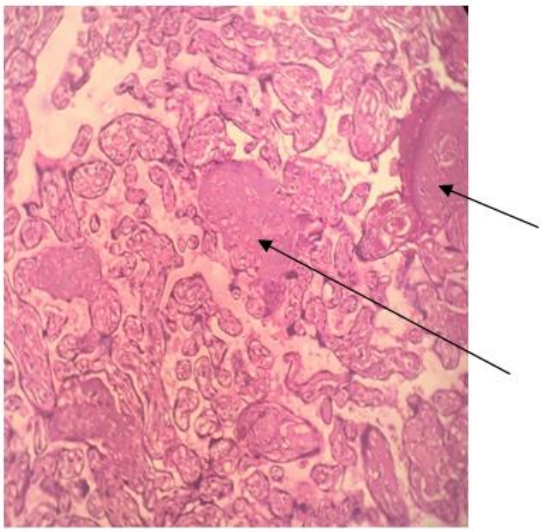

Fig 4: Microphotograph showing Fibrinoid necrosis (H& E stain,100 x)

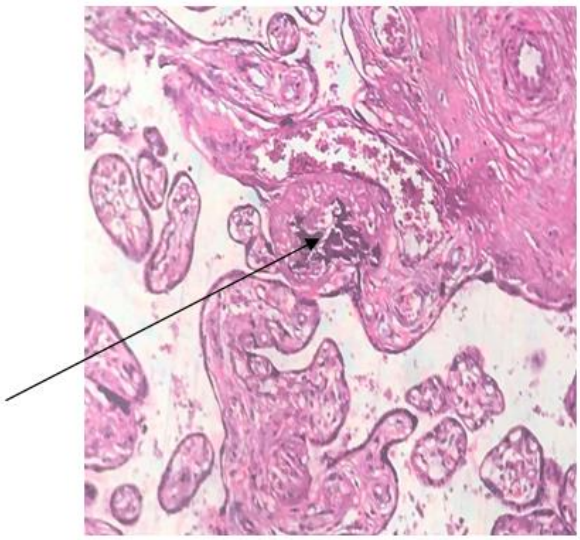

Fig 5: Microphotograph showing Calcification (H& E stain,100 x)

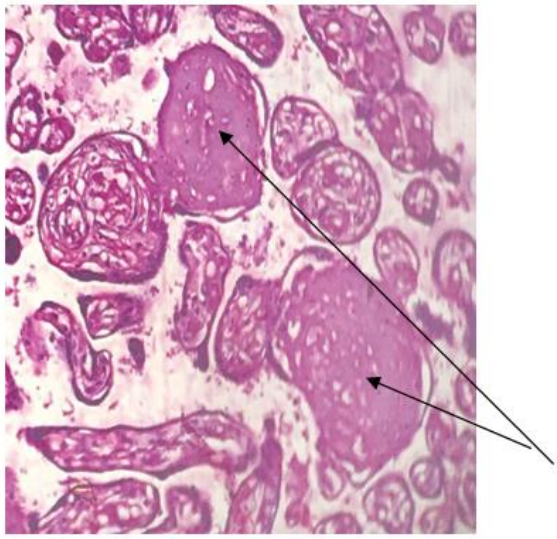

Fig 6: Microphotograph showing Hyalinized villi (H& E stain,100 x)

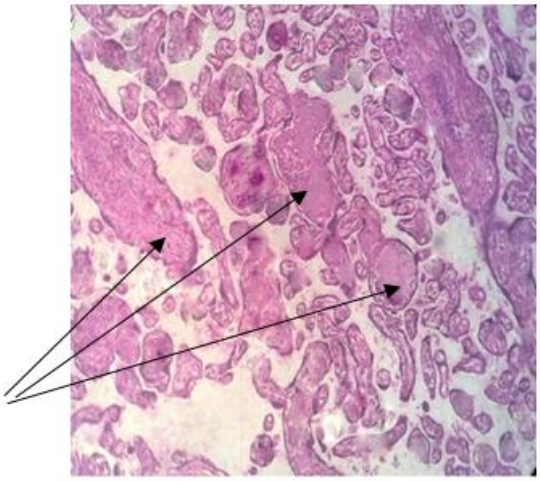

Fig 7: Microphotograph showing Hypovascular Villi (H& E stain,100 x)

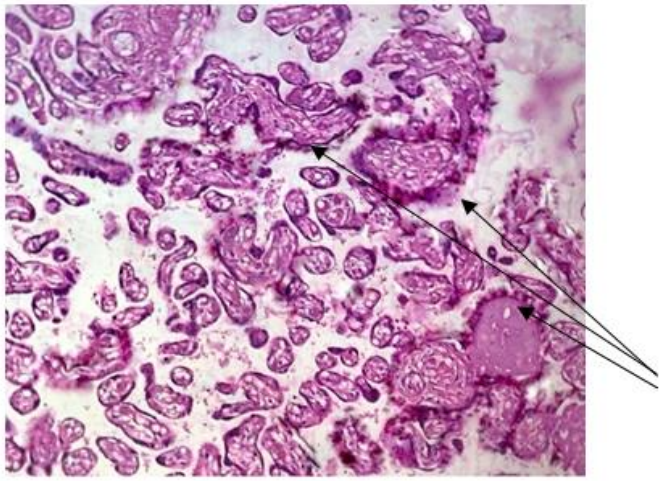

Fig 8: Microphotograph showing Perivillous fibrin deposition (H& E

Table 5: Morphometric and Microscopic Findings of the placenta in pregnant women-

Parameter	**Control group (n=50)**	**Hypertensive group (n=150)**	Statistical significance $p<0.05$
Placental weight(gm)	482.34±21.50	381.54±15.52	significant
Thickness(cm)	2.60±0.37	2.25±0.60	significant
Shape	Circular-38 Oval-12	Circular-37 Oval- 13	Not significant
Surface area(cm^2)	225.40±32.04	91.35±19.12	significant
Mean no of cotyledons per placenta	16.6±1.66	10.94±1.87	Significant
Mean no of calcified areas per placenta per lpf	1.4±1.07	16.36±2.52	Significant

Mean no of areas of Syncytial knot formation per lpf	5.04±1.16	24.48±2.05	Significant
Mean no of areas of Fibrinoid necrosis per lpf	1.82±1.49	10.86±1.61	Significant
Mean no of areas of hyalinised villi per lpf	1.77±1.17	10.8±1.76	Significant
Mean no of areas of Perivillous fibrin deposition per lpf	1.31±1.18	4.68±2.01	Significant
Mean no of areas of intervillous space per lpf	1.25±1.15	6.9±3.03	Significant
Mean no of areas of Hypovascular villi per lpf	3.62±1.09	6.94±1.20	Significant

Student t-test applied. Variables are presented as mean ± SD. The * represents significant at $p < 0.05$

Discussion

The placenta is a highly specialized organ of pregnancy that supports normal growth and development of the fetus in uterus. Its growth and functions are precisely regulated and coordinated to ensure the exchange of nutrients and waste products between maternal and fetal circulatory systems and it shares same stress and strain to which the fetus is exposed. Thus, any disease affecting mother and fetus also has great impact on placenta.[5]

Some previous studies suggested that neonatal haematological parameters are influenced by genetic, socio-economic status as well as various environmental factors experienced by the pregnant mother during her pregnancy. In hypertensive group neutropenia and lymphocytopenia suggest that there may be some uteroplacental failure due to hypoxia, decrease in neutrophil count might be caused by a decrease in growth factors which increases neutrophil production, decrease in response of proginator cells to growth factors and presence of inhibitor substance which inhibit neutrophil production. Thrombocytopenia in pregnancy induced hypertension is mostly caused due to increase consumption of platelet which may be due to adherence of platelet at the site of damaged vascular endothelium. Severity of pregnancy induced hypertension and thrombocytopenia observed are closely correlated which indicates that thrombocytopenia is directly proportional to the severity of pregnancy induced hypertension. So, neutropenia, Lymphopenia and thrombocytopenia might be due to inhibitor of neutrophil production. Neutropenia and Lymphocytopenia suggest that there may be some uteroplacental failure due to hypoxia. In hypertension, the uteroplacental circulation is compromised and the villi are exposed to a more hypoxic conditions resulting in a shift towards branching angiogenesis.

Syncytial knots might be increased in conditions of utero-placental malperfusion such as in hypertension. There would be a disturbance in the hormonal factors in pregnancy induced hypertensive mothers, which may probably lead to altered morphometry of placenta and low birth weight babies.

Conclusion:

The results indicate that hypertensive mothers show lower gestational age and greater incidence of cesarean sections with more number of premature and lower birthweight babies as compared to normal group. Also, neutropenia, lymphocytopenia and hypertension induced thrombocytopenia was more common in such women.

In conclusion,, hypertension in pregnancy influence haematological changes in cord blood and morphology of placenta which in turn adversely affect the perinatal outcome.

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