A COMPARATIVE STUDY OF PLACENTAL MORPHOMETRY AND HISTOMORPHOLOGY IN NORMAL AND HYPERTENSIVE PREGNANCIES

Dissertation submitted in

partial fulfilment of the requirements for the degree of

M.D. (PATHOLOGY)

BRANCH - III

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MADRAS MEDICAL COLLEGE
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THE TAMIL NADU
DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI

OCTOBER 2015

CERTIFICATE

This is to certify that this Dissertation entitled **"A COMPARATIVE STUDY OF PLACENTAL MORPHOMETRY AND HISTOMORPHOLOGY IN NORMAL AND HYPERTENSIVE PREGNANCIES"** is the bonafide original work of **DR.A.PRATHIBA** in partial fulfillment of the requirement for M.D., (Branch III) in Pathology examination of the Tamil Nadu Dr.M.G.R Medical University to be held in October 2015.

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DECLARATION

I, **Dr.A.Prathiba,** solemnly declare that the dissertation titled **"A COMPARATIVE STUDY OF PLACENTAL MORPHOMETRY AND HISTOMORPHOLOGY IN NORMAL AND HYPERTENSIVE PREGNANCIES"** is the bonafide work done by me at Institute of Pathology, Madras Medical College under the expert guidance and supervision of **PROF. DR.M.P.KANCHANA, M.D.,** Professor of Pathology, Institute of Obstetrics and Gynaecology, Madras Medical College. The dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University towards partial fulfillment of requirement for the award of M.D., Degree (Branch III) in Pathology.

Place: Chennai

Date: **DR.A.PRATHIBA**

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INSTITUTIONAL ETHICS COMMITTEE
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CERTIFICATE OF APPROVAL

To
Dr. A. Prathiba,
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Dear Dr. A. Prathiba,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"A Comparative Study of Placental Morphometry and Histomorphology in Normal and Hypertensive Pregnancies"** No.29062014

The following members of Ethics Committee were present in the meeting held on 03.06.2014 conducted at Madras Medical College, Chennai-3.

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12.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

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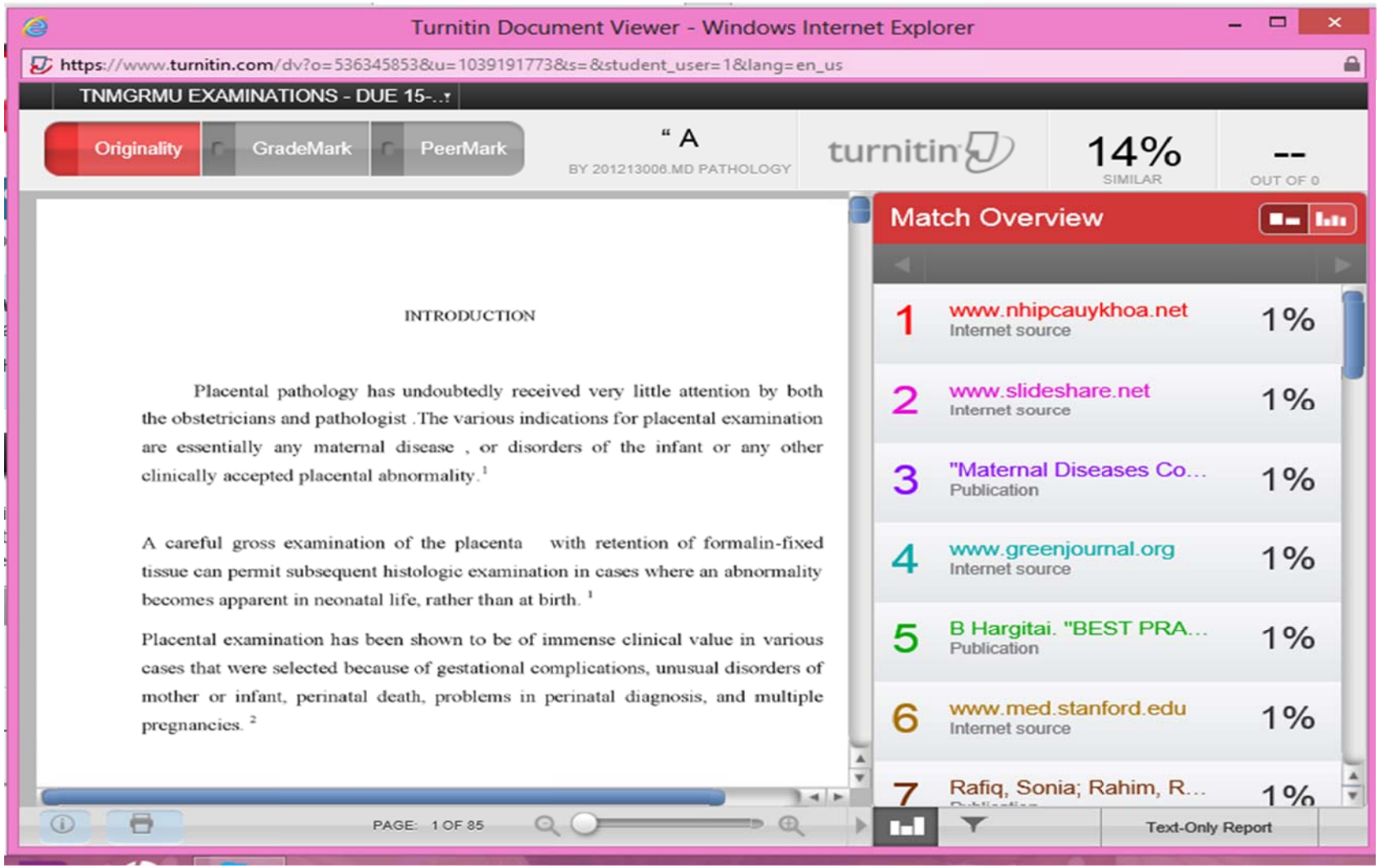
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INTRODUCTION
Placental pathology has undoubtedly received very little attention by both the obstetricians and pathologist .The various indications for placental examination are essentially any maternal disease , or disorders of the infant or any other clinically accepted placental abnormality.[1]
A careful gross examination of the placenta with retention of formalin-fixed tissue can permit subsequent histologic examination in cases where an abnormality becomes apparent in neonatal life, rather than at birth. [1]
Placental examination has been shown to be of immense clinical value in various cases that were selected because of gestational complications, unusual disorders of mother or infant, perinatal death, problems in perinatal diagnosis, and multiple pregnancies. [2]
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Placental examination has been shown to be of immense clinical value in various cases that were selected because of gestational complications, neonatal disorders of mother or infant, perinatal death, problems in perinatal diagnosis, and multiple pregnancies.[3]

Placental examination forms an integral part of perinatal or fetal autopsy and helps in adding important or conclusive information.[4]

Examination of the placenta in a problematic pregnancy has its own value, it yields information regarding the nature and duration of processes that has occurred during the gestational period. Such evaluation requires thorough and thoughtful gross examination, careful sectioning, and a clear understanding of the basic macroscopic features and the numerous changes in a whole list of pathologic processes.[5]

ABBREVIATIONS

PE	:	Preecampsia
SCT	:	Syncytiotrophoblast
CT	:	Cytotrophoblast
TBM	:	Trophoblastic Basement Membrane
IVS	:	Intervillous space
VSM	:	Vasculo syncytial membrane
EVCT	:	Extra villous cytotrophoblast
IIV	:	Immature intermediate vili
MIV	:	Mature intermediate villi
RPH	:	Retroplacental hematoma
SCF	:	Subchorionic fibrin
SK	:	Syncytial knot
VFD	:	Villous fibrinoid degeneration
IUGR	:	Intra uterine growth restriction
RBC	:	Red blood cell
SGA	:	Small for gestational age
S	:	Significant
NS	:	Not Significant
USG	:	Ultrasonogram
VOCAL	:	Visual Organ Computer – aided Analysis
BP	:	Blood pressure

ALT	:	Alanine transaminase
AST	:	Aspartate transaminase
LDH	:	Lactate dehydrogenase
IL 1	:	Interleukin 1
IL 6	:	Interleukin 6
TNF	:	Tumor necrosis factor
PGI 2	:	Prostacyclin
TXA2	:	Thromboxane A2
HLA	:	Human leucocyte antigen
C/s	:	cross section

CONTENTS

A COMPARATIVE STUDY OF PLACENTAL MORPHOMETRY AND HISTOMORPHOLOGY IN NORMAL AND HYPERTENSIVE PREGNANCIES

ABSTRACT

In preeclampsia, there is increased resistance to uteroplacental circulation which adversely affects the placental morphology (macroscopically and microscopically) and in turn the fetal growth.

OBJECTIVES :

To study the morphometry , gross and histomorphologic changes of placenta in preeclampsia & to correlate these changes with severity of preeclampsia , as well as fetal outcome.

METHODS :

200 placentae (100 normal ; 100 preeclamptic) were studied .Fetal outcome, Placental morphometry, gross and histomorphologic features were studied in the two groups and the results were compared and correlated using statistical analysis .

RESULTS :

The placental weight , volume and surface area were significantly decreased in the preeclamptic group . The incidence of retroplacental hematoma and infarction was significantly more in the study group and was also associated with a poor fetal outcome. The microscopic features of areas of syncytial knot formation , cytotrophoblastic cellular proliferation , irregular thickening of trophoblastic basement membrane , villous fibrinoid degeneration and villous

stromal fibrosis were all found in agreater amount in the preeclamptic placentae than the control group . And these changes statistically correlated with severity of preeclampsia , aswell as with fetal outcome .

CONCLUSION :

Preeclampsia adversely influences the morphometry and morphology of the placenta with an impact on the fetal outcome. However, none of the pathological changes are specific to preeclampsia. This study further emphasizes the importance of in-utero measurement of placental volume and thus better management of at risk fetuses.

KEY WORDS :

Placenta, preeclampsia, morphometry, morphology.

INTRODUCTION

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A careful gross examination of the placenta with retention of formalin-fixed tissue can permit subsequent histologic examination in cases where an abnormality becomes apparent in neonatal life, rather than at birth. [1]

Placental examination has been shown to be of immense clinical value in various cases that were selected because of gestational complications, unusual disorders of mother or infant, perinatal death, problems in perinatal diagnosis, and multiple pregnancies. [2]

Placental examination forms an integral part of prenatal or fetal autopsy and helps in adding important or conclusive information. [3]

Examination of the placenta in a problematic pregnancy has its own value, it yields information regarding the nature and duration of processes that has occurred during the gestational period. Such evaluation requires thorough and thoughtful gross examination, careful sectioning,

and a clear understanding of the basic microscopic features and the numerous changes in a whole list of pathologic processes. [4]

Toxemia of pregnancy is one of the known leading cause of maternal mortality and stands to be an important factor in terms of fetal wastage as well.[5] They form one of the deadly triad along with hemorrhage and infection which together contribute to maternal morbidity and mortality. In addition, preeclamptic pregnancies are known to be associated with prematurity and fetal growth restriction, contributing largely to perinatal mortality and morbidity.

In India, preeclampsia has an incidence of 1.5%. In most of the previous studies, gross abnormalities of placenta have received undue attention and undeserved status. Recently, morphological changes in the chorionic villi have been proven to bear a strong relationship with the fetal well-being.[6]

The placenta has been referred to as the mirror of intrauterine fetal experience. Not only that, it stays to be the best record of the prenatal experience of every infant. A glance at the literature reveals that the preeclampsia-eclampsia syndrome does exert its deleterious effects on the placenta.[5]

Grossly, the preeclamptic placentae is lesser in weight, diameter and thickness, with an increase in the incidence of abnormal shape and cord insertion, with diminished fetoplacental ratio. Also there seems to be a higher incidence of infarction and retroplacental hematoma, in preeclamptic placentae.

The numerous placental changes bear a direct relation to severity and duration of the disease process. The fetal outcome is adversely influenced by the pathological changes in the placenta.

Thus there is a need for a thorough examination of placenta which may help in revealing the various abnormalities that contribute to the disorder of pregnancy, toxemia, in the present study. This study is an attempt to observe and to compare the morphometric and the morphological features, both gross and microscopic in preeclamptic and normal placentae.

Aims and Objectives

AIMS & OBJECTIVES

1. To record the data on morphometry, morphology and histology of normal and preeclamptic placentae, respectively.

2. To compare and analyse the placental morphometry and placental morphology (gross and microscopic) in normal and hypertensive pregnancies.

3. To correlate the severity of pre-eclampsia with morphometry and extent of histomorphologic changes.

4. To correlate the fetal outcome with morphometric findings of placenta

Review of Literature

REVIEW OF LITERATURE

PLACENTAL DEVELOPMENT :

Development of human placenta is initiated at the time when the fetal membranes have established stable and close contacts with the uterine endometrium, or in other words when the blastocyst implants.

The placenta develops in three stages [7]

1. Prelacunar stage
2. Lacunar stage
3. Villous stage

Prelacunar stage:

The implanting blastocyst is made of around 107 to 256 cells [8,9] . The cells forming the outer wall surrounding the blastocystic cavity are called **trophoblast.** These trophoblastic cells are the ultimate forerunners of the fetal membranes, including the placenta.

The inner cell mass is called **embryoblast** and this pole of the cavity is called **embryonic pole**. The embryoblast gives rise to the embryo, umbilical cord and the amnion. Apart from these, the embryoblast's mesenchyme and blood vessels also contribute to the formation of the placenta.[7]

After invading the endometrium, the trophoblastic cells proliferate to form two layers.[10]

- Outer syncytiotrophoblast
- Inner cytotrophoblast

This initial stage where the outer syncytiotrophoblast forms a rather soiled mass is the 'Prelacunar stage'.[11]

Lacunar Stage:

At this stage, small vacuoles start appearing in the syncytium, which expand and coalasce to form a system of lacunae. The interventing pillars and lamellae of SCT are called **trabeculae.**

The trophoblastic wall at implantation pole is much thicker **(Chorionfrondosum**) as the formation of SCT started much earlier here and this forms the placenta. And the remaining circumferential thinner trophoblastic layer undergoes regressive transformations to form the smooth chorion (**Chorionleavae)**, the fetal membranes.[9]

With the formation of lacunae, the trophoblastic covering is divided into **three layers.**

a) Primary chorionic plate, which lies towards the blastocystic cavity.
b) Lacunar system along with trabeculae.
c) Trophoblastic shell that faces endometrium

With further invasion, the maternal blood vessels are disintegrated by the invading SCT. With this maternal blood fills the lacunae.[9] Likewise, the walls of the disintegrating capillaries and spiral arteries are completely replaced by the basally expanding SCT in a step wise fashion[12].

Early villous stage :

Once the maternal circulation is established, there is an increase in trophoblastic proliferation with further fusion. This paves way to the formation of **primary villi,** which are composed of buds or projection of SCT invaded by proliferating CT. With further branching, they give rise to primitive villous trees, which are called **anchoring villi** when they remain in contact with trophoblastic shell. Now the lacunar system is called **intervillous space.**

Sooner, the extraembryonic mesenchyme present on the innersurface of primary chorionic plate begins to invade, leading to formation of **secondary villi.**

The expanding villous mesenchyme does not reach the basal part of the trophoblastic shell. These basal segments of the trabeculae persist in primary villous stages. There are referred to as **cell columns**. They are the source of **extravillous CT**. Similarly, in some free floating villi the

proliferating villous tips are not invaded by mesenchyme and these form the **trophoblastic cell islands.**

The appearance of first fetal capillaries in the mesenchyme marks the formation of the **tertiary villi**. These fetal capillaries get their origin from hemangioblastic progenitor cells which in turn are believed to differentiate from the mesenchyme[13,14].

The placenta always forms a barrier between the maternal and fetal circulation. This **barrier** is made of the following layers;

1. SCT - Continuous layer lining the IVS and covering the villous surface.
2. CT (Langhans cells.)
3. Basal lamina of the trophoblastic layer.
4. Connective tissue
5. Fetal endothelium surrounded by basal lamina.

TEMPORAL VARIATION IN VILLOUS STRUCTURE:

Growth and maturation of the villous tree

This temporal variation in villous structure is a reflection of the ongoing maturation and branching of the villous tree. And this relation was formally documented; mostly by the work of Kaufmann and his colleagues [15-22].

There are **five types** of vill:

1. **Mesenchymal villi:**
    a. These represent the first generation of any newly formed villi.
    b. Derived from mesenchymal invasion and vascularisation of trophoblastic sprouts.
    c. Differentiate into : mature or immature intermediate villi.
    d. Trophoblastic layer : complete, syncytial nuclei is dispersed regularly.
    e. Stroma : Immature and abundant with few hofbauer cells and ill formed fetal capillaries.
    f. Time Scale : Mainly during early pregnancy. At term – few are seen in the centre of lobules.

2. **Immature intermediate villi:**

- These are stem villi's peripheral extensions.
    - Trophoblastic layer:
        - Well preserved
        - Numerous CT
        - SCT nuclei evenly dispersed
        - No syncytial knots or vasculosyncytial membranes.

- Stroma:
    - Abundant and loose with numerous hofbauer cells; venules, arterioles and capillaries.
- Time scale:
    - Predominant form in immature placenta.
    - At term : some seen in the centre of the lobules representing persistant growth zone[23-26].

3. Stem Villi

- These are the stems that connect the villous tree to the chorionic plate.
- Towards term, the trophoblastic layer is mostly replaced by fibrinoid.
- They contain arteries and veins with appreciable muscle walls, surrounded in turn by a compact fibrous stroma.
- At term : makes up 1/3rd of total villous volume. Maximally concentrated in the central subchorial part.

4. **Mature intermediate villi**:

- Derived from peripheral ramification of villous stems.
- Differentiate into terminal villi
- SCT : uniform no knots or VSM.

- Stroma : Loose stroma containing capillaries along with small arterioles and venules.
- Term Placenta : constitutes 1/4th of the total villous volume.

5. Terminal Villi:

- Final, grape like outgrowths of mature intermediate villi.
- SCT : Thin, syncytial nuclei dispersed irregularly, syncytial knots & VSM seen.
- Stroma : Contains sinusoidally dilated capillaries filling most of the cross sectional diameter of the villi.
- At term : constitutes 60% of the villi
- Best differentiated for materno – fetal transfer.

Pattern of development, as detailed by Kaufmann and his colleagues:

- Early weeks of pregnancy : all villi are menenchymal villi.
- 7th& 8th Weeks GA :

Mesenchymal villi begin to transform into

↓

Immature intermediate villi

(subsequenty transform into)

↓

Stem Villi

- End of 2nd trimester : formation of further IIV stops.

- Beginning of 3rtrimester : There occurs a **"SWITCH"**[27-28]
- **From** "**Branching angiogenesis**", which is responsible for IIV formation.
- **To** "**Non Branching angiogenesis**", which is responsible for MIV formation characterized by long, ill branched capillary loops.
- Soon after terminal villi develop from MIV & predominate at term. These form when longitudinal capillary growth overcomes longitudual villous growth.

REGIONAL VARIATION IN VILLOUS MORPHOLOGY :

At term, towards

Fetal surface : Stem villi & intermediate villi are prominent.

Basal plate : terminal villi are prominent.

The terminal villi

- (**Subchorial vs basal plate)** [29,30]

  Subchorial villi have:

  - More collagenous stroma
  - Thicker TBM
  - Fewer VSM

- Greater number of easily visible CT

- **Peripheral vs Central villi**

  Peripheral villi have:-

  - More fibrotic stroma
  - Thicker TBM
  - Fewer VSM

These variations bear a relationship to the flow dynamics of maternal blood in IVS & subsequent villous oxygenation.

NORMAL HISTOLOGY OF PLACENTA

Basic Villous structure:

The microscopic appearance of placental villi varies according to gestational age and the stage of development of the villous tree. Despite these facts, the villi possess a basic structure which is independent of all these variables.

The trophoblastic mantle is divided into

a) Inner layer of cytotrophoblastic cells (Langhan's cell).
b) Outer layer of syncytiotrophoblast

CYTOTROPHOBLAST :

The Langhan's cells appear ovoid, cuboidal or polyhredral with well defined cell borders, clear to slightly granular cytoplasm and a pale staining nucleus with finely dispersed chromatin.

These cells are quite prominent and complete in the 1st trimester but they are discontinuous and **less conspicuous in the 2nd and 3rd trimester.** These are the stem cells which helps in the trophoblastic growth by promoting proliferation and subsequent fusion.

At term the CT is seen in only around 30% of the total villous surface. But this doesn't mean that there is a decrease in the absolute number of CT at term, they continue to increase during the entire length of pregnancy. (31)

SYNCYTIOTROPHOBLAST :

The villi are ultimately covered by SCT. This is a surface epithelial layer which is bathed on its outer surface by the maternal blood. The final and **ultimate decisive barrier** that either limits or permits the various transplacental process is the SCT.

This syncytium is **devoid of generative potency. T**his lack of necessity to take part in cell division, permits the entire metabolic activity of this tissue to be channelized to its transfer function.(32)

SCT is formed by the fusion of neighbouring trophoblastic cells, that come in contact with the maternal tissue. And it is worth noting that this happens to be the **one and only true syncytium** occurring in the human body.

During the first trimester, the syncytial nuclei are smaller, darkly stained and regularly placed. Their cytoplasm is finely granular, homogenous or commonly vacuolated of which some vacuoles may contain lipid. Apart from this we can also see a delicate brush border on the surface of the young villi .

In the **term** placenta, the **syncytial nuclei are dispersed irregularly** and aggregate to form multinucleated protrusions from the villous surface. These are termed syncytial knots.

Syncytial knots, syncytial sprouts and syncytial buds belong to a rather heterogeneous group of specialization in SCT. But they share one feature in common, ie. **Remarkable collection of nuclei**. [33,34]

Syncytial sprouts actually represent the early stages in the formation of lateral villi. Those of them which don't become a villi become predunculated and ultimately breaks off to enter the intervillous space and then the maternal circulation.

Syncytial Buds are the free multinucleated bodies in the villous stroma. These occur as a result of separation of the invaginating trophoblast into the villous stroma[34]. But there is always a possibility that these buds, could in reality represent the tangential rectioning of an indenting villous surface trophoblast.

Bared on the descriptions of Cantle et al and Huppertz et al[35,36], the criteria that has been suggested for differentiating between true specialization of trophoblastic layer and tangential sections is as follows :

True syncytial sprouting

- Arise due to trophoblastic proliferation

They have

- Smooth surfaces
- Loosely scattered oval nuclei
- Incidental syncytial bridges

Degenerative, apoptotic, Knotting

They have

- Knot or sprout like structures with smooth surfaces
- Devoid of microvilli

- Nuclei are densely packed showing extremely condensed chromatin

Flat sections (syncytial knotting, Tenney, Parker changes)

- Irregularly shaped and notched sprouts, knots and bridges
- Nuclear shapes are heterogenous which is characteristic for syncytiotrophoblast.
- The apparent number of nuclei, increases with the thickness of the section.

Syncytial bridges

Yet another finding that has had intense discussion is the syncytial bridges. This was first described by Langhans 1870. Following that this has been reported by Stieve (1936, 1941), Peter (1943, 1951), Ortman (1941) ,Jones and Fox (1977) and Kaufmann &Stegner (1972).[37-44]

Studies by Kusterman (1981), Burton (1986a) Cantle et al (1987) concluded that these are artifacts due to tangential sectioning of villous branches. [35,45,46]

However, the studies by Burton and cantle et al (1987) have clearly stated and convinced that apart from artifactual effects, real syncytial bridges do exist.

Evidence was provided by the studies of Kaufmann & Stegner (1972) Jones, & fox (1977) Horman (1953) and Cantle et al (1987) , stating that true bridges are a consequence of fusion of neighbouring villous surfaces, which have a prolonged close contact[35,43-44,47]. Initially, the intercellular gaps between the adjacent villi are bridged through desmosomes. On a later stage, these distinguishing membranes disintegrate leading to the formation of true syncytial bridges.

Syncytial knotting – influence by the section thickness[35,45-46]

- Ultrathin sections (0.05 – 0.1mm) made for electron microscopy : exhibits very few sprouts or knot like findings.
- In semithin functions, these findings are rare.
- Paraffin section (5-10 mm) shows syncytial knotting as a frequent feature owing to its thickness.

Syncytial knotting : Diagnostic value

Despite various studies referring this as sectional artifact, Kaufman et al (1987) stood by the fact that syncytial knotting as a two dimensional finding still has a diagnostic value.[48]

These can be considered as significant artifacts that point to an underlying deformity in the terminal villi. This can further be attributed to

abnormal villous angiogenesis due to defective oxygenation of the placenta as in hypoxic or preclamptic placentae.

Apart from structural changes, the two factors that can be helpful in differentiating between true sprouting, apoptotic knotting & trophoblastic flat sectioning are :-

- Stage of pregnancy
- Type of villi involved

Young placenta with sprouts arising from immature intermediate and mesenchymal villi represents signs of actual villous sprouting.

In contrast, in term placenta a vast majority of the knots are due to flat sectioning and these are found in aggregates of terminal villi which arise from the curved surface of a mature intermediate villi. But a minority of those emanating from immature intermediate villi present in the centre of villous trees is a representation of true villous sprouting.

SCT is known to be a continuous structure in every placenta. Only during advanced pregnancy as a result of focal syncytiotrophoblastic degeneration, fibrinoid plaques separate small islands of these SCT from the remaining syncytial continum. To be precise, wherever the SCT is interrupted due to degeneration, that gap is occupied by fibrin type fibrinoid.

TROPHOBLASTIC BASEMENT MEMBRANE

The villous trophoblast is limited from the villous stroma by the T.B.M.which on an average measures from 20 to 50mm thickness and has a fibrillary structure microscopically Its constituents are laminin collagen IV and heparin sulphate .[49]

VILLOUS STROMA

This stroma is composed of undifferentiated mesenchymal cells, mature (retriculum) mesenchymal cells, fibroblasts, myofibroblasts, precollagen and collagen firbes. The relative proportion of these constituents vary with gestational age as well as stage of villous development[17,18,50-56]. Few mast cells can also be present in the villous stroma [57,58].

HofbauerCells :

These are simple tissue macrophages present in the villous stroma[59-61]. These cells can be ovoid, round or reniform, measuring around 25μm in diameter with a nucleus placed eccentrically. The cytoplasm in the early stage of gestation is coarsely vacuolated but, as pregnancy advances, there is a decrease in the size and number of vacuoles with more prominence of the intracytoplasmic granules[62].

Hofbauer cells are an important source of cytokines in the placenta. They mediate both non-immune and immune phagocytosis, as well as are capable of trapping maternal antibodies coming into the placental tissue.

Fetal villous vessels:

The exact time of appearance of the first villous vessels is variable. Generally, by the second month end, well developed vessels that are lined with large, immature, endothelial cells are seen. The vessels of the terminal villi in term placenta are in capillary size, some can appear with sinusoidal dilatation. These endothelial cells are connected by tight functions and supported by the delicate basal lamina containing laminin, fibronection, and collagen type IV. [54,63]

NON VILLOUS COMPONENTS

The placenta is limited on the fetal side by the amniotic membrane and chorionic plate and on maternal ride by the basal plate. In between these two, lies the intervillous space containing stem villi with their branches.

Amnion:

It consists of a single layer of cubical epithelium loosely attached to the adjacent chorionic plate. It takes no part in formation of the placenta and is avascular.

Chorionic plate:

From within outwards, it consists of

1. Primitive chorionic mesoderm consisting of branches of umbilical vessels.
2. A layer of CT.
3. Syncytiotrophoblast: The stem villi arise from the plate.

Basal Plate:

From inside out, it consists of the following layers.

1. Basal plate syncytiotrophoblast
2. Rohr's fibrinoid stria (encasing extra villous trophoblastic cells)
3. Extravillous trophoblast layer
4. Nitabuch's fibrinoid layer (Uteroplacental fibrinoid)
5. Part of the compact and spongy layer of the deciduasbasalis.

The basalplate is perforated by spiral artery branches of uterine vessels through which the maternal blood flows into the intervillous space.

Intervillous space:

It is bounded on the inner side by the chorionic plate and on the outer side by the basal plate; limited on the periphery by the fusion of the

two plates. It is lined internally on all sides by the SCT and is filled with slow flowing maternal blood.

Numerous branching villi, which arise from the stem villi and project into this space are the chief constituents of the IVS.

Extravillous trophoblast cells:

This term applies to all the trophoblastic cells that lie outside the villi in the

- Cell islands
- Chorionic plate
- Basal plate
- Septa
- Membranes
- Cell column

These are further categorized into

- Proliferating stem cells (connected to the basal lamina)
- Nonproliferating cells (have lost contact with basal llamina).

Microscopic :

EVCT are either isolated or clustered in strings. They have a round to spindle or polygonal shape and in paraffin sections, their nuclear cross

sections are always seen. This point is of significance when trying to differentiate it from a decidual cell.

Decidual Cells:

These are the stromal cells that are enlarged and elongated. In a section, all the cells will show the same shape depending on the angle at which the section was taken. Owing to the elongated cell bodies, the cut section will rarely include the ovoid nuclei.

Uteroplacental veins:

These are seen admixed, within the decidual and extra villous trophoblastic cells, the trophoblastic cells might invade the venous wall, rarely, but never invades the lumen of the uteroplacental vein.

Uteroplacental arteries:

They traverse spirally in the basal plate and they serve the connection between the intervillous space and maternal uterine arteries. Owing to their spirality, we can see several cut sections of uteroplacental arteries.

As against the uteroplacental veins, a distinguisting feature of uteroplacental arteries is that their endothelial lining is to a great extent replaced by the cells termed “intravascular trophoblast”. These cells lead to the formations of large plugs that can either occlude or narrow the

arterial lumen. Sooner the adventitia as well as the media are also replaced by fibrinoid and trophoblastic cells.

The placenta at term:

The expelled placenta is a flattened discoidal mass with an approximately circular or oval outline, with an :

- Avg. volume 500ml (range 200-950 ml)
- Avg. weight 500gms (range 200-800 gms)
- Avg. diameter 185mm (range 150-200 mm)
- Avg. thickness 23mm (range 10-40 mm)
- Avg. Surface ara, 30,000mm

Thickest at its centre, it rapidly diminishes in thickness towards its periphery.

Umbilical cord:

The normal length of umbilical cord at term is between 40 and 70cm. Short cords are those less than 32cm and long cords are those more than 100cm. The normal coiling index is 1 coil / 5 cm. The cord contains, three vessels (two arteries and one vein) and this needs to be assessed at a minimum of 5cm from placental insertion. Embryonic remnants of the urachus & vitelline duct are normal findings from which cysts can arise.

These remnants may need to be differentiated from hemangiomas and teratomas.

The cord normally inserts near the centre than elsewhere. Battledore placenta with marginal insertion is seen in around 7% of term placentae and velamentous insertion in around 1% of term placentae.

Extraplacental membranes and fetal surface

The significance of circumvallate and circummarginate placenta is uncertain .An association has been proposed between IUGR and acute and chronic maternal hemorrhage in circumvallate placentas. Amnion nodosum is a sign of oligohydramnios but sq. metaplasia of amnion is again a normal finding.

Langhan's fribinoid (subchorionic fibrin deposition) in small, amounts is not pathological since it collects due to eddying of the intervillous flow.

FUNCTIONS OF THE PLACENTA:

The placenta is a very unique organ as it takes charge of the function, of most of the fetal organs, with exception of the central nervous system and locomotor apparatus. The various functions accomplished by the placenta are:-

a. Excretory function, pH regulations, water balance (kidney function).
b. Gaseous exchange (Lung's function)
c. Resorptive and Catabolic function (Gut's function)
d. Synthesis and recreation of substances like the endocrine glands.
e. Hematopoises (Bone marrow function)
f. Numerous secretary and metabolic functions of the liver.

PLACENTA - MACROSCOPIC FEATURES

Deviation from the round or oval shape such as irregularly shaped, multiobed or bilobed placenta may be attributed to uterine abnormalities or disturbed implantation. However this can be assessed only in clinicipathological context.

The gross lesions of the placenta can be categorized as :

1. Due to disturbances in maternal blood flow to or through the placenta.

2. Disturbances of fetal blood flow to or through the placenta.
3. Thrombi & hematomas.
4. Non-vascular lesions.

1. **Lesions due to disturbances of maternal blood flow**.

a) Massive pervillous fibrin deposition :

Plaques of this fibrin is seen in around 22% of normal, uncomplicated full term placenta[64]. This deposition is known to occur in the setting of a good maternal blood flow across the placenta.

Grossly, seen commonly in prepheral area in the marginal angle. It can also be present centrally. It is hard and sharply demarcated. The C/s is white or with a slight yellow tinge with a granular or smooth surface.

Microscopically, this plaque contains widely separated villi entrapped in fibrin which obliterates the intervillous space completely. In older plaques, the SCT is lost, CT persist, TBM is thickened with progressive fibrosis of the villi making it avascular.

B) *SubchorionicFibrin plaque :*

This is seen in around 20% of normal, uncomplicated term placenta. This finding is unaffected by the maternal factors and does not interfere with fetal growth. These plaques are solely made of fibrin. This

deposition of fibrin is a consequence of maternal blood stasis in the subchorionic region of intervillous space[65].

Gross :

Mostly a triangular sharply demarcated laminated white plaque with the base abutting the chorionic plate and apex pointing into placental substance.

Microscopy :

The plaque is composed of solely laminated fibrin. No entrapped villi are seen.

C) *Maternal floor Infarction :*

The incidence of this lesion has divergent views. As per Naeye , it occurs in 0.5% of placentas[66]. But Andres et al said the incidence was only 0.09% and fox says, the incidence is even less. [67]

The etiology and pathogenesis of this finding is completely unknown. However, there are varying views. Rushton (1987) believed, these changes occur only after fetal death[68]. As against this, sufficient cases associated with a healthy born infant have been reported [69,70].

Andres et al, 1990 ; Mandsager et al, (1994) Naeye (1988) believe it to be representative of an end period of various disorders[66,67,71] , whilst

Bernischke and Kaufmann (1995) said it could be caused by an abnormal host placental interaction[72].

There is a general agreement that this lesion is connected to IUGR and high incidence of fetal death probably because fibrin interferes with maternal blood perfusion of IVS[66,67,71,73,74] .

Gross :

The matural surface is greyish yellow with a gyriform appearance. There is marked thickening of the basal plate with firm white material.

Microscopy :

This lesion is compound of excess fibrin deposited in the basal plate, entrapped villi are seen within the expanding fibrin mass.

D) *Infarct*

A placental infarct is defined as a localized region of Ischaemic villous necrosis.

In normal uncomplicated term placentae, less than 5% of villous tissue may be infarcted whereas in pre-edamptic placentae, the percentage is > 5% of villous tissue.

There are various views regarding its etiology.

Barthomew concluded that infarction is primarily due to an obstruction in the fetal stem vein with resultant congestion and swelling of villi finally leading to obliteration of IVS and their infarction. This view was supported by Hunt et al 1940, Falkiner 1942, Diekmann 1952, Steigrad 1952, Thomsen 1954, Gregor 1961, Becker 1963[75-81] . Further Roig (1963) said this obstruction occurs in umbilical vein due to cord knotting[82].

However over the years, various studies have accepted that thrombotic occlusion of the maternal uteroplacental vessel, some being secondary to a retro placental hematoma is responsible for the placental infarct[83-93] .

Gross :

Infarcts are more common in periphery than in central areas. The infarct is most of the times attached to the basal plate extending into the placental tissue. A fresh infarct is dark red and firmer with a shiny cut surface. Older infarcts are more firm and brown yellow or white in colour.

Microscopy :

Early infarct is composed of crowded villi with extreme obliteration of IVS. The villous vessels are congested and dilated. The

SCT nuclei undergo pyknosis and eventually disappear. No TBM thickening or CT proliferation seen. Older infarct is composed of crowded ghost villi with a thin layer of intervening firbrin.

II. Lesions due to fetal blood flow disturbances

Fetal artery thrombosis :

Thrombotic occlusion of the fetal villous stem artery creates a sharply delineated area of villous avascularity.

Incidence :

Fox reported that single fetal artery thrombosis was seen in 4.5% of normal term placenta. There are no specific factors that predispose to thrombus formation.

The placenta can withstand the loss of upto 30% of its villi, provided the maternal circulation is intact. So, thrombus of a single fetal artery which will not deprive 75% of villi is of no significance.

However, they are found with increasing frequency in placenta from diabetic mother or maternal coagulation disorders[94,95].

Gross :

Well delineated roughly triangular pallor area within the placental substance with the base facing the basal plate.

Microscopy :

This union appears as a sharply demarcated area of avascular villi. In these avascular villi,

- SCT shows excessive knotting
- CT : no proliferation
- TBM : no thickening
- Villous stroma : excessive stomal fibrous tissue.

Intervillous space is patent with maternal blood. No fibrin deposition.

III. Thrombi & Hematoma:

A) *Massive Subchorial thrombosis (Breus mole)*

This is a red thrombus that measures around more than 1cm in thickness, separating the chorionic plate from underlying villous tissue.

Small subchorial thrombi are much more common than is generally recognized as they are easily missed or ignored.[96]

There has always been a controversy regarding its origin. Shanklin & Scot, (1975) reported that blood in the thrombus is of maternal origin. Whilst, Ho (1983) said it was of fetal origin as it has nucleated RBCs. Hart (1902) proposed that the reason could be a sudden marked slowing

of the blood flow in the IVS. Which is attributed to marked obliteration of venous channels draining the space.[97-99]

Gross :

These appear as thick nodular masses of red thrombi distorting the fetal surface of placenta. It can extend to the basal plate to form a transplacental thrombus.

Microscopy :

The lesion contains only laminated thrombus. No villi are seen within it.

B) *Retroplacental hematoma*:

This lies between the uterine wall and the basal plate of placenta.

Fox reported its incidence as 4.5% of all placenta. This was the same as reported by Bermischke & Gille, (1977). Its incidence was however elevated in preeclampsia.[100,101]

The various etiological factors proposed are;

- Maternal hypertension & preeclampsia.
- Obstruction to the venous drainage of placenta [102-105] .
- Coccaine usage [106-110]
- Cigarette Smoking [111-116]

- Anticardiolipin Antibodies [117]
- Blunt trauma to abdomen [118,119]

The significance of the lesion depends on its size. Where as there can be an involvement of 20-25% of villous parenchyma without any untoward consequence of the fetus.

Gross :

The lesion can extremely vary in size from 1 cm to fully involving the maternal surface. Frank hematoma is soft, red and can be easily detached from placental maternal surface leaving behind a crateriform depression.

Older hematoma appears brown, hard and firmly adherent to the placenta. ,compressing the overlying placenta which is often infarcted. For differentiation purpose, a simple adherent blood clot can be easily stripped from the maternal surface and never indents the placental substance.

Microscopy :

Early stages	:	RPH c/o solely RBCs and few strands of fibrin.
As lesion ages	:	RBCs degenerate
		Amount of fibrin increases
		Leucocyte and macrophage infiltration.

Later Stages : hemoriderin laiden macrophages in basal plate.

In all, overlying basal plate may be normal or necrotic or may contain a heavy infiltration of polymorphonuclear leucocytes.

C) *Marginal hematoma*

This is formed at the lateral margin of the placenta. This is referred as subchorionic hemorrhage by USG.

Incidence :

Wilkin (1965) found marginal hematoma in 0.74% of placentas.

There seems to be no association with maternal preeclampsia.

D) *Intervillous thrombi*:

These are villous free, nodular foci of coagulated blood in IVS. They however don't fulfill the criteria for thrombus in that they lack platelets. Villi are absent from this thrombus.

Incidence varies from 3 - 50% in full term, uncomplicated pregnancies. It is increased in materno-fetal rhesus compatibility[120-122]

E) *Kline's hemorrhage*:

There are vague hemorrhagic areas in placental substance. Fox refers to this as a very fresh intervillous thrombus.

F) *Subamniotic hematoma*:

This refers to the accumulation of blood between the amnion & chorion on fetal surface. This is known to arise due to trauma to the venous tributaries of umbilical vein at the time of excessive traction.

IV. Non Vascular lesion:

Calcification:

The incidence of gross calcification in the placenta varies in various studies, from 14-37%[123-127]. Schonig has conceded that two forms of calcification exist.[128]

a) Physiologic – First 6 months - not visible to naked eye.
b) Dystrophic – Later pregnancy period – Grossly valuable.

Pathologist can identify only the second type of calcification.

Calcification is less common in placenta with less than 36 weeks gestational age and it increases as the term approaches.

Various studies have proved that gross placental calcification is of no pathological or clinical significance[125,127,129]. There is no significant increase in calcification of placentas from prolonged pregnancies[125,130,131], Maternal pre eclampsia ,essential hypertension or diabetes mellitus [100,127].

Various studies have proposed that serum calcium level in the mother is a factor in the pathogenesis[133,134]. But Tindall & Scott have indicated that further mechanism apart from maternal serum calcium level are involved. The occurrence of placental calcification has been associated with primigravidity[124,129] and also with high socio-economic status in community[131].

Gross

Seen as small, hard, scattered flicks on the maternal surface, mainly seen in the basal plate and septa. It is unusual to see it in the chorionic plate. There can be calcium deposition in old infarcts and perivillous or subchorionic fibrin.

Microscopy :

Seen as structureless, basophilic material deposited either as plaques or coarse granules. Calcification of villi may be seen at times.

DEFINITION AND CLASSIFICATION OF HYPERTENSIVE DISORDERS OF PREGNANCY[134,135]

Pre-eclampsia is a pregnancy specific syndrome characterized by elevation of blood pressure of more than 140mm of Hg systolic or more than 90mm of Hg diastolic with proteinuria after 20 weeks of gestation.

Eclampsia is defined as the occurrence of seizures in a women with preeclampsia, that cannot be attributed to other causes.

Multiple classifications have been proposed to classify the hypertensive disorders of pregnancy. The working group of National High Blood Pressure Education Programme (2000) recommended the following classification.

GESTATIONAL HYPERTENSION:

- BP $\geq$ 140/90 mm of Hg for first time during pregnancy no proteinuria.
- BP returns to normal <12 weeks post partum.
- Final diagnosis made only post partum.
- May have other signs of pre-eclampsia, for example, epigastric discomfort or thrombocytopenia.

PRE-ECLAMPSIA:

Minimum criteria:

- BP $\geq$ 140/90 mm Hg after 20 weeks for gestation.
- Proteinuria $\geq$ 300mg/24 hours or $\geq$ 1+dipstick

Increased certinity of preeclampsia

- BP $\geq$ 160/110 mm of Hg.
- Proteinuria 2.0g/24 hours or $\geq$ 2 + dipstick
- S.creatinine> 1.2 mg/dl unless known to be previously elevated
- Platelet < 1,00,000/mm^3
- Microangiopathic hemolysis (increased LDH)
- Elevated ALT or AST
- Persistent headache or other cerebral or visual disturbance
- Persistent epigastric pain.

ECLAMPSIA:

Seizures that cannot be attributed to other causes in a woman with pre-eclampsia.

Super imposed pre-eclampsia (on chronic hypertension)

New onset proteinuria $\geq$300mg/24 hours in hypertensive women but no proteinuria before 20 weeks gestation.

A sudden increase in proteinuria or blood pressure or platelet count <1,00,000/mm^3 in women with hypertension and proteinuria before 20 weeks gestation.

CHRONIC HYPERTENSION:

- BP ≥ 140/90 mm of Hg before pregnancy or diagnosed before 20 weeks of gestation.
- Hypertension first diagnosed after 20 weeks of gestation and persistent after 12 weeks post partum.

Hypertensive disorders during pregnancy : Indicators of severity

Abnormality	Mild	Severe
Diastolic blood pressure	<100 mmHg	110mm Hg or higher
Proteinuria	Trace to 1+	Persistent 2+ or more
Headache	Absent	Present
Visual disturbance	Absent	Present
Upper abdominal pain	Absent	Present
Oliguria	Absent	Present
Convulsion	Absent	Present
Serum Creatinine	Normal	Eclampsia elevated
Thrombocytopenia	Absent	Present
Liver enzyme elevation	Minimal	Marked
Fetal growth restriction	Absent	Obvious
Pulmonary oedema	Absent	Present

WHO Classification[136]:

Uses the limit of 90 mmHg diastolic blood pressure, but specifies that woman should be normotensive before 20th week of pregnancy.

In a previously hypertensive woman, pre-eclampsia is diagnosed if there is an increment of 15mm of Hgt in diastolic pressure and/or development of proteinuria.

A diastolic pressure of 90mmHg, but measured twice at least 4 hours apart, diminishing the influence of "white coat hypertension".

A diastolic pressure of 110mmHg is sufficient for the diagnosis if measured only once.

RISK FACTORS FOR PRE-ECLAMPSIA[137,138]

Pre-conceptional and/or chronic risk factors:

Partner related risk factors

- Nulliparity / primipaternity / teenage pregnancy
- Limited sperm exposure, donor insemination oocyte donation
- Partner who fathered a pre-eclampsia pregnancy in another woman.

Non partner related risk factors

- History of previous pre eclampsia
- Age, interval between pregnancies
- Family history

Presence of specific underlying disorders

- Chronic hypertension and renal disease, obesity, insulin resistance, low birth weight gestational diabetes, type I diabetes mellitus.
- Activated protein C resistance, protein S deficiency.
- Antiphospholipid antibodies.
- Hyper homocysteinemia
- Sickle cell disease, sickle cell trait

ETIOLOGY AND PATHOPHYSIOLOGY OF PRE-ECLAMPSIA[135,139-148]

The cause of pre-eclampsia is not known. Many consider the placenta the pathogenic focus for all manifestations of pre-eclampsia because delivery is the only definitive cure for this disease.

The four main etiological factors believed be involved in development of pre eclampsia are;

1) PLACENTAL ISCHAEMIA HYPOTHESIS:

Reduced placental perfusion plays a major role in pregnancies complicated by pre-eclampsia.

In normal pregnancy due to the trophoblastic invasion, the diameter of the spiral arteries proximal to the trumpet shape outlet increases 4-6

fold, relative to that of non pregnant women. The endothelium is replaced by trophoblast and the internal elastic lamina is replaced by trophoblast and an amorphous matrix that predominantly consists of fibrin deposits. These vascular changes extends from the intervillous space upto the inner third of the myometrium. By contrast these changes develop defectively in pre-eclamptic women and are also limited to the decidual portion of the spiral arteries, the myometrial segment maintaining the smooth muscle layer.

The consequence of this abnormal invasion of the spiral arteries is the deficient uteroplacental circulation already at the end of first trimester.

The placental under perfusion results in the release of various toxins into the circulation, such as oxygen free radicals and lipid peroxides, causing oxidative stress or impaired antioxidant defenses, activation of leucocytes, and release of cytokines. The result is widespread endothelial dysfunction and cellular activation.

2) OXIDATIVE STRESS THEORY:

Activated / injured endothelial cells, release procoagulants, vasoconstrictors, and mitogens that promote platelet agglutination and activate coagulation cascade.

Role of oxidative stress:

Oxidative process has been proposed to play an important role in the etiology of uteroplacental vascular endothelial damage in hypertensive disorders of pregnancy. Oxidative processes such as lipid peroxidation, the conversion of unsaturated fatty acids by free radicals to lipid peroxides, occur normally at low levels in all cells and tissues. Control of the potentially self perpetuating lipid peroxidation chain is regulated through anti-oxidant systems such as vitamin E and selenium. An imbalance between oxidative and antioxidative system leads to a steady state with high levels of free reactive oxygen species and lipid peroxides; this imbalance is termed oxidative stress. It causes disruptive membrane damage in endothelium.

Markers of oxidative stress such as glutathion peroxidase and malondialdehyde are increased. Additional evidence is given by the elevated levels of cytokines such as TNF-alpha and intcrleukines. These cytokines are strong initiators of oxidative processes.

3) IMMUNE MALADAPTATION HYPOTHESIS:

- Pre-eclampsia may result from an abnormal maternal immune response to paternally derived antigens on the trophoblast.

- It is postulated that activated immune cells from decidua release mediators like plasma elastase, toxic proteases and cytokine like TNF-alpha, IL-1, IL-6 which cause endothelial damage.
- Elastase - destroys the integrity of endothelium.

TNF-alpha, **IL-1** :

Increased generation of thrombin, platelet activating factor, endothelial cell permeability, increased expression of ICAM-**1,**VCAM-**1**(which mediate adherence of inflammatory cells and activate endothelial cells).

IL-6 :

Increases vascular permeability, stimulate platelet derived growth factor synthesis, impairment of PGI2 synthesis.

Lipid peroxides formed as a result of increased oxidative stress inhibit PGI2 synthesis, favours production of platelet derived thromboxane A2 (TXA2), alters the capillary permeability to proteins and triggers thrombosis formation.

This leads to generalized vasospasm, oedema, and proteinuria and thrombus formation.

4) PREECLAMPSIA AS A GENETIC DISEASE :

Genetic predisposition could be involved in

a) Any aspect of pre-eclampsia etiology :

Immune maladaptation/ placental ischaemia/ oxidative stress.

b) Genes involved in blood pressure regulation/ placentation / vascular injury / remodeling etc.

eg: Ag-1 gene (angiotensiongen gene)

E-Nosgene (endothelial nitric oxide synthetase gene)

ET-1 gene (endothelin - 1 gene)

- HLA's are involved in immune tolerance and thus deviation from normal expression plays a role in immune maladaptation.

PATHOLOGY OF PLACENTA IN PRE-ECLAMPSIA

Placenta from preeclamptic women tend, on average to be smaller than those from uncomplicated pregnancies. But, the decrease is only slight and a proportion of such placentae are unusually large.

The various morphometric parameters like weight, volume, surface area have been shown in a number of studies to be significantly lower in hypertensive pregnancies than normal term pregnancies.

As far as macroscopic features are concerned, there is no significant increase in the incidence of extrachorial placentation or of abnormal cord insertion in preeclamptic placentae.

The only two gross lesions that are significant in preeclamptic placentae are;

- Infarction
- Retroplacental hematomas

Infarction:

The incidence of placental infarction ranges from about 33% in cases of mild preeclampsia to approximately 60% in patients with severe form of the disease. [149]

Extensive infarction (involving more than 10% of parenchyma) is found in about 30% of placentae from cases of severe preeclampsia, but not a feature of the milder forms of this disease[149].

Infarction is the dramatic and easily recognized visible sign of maternal uteroplacental vascular unsufficiency. Infarcts are more significant when they are central and greater than 3 cm in greatest dimensions. Infarction is associated with significant perinatal mortality and morbidity, including IUD , fetal hypoxia and neonatal mortality and morbidity.

Thus, extensive infarction occurs only against a background of markedly abnormal maternal vasculature and a restricted maternal blood flow to the placenta and it is these factors rather than the loss of villi due to infarction which are the real cause of the fetal complications. The true significance of extensive placental infarction is therefore that it is the visibile hallmark of a severely compromised circulation to the placenta.

Retroplacental hematoma (RPH)

Retro placental hematomas are found unduly frequently in preeclamptic placenta occurring in about 12-15% of all cases.

There is a majority of opinion saying, this hemorrhage is a result of rupture of a maternal decidual arteriole, which is believed to be a catastrophe occurring in the vessel wall that has been weakened due to changes in preeclampsia.[150-156]

Initially abruption was considered specific and integral part of preeclamptic process[157,158]. In support of this, in various reviews on abruption, there was a high percentage of patients affected by preeclampsia[159-162]. However in some reviews on abruption, the percentage of preclamptic patients has been on a lower level[163,164].

Williams et al (1991b) in his study[165], concluded that though there was a high risk of placental abruption with essential hypertension, this was certainly not the case with preeclampsia. This fell in accordance with the study of Abdella et al (1934) who found that the incidence of abruption in patients with preeclampsia was 2.5% , while in those with essential hypertension was 10% .And the highest incidence was in women with eclampsia, ie.23.6%[166].

So, it would be fair to say that the pregnancy of RPH is increased in preeclamptic placentae.

Large lesions where in 40% or more of villous population is acutely deprived of blood supply are associated with high incidence of fetal hypoxia, death.

Subamniotic hematoma, marginal hematoma, massive sub chorial thrombosis intervillous thrombosis are of not much clinical significance.

Placental calcification, often regarded as evidence of either placental senescence or degeneration and of no pathological or clinical significance and not associated with any fetal complication.

Histological findings :

As per fox, villi of most preclamptic placentas have normal maturity for that gestational period. However in a few cases, there is notable delay in villous maturation and it was found that this was by large restricted to severely preeclamptic pregnancies with resultant severe growth retarded fetus[167,168]. Still on the contrary some preeclamptic placenta showed evidence of accelerated villous maturation as per Fox.

The most characteristic and striking features of villi in pre-eclampsia are

- Undue number as well as prominence of villous CT cells.
- Irregular thickening of trophoblastic basement membrane and this can best be appreciated when stained with PAS.
- The intensity of these changes correlate with duration and severity of maternal preeclampsia.
- Occasional villi with a thickened TBM are found in about 1/3rd fetal placenta.

A striking increase in the proportion of villi with unduly thick TBM is common feature in preeclamptic placenta. Fetuses whose placenta contain a marked excess of villi with abnormally thick TBM have a much higher incidence of clinical hypoxia than do those in which the changes are absent. However, various studies say that the high

incidence of fetal hypoxia found in association with this abnormally is due, not to basement membrane changes, but to the ischemia which is responsible both for the histologic changes and fetal complications.

The vascularisation of the villi is often normal but a significant percentage of placental villi are hypovascular. They contain relatively inconspicuous, non-dilated, small vessels. This particular change correlates with the level of obliterative endarteritis of fetal stem arteries[169,170], which is found in around one third of preeclamptic placentae.

These hypovascular villi which are inadequately perfused from fetal side show.

- Abundant syncytial knotting
- Lack VSM
- Increased amount of stromal collagen.

The hypoxic placenta in preeclampsia is composed of numerous branched, short and fist like appearance of terminal villi. This greatly enhances the degree of syncytial knotting (flat sections), that a net like appearance may be discovered in the two dimensional picture.

Villous edema

It has been widely appreciated that villous edema may also be found in placenta from women with preeclampsia.

The cause of villous edema is unknown, it has been attributed to functional insufficiency of fetal circulation, increased size of the edematous villi may decrease the capacity of IVS and thus limit the maternal flow through the placenta.

Fibrinoid degeneration of villi :

The first stage in the evolution of this lesion in the appearance of a small nodule of homogenous, acidophulic, PAS positive material at one point in the villious trophoblast. This nodule progressively enlarges as fresh fibrinoid material is laid down on its deep aspect so as to form a mass which gradually bulges into and compresses the villous stroma, this process continuing until the whole villous is converted into a fibrinoid nodule.

The incidence of villous fibrinoid necrosis is found to be moderately increased in preeclamptic placentas.

The lesion has been attributed to an immunological reaction within villous tissue and to amyloid deposition as an ageing change.

The pathologist noting an excess of villi showing fibrinoid necrosis in a placenta is therefore not, at the moment in a position to arrive at any valid conclusion from this finding, though the possibility that it represents an immune attack on trophoblastic tissue cannot be totally discarded and should be borne in mind.

PATHOGENESIS OF MORPHOLOGIC CHANGES

As agreed by most of them, all of the changes in preclamptic placentae except VFN are a consequence of abnormal maternal uteroplacental vasculaure . This fact of reduced blood flow has been well established over many years[171-174] .

This has also been confirmed with Doppler studies[175-180]. It is a well known fact that this uteroplacental insufficiency is a result of incomplete trophoblastic invasion of placental bed spiral arteries and thus the spiral arteries are inadequately converted to uteroplacental vessels.

The increase in incidence of placental infarction in preeclampsia is attributed to atherosis in spiral arteries.

Cytotrophoblastic hyperplasia is a specific response and TBM thickening a non specific response to placental ischemia. Thus these are direct effects of reduced maternal blood flow.

The excess of syncytial knots and villous stromal fibrosis are a result of reduced villous perfusion due to obliterative endarteritis of fetal stem vessels, which is a hallmark for prolonged vasoconstriction of these stem vessels. This leads to rise in placental vascular resistance[181]. All this represents the fetal hemodynamic response to uteroplacental ischemia[182-189]. This reduction in placental fetal perfusion is in fact a compensatory mechanism by which there is preferential diversion of blood to the vital cerebral and cardiac circulation of fetus.

Itskovitz et al considered that the villous tissue can enhance oxygen extraction in the face of decreased blood flow and can withstand a reduction of 50% blood flow without having any adverse effect on fetal oxygenation[190].

FETUS IN PRE ECLAMPSIA

Fetal growth restriction (FGR) is the end point of a number of pregnancy associated conditions and pre-eclampsia(PE) is one of them. PE is regarded as a syndrome of heterogeneous origin and fetal growth is very often restricted in it. Preeclampsia with shallow trophoblastic invasion of decidual arteries, reduce placental perfusion and cause insufficient transport of nutrients to fetus. Placental morphologic changes vary substantially in PE and it has been hypothesized that FGR depends on abnormal placental development. Pathophysiological process of FGR

and the responses of fetus to the restricted nutrition and oxygen supply are very complex and far from fully understood..

Odegard et al in 2000 made a study and reported the following observations that PE was associated with a 5% reduction in birth weight. In severe PE, the reduction was 12% and in early onset disease, birth weight was 23% lower than expected. The risk of SGA was four times higher in infants bom to women with PE among nullipara, PE associated with threefold higher risk of SGA and among parous, the risk of SGA was particularly high after recurrent PE. They concluded that factors like multiparity, severity of disease (mild, moderate and severe) and late versus early onset disease play a synergistic role in FGR in PE. Though the possibility that it represents an immune attack on trophoblastic tissue cannot be totally discarded and should be borne in mind[191] .

Materials and Methods

MATERIALS AND METHODS

Study Design : Prospective Study.

Study period : June 2014 to December 2014

Study Place : Institute of Obstetrics and Gynaecology, Madras Medical College, Chennai-3

Sample size :

Study group : 100 cases

Control group : 100cases

Inclusion criteria

Study Group :

1. Singleton pregnancy
2. Pre-eclampsia BP>140/90 ; Urine albumin +
3. Eclampsia

Control Group:

1. Singleton pregnancy
2. Normotensive

Exclusion criteria

1. Women with multiple pregnancy
2. Women with pre existing hypertension
3. Preeclampsia with comorbid conditions

METHODOLOGY

Detailed history of the mother such as name, age, parity, address, occupation, marital history, previous obstetric history, past history of major illness, present medical history and habits were recorded on predesigned proforma with regard to the baby's gestational age. Birth weight and Apgar scores were observed from the record.

All placentas were collected immediately after delivery and washed in tap water which removed the blood collected in membranes and clots.

Grossing procedure

Placenta was examined in fresh state after delivery, handling the specimen with great care avoiding lacerations.

Membranes:

Distance from the placental margin to the nearest point of rupture was measured. Membranes were examined for completeness, insertion, decidual necrosis, edema, extra-amniotic pregnancy, retromembranous hemorrhage, meconium staining, colour and transparency. A long 2-3cm wide section of membranes beginning with the point of rupture and extending to and including a small portion of placental margin were taken and rolled with amniotic surface inward, fixed for 24 hours and 3mm

section was taken from the centre. Trim the remaining membranes from the placental margin

Umbilical cord:

The length of the cord and the shortest distance from the cord insertion to the placental margin were measured. Cord was examined for insertion, number of umbilical vessels, colour, true knots, torsion, stricture, hematoma and thrombosis. Cord was removed from the placenta 3cm proximal to the insertion , 2-4cm segment from its midpoint was taken, fixed for 24hours and 3mm section was taken.

The disc weight should be obtained once the membranes, cord, and extraeneous clot have been removed. A major variable in placental weight is the amount of fetal blood present in the placenta.

Measurements of the generally ovoid disc should be taken along the greatest and shortest diameter. The thickness is best measured after cutting .

With these basic measurements, using standard mathematical formulae, the values for placental surface area and placental volume were derived.

Placental surface area (cm^2) = (π x largest diameter x shortest diameter)/ 4

Placental volume (cm^3) = surface area x thickness at centre

The placenta along with cord and membranes will be coded and preserved in 10% formalin .

Fetal surface:

Examination for colour, opacity, subchorionic fibrin, cysts, amnion nodosum, squamous metaplasia, thrombosis of fetal surface vessels and chorangioma was done.

Maternal surface:

Examination for completeness, normal fissures, laceration, depressed areas, retroplacental hemorrhage was done.

The parenchyma should be sectioned in a "bread –loaf fashion" at approximately 1 to 2 cms interval, cutting with either the fetal or maternal side down. The cut slices should be examined for the presence of focal lesions such as infarcts , thrombi , and , excessive fibrin.

Sections of the villous parenchyma should be taken to include the full thickness of the placenta, extending from the maternal to fetal surface, including both amnion and decidua.

- The placental changes were compared in the two groups.
- Placental changes were correlated with duration and severity of peeclampsia.
- Placental findings were correlated with fetal outcome.

STATISTICAL ANALYSIS :

Comparision of various parameters between the study groups will be analysed by ANOVA and by student's "t" test.

Categorical data will be analysed by Chi-square test.

Observation and Results

OBSERVATIONS AND RESULTS

TABLE 1: DISTRIBUTION OF CASES ACCORDING TO GESTATIONAL AGE

	GROUP	
	CASE	CONTROL
28 - 32	21	11
33 - 36	21	11
37 - 40	58	78
TOTAL	100	100

In the present study , more number of preterm delivered cases belonged to the hypertensive group.

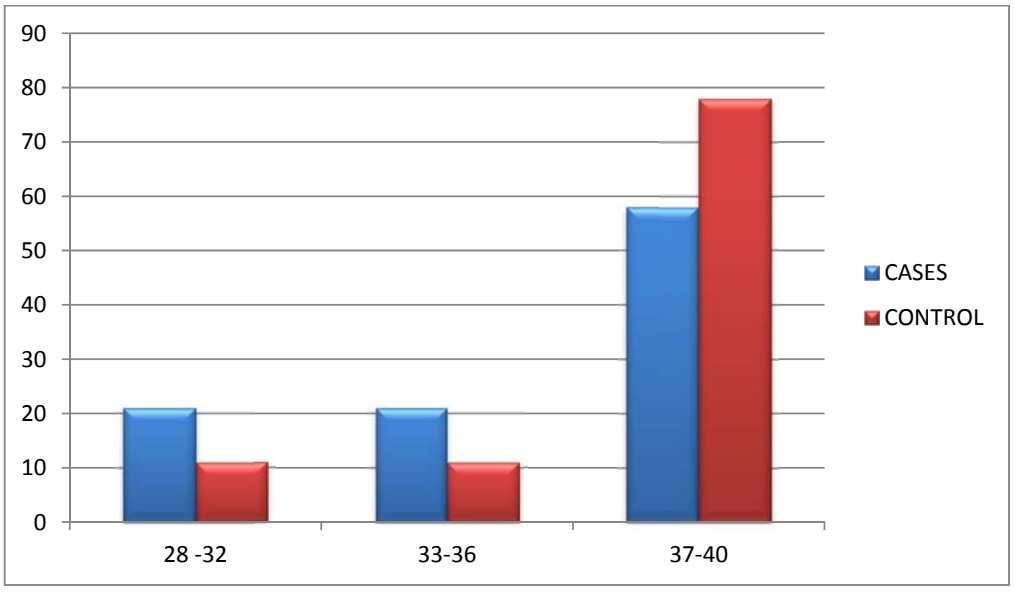


TABLE 2 : COMPARISION OF THE FETAL BIRTH WEIGHT

	CASE (mean ± S.D)	**CONTROLE (mean ± S.D)**	**p -Value**
Fetal Birth Weight [gms]	2271.2±788.04	2584±682.35	0.003

The mean birth weight in preeclamptic group is 2271.2 ± 788.04 gms

The mean birth weight in the control group is 2584 ± 682.35 gms

p – value : 0.003 (statistically significant)

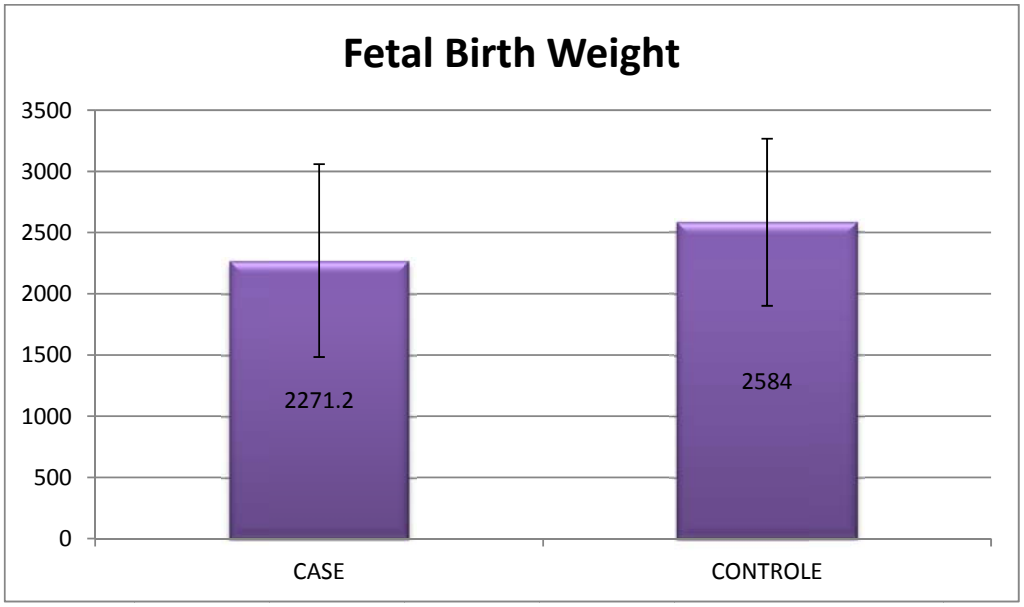


TABLE 3 : COMPARISION OF PLACENTAL MORPHOMETRY

	CASE (mean ± S.D)	CONTROLE (mean ± S.D)	p - Value
Placental Weight (gms)	421.8±120.09	461.75±99.08	0.011
Placental Surface Area (sq.cm)	172.77±60.82	195.25±58.82	0.009
Placental Volume (cu.cm)	270.8±132	385.01±142.66	0.001

The mean placental weight is reduced in preeclampsia. This is statistically significant.

The mean placental surface area is reduced in the preeclamptic group and is statistically significant.

The mean placental volume is again decreased in the preeclamptic group when compared with the control group. This is also statistically very significant.

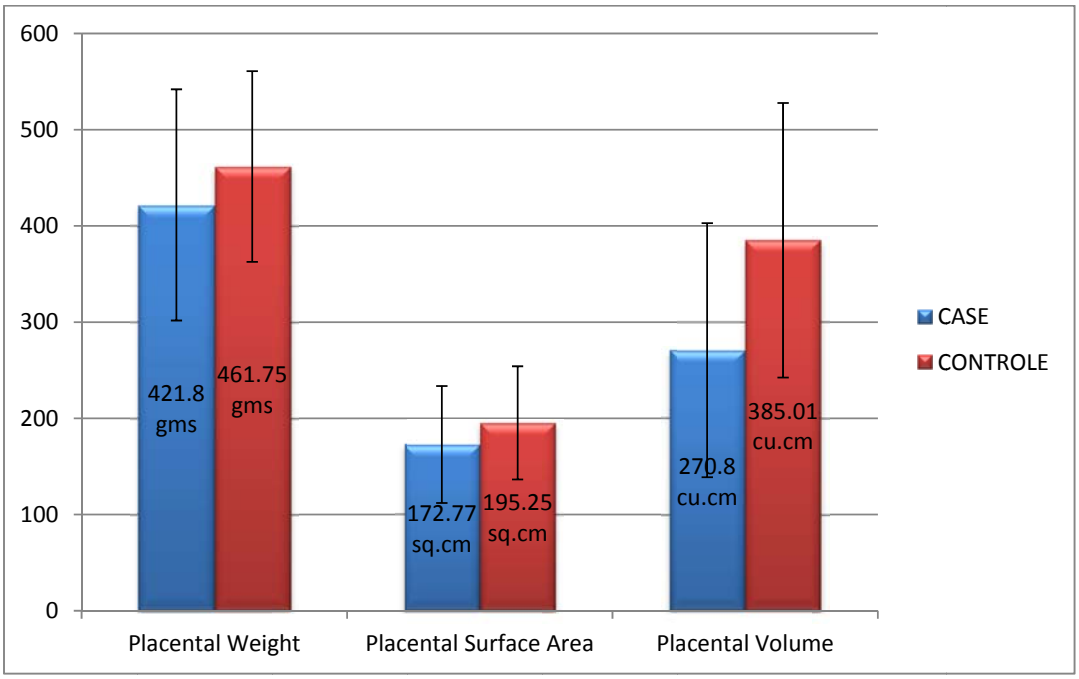


TABLE 4 : COMPARISION OF PLACENTAL GROSS MORPHOLOGY

		CASES	CONTROL	p-value
SUB CHRONIC FIBRIN	Present	3	6	0.306 (NS)
	Absent	97	94	
RPH	Present	26	2	<0.001 (S)
	Absent	74	98	
INFARCTION	Present	44	5	<0.001 (S)
	Absent	56	95	
CALCIFICATION	Present	17	15	0.700 (S)
	Absent	83	85	

The incidence of retroplacental hematoma and infarction is significantly raised in the study group in comparison to control group. But, there is no significant difference in the occurrence of sub chorionic fibrin and calcification between the two groups.

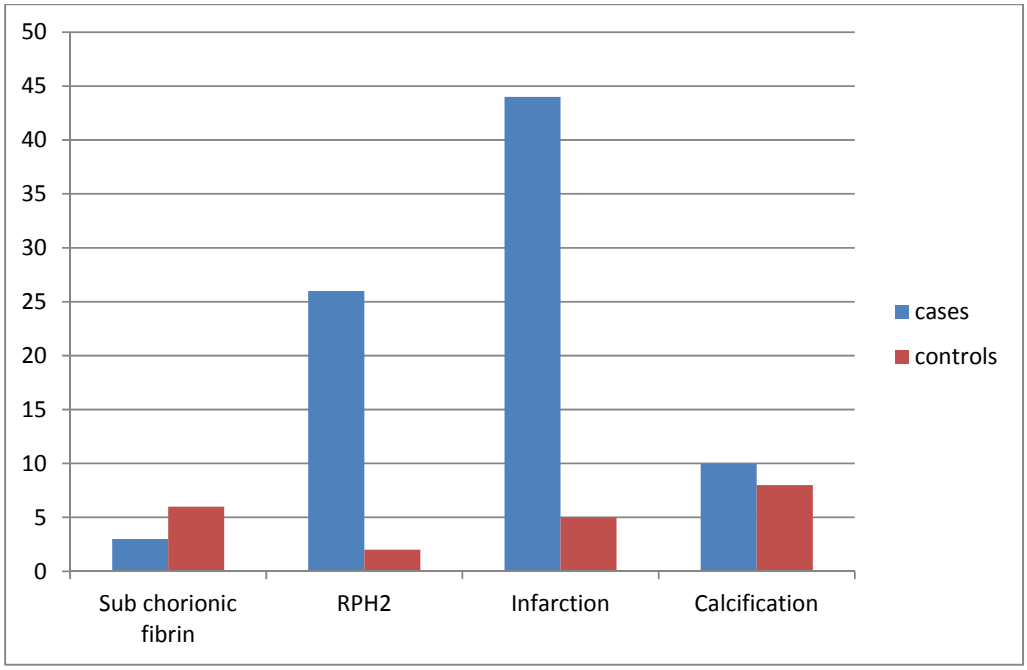
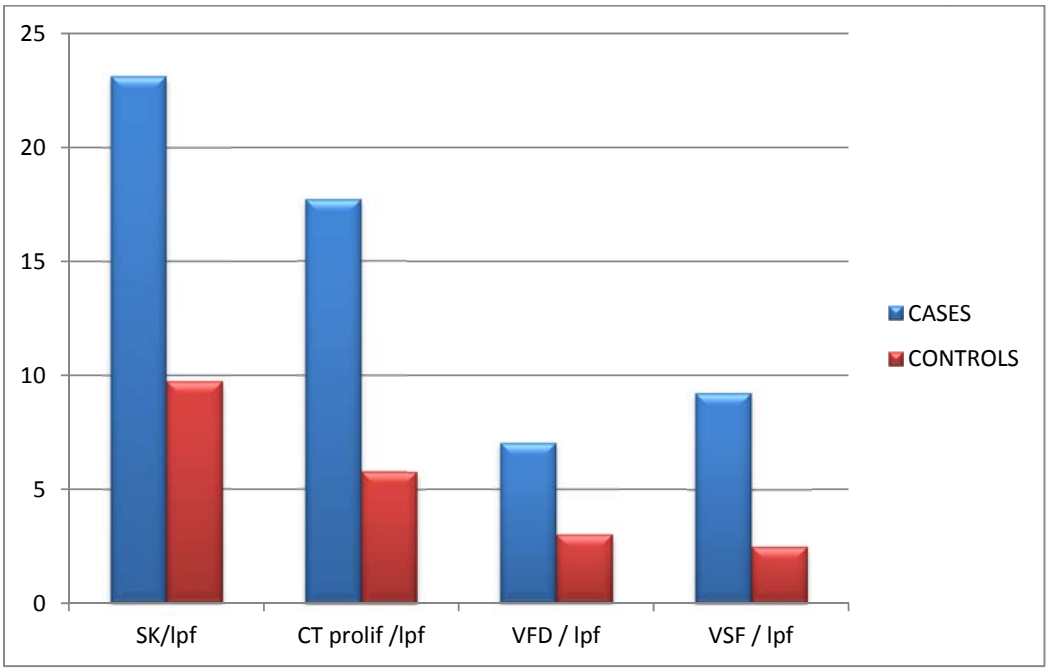


TABLE 5 : COMPARISION OF PLACENTAL HISTOMORPHOLOGY

5 (A)

PLACENTAL HISTOMORPHOLOGY	GROUP		p VALUE
	CASE	CONTROL	
	Mean ±S.D	Mean ± S.D	
Mean no of areas of Syncytial knot formation/ LPF	23.15 ± 4.84	9.75 ± 3.18	< 0.001
Mean no of areas of Cytotrophoblastic cellular proliferation / LPF	17.72 ± 2.63	5.78 ± 1.31	< 0.001
Mean no of areas of villous Fibrinoid degeneration /LPF	7.05 ± 2.87	3.04 ± 1.24	< 0.001
Mean no of areas of villous Stromal fibrosis/ LPF	9.22 ± 2.19	2.47 ± 1.01	< 0.001

In the preeclamptic group, there is an increase in the mean no. of areas / lpf of syncytial knot formation , cytotrophoblastic cellular proliferation , villous fibrinoid degeneration & villous stromal fibrosis. This difference is statistically significant.



5 (B):

TBM THICKENING	CASE	CONTROL	p - Value
< 3%	38.10%	61.90%	< 0.001
> 3%	70.30%	29.70%	

The incidence of irregular thickening of trophoblastic basement membrane is increased in the study group. This is statistically significant.

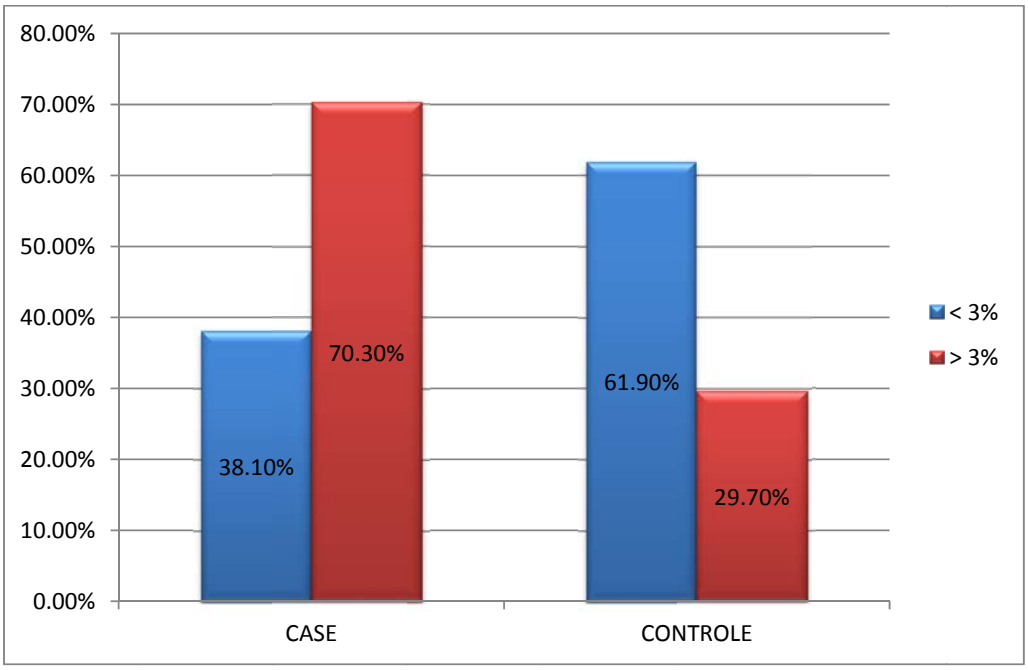


TABLE 6: CORRELATION OF PLACENTAL MORPHOMETRY WITH SEVERITY OF PREECLAMPSIA IN STUDY GROUP

	Placental Weight	Placental Volume	Placental Surface Area
DIASTOLIC BP	-0.197	-0.159	-0.132

In this study , there is a negative correlation between severity of preeclampsia and the placental morphometric features like , placental weight , volume and surface area. (i.e.) With increasing severity of preeclampsia, there is a significant decrease in the placental weight , volume and surface area

TABLE 7: CORRELATION OF PLACENTAL HISTOMORPHOLOGY WITH SEVERITY OF PREECLAMPSIA IN STUDY GROUP

	SK / LPF	**CT prolif / LPF**	**VFD / LPF**	**VSF / LPF**
DIASTOLIC BP	+0.642	+0.471	+0.510	+0.505

In this study, there is a positive correlation between the severity of preeclampsia and histomorphologic features. ie. With an increase in the severity of preeclampsia , there is statistically significant increase in the mean number of areas of syncytial knot formation / lpf , cytotrophoblastic cellular proliferation / lpf , villous fibrinoid degeneration / lpf and villous stromal fibrosis / lpf .

TABLE 8 : CORRELATION OF PLACENTAL MORPHOMETRY WITH HISTOMORPHOLOGY IN THE STUDY GROUP

	SK / LPF	CT prolif / LPF	VFD / LPF	VSF / LPF
Placental Weight	- 0.137	- 0.111	- 0.225	- 0.151
Placental Surface Area	- 0.141	- 0.013	- 0.211	- 0.117
Placental Volume	- 0.215	- 0.082	- 0.331	- 0.157

In this study, there is a negative correlation between placental morphometry and intensity of microscopic changes, ie. With a decrease in the morphometric values , there is an increase in the extent of microscopic changes .

TABLE 9: CORRELATION OF PLACENTAL MORPHOMETRY WITH FETAL OUTCOME

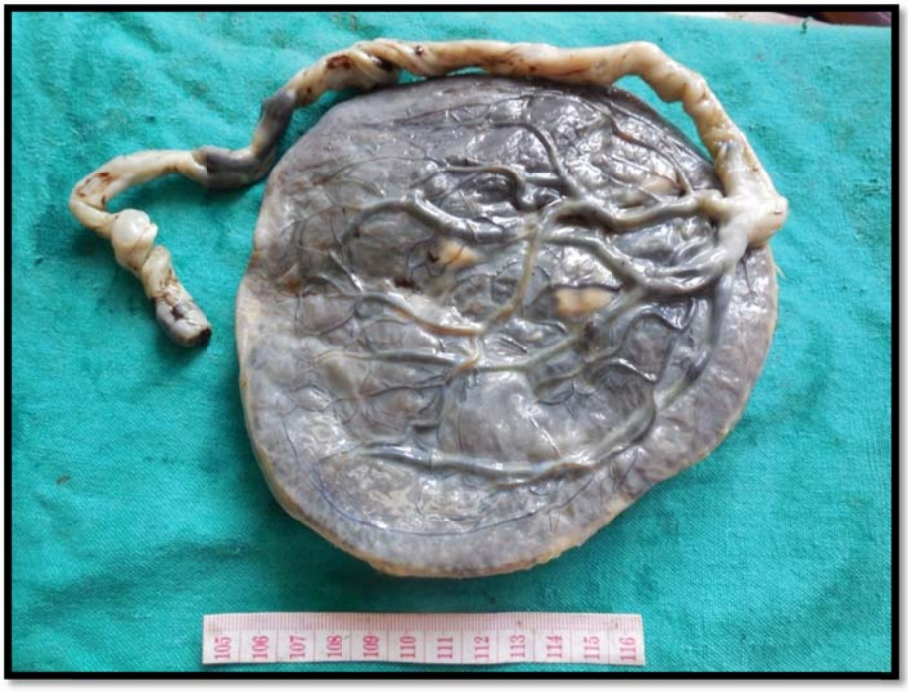
	FETAL BIRTH WEIGHT	APGAR
Placental Weight	+ 0.841	+ 0.668
Placental Surface Area	+ 0.536	+ 0.488
Placental Volume	+ 0.574	+ 0.435

In this study, there is a highly significant positive correlation between placental morphometry and fetal outcome , ie. With a decrease in placental morphometric values , the fetal outcome will be adversely affected.

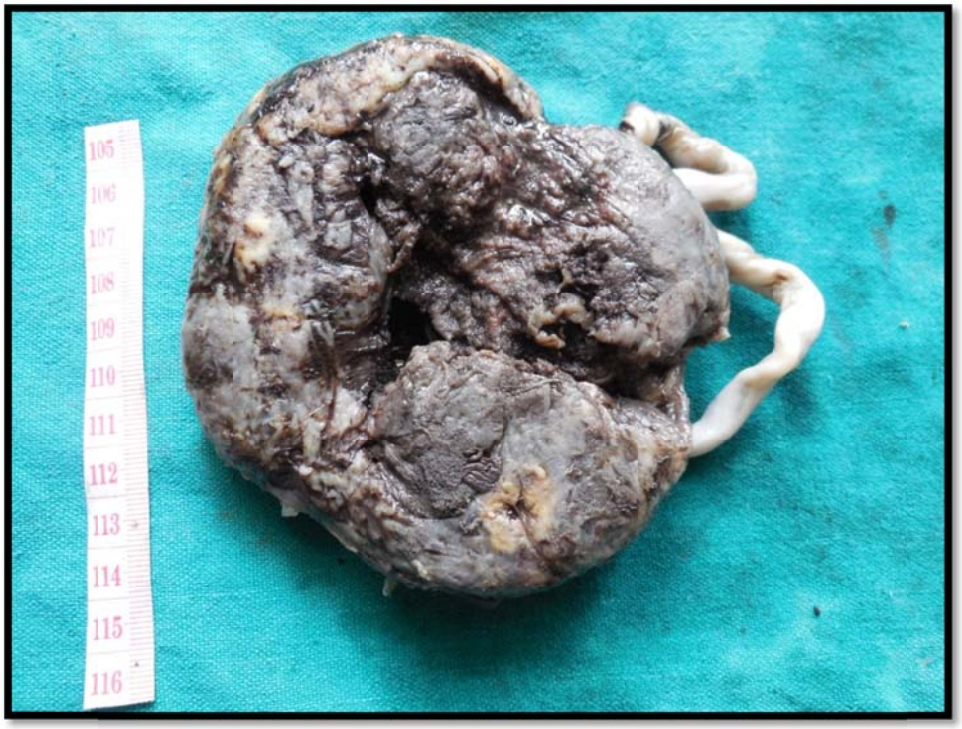
Colour Plates

SMALL PREECLAMPTIC PLACENTA

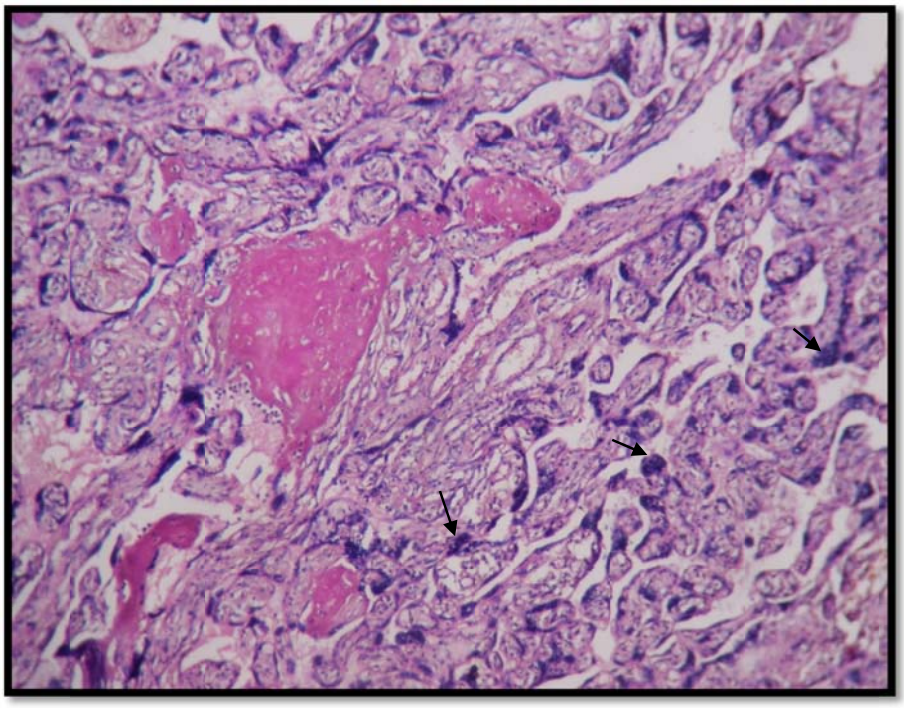
MARGINAL INSERTION



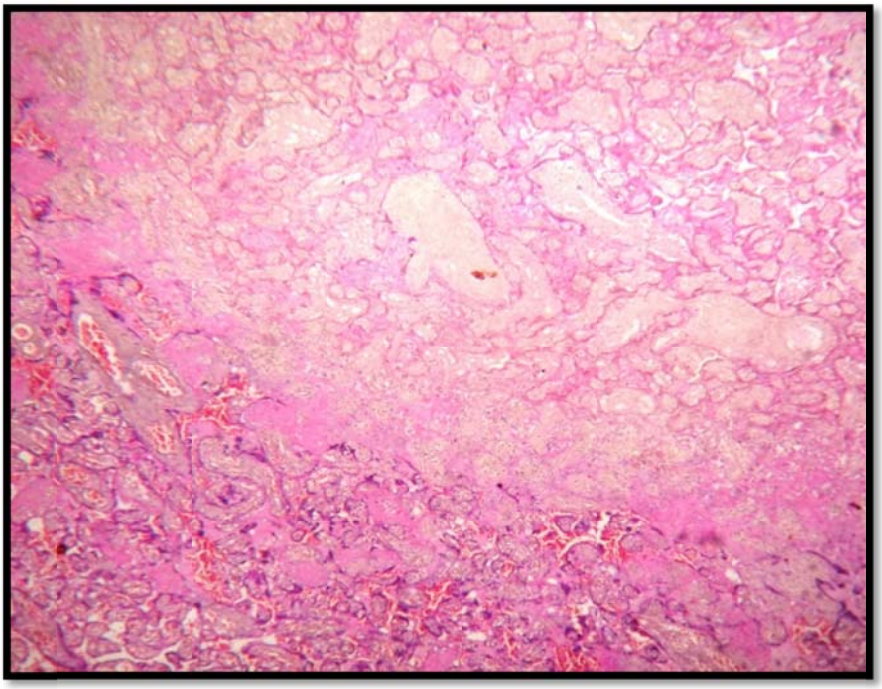
RETROPLACENTAL HEMATOMA



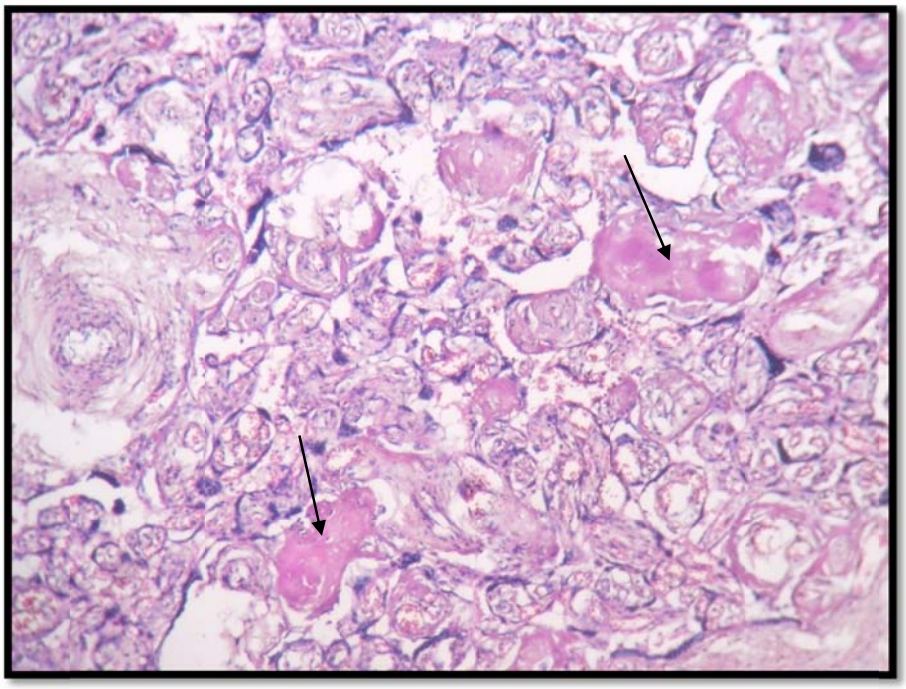
SYNCYTIAL KNOT



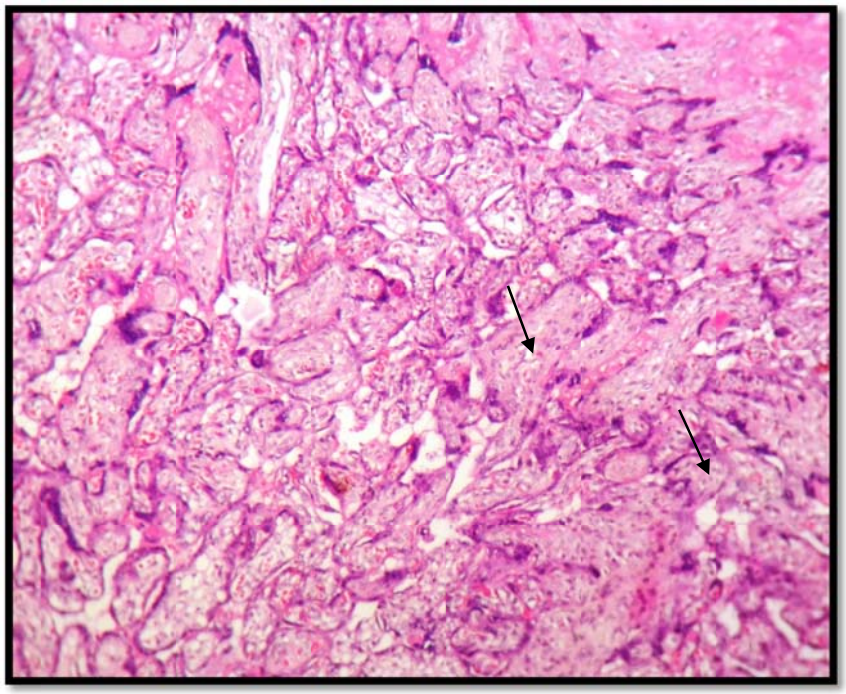
INFARCTION



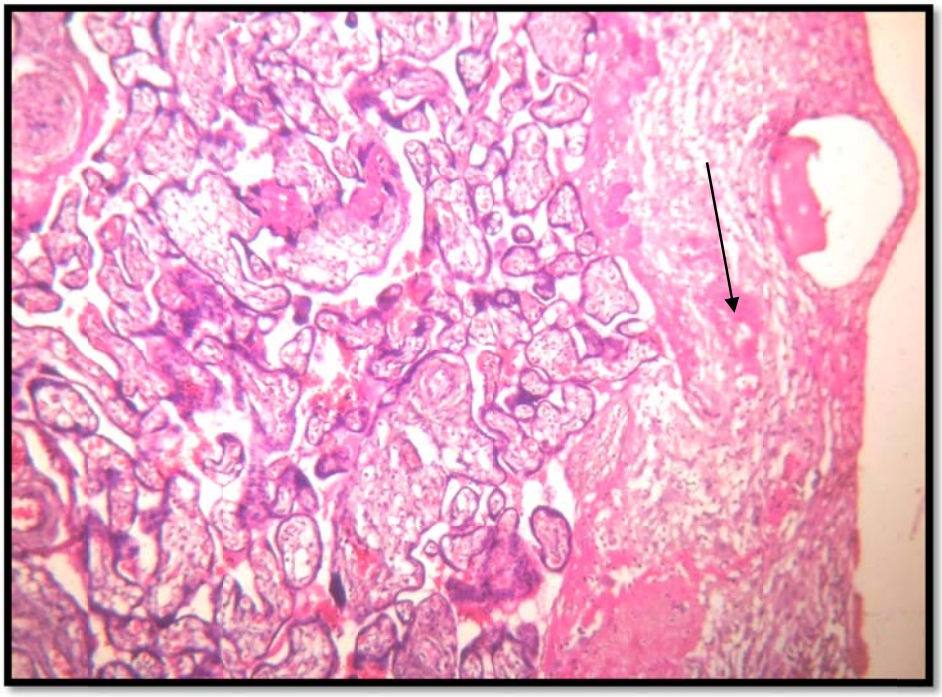
VILLOUS FIBRINOID DEGENERATION



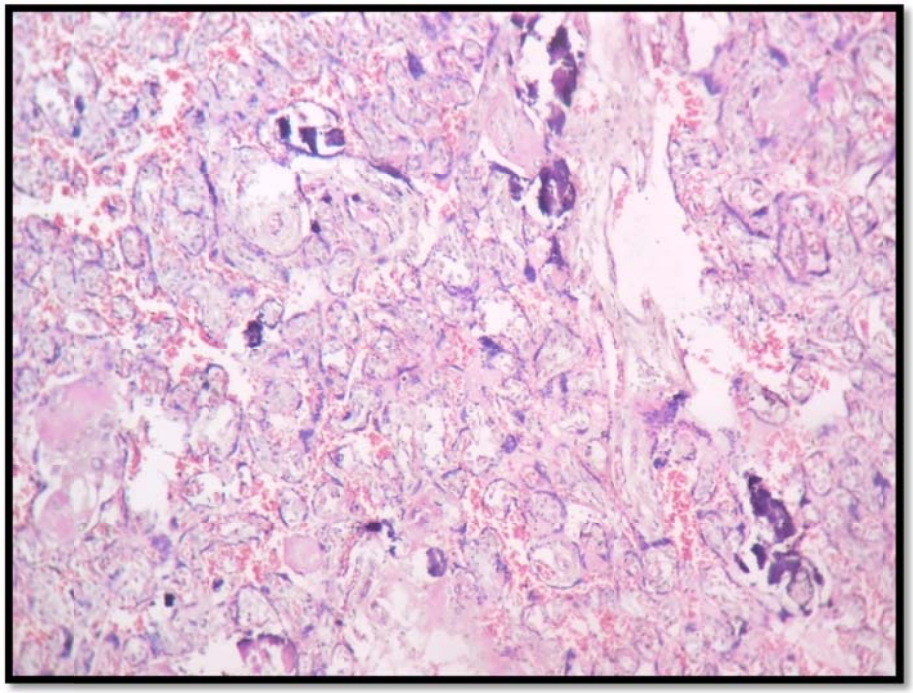
VILLOUS STROMAL FIBROSIS



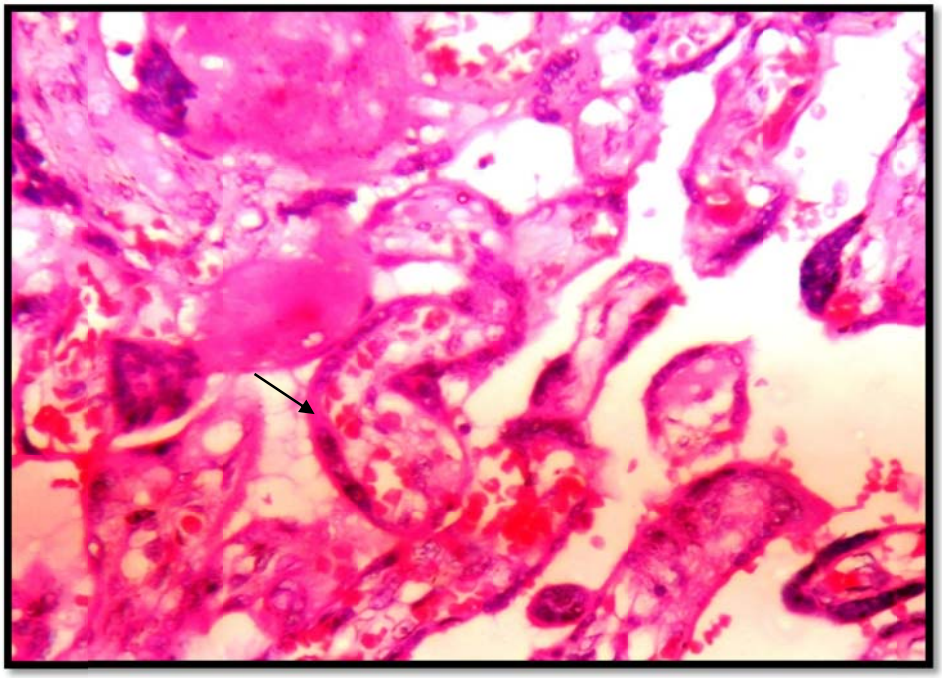
SUB CHORIONIC FIBRIN



CALCIFICATION



TROPHOBLASTIC BASEMENT MEMBRANE THICKENING



Discussion

DISCUSSION

Preeclampsia is one of the leading causes of maternal as well as perinatal mortality and morbidity. The etio-pathogenesis of preeclampsia still remains a subject of controversy. The classical view in this regard focuses on the placenta and uteroplacental circulation.

Pregnancy induced hypertension clinically presents with hypertension, proteinuria and edema. Typically once the uterus is emptied of the fetus & the placenta, the disease process ceases . Infact immediate post partum curettage of the placental bed, brings down the maternal blood pressure at a faster pace than in places where curettage is not done. The fact that PIH occurs even in the absence of the fetus, for eg . in hydatidiform moles , shows clearly that PIH is ultimately dependent on the presence of placental tissue.

Although the study of placenta is retrospective in nature, yet it provides a reflection of hazards, the fetus has been subjected to, during its growth and development.

In the earlier studies of the effect of maternal disease on placenta, gross abnormalities have received undue attention. It is difficult to define the normal placental findings and differentiate it from the abnormal,

because of the structural complexity and rapid evolution of the placenta. Fox (1978) suggested that placental pathology is quantitative rather than qualitative[192]. Bernischke and kaufman (2000) stressed the significance of placental findings only when these had a bearing on the fetal outcome[7].

Fetal outcome :

Fetal and placental growth restriction are frequently encountered manifestations of preeclampsia. The correlation of various placental findings with fetal outcome measured in terms of birth weight and APGAR will be dealt in the following discussion. Apart from growth restriction , there are many sporadic reports of thrombocytopenia and other hematological disorders in babies of preeclamptic mothers[193,194] .

Fetal birth weight :

This study shows fetal weight is significantly reduced in the hypertensive group than in the control group .These findings corroborate with studies of other workers Damania(1989), Fox (1994), Kalousek (1994), Pradeep S Londhe(2011)[195-198] . Rath in 1994 quoted that the intercotyledonous vasculature is altered, ending in low birth weight of infants[199].

As per this study , with increasing severity of preeclampsia , there is corresponding decrease in the fetal birth weight.

PLACENTAL MORPHOMETRY

Placental weight :

Normally, a placenta weighs from 400 to 800 gms . This study observed the reduction of placental weight in the preeclamptic group . Similar findings were reported by Bandana Das et al(1996), Dutta (1989), and Nobi's Das(1991), Pradeep S Londhe(2011)[198,200-202].

The decrease in placental weight has a significant negative correlation with increasing severity of preeclampsia and the extent of morphologic changes. Similar results were obtained by Majumdar et al in his study[203] .

Placental surface area :

The mean placental surface area is significantly decreased in preeclamptic placentae. This is in concordance with the study of Pradeep et al and Majumder et al[198,203]. In a recent study by Rath et al (2000)[199], the mean placental surface area in preeclamptic group was 209.36 cm^2 and that in the control group is 254.63 cm^2 .

This finding also has a significant negative correlation with increasing severity of preeclampsia and a significant positive correlation

with fetal outcome . Similar results were obtained by Majumder et al, Bandana Das and Kaizad et al[200,203,204] .

Feto-placental ratio :

At term , the feto-placental ratio varies between 6:1 and 8:1. The present study noted that there was a reduction in feto-placental weight ratio in the preeclamptic group compared to normotensive group. Similar results were obtained by Bandana Das(1996) and Kher zawar (1981)[200,205]. These findings also corroborate with the findings of Thompson et al, Nummi, and Soma[206-208].

PLACENTAL GROSS MORPHOLOGY:

Sub chorionic fibrin :

Sub chorionic fibrin was not found to be increased in this study. Most of the studies (Fox 1967, Mallik et al 1979) did not record the increased incidence of sub chorionic fibrin in preeclamptic placentae [149,209].However, Bandana Das (1996) noted an increase in the incidence of sub-chorionic fibrin, but still it did not have any effect on the fetal outcome.[200]

Sub chorionic fibrin plaques are not of any clinical significance and does not interfere with fetal growth or development[149]

Retro-placental Hematoma :

This study showed a highly significant increase in the incidence of retro placental hematoma in preeclamptic pregnancies when compared to the control group.

In most reviews, by Fox (1978) and Mohan et al (1989), Daro et al, Bevis, Vermelin & Braye and Hsu et al, they have reported that a high proportion of placentae with retro-placental hematoma belonged to the preeclamptic group[159-162,192,210] .

Whether a RPH has a significant effect on the fetus mainly depends on the size. Small lesions are insignificant . Where as large hematomas, lead to extensive areas of infarction by creating a plane of separation between maternal blood vessels and a proportion of overlying villi. Thus the important and functionally significant lesion is the resultant infarct rather than the hematoma. When such a lesion involves more than 40% of maternal surface , a significant proportion of the villi are deprived of their oxygen supply with an adverse impact on fetal outcome.

Tatum (1953), Dyer & Mc Caughey (1959), Hibbard & Hibbard (1963) emphasized the fact that abruption / RPH is not diagnostic of preeclampsia as was earlier believed[211-213] .

Infarction :

In this study , there was a definite increase in the incidence of infarction in the preeclamptic group and the incidence increases with increasing severity of the disease. Similar findings were observed by Fox (1967 b), Bandana Das et al, Wallenburg (1969), Budliger (1964) [149,200,214,15]. The incidence of infarction in the control group was 5%.

Wentworth (1967), in his study showed that there was a significant increase in incidence of infarcts (67%) in severely toxemic patients , where as mildly toxemic patients had only 11.7% incidence of infarcts[216]. Fox(1967) and Udania et al (2004) had observed a similar raise in the incidence of placental infarction with severity of toxemia.[149,217]

Fox says , extensive infarction , ie. Infarction involving more than 5% of placental tissue occurs in 30% of placentae from severe preeclamptic patients , where as it is present in only 2% of mild preeclamptic placentae[149].

According to the work of Kloosterman & Huidekoper (1952, 1954), Little (1960), and Wigglesworth(1964) there can be no doubt that commonly occurring minor degree of placental infarction (which involves less than 5% of parenchyma) is of no clinical significance. But extensive

placental infarction is associated with a high incidence of fetal hypoxia , IUGR & death[218-221].

Richard Naeye(1977) deduced in his study , that placental infarction caused 2.26/1000 perinatal deaths and that fatal infarcts were strongly associated with diastolic pressures over 90 mmHg in the gravid[222].

Wallenburg (1969) noted a significant correlation of infarction with low APGAR score and low birth weight[214].

Calcification :

The incidence of calcification was 17% in cases and 15% in control groups. This is not statistically significant . Similar findings were given by Fox (1966a) ,Brandt (1973). [100,127]

The view that calcification is a hallmark of placental senescence or degeneration is no longer tenable . various studies have associated calcification with primigravidity[124,125,127,129,223] , young age , higher socio-economic groups[131] and maternal serum calcium levels [132,133].

PLACENTAL HISTOMORPHOLOGY

The histology of placenta from preeclamptic pregnancies shows a significant increase in villous cytotrophoblastic proliferation, villous

syncytial knot formation , irregular thickening of trophoblastic basement membrane, patchy villous fibrinoid degeneration and villous stromal fibrosis, in the study group when compared to the control group.

This is very much in accordance with previous studies conducted by Jones & Fox(1980). Genset (1992) reported that stromal fibrosis and excessive syncytial knot formation are seen in generalized form , occurring due to overall reduction of fetal perfusion of placenta.[224,225]

Teasdale (1980) and Udainia et al (2004) quoted that localized villous fibrinoid degeneration could be the aftermath of hypertension.[217,226]

Tenny & Parker (1940) quoted that the influence of maternal factors is best shown in preeclampsia where the decreased intervillous blood flow finally leads to increased syncytial knotting, so called the Tenny- Parker changes. He emphasized that the increased bridging of placental syncytium producing knots, is very much characteristic of preeclampsia. Syncytial knots are also seen normally in term and preterm placentae but there number is much increased in toxemia.[227]

Mohan Harsh et al (1989) analysed the macroscopic lesions and villous alterations seen in placentae of toxemia of pregnancy and correlated with fetal outcome[210]. It was observed that lighter placentae

were associated with low birth weight new borns. The most striking villous lesions seen in placenta were cytotrophoblastic cellular proliferation , thickening of trophoblastic basement membrane and these lesions were associated with fetal complications like low birth weight, birth asphyxia and still birth. Similar findings were reported by Kher.AV. Zauer(1918) and Kalra VB et al (1985)[205,228]

Summary

SUMMARY

The observations noted in the present study are :

1. More number of preterm delivered cases belonged to preeclamptic group.

2. Fetal birth weight was significantly reduced in preeclamptic group.

3. The placental morphometry , ie. Placental weight , surface area and volume was significantly decreased in preeclamptic group.

4. There was a net reduction in feto-placental ratio in preeclamptic group .

5. Incidence of sub chorionic fibrin was not increased in preeclamptic group

6. Significant increase in the incidence of retro placental hematoma was noted in the preeclamptic group.

7. Incidence of still birth was increased in the presence of retro-placental hematoma.

8. Significant increase in the incidence of infarction was noted in the preeclamptic group.

9. Presence of infarction was associated with poor fetal outcome.

10. There was no significant increase in the incidence of calcification in the preeclamptic group.

11. There was a significant increase in the mean number of areas /lpf of the following findings in the preeclamptic group . And these also showed an increase in the intensity with increasing severity of preeclampsia.

- Villous syncytial knotting / lpf
- Villous cytotrophoblastic cellular proliferation/ lpf
- Irregular thickening of trophoblastic basement membrane (>3%)
- Villous fibrinoid degeneration / lpf
- Villous stromal fibrosis / lpf

12. There was a significant negative correlation between severity of preeclampsia and placental morphometry, ie. With increasing severity, there was a decrease in the values of placental weight , volume and surface area.

13. This study showed a significant positive correlation between the severity of preeclampsia and the gross findings of RPH &

infarction, ie. With increasing severity of preeclampsia, there is an increase in the incidence of these values .

14. This study showed a significant negative correlation between placental morphometry and placental histomorphology in the preeclamptic group, ie. With decrease in morphometric values , there was an increase in the intensity of microscopic features .

15. Ultimately , this study revealed a significant positive correlation between placental morphometry and fetal outcome in the preeclamptic group, ie. The placentae with decreased morphometric values produced fetuses with low birth weight and a considerable decrease in the APGAR score.

Conclusion

CONCLUSION

From the present study , it can be concluded that although placenta readily adapts to hypoxia due to uteroplacental insufficiency , the compensatory changes are insufficient and result in a primary failure to develop and form an adequate placental mass, thereby adversely influencing the placental morphometry , gross and histomorphology.

The pathologic changes, including the placental morphometry and in particular, retroplacental hematoma and infarction adversely influence the perinatal outcome.

Although there are various combinations of histologic and gross changes which are characteristic of placenta in preeclampsia , there is no single lesion which is invariably found in such placenta and none of the abnormalities are specific to preeclamptic placentae.

There are numerous cases where the preeclamptic placenta is virtually normal, mainly if the disease was mild and of a shorter duration. In severe preeclampsia, the lesions are however more prominent and accentuated and at the same time the duration of the disease is of importance.

This study greatly emphasizes the importance of placental morphometry and its correlation with fetal outcome. Currently , with the help of three dimensional ultrasonography and Virtual Organ Computer – Aided Analysis (VOCAL), the placental volume can be ascertained in utero and a correlation with the fetal growth can be obtained.

Thus , based on this study, a suggestion can be made that in-utero measurement of placental volume be included in the routine monitoring of fetal well being in preeclamptic pregnancies, thereby paving way for better management of at risk fetus.

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Annexures

ANNEXURE I

DISSERTATION PROFORMA

I) CLINICAL HISTORY

Name :

Age : IP No :

Maternal gravidity/ parity /live /abortions :

Gestational age :

Blood pressure :

H/O previous child birth :

Any other relevant information :

II) INVESTIGATIONS :

Blood sugar :

Blood urea / serum creatinine :

Hemoglobin :

Urine for albumin & pus cells :

MODE OF DELIVERY :

III) NEWBORN DETAILS :

Birth weight of baby :

APGAR score :

Any congenital anomalies :

IV) PLACENTAL WORKSHEET :

A) MORPHOMETRY :

1. Umbilical cord :
    - Cord insertion from margin (cm)
    - Cord length (cm)
    - No. of cord twists in 5cm
2. Placenta :
    - Trimmed placental weight (gm)
    - Placental diameter (greatest / smallest)
    - Placental central thickness
    - Placental volume (cc)
    - Placental surface area
    - Feto-placental ratio

B) GROSS EXAMINATION :

1.Umbilical cord :

- Cord colour
- No. of vessels
- Other cord findings

2.Membranes :

- Membrane colour
- Other findings

3.Placenta :

- Marginal vein for any thrombus
- Fetal surface findings
- Maternal surface findings
- Parenchyma
- Presence of infarction
- Presence of calcification

C) MICROSCOPIC EXAMINATION :

- Villous cytotrophoblastic proliferation
- Thickening of trophoblastic basement membrane
- Syncytial knotting
- Villous edema
- Villous fibrinoid necrosis
- Villous stromal fibrosis

ANNEXURE II

INDICATIONS FOR PLACENTAL EXAMINATION

Pediatric

- Prematurity/postdates
- Growth indices: intrauterine growth restriction/macrosomia
- Unexpected adverse outcome
- Congenital anomalies
- Suspicion of fetal infection
- Fetal hydrops
- Fetal hematologic abnormalities

Obstetric

- Stillbirth (important site to obtain tissue for culture for karyotype)
- Poor obstetric history
- Maternal disease/death
- Hypertension
- Maternal infection
- Oligo/polyhydramnios
- Excessive bleeding per vagina
- Abnormal fetal monitoring
- In utero therapy
- Maternal toxin exposure
- Abnormal placenta noted at delivery

ANNEXURE III

I. HAEMATOXYLIN AND EOSIN STAINING

Fixation – 10% Formalin

Technic – Paraffin section cut at 4 microns

SOLUTION PREPARATION

Haematoxylin - 10gram is dissolved in Absolute alcohol - 100ml with light heat. Aluminum Potassium sulphate 200 gram dissolved in 2 liters of warm distilled water. Both were mixed and boiled: 5 gms of mercuric oxide was added while boiling and cooled after two minutes. Prior to use, 3 ml of acetic acid for 100 ml of hematoxylin was added.

1% ACID ALCOHOL

70% alcohol - 990 ml.

Con.HCI - 10 ml**.**

Eosin

Eosin - 10 gram D.H2O - 100 ml.	dissolved

Phloxine ‘B’ - 100 mg D.H2O - 20 ml	dissolved

Both were mixed and 780 ml of 90% alcohol was added. 4 ml of glacial cetic acid and saturated Lithium carbonate were added.

PROCEDURE

1. The slide was kept in xyline for 15 minutes.
2. It was washed in graded alcohol absolute 90% : 80% each 2 dips
3. Slide was washed in water for 5 minutes.
4. Stained in haematoxylin for 5 minutes.

5. It was washed in water for 5 minutes.
6. Differentiated in 1% acid alcohol 2 dips
7. Washed in water for 2 minutes.
8. Dipped twice in Lithium carbonate for blueing
9. Washed in water for 10 minutes
10. Dipped in 80% alcohol
11. Stained with eosin for 5 minutes.
12. Dehydrated in graded alcohol 80%, 90% then absolute alcohol
13. Cleared in xylene.
14. Mounted in D.P.X.

Result

Nuclei	-	Blue
Cytoplasm	-	Pink

Master Chart

MASTER CHART - CONTROLS

S.NO	age	parity	gestational age	systolic B.P	diastolic B.P	proteinuria	fetal birth wt (gm)	APGAR SCORE	live/still birth	placental morphometry				gross				placental histomorphology				
										placental wt(gm)	placental surface area (sq.cm)	placental volume(cc)	feto-placental ratio	subchorionic fibrin	retroplacental hematoma	infarction	calcification	mean no. of areas of syncytial knot formation / LPF	mean no. of areas of cytotrophoblastic cellular proliferation / LPF	irregular thickening of trophoblastic basement membrane (%)	mean no. of areas of villous fibrinoid degeneration / LPF	mean no. of areas of villous stromal fibrosis / LPF
D1	24	G3P2L2	38	120	80	Nil	3100	8	LB	650	296.7	593.5	4.8	-	-	-	-	9	6	<3%	2	2
D2	25	G4P3L3	39	120	80	Nil	3200	8	LB	500	226.1	339.1	6.4	-	-	-	-	8	5	<3%	3	3
D3	26	G2P1L1	38	120	80	Nil	3000	8	LB	450	251.2	502.4	6.7	-	-	-	-	11	6	<3%	2	2
D4	20	Primi	40	120	80	Nil	3000	9	LB	450	153.1	199	6.7	-	-	-	-	7	5	<3%	4	2
D5	35	G5P4L4	39	130	80	Nil	2500	8	LB	300	188.4	282.6	8.3	-	-	-	-	8	6	<3%	2	1
D6	20	G3P1L1	38	120	80	Nil	1500	1	LB	200	213.5	320.3	7.5	-	-	-	-	9	7	<3%	2	2
D7	25	Primi	40	130	80	Nil	3070	8	LB	550	212	317.9	5.6	-	-	-	-	10	6	<3%	5	5
D8	25	Primi	40	120	80	Nil	2800	9	LB	500	226.1	293.9	5.6	-	-	-	-	9	6	<3%	3	1
D9	25	Primi	38	110	80	Nil	2700	7	LB	450	226.1	339.1	6	+	-	-	+	8	7	>3%	2	5
D10	21	G2P1L1	38	120	80	Nil	2500	8	LB	400	141.3	212	6.3	-	-	-	-	8	7	<3%	4	2
D11	28	G2P1L1	39	120	80	Nil	2100	9	LB	350	109.9	219.8	6	+	-	-	-	9	6	<3%	2	2
D12	24	G3P2L2	40	140	80	Nil	2900	8	LB	550	160.1	320.3	5.3	-	-	-	-	10	5	>3%	2	1
D13	26	Primi	40	120	70	Nil	2700	8	LB	550	212	423.9	4.9	-	-	-	-	11	5	<3%	3	3
D14	28	G2P1L1	40	130	70	Nil	3300	8	LB	580	213.5	533.8	5.7	+	-	-	-	10	5	>3%	2	2
D15	23	Primi	38	120	80	Nil	2500	9	LB	450	109.9	274.8	5.6	-	-	-	-	10	6	<3%	3	2

D16	20	Primi	38	120	70	Nil	2500	8	LB	400	131.9	263.8	6.3	+	-	-	+	12	7	<3%	2	3
D17	23	G2P1L1	38	130	80	Nil	2500	8	LB	500	226.1	452.2	5	-	-	-	-	10	7	<3%	1	2
D18	29	G3A2	39	120	70	Nil	2560	8	LB	650	153.1	229.6	3.9	+	-	-	-	9	7	<3%	1	3
D19	21	Primi	38	130	70	Nil	3460	8	LB	550	141.3	353.3	6.3	-	-	-	-	9	7	<3%	5	1
D20	30	G4P3L3	28	110	70	Nil	1200	0	SB	220	70.65	141.3	5.5	-	-	+	-	13	6	>3%	4	2
D21	25	G4P3L0	40	110	60	Nil	2300	8	LB	400	120.9	241.8	5.8	-	-	-	-	12	6	<3%	6	3
D22	25	G4P1L2	38	110	70	Nil	2640	9	LB	520	122.5	306.2	5.1	+	-	-	-	15	6	>3%	2	2
D23	22	G3P1L1A1	38	110	70	Nil	3050	8	LB	550	84.78	169.6	5.5	-	-	-	-	12	5	<3%	2	1
D24	20	Primi	39	120	80	Nil	2800	8	LB	520	94.2	235.5	5.4	-	-	-	-	9	7	>3%	3	3
D25	25	G3P1L1A1	39	120	80	Nil	3150	8	LB	560	282.6	706.5	5.6	-	-	-	+	9	6	<3%	3	2
D26	25	G4P2L2	40	120	80	Nil	2500	9	LB	450	141.3	282.6	5.6	-	-	-	-	9	7	<3%	5	2
D27	23	G2P1L1	38	110	70	Nil	2530	8	LB	600	251.2	628	4.2	-	-	-	-	8	6	<3%	1	3
D28	22	G2P1L1	38	110	80	Nil	2900	8	LB	560	268.5	671.2	5.2	-	-	-	-	9	7	<3%	2	2
D29	22	G2A2	32	110	70	Nil	1450	8	LB	300	282.6	565.2	4.8	-	-	-	-	7	5	<3%	4	3
D30	35	G4P2L1	39	120	80	Nil	2930	9	LB	520	103.6	259.1	5.6	-	-	-	+	5	7	<3%	5	2
D31	23	G2P1L1	40	120	70	Nil	3500	9	LB	500	175.8	351.7	7	-	-	-	-	7	6	<3%	2	3
D32	18	Primi	38	120	80	Nil	2600	9	LB	450	142.9	285.7	5.8	-	-	-	-	15	5	>3%	2	2
D33	21	G2A1	38	100	80	Nil	3500	9	LB	520	213.5	427	6.7	-	-	-	-	18	3	>3%	1	3
D34	33	G2P1L1	34	110	70	Nil	2250	8	LB	400	200.2	500.4	5.6	-	-	-	-	20	2	<3%	3	2
D35	22	G2P1L1	39	120	80	Nil	3350	8	LB	600	298.3	596.6	5.6	-	-	-	-	14	5	<3%	3	3
D36	26	G2P1L1	39	110	70	Nil	2830	9	LB	620	153.1	306.2	4.6	-	-	-	-	7	7	<3%	3	4
D37	22	G2A1	28	120	80	Nil	1060	8	LB	320	31.4	125.6	6.4	-	-	-	-	7	4	<3%	3	2

D38	22	G2P1L1	40	120	80	Nil	3500	9	LB	550	141.3	282.6	4.9	-	-	-	-	8	6	<3%	3	2
D39	20	Primi	39	110	70	Nil	2550	8	LB	525	313.2	626.4	4.5	-	-	-	-	9	4	<3%	2	1
D40	19	Primi	34	110	70	Nil	1800	9	LB	400	153.1	306.2	5.4	-	-	-	+	2	7	<3%	4	1
D41	26	G3P2L1	38	120	80	Nil	2700	8	LB	500	213.5	533.8	5.4	-	-	-	-	14	6	>3%	2	2
D42	30	G2P1L1	39	120	80	Nil	2700	8	LB	500	186.8	280.3	7.1	-	-	+	-	17	8	<3%	2	2
D43	25	G2P1L1	39	110	70	Nil	3200	9	LB	450	164.9	412.1	6.1	-	-	-	-	13	5	<3%	3	3
D44	27	G3P1L1A1	38	120	80	Nil	3250	9	LB	530	200.2	400.4	7.1	-	-	-	-	13	3	<3%	1	3
D45	26	Primi	38	110	70	Nil	3400	8	LB	480	153.1	306.2	6.1	-	-	-	-	11	6	<3%	3	4
D46	30	G2P1L1	40	120	80	Nil	3350	8	LB	550	266.9	667.3	6.7	-	-	-	-	9	2	<3%	4	2
D47	22	G2P1L1	40	110	70	Nil	3030	9	LB	450	142.9	285.7	6.3	-	-	-	-	8	4	<3%	2	4
D48	23	G1PIL1	38	120	80	Nil	3500	8	LB	560	200.2	400.4	5.2	-	-	-	-	5	5	<3%	2	2
D49	24	Primi	38	110	70	Nil	2600	8	LB	500	213.5	640.6	7.7	-	-	-	-	14	7	<3%	3	2
D50	25	G2P1L1	39	120	80	Nil	3450	8	LB	450	186.8	460.1	5.9	-	-	-	-	7	8	<3%	2	5
D51	22	G2P1L1	40	120	80	Nil	3080	8	LB	520	213.5	427	5.4	-	-	-	-	13	4	<3%	2	2
D52	20	Primi	38	120	80	Nil	1960	8	LB	360	240.2	600.5	5.7	-	-	+	+	9	6	<3%	3	3
D53	25	Primi	40	120	80	Nil	2580	8	LB	450	213.5	427	5.5	-	-	-	+	9	5	>3%	2	6
D54	26	G2P1L1	38	120	80	Nil	3000	8	LB	550	240.2	480.4	4.9	-	-	-	-	9	8	<3%	2	2
D55	22	G3P2L2	38	120	80	Nil	2440	8	LB	500	200.2	300.3	6	-	-	-	-	8	7	<3%	1	2
D56	19	Primi	39	110	70	Nil	3280	9	LB	550	212	317.9	4.4	-	-	-	-	5	6	>3%	1	1
D57	29	G3 P2L2	34	120	80	Nil	1980	9	LB	450	213.5	320.3	5.8	-	-	-	-	12	7	<3%	2	3
D58	25	Primi	40	110	70	Nil	2780	9	LB	480	212	317.9	8.1	-	-	-	-	10	6	>3%	2	2
D59	30	G2P1L1	30	120	80	Nil	2420	8	LB	300	164.9	329.7	8.1	-	-	-	+	7	7	<3%	2	1

D60	30	G3P2L2	39	120	80	Nil	4120	8	LB	620	282.6	565.2	6.6	-	-	-	-	11	5	<3%	3	2
D61	28	Primi	40	120	80	Nil	2920	8	LB	500	200.2	500.5	5.8	-	-	-	-	9	7	<3%	2	2
D62	25	Primi	39	130	80	Nil	2400	8	LB	520	226.1	565.2	4.6	-	-	-	-	6	6	<3%	3	1
D63	25	G2P1L1	39	120	70	Nil	3200	8	LB	480	282.6	423.9	6.7	-	-	-	-	8	5	<3%	4	2
D64	24	G2P1L1	40	120	80	Nil	3100	9	LB	520	253.6	507.1	6	-	-	-	-	5	6	<3%	4	1
D65	23	G2P1L0	38	110	70	Nil	2400	9	LB	500	141.3	282.6	4.8	-	-	-	-	4	6	<3%	3	2
D66	23	G3P2L1	36	110	70	Nil	2000	9	LB	350	142.9	357.2	5.7	-	+	+	-	8	8	<3%	4	3
D67	25	G2P1L1	28	120	80	Nil	1260	8	LB	300	142.9	214.3	4.2	-	-	-	-	8	4	>3%	4	2
D68	19	G2P1L1	40	120	80	Nil	2100	9	LB	500	150.7	301.4	4.2	-	-	-	-	12	3	>3%	4	3
D69	20	Primi	40	110	70	Nil	2220	8	LB	550	200.2	400.4	4	-	-	-	+	15	6	<3%	2	2
D70	30	G4P2L0	39	120	80	Nil	1420	9	LB	400	164.9	247.3	3.6	-	-	-	-	9	7	>3%	2	3
D71	22	G2P1L0	30	110	70	Nil	1950	8	LB	380	175.8	351.7	5.1	-	-	-	+	19	4	<3%	3	3
D72	21	G2A1	32	120	80	Nil	2320	9	LB	400	212	424	5.8	-	-	-	-	7	6	<3%	4	2
D73	28	G4P3L3	30	110	70	Nil	1520	8	LB	360	142.9	285.7	4.2	-	-	-	-	9	3	<3%	2	4
D74	26	G7A6	28	110	70	Nil	1700	8	LB	330	141.3	212	5.2	-	-	-	-	9	8	<3%	3	3
D75	23	G3P2L1	36	110	70	Nil	2000	8	LB	400	200.2	500.4	5	-	-	-	-	9	7	>3%	3	4
D76	22	G2A1	40	100	70	Nil	3600	9	LB	500	226.1	339.1	7.2	-	-	-	-	8	7	>3%	3	2
D77	18	Primi	39	120	80	Nil	3000	9	LB	450	266.9	400.4	6.7	-	-	-	-	13	6	<3%	4	2
D78	20	Primi	39	120	80	Nil	2600	9	LB	520	345.4	690.8	5	-	-	-	-	12	7	>3%	2	3
D79	26	G2P1L1	38	110	70	Nil	3000	8	LB	480	212	212	6.3	-	-	-	+	9	6	<3%	4	4
D80	24	G3P2L2	40	100	70	Nil	3500	9	LB	480	251.2	376.8	7.3	-	-	-	-	10	7	<3%	4	1
D81	19	Primi	39	120	70	Nil	3250	8	LB	500	153.1	229.6	6.5	-	-	-	-	19	6	>3%	3	2

D82	20	Primi	36	100	70	Nil	2300	9	LB	450	131.9	263.8	5.1	-	-	-	-	11	7	<3%	4	3
D83	23	G2P1	36	110	70	Nil	2060	8	LB	480	188.4	376.8	4.3	-	-	-	-	11	5	<3%	3	4
D84	24	G2A1	38	110	70	Nil	2450	9	LB	450	186.8	280.3	5.4	-	-	-	-	13	5	>3%	4	2
D85	26	G2P1L1	32	120	80	Nil	2400	8	LB	400	212	317.9	6	-	-	-	-	9	4	<3%	4	2
D86	21	Primi	36	120	80	Nil	1600	8	LB	250	142.9	357.2	6.4	-	+	+	-	9	7	<3%	3	1
D87	29	Primi	38	120	80	Nil	1500	9	LB	280	131.9	263.8	5.4	-	-	-	+	8	4	<3%	4	3
D88	28	G2A1	38	120	80	Nil	1450	9	LB	300	164.9	329.7	4.8	-	-	-	-	9	7	<3%	3	2
D89	24	Primi	39	120	80	Nil	1040	9	LB	320	142.9	285.7	3.3	-	-	-	-	8	6	<3%	2	3
D90	19	Primi	39	120	80	Nil	1100	8	LB	250	162.8	244.1	4.4	-	-	-	+	8	5	<3%	4	4
D91	32	G3P2L2	40	120	80	Nil	2600	8	LB	300	213.5	427	8.7	-	-	-	-	7	5	<3%	5	2
D92	26	Primi	30	110	70	Nil	1440	9	LB	350	226.1	339.1	4.1	-	-	-	-	9	6	<3%	6	2
D93	29	G2P2L2	34	110	70	Nil	2500	8	LB	400	200.2	300.3	6.3	-	-	-	+	8	6	>3%	4	3
D94	30	G2P1L1	40	120	80	Nil	2300	8	LB	450	226.1	452.2	5.1	-	-	-	-	11	5	<3%	7	4
D95	21	Primi	36	120	80	Nil	1700	9	LB	400	213.5	320.3	4.3	-	-	-	-	9	4	<3%	3	2
D96	20	Primi	39	110	70	Nil	2200	8	LB	500	226.1	565.2	4.4	-	-	-	-	7	6	<3%	5	4
D97	23	G2P1L1	38	120	80	Nil	2700	8	LB	550	282.6	706.5	4.9	-	-	-	-	12	4	<3%	5	3
D98	29	G4P3L3	39	110	70	Nil	3920	9	LB	650	345.4	690.8	6	-	-	-	+	8	6	<3%	4	2
D99	22	Primi	38	120	80	Nil	3080	8	LB	550	282.6	565.2	5.6	-	-	-	-	8	6	<3%	5	3
D100	27	G2P1L1	36	120	80	Nil	3500	9	LB	560	253.6	633.9	6.3	-	-	-	-	6	7	>3%	5	2

MASTER CHART - CASES

HPE NO.	age	parity	gestational age	systolic B.P	diastolic B.P	proteinuria	fetal birth wt (gm)	APGAR	live/still birth	placental weight (gm)	placental surface area(sq.cm)	placental volume (cc)	feto-placental ratio	sub chorionic fibrin	retroplacental hematoma	infarction	calcification	mean no. of areas of syncytial knot formation / LPF	mean no. of areas of cytotrophoblastic cellular proliferation / LPF	irregular thickening of trophoblastic basement membrane (%)	mean no. of areas of villous fibrinoid degeneration / LPF	mean no. of areas of villous stromal fibrosis / LPF
DP1	19	Primi	28	170	120	L	1200	0	SB	250	62.8	125.6	4.8	-	-	+	+	27	18	>3%	7	10
DP2	25	Primi	34	180	110	+	1750	8	LB	250	102.05	102.05	7	-	-	-	-	28	17	>3%	9	11
DP3	19	Primi	40	160	110	Nil	2400	8	LB	450	186.83	280.25	5.3	-	-	+	-	26	20	>3%	6	9
DP4	19	Primi	38	180	120	L	2750	8	LB	450	251.2	376.8	6.1	-	-	-	-	28	19	<3%	9	11
DP5	19	Primi	28	160	100	I	1200	0	SB	200	94.2	141.3	6	-	-	+	-	21	15	<3%	4	8
DP6	25	Primi	36	140	100	++	1100	0	SB	230	120.89	120.89	4.8	-	-	+	-	22	14	<3%	5	9
DP7	19	Primi	34	150	110	L	1750	8	LB	400	163.3	326.56	4.4	-	-	+	-	27	19	>3%	8	11
DP8	27	G3P1L1A1	34	150	120	L	1800	5	LB	350	226.08	452.16	5.1	-	-	-	-	29	18	>3%		10
DP9	19	Primi	36	140	100	Nil	2000	8	LB	350	211.95	423.9	5.7	-	-	-	+	20	14	<3%	4	8
DP10	23	Primi	40	150	110	++	2900	8	LB	500	200.18	300.3	5.8	-	-	-	-	26	19	>3%	6	10
DP11	24	G5P2L2A2	38	150	100	Nil	3200	8	LB	550	266.9	533.8	5.8	-	-	-	-	24	16	<3%	5	8
DP12	25	G2P1L1	39	170	96	Nil	2350	8	LB	550	226.08	678.24	4.3	-	-	-	-	17	14	<3%	2	8
DP13	25	Primi	34	140	100	+++	1200	5	LB	400	120.89	181.34	3	-	-	+	-	19	15	<3%	3	7
DP14	20	G3P1L1A1	38	160	114	Nil	2750	8	LB	450	163.28	163.28	6.1	-	-	+	-	25	16	>3%	8	10
DP15	30	G3P1L1A1	39	140	90	Nil	3250	4	LB	530	141.3	282.6	6.1	-	-	-	-	19	16	<3%	3	8
DP16	26	Primi	34	160	110	L	1200	4	LB	400	129.53	194.28	3	-	-	-	-	26	14	>3%	8	10
DP17	23	Primi	38	180	110	L	3900	8	LB	600	186.8	560.5	6.5	-	-	-	-	25	19	>3%	6	10
DP18	40	G5P3A1	34	160	114	L	1360	0	SB	250	43.96	65.94	5.4	-	-	-	-	27	19	>3%	9	11
DP19	32	G3P2L2	40	160	110	Nil	2360	8	LB	500	94.2	141.3	4.7	-	-	+	-	21	16	<3%	8	7
DP20	27	G3P2L1	32	160	120	Nil	1900	0	SB	300	62.8	125.6	6.3	-	-	+	-	22	20	<3%	8	7
DP21	25	G3P2L2	40	150	110	+	3200	8	LB	550	102.05	255.13	5.8	-	-	-	-	26	21	>3%	9	8
DP22	20	Primi	30	210	150	L	1100	0	SB	250	94.2	141.3	4.4	-	-	-	-	29	20	>3%	7	10
DP23	36	G3P1L1A1	34	204	106	Nil	2400	8	LB	350	197.82	395.64	6.9	-	-	-	-	17	17	>3%	3	7
DP24	30	G3P1L1A1	30	130	90	+	1250	0	SB	250	77.72	116.57	5	-	+	-	-	15	16	<3%	5	6

DP25	21	Primi	34	130	90	+++	1400	8	LB	250	94.2	188.4	5.6	-	-	+	-	14	14	>3%	4	7
DP26	25	G2A1	36	150	110	++	2100	8	LB	300	141.3	211.95	7	-	-	-	-	19	20	<3%	6	6
DP27	24	G2A1	38	180	130	L	2500	8	LB	450	253.5	379.5	5.6	-	+	+	-	28	21	>3%	9	10
DP28	21	Primi	28	170	80	L	1200	0	SB	230	94.2	141.3	5.2	-	-	+	-	15	16	>3%	4	8
DP29	23	Primi	38	190	110	++	2500	8	LB	500	163.3	244.92	5	-	-	-	+	18	17	<3%	6	7
DP30	21	Primi	38	170	110	+++	2760	8	LB	600	153.08	229.61	4.6	-	-	-	-	19	16	<3%	3	7
DP31	24	Primi	40	170	100	++	2600	8	LB	500	188.4	376.8	5.2	-	-	-	+	13	13	<3%	6	6
DP32	26	G2P4	40	150	100	+	3600	8	LB	450	164.8	331.6	8	-	-	-	-	17	15	<3%	6	9
DP33	20	Primi	38	160	90	++	2400	8	LB	450	141.3	282.6	5.3	-	-	-	-	14	14	<3%	5	5
DP34	28	G3A2	39	170	120	L	2650	8	LB	450	197.82	395.64	5.9	-	+	+	+	27	21	>3%	10	10
DP35	22	G2P1L1	38	150	100	-	3450	8	LB	500	251.2	628	6.9	-	-	+	-	16	16	<3%	4	7
DP36	27	G2P1L1	39	170	110	L	1450	5	LB	300	129.53	194.29	4.8	-	-	-	-	19	17	<3%	6	8
DP37	25	G2P1L1	38	160	90	+++	2220	5	LB	350	175.84	175.84	6.3	-	-	-	-	14	14	<3%	5	6
DP38	28	G3P1L1A1	40	150	100	-	2960	8	LB	550	238.64	357.9	5.4	-	-	+	-	18	16	>3%	4	6
DP39	30	G2P1L1	34	200	130	L	2300	6	LB	300	131.88	197.82	7.7	-	-	+	-	29	21	>3%	11	12
DP40	26	Primi	33	140	100	-	2300	5	LB	350	175.84	263.76	6.6	-	+	+	-	17	15	<3%	6	7
DP41	29	G2P1L1	38	150	106	++	2800	9	LB	550	211.95	211.95	5.1	-	+	-	-	16	14	<3%	5	6
DP42	28	G2P1L1	40	150	100	-	3160	8	LB	500	266.9	320.28	6.3	-	-	+	-	29	21	>3%	12	7
DP43	22	G2P1L1	32	170	110	+++	1840	5	LB	300	153.08	229.61	6.1	-	-	+	+	28	22	>3%	14	7
DP44	32	Primi	40	170	100	+++	3860	8	LB	550	226.08	339.12	7	-	+	-	-	22	14	<3%	7	10
DP45	27	G2P1L1	38	170	90	++	3500	9	LB	600	223.72	355.52	5.8	-	+	+	-	15	16	<3%	5	10
DP46	22	G2P1L1	34	160	100	++	1900	5	LB	400	208.81	313.22	4.8	-	-	+	-	26	20	>3%	9	11
DP47	25	G2A1	34	170	100	L	1300	0	SB	350	129.53	155.43	3.7	-	-	-	-	21	15	<3%	5	8
DP48	22	Primi	39	150	90	+	3220	9	LB	500	186.83	280.24	6.4	-	-	-	-	19	18	<3%	4	8
DP49	19	Primi	40	160	100	+	3210	9	LB	400	197.82	296.73	8	-	-	-	-	24	21	>3%	7	10
DP50	28	G3P3L1	36	170	110	L	2600	8	LB	500	223.73	233.73	5.2	-	-	-	-	24	18	>3%	6	8
DP51	27	Primi	40	170	90	++	1900	8	LB	350	213.52	320.28	5.4	-	-	+	-	18	15	<3%	5	9
DP52	26	G5P4L2	40	150	110	L	2480	9	LB	450	253.56	380.33	5.5	-	-	-	-	24	20	>3%	7	9
DP53	22	Primi	38	190	120	L	1020	0	SB	300	153.08	153.08	3.4	+	+	+	+	29	21	>3%	12	10
DP54	26	G3P1LO	30	180	110	L	1520	5	LB	320	175.84	117.23	4.8	-	-	+	-	27	21	>3%	12	11
DP55	22	Primi	39	170	90	L	2400	8	LB	500	213.52	213.53	4.8	-	-	-	-	19	17	<3%	8	9

DP56	21	Primi	39	150	90	+	3000	6	LB	600	253.6	253.6	5	-	-	-	+	21	17	<3%	6	9
DP57	23	Primi	40	140	90	++	2520	8	LB	500	223.73	335.59	5	-	-	-	-	20	15	<3%	6	9
DP58	22	G2P1L1	32	190	110	L	1200	0	SB	400	211.95	317.93	3	-	+	++	-	28	21	>3%	13	12
DP59	25	G2P1L0	32	190	120	L	1600	4	LB	300	253.6	380.33	5.3	-	+	++	-	29	22	>3%	12	13
DP60	26	G2A1	28	160	110	L	1210	4	LB	250	141.3	211.95	4.8	-	-	-	-	30	21	>3%	12	13
DP61	28	Primi	28	170	100	L	1500	4	LB	280	131.9	131.9	5.4	-	-	-	-	21	20	<3%	7	9
DP62	32	G3P2L0	32	160	100	+++	1240	0	SB	250	102.05	153.08	5	-	-	+	-	20	16	<3%	4	9
DP63	23	Primi	40	150	100	-	3000	8	LB	550	223.73	223.73	5.5	-	-	++	-	20	14	<3%	4	7
DP64	32	Primi	38	150	110	-	2000	8	LB	450	117.8	117.8	4.4	-	-	-	+	29	21	>3%	9	13
DP65	23	G3A2	38	150	110	++	1280	0	SB	300	150.72	180.86	4.3	-	+	-	-	28	22	>3%	4	13
DP66	32	G5A4	39	160	80	+	2460	8	LB	550	197.82	395.64	4.5	-	+	-	-	24	17	<3%	5	9
DP67	20	Primi	39	200	120	L	2560	8	LB	500	223.73	335.59	5.1	-	+	+	-	29	20	>3%	8	13
DP68	24	Primi	40	180	100	++	3000	8	LB	450	226.08	339.12	6.7	-	+	++	-	19	16	<3%	5	8
DP69	24	Primi	40	140	90	++	2000	8	LB	400	253.6	304.27	5	-	+	-	+	21	15	<3%	7	9
DP70	24	Primi	38	150	100	-	2580	8	LB	500	211.95	317.93	5.2	-	-	-	-	20	16	<3%	4	8
DP71	25	G4P3L2	30	180	110	L	1620	5	LB	300	112.26	112.26	5.4	-	+	-	-	28	21	>3%	11	12
DP72	28	Primi	28	170	100	L	3160	9	LB	450	211.95	317.9	7	-	-	+	-	19	18	<3%	7	8
DP73	22	G2A1	39	180	100	L	3380	9	LB	500	266.9	533.8	6.8	+	-	-	-	12	14	<3%	4	7
DP74	29	G3P1L1A1	34	180	100	+	1980	5	LB	380	211.95	423.9	5.2	-	-	-	-	21	17	<3%	4	8
DP75	19	Primi	38	190	100	L	2280	8	LB	500	226.08	565.2	4.6	-	-	+	-	23	18	>3%	6	7
DP76	20	Primi	32	150	100	L	1820	8	LB	250	94.2	94.2	7.3	-	-	++	-	23	15	>3%	8	6
DP77	30	G4P3L3	32	150	90	L	1880	8	LB	300	129.53	155.43	6.3	-	-	+	+	24	16	>3%	9	9
DP78	34	G3P1L1A1	34	170	100	+++	1200	0	SB	350	200.18	300.26	3.4	-	+	-	-	19	14	<3%	5	8
DP79	20	Primi	20	170	110	+	1000	2	LB	300	211.95	423.9	3.3	-	-	++	-	29	21	>3%	11	13
DP80	24	Primi	30	160	120	++	1490	5	LB	250	84.78	84.78	6	-	+	++	-	30	22	>3%	13	13
DP81	24	G2P1LO	38	170	100	-	3900	8	LB	600	296.73	593.46	6.5	-	-	-	-	23	17	>3%	4	9
DP82	28	G2P1L0	40	160	90	++	3000	9	LB	550	211.95	423.9	5.5	-	+	+	-	21	21	<3%	5	8
DP83	30	Primi	28	170	100	+++	1100	3	LB	240	112.26	224.51	4.6	-	-	+	+	26	22	>3%	6	11
DP84	26	Primi	34	180	110	++	1200	3	LB	320	131.88	158.26	3.8	-	-	-	-	28	20	>3%	9	10
DP85	30	G3P1L1A1	38	150	110	-	3250	8	LB	650	328.13	393.76	5	-	-	-	-	27	21	>3%	9	12
DP86	26	G2P1L1	39	170	100	++	3600	9	LB	600	282.6	339.12	6	-	-	-	-	24	19	<3%	5	7

DP87	21	Primi	40	180	120	L	2760	9	LB	550	211.95	317.93	5	-	-	-	+	29	23	>3%	10	13
DP88	35	G4P3L3	40	180	130	L	2500	8	LB	400	117.75	235.5	6.3	-	+	++	-	30	18	>3%	12	14
DP89	23	Primi	38	180	100	-	2550	8	LB	500	141.3	282.6	5.1	-	+	-	+	24	16	<3%	11	9
DP90	24	Primi	38	160	90	+	3200	8	LB	600	175.84	211.01	5.3	-	+	+	-	21	16	<3%	5	6
DP91	23	Primi	38	170	100	+	2500	8	LB	550	141.3	282.6	4.5	-	+	-	-	25	18	>3%	6	11
DP92	23	Primi	39	160	120	L	3400	9	LB	700	94.2	113.04	4.9	-	-	-	-	29	19	>3%	9	13
DP93	25	G4P1L1A2	39	150	100	-	2600	9	LB	550	112.26	134.71	4.7	-	-	-	-	25	15	>3%	11	8
DP94	27	G3P2L1	32	160	110	L	1900	6	LB	400	131.88	184.63	4.8	-	-	-	+	29	15	>3%	9	13
DP95	30	G3P2L2	38	150	100	-	3200	8	LB	550	238.64	381.82	5.8	+	+	+	-	24	17	<3%	6	9
DP96	18	Primi	38	150	110	-	2300	8	LB	400	131.88	197.82	5.8	-	-	-	-	30	18	>3%	12	13
DP97	20	G2P1L0	34	170	120	L	1800	6	LB	300	84.78	84.78	6	-	+	++	+	31	16	>3%	12	14
DP98	21	Primi	38	150	80	L	1930	6	LB	400	102.1	102.1	4.8	-	-	++	+	24	21	<3%	5	9
DP99	23	Primi	38	170	100	L	2900	8	LB	600	211.95	317.93	4.8	-	-	++	-	25	20	<3%	4	9
DP100	25	G3A2	35	170	120	L	1200	0	SB	400	84.78	84.78	3	-	+	-	-	29	20	>3%	12	11

KEY TO MASTER CHART

G	:	GRAVIDITY
P	:	PARITY
L	:	LIVE
A	:	ABORTION
B.P	:	BLOOD PRESSURE
LB	:	LIVE BIRTH
SB	:	STILL BIRTH
“+”	:	PRESENT
“-“	:	ABSENT
LPF	:	LOW POWER FIELD