COMPARISON OF GROSS MORPHOLOGICAL AND HISTOLOGICAL FEATURES OF PLACENTA BETWEENHYPERTENSIVE PREGNANT WOMEN AND NON-HYPERTENSIVE PREGNANT WOMEN ATTENDING MUHIMBILI NATIONAL HOSPITAL

Antipas Furaha, (MSc Anatomy)

A Research Report Submitted in Partial Fulfillment of the Requirements of the Degree of Master of Science in Anatomy of the Muhimbili University of Health and Allied

Sciences

October, 2020

Muhimbili University of Health and Allied Sciences

Department of anatomy



COMPARISON OF GROSS MORPHOLOGICAL AND HISTOLOGICAL FEATURES OF PLACENTA BETWEENHYPERTENSIVE PREGNANT WOMEN AND NON-HYPERTENSIVE PREGNANT WOMEN ATTENDING MUHIMBILI NATIONAL HOSPITAL

By

Antipas Furaha

A Research Report Submitted in Partial Fulfillment of the Requirements of the Degree of Master of Science in Anatomy of the Muhimbili University of Health and Allied Sciences

October, 2020

CERTIFICATION

The undersigned certify that, they have read and hereby recommend for examination of the dissertation entitled "Comparison of gross morphological and histological features of placenta betweenhypertensive pregnant women and non-hypertensive pregnant women attending muhimbili national hospital" in fulfillment of the requirements for the degree of Master of Science in Anatomy at Muhimbili University of Health and Allied Sciences.

Dr. Dennis Russa (Supervisor)

Date

DECLARATION AND COPYRIGHT

I, Antipas Eugen Furaha, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature_____ Date_____

This dissertation is a copyright material protected under the Berne Convention, the Copyright Act 1999 and other international and national enactments, in that behalf, on intellectual property. It may not be reproduced by any means, in full or in part, except for short extracts in fair dealing, for research or private study, critical scholarly review or discourse with an acknowledgement, without the written permission of the Directorate of Postgraduate Studies, on behalf of both the author and the Muhimbili University of Health and Allied Sciences.

ACKNOWLEDGMENT

First and foremost I would like to thank GOD for his favor, gift of life, daily provision and ability to develop and succesfully complete this dissertation.

I extend my special thanks to Muhimbili University of Health and Allied Sciences(MUHAS) for the support during my two years of training and for the knowledge and competency I acquired during my training. I also would like to acknowledge Muhimbili National Hospital(MNH) for allowing me to do my study and in Muhimbili National Hospital Labor ward number 34 and ward 35 and obstetric thietre for their extreme support during data collection.

I am extremely thankful to my supervisors Dr Dennis Russa for his time, endless support, patience and guidance during the time of this project.

I would like to express my sincere thanks to all members of faculty MUHAS Anatomy department under Dr Dennis Russa. The achievement of this project is the result of their support and sharing of their knowledge.

I owe sincere thanks to my family members for their love, support, encouragement and patience. Last but not least to my fellow residents for the great time and experience we shared during our training period.

ABSTRACT

BACKGROUND: Placenta is the fetomaternal vital organ which is responsible for the maintenance of the pregnancy and promotion of fetal growth and development. The optimal survival, growth and development of the fetus are correspondence to the appropriate formation and development of the placenta. Hypertensive disorders of pregnancy exert great impact on placenta and thus reflects changes both morphological and histological. There were very few studies done on this topic and most of them were done among Caucasians. This study was not done in our settings. We did this study in order to see if these differences exist in our setting and being important in providing comparative analysis with other studies so as to confirm the magnitude of changes caused by hypertensive pregnant disease to human placenta and add knowledge on this topic. We expected the knowledge obtained from this study to increase awareness on placental impact of the disease particularly with reference to our population and to make comparative analysis with other populations.

AIM: This study compared the morphological and histological features of placenta between hypertensive pregnant mothers and non-hypertensive pregnant mothers attended Muhimbili National Hospital (MNH).

METHODS: A hospital based comparative cross sectional study was conducted from June 2020 to August 2020 at Muhimbili National Hospital (MNH). A total of 80 placenta were studied morphologically and histologically, of which 40 placenta were from hypertensive pregnant mothers and 40 placenta were from normotensive pregnant mothers. In the morphological aspect, the shape, weight, the site of insertion of the umbilical cord, the number of cotyledons of each placenta and thickness of placenta were noted. In the histological part Neutral buffered formalin (NBF) was used the routine staining technique which was Hematoxylin and Eosin (H&E) and light microscope were used. The data were analyzed by using SPSS version 20 computer software and results were summarized in means and proportions.

Statistical significance of difference between two groups in the aspect of the data that was expressed in 'means' was calculated by using Students "t" test. A difference between the two groups was considered to be significant when p<0.05. In the aspect of the data that was expressed in percentage/proportion was calculated by using chi-square test. A difference between two groups will be considered to be significant when p<0.05.

RESULTS: The irregular shape of placenta and marginal insertion of umbilical cord were more in the hypertensive group and were statistically significant (p>0.001). The mean placenta weight, mean placenta thickness and mean numbers of cotyledons were significantly less in hypertensive group compared to normotensive group (p<0.01). Microscopic study of the placenta revealed the presence of fibrinoid necrosis, syntial knots, calcifications and villous hypoplasia in both normotensive and hypertensive group however these findings were significantly higher in the hypertensive group (p>0.01).

CONCLUSION: Hypertensive disorders of pregnancy (HDP) exert profound impact on placenta. Morphologically altering its dimensions andhistologically fibrinoid necrosis, calcifications, syntial knots and villous hypoplasia were significantly more in hypertensive group than in normotensive (p>0.001).

RECOMMENDATION: Screening of the pregnant women for the Hypertensive Disorders of Pregnancy (HDP) and proper and effective management of the pregnant women with hypertensive disorder of pregnancy (HDP) is of paramount importance since we have found significantly more placental ischemic lesions which are fibrinoid necrosis and calcifications which threaten the fetal outcomes.

Further studies should be done on the association of the gross and histological features and fetal and maternal outcomes.

Table of Contents	
CERTIFICATION	i
DECLARATION AND COPYRIGHT	ii
ACKNOWLEDGMENT	iii
ABSTRACT	iv
ABBREVIATIONS	X
DEFINITION OF KEY TERMS	xii
CHAPTER ONE	1
1.1 INTRODUCTION	1
1.2 PROBLEM STATEMENT	3
1.3 CONCEPTUAL FRAMEWORK.	4
1.5 RESEARCH QUESTION	6
1.6 RESEARCH OBJECTIVES	6
1.6.1 Broad objectives	6
1.6.2 Specific objectives	6
1.7 LITERATURE REVIEW	7
1.7.1Morphometrical review	7
1.7.2Histological review	8
CHAPTER TWO	11
2.0 MATERIALS AND METHODS	11
2.1. STUDY DESIGN, STUDY POPULATION AND STUDY AREA	11
2.1.1 Type of study:	11
2.1.2Study population:	11
2.1.3Study area	11

2.1.4Study settings	11
2.2 SAMPLE SIZE AND SELECTION	13
2.2.1 Sample Size	13
2.2.2 Sampling technique	14
2.2.3Inclusion criteria:	14
2.2.4Exclusion criteria:	14
2.3 VARIABLES	14
2.3.1 Independent variable	14
2.3.2 Dependent variable	14
2.4 DATA COLLECTIONMETHODS	15
2.4.1 Blood pressure measurement	16
2.4.1 Collection and gross examination of placenta:	16
2.4.2 Light Microscopic examination.	17
2.5 DATA COLLECTION TOOL	17
2.6 DATA MANAGEMENT AND ANALYSIS	
2.7 ETHICAL ISSUES	
2.7.1 Ethical clearance	
2.7.2Ethical Consideration	19
CHAPTER THREE	21
3.0 RESULTS	21
3.1 MATERNAL CHARACTERISTICS	21
3.2 GROSS MORPHOLOGICAL FEATURES	23
CHAPTER FOUR	29
4.0 DISCUSSION	

CONCLUSION	32
RECOMMENDATION	32
REFERENCES	33
APPENDIX	36
Structured checklist	36
CONSENT FORM-ENGLISH	37
CONSENT FORM-SWAHILI	

LIST OF TABLES

Table 1. Maternal characteristics between hypertensive and normotensive	
group22	2
Table 2. Gross morphological features of placenta between hypertensive and normotensive	
group2	5
Table 3. Comparison of placental histological features in hypertensive and	
normotensive	,

LIST OF FIGURES

Figure 1: Conceptual Framework	4
Fig 2: Gross morphological features of the placenta	24
Fig 3: Photomicrographs of the placenta stained by Haematoxylin and	
eosin	27
Fig 4: Photomicrographs of the placenta by stained by Haematoxylin and	
Eosin	2

ABBREVIATIONS

ANC:	Antenatal care
AP:	Atheromatous plaque
BIHS:	British and Irish Hypertension Society
Cm:	Centimeter
ESH:	European Society of Hypertension
Gm:	Gram
Gm/l:	Gram per litre
HDP:	Hypertensive disorders of pregnancy.
Н&Е:	Haematoxylin and Eosin
HPW:	Hypertensive Pregnant Woman.
IFGR:	Intrauterine fetal growth restriction.
Mg/ml:	Milligram per milliliter
MNH:	Muhimbili National Hospital.
MSc Anatomy:	Master of Science in Human Anatomy
MUHAS:	Muhimbili University of Health and Allied Sciences
NBF:	Neutral Buffered Formalin
NHPW:	Non- hypertensive Pregnant Woman.
PIH:	Pregnancy induced hypertension.
PV:Perivasculitis	
PVF:	perivillous fibrin.

SPSS Statistical Package for Social Science

S.V.S Medical College: Sri Venkata Sai Medical College

TV:Terminal villi

TZ:Tanzania

WHO: World Health Organization

DEFINITION OF KEY TERMS

Blastocyst: A thin-walled hollow structure in early embryonic development that contains a cluster of cells called the inner cell mass from which the embryo arises.

Categorical variable: This is the variable which does not take numerical values, but are recorded and reported in categories, such as shape of the placenta which can be ovoid or irregular, site of insertion of umbilical cord which can be central or not central.

Chorion frondosum: The part of the chorion that has persistent villi and that with the decidua basalis forms the placenta.

Continuous variable: This is the variable which takes numerical values and takes any value within meaningful extremes such as weight of placenta.

Desidua basalis: The part of the endometrium in the pregnant human female that participates with the chorion in the formation of the placenta.

Eclampsia: Eclampsia was defined as the presence of new-onset grand mal seizures in a woman with preeclampsia. Eclampsia can occur before, during or after labor.

Gestational hypertension: Blood pressure >140/90 presenting after 20 weeks of pregnancywithout significant proteinuria.

Histological features of placenta: These are the features of the placenta which are seen

microscopically which are numerous villi, syncytial knots and stroma.

Intrauterine fetal growth restriction: fetal growth less than the normal growth potential specific infant because of genetic or environmental factors.

Morphological features of placenta: These are the features of the placenta which are seen grossly, these are shape, number of cotyledons, weight, and site of insertion of umbilical cord **Placenta:** is the fetal organ providing the interchange between mother and fetus.

Placenta abruptio: is defined as the premature separation of the placenta from the uterus.

Placental calcification: is a condition in which there is a slow but continuous process of calciumdepositions in the placenta.

Placental infarction: refers to a localized area of ischemic villous necrosis

Pre-eclampsia: Blood pressure >140/90 presenting after 20 weeks of pregnancy with significant proteinuria (>30 mg/ml, or >300 mg/day or at least 1g/L [2+] on dipstick testing).

Severe pre-eclampsia: Blood pressure >160/110 presenting after 20 weeks of pregnancy with

significant proteinuria (>30 mg/ml, or >300 mg/day or at least 1g/L [2+]on dipstick testing) with symptomatic manifestation.

Syncytial knots: A localized aggregation of syncytiotrophoblastic nuclei in the villi of the placenta during early pregnancy.

Umbilical cord: The cord that connects the developing fetus with the placenta while the fetus

CHAPTER ONE

1.1 INTRODUCTION

Placenta is the fetomaternal vital organ which is responsible for the maintenance of the pregnancy and promotion of fetal growth and development(Yibeltal et al., 2017). It connects the fetus to the uterine wall thus providing nutrients and oxygen to the fetus, eliminating waste products from the fetus thus works as digestive system, lung and kidney respectively. The optimal survival, growth and development of the fetus is correspondence to the appropriate formation and development of the placenta(Wang et al., 2010). It develops after conception at the time of implantation of the blastocyst in the uterus, and is generally discharged from the uterus following infant birth. It develops from the fetal tissue that is chorion frondosum and maternal tissue that is decidua basalis. The normal "term placenta" is round and flat in shape and is about (400 - 600) gm in weight, (15 - 25) cm in diameter, (2 - 3) cm in thickness and 15 to 20 cotyledons however there is a considerable variation from placenta to placenta, which strongly depend on the mode of delivery(Huppertz, 2008). The histology of the normal placenta, the chorionic surface shows cuboidal to columnar cells in the areolar region and the villi clumps which have a randomized distribution form the micro cotyledons which are sometimes branched(Avagliano et al., 2016). Studying the morphological and histological features of the placenta is the stepping stone of predicting fetal outcomes. Some placental parameters such as placental weight and number of cotyledons can be clinically used in the prediction of fetal outcome.(Lilungulu, 2019)

Hypertensive disorders of pregnancy are common and basically refers to a cluster of disease ranging from chronic hypertension and gestational hypertension to pre-eclampsia –eclampsia. Hypertensive disorders of pregnancy (HDP) is thought to be a kind of syndrome, composed of some types of diseases that are respectively caused by influence of both genetic and acquired factors. There has been little consensus regarding international classifications; however, various classifications have been described. A Japanese consensus for pregnancy induced hypertension proposed in 2004, consists of 4 subtypes according to symptoms and onset; gestational hypertension, pre-eclampsia, super imposed pre-eclampsia and eclampsia.

associated with increased risk of adverse outcomes to both mother and fetus and the common ones are; placenta abruption, intrauterine fetal growth restriction (IFGR), premature delivery and stillbirth, thus, form one of the deadly triad along with hemorrhage and infection. Hypertensive Disorders of Pregnancy (HDP), gestational hypertension and pre-eclampsia affect about 5.2%-8.2%, 1.8%-4.4%, 0.9%-9.2%, respectively globally (Umesawa and Kobashi, 2017). The hypertensive disorders of pregnancy affect about 10% of pregnant women in Africa(Noubiap et al., 2019)Pre-eclampsia/eclampsia is a major cause of maternal deaths contributing about 19.9% of all maternal deaths(Pembe et al., 2014).

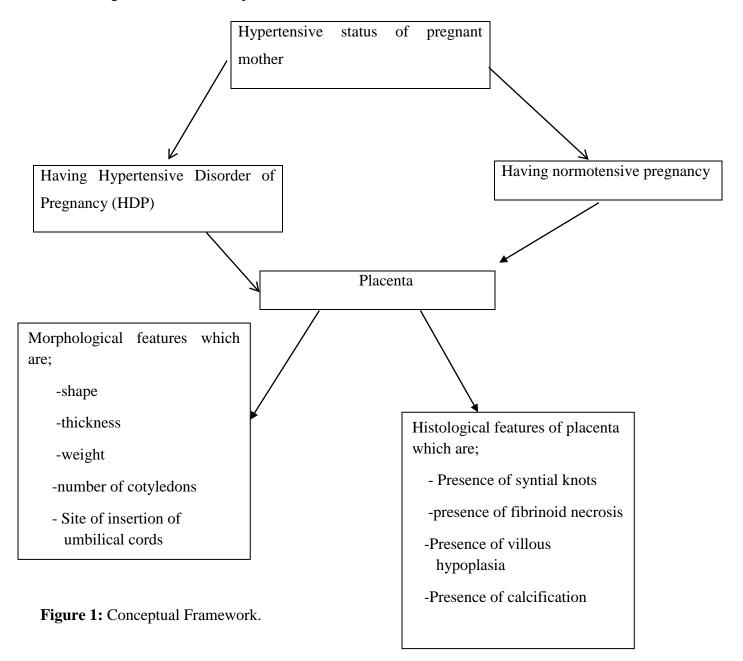
Hypertensive disorders of pregnancy can be classified into 4 categories which are; gestational hypertension, chronic hypertension, pre -eclampsia and pre-eclampsia superimposed on chronic hypertension(Singh and Singh, 2015). The etiology of pre-eclampsia is not clear though combinations of fetal and placental factors are likely to play part. Inappropriate formation of the placenta leading to abnormal angiogenic factor production and abnormal systemic endothelial dysfunction as well as genetic and immunological factors are said to contribute(Shah and Gupta, 2019). The examination of the placenta gives a clue on what happened with it when it was in the mother's womb and can predict the future of the fetus, thus the placenta is the mirror of the maternal and fetal status. The hypertensive disorders of pregnancy particularly pregnancy induced hypertension (PIH) are reflected on the placenta both macroscopically and microscopically. Several studies revealed that the utero-placenta blood flow is decreased in PIH secondary to maternal vasospasm, eventually will cause constriction of fetal stem arteries and will lead to changes seen on the placenta of preeclamptic mothers(Salmani et al., 2014). The healthy placenta is essential for a healthy pregnancy. Conversely, abnormal placenta structure and function is seen in conditions such as Hypertensive Disorders of Pregnancy (HDP). These abnormalities can range from a reduction in placental size to microscopic changes in placenta villous architecture. These can lead to poor fetal outcomes such as intrauterine growth restriction, prematurity, stillbirth and low birthweight (Heazell, 2015).

1.2 PROBLEM STATEMENT

Hypertensive disorders in pregnancy (HDP) represent some of the important problems faced by public health because is a major cause of maternal and prenatal morbidity and mortality especially in resource limited settings. The prevalence of HDP, gestational hypertension and pre-eclampsia globally are 5.2%-8.2%, 1.4%-4.4% and 0.2%-9.2% respectively (Umesawa and Kobashi, 2017). The hypertensive disorders of pregnancy affect about 10% of pregnant women in Africa (Noubiap et al., 2019). Pre-eclampsia/eclampsia is a major cause of maternal deaths contributing about 19.9% of all maternal deaths at Muhimbili National Hospital in Dares-salaam, Tanzania (Pembe et al., 2014). The healthy placenta is essential for a healthy pregnancy. Conversely, abnormal placenta structure and function is seen in conditions such as Hypertensive Disorders of Pregnancy (HDP). These abnormalities can range from a reduction in placental size to microscopic changes in placenta villous architecture. These can lead to poor fetal outcomes such as intrauterine growth restriction, prematurity, stillbirth and low birthweight(Heazell, 2015). Hypertensive disorders of pregnancy exert great impact on placenta and thus reflects changes both morphological and histological (Bandekar and Kale, 2018). Some studies have shown that the mean placenta weight, mean number of cotyledons were significantly lower in placenta of hypertensive pregnant mothers compared to normotensivepregnant mothers. Irregular shaped placenta were more common in hypertensive group. Histologically syntial knots, cytotrophoblastic cellular proliferation, hyalinized area, proliferation of medium sized blood vessels, stromal fibrosis and fibrinoid necrosis was significantly higher in hypertensive group (Chhatwal, Chaudhary and Chauhan, 2018). These studies done on this topic, most of them have been done among Caucasians. This study was not done in our settings. These features were from studies done among Caucasians and we didn't know if these differences existed in our population because none of the studies involved our population and these studies have shown different findings in different populations even among Caucasians.

1.3CONCEPTUAL FRAMEWORK.

The following was the conceptual framework in which the independent variable was the hypertensive status of the pregnant woman and the dependent variables were morphological and histological features of the placenta.



1.4 RATIONALE

Placental changes and variations have an important impact on fetal wellbeing and pregnancy outcome and these changes are affected by the hypertensive status of the pregnant woman hence it is important to study the morphological and histological changes of placenta of hypertensive pregnant mothers. There were very few studies done on this topic and most of them were done among Caucasians. This study was not done in our settings. We did this study in order to see if these differences existed in our setting and to add knowledge on this topic. We expected the knowledge obtained to increase awareness on placental impact of the disease particularly with reference to our population and to make comparative analysis with other populations. Also we expected the knowledge obtained to be a stepping stone towards studying the association of these features with fetal outcomes and maternal outcomes. This study was also conducted as a partial fulfillment of the requirement for the degree of Master of Science in human anatomy (MSc. Anatomy) of the Muhimbili University of Health and Allied Sciences (MUHAS).

1.5 RESEARCH QUESTION

Is there any morphological and histological difference between placentas of hypertensive pregnant mothers and placentas of normotensive pregnant mothers?

1.6 RESEARCH OBJECTIVES

1.6.1 Broad objectives.

- To compare gross morphological and histological features of placentas between hypertensive pregnant mothers and non-hypertensive pregnant mothers attending Muhimbili National Hospital

1.6.2 Specific objectives.

- i. To compare the morphometry of placentas between hypertensive pregnant mothers and non-hypertensive pregnant mothers attending Muhimbili National Hospital
- To compare the histological features of placentas between hypertensive pregnant mothers and non-hypertensive pregnant mothers attending Muhimbili National Hospital.

1.7 LITERATURE REVIEW

Hypertensive disorders in pregnancy (HDP) represent some of the important problems faced by public health because is a major cause of maternal and prenatal morbidity and mortality especially in resource limited settings. They are associated with increased risk of adverse outcomes to both mother and fetus and the common ones are; placenta abruption, intrauterine fetal growth restriction (IFGR), premature delivery and stillbirth, thus, form one of the deadly triad along with hemorrhage and infection(Umesawa and Kobashi, 2017).The maternal and fetal status are reflected on the placenta thus, placenta is a predictor of outcome of pregnancy. Hypertensive disorders of pregnancy exert great impact on placenta and thus reflects changes both morphological and histological changes. (Bandekar and Kale, 2018).

1.7.1Morphometrical review

In the study which was done by Yibeltal et al., 2017 at Gandhi Memorial and Black lion Specialized Hospitals, Addis Ababa, Ethiopia with the objective of assessing the macro architectural changes of placenta in pre-eclampsia mothers as compared to normotensive mothers revealed that the majority of the placenta of the pre-eclamptic mothers and normotensive mothers grossly were circular in shape. The majority of the irregular shaped placenta were obtained from the pre-eclamptic mothers. The placenta weight and number of cotyledons were significantly decreased in pre-eclamptic mothers as compared to normotensive of finding out the morbid changes in the placenta of hypertensive mothers in comparison with normal pregnancy revealed that the morphometry of placenta (mean placenta weight and number of cotyledons) were significantly less in hypertensive group as compared to normotensive group. The marginal insertion of the umbilical cord was significantly higher in hypertensive group compared to normotensive group. (Nag et al., 2013).

In the study done by Goswami et al., 2016at Obstetrics and Gynecology Department at Bhavnagar tertiary care hospital in Indiawith the objective of studying gross changes of placenta in mothers with pregnancy induced hypertension and compare with mothers with normal blood pressure showed that the placenta from mothers in the hypertensive group had significantly altered shapes like oval and irregular whereas the placenta from mothers in the normotensive group had circular shape in majority. The attachment of umbilical cords were more marginal and eccentric than central in the hypertensive group. The mean cotyledon number, placental weights were less in hypertensive group compared to normotensive group.(Goswami et al., 2016)In the study which was done by Sankar et al., 2013 in the Department of Anatomy in Narayana Medical college in India with the objective of comparing morphological and histomorphometrical changes in placentas from mothers with pre-eclampsia with those in placentas from normotensive mothers, in relation to the surface area and diameter of terminal villi (TV) and blood vessels, gross placental morphometrical study showed that the mean placenta weight was significantly lower in the placentas with pre-eclampsia as compared to placentas from normotensive mothers(Sankar et al., 2013)

Chhatwal et al., 2018 did the study in the department of Obstetrics and Gynecology in collaboration with the Department of Pathology, Himalayan Institute of Medical Sciences in India with the objective of investigating the morphological and histological changes in the placenta in hypertensive pregnancyrevealed that the mean placental weight of the hypertensive mothers was significantly higher than that of the normotensive mothers(Chhatwal et al., 2018)In the study done by Salmani et al 2014 in the department of Anatomy in collaboration with the department of Obstetrics and Gynecology S.V.S Medical College, a tertiary care hospital, Mahabubnagar, Andhra Pradesh in India with the objective of studying the morbid changes in placenta in cases of Pregnancy Induced Hypertension (PIH) showed that the weight of the placenta was less in pre-eclamptic and eclamptic mothers as compared to placenta of the normotensive mothers. The majority of placentas were oval and the rest were round and irregular in shape. The majority of the placenta had eccentric insertion of the umbilical cord while the rest had central insertion of the umbilical cord. The number of cotyledons varied from 18 to 23 in all groups(Salmani et al., 2014).

1.7.2Histological review

In the study done by Parmar et al., 2019 in Anatomy Department of SBKS Medical College and Research Centre, Vadodara with the objective of evaluating histological changes of placenta in hypertensive pregnancies revealed the presence of calcification, infarction, fibrinoid necrosis, villous hyalinization, syncytial knots and cytotrophoblastic cellular proliferation in both hypertensive pregnant mothers and normotensive pregnant mothers however these histological features were seen more in hypertensive mothers.(Parmar et al., 2019)In the study done by Salmani et al., 2014 in the department of Anatomy in collaboration with the department of Obstetrics and Gynecology S.V.S Medical College, a tertiary care hospital, Mahabubnagar, Andhra Pradesh in India with the objective of studying the morbid changes in placenta in cases of Pregnancy Induced Hypertension (PIH), histological study of placenta showed significant number of syncytial knots, fibrinoid necrosis, areas of calcification and hyalinization and areas of medial coat proliferation of medium sized blood vessels in the hypertensive pregnant mothers(Salmani et al., 2014).

Nag et al, 2013 did the study with the objective of finding out the morbid changes in the placenta of hypertensive mothers in comparison with normal pregnancy ; histological evaluation showed that the number of syncytial knots, cytotrophoblastic cellular proliferation, fibrinoid necrosis, endothelial proliferation, calcified and hyalinised villous spots were significantly higher in hypertensive group compared to normotensive group(Nag et al., 2013). In the study which was done by Sankar et al, 2013 in the Department of Anatomy in Narayana Medical college in India with the objective of comparing morphological and histomorphometrical changes in placentas from mothers with pre-eclampsia with those in placentas from normotensive mothers , in relation to the surface area and diameter of terminal villi (TV) and blood vessels, histological evaluation come up with the following findings; perivasculitis (PV) of fetal vessels, thrombosis and atheromatous plaque (AP) formation in the fetal vessels, perivillous fibrin (PVF) deposition in the placentas with pre-eclampsia.(Sankar et al., 2013).

Chhatwal et al, 2018 did the study in the department of Obstetrics and Gynecology in collaboration with the Department of Pathology, Himalayan Institute of Medical Sciences in India with the objective of investigating the morphological and histological changes in the placenta in hypertensive pregnancy histological study of the placentas of hypertensive mothers

revealed syncytial knots, cytotrophoblastic cellular proliferation, hyalinized area and proliferation of medium sized blood vessels, stromal fibrosis and fibroid necrosis was significantly higher among the hypertensive mothers.(Chhatwal, Chaudhary and Chauhan, 2018)In the study done by Tateishi et al., 2018, at the Shinshu university Hospital Matsumoto in Japan with the objective of evaluating histopathological features of pregnancy induced hypertensive pregnant mothers were multiple infarctions, acute atherosis from incomplete remodeling of spiral arteries, distal villous hypoplasia and increased syntial knots reflecting placental hypoxia or ischemia(Tateishi et al., 2018).In the study done by Kartha et al, 2014 at department of Pathology, Government Medical College Kottayam in India with the objective of studying morphometric features, gross and histological changes of placenta in pregnancy induced hypertension (PIH) irrespective of the severity the following histological findings were revealed; atherosis, fibrinoid necrosis, endothelial proliferation, calcification and infarction.

CHAPTER TWO

2.0 MATERIALS AND METHODS

The chapter included research approach and techniques applied from sample and sampling technique, data collection, data analysis and interpretation. The research design covered the reasons for data sources, data analysis and a brief note on ethical issues.

The study was conducted for the period of 4months from June 2020 to September 2020, after clearance from the MUHAS Ethical Committee.

2.1. STUDY DESIGN, STUDY POPULATION AND STUDY AREA

2.1.1 Type of study:

The type of study conducted wascomparative cross sectional study.

2.1.2Study population:

All Pregnant women admitted in maternal block at Muhimbili National Hospital (MNH) at gestational age of 34 to 42weeks.

2.1.3Study area

Muhimbili National Hospital (MNH) Department of Obstetrics and Gynecology in collaboration with the Department of Anatomy Muhimbili University of Health and Allied Science located in Dar-es-salaam, Tanzania.

2.1.4Study settings

The study was conducted at Muhimbili National hospital, and teaching hospital for Muhimbili University of Health and Allied Sciences. It caters for a population of about 4.4 million Dar es Salaam residents and referred patients from up-country. The hospital receives patients from 3 Regional hospitals and other hospitals within the city and upcountry. Being a tertiary hospital it receives many patients with severe morbidities that need specialized care.

The department of obstetrics and gynecology has 6 units which includes General obstetric unit, General gynecology unit, acute care unit /fetal maternal medicine unit, Gynecology oncology unit, Urogynecology unit and Reproductive endocrinology and infertility unit. The general obstetric unit has 4 firms namely firm I, II, III and IV, the unit has more than four wards including ward 41, 42 and annex.

These firms admit patients with variety of conditions including Pregnancy induced hypertension, patients for prenatal care, intranatal care and post-natal care, puerperal psychosis, puerperal sepsis, anemia in pregnancy, UTI in pregnancy etc. Each firm runs an outpatient clinic to follow up patients attending antenatal care including those discharged from the wards and new patients referred from other centers but do not need admission. During clinic days, pregnant women are supposed to report at 07:00hrs whereby the new patients have to start with registrations. Then all pregnant women the new ones and follow ups are given health education followed by measuring their blood pressure and body weight. After taking their blood pressures they are attended one by another by their respective doctors. The routine laboratory tests taken are; tests for malaria parasites, hemoglobin level, blood group, syphilis and urinalysis including protein in urine.

Maternity unit accept pregnant women straight from home as well as referral from all regional and district hospital in the city. The hospital has 2 maternity blocks which comprises of 7 wards; labor ward, antenatal and postnatal wards and private wards with each ward having a bed capacity of 50 beds, cases with severe preeclampsia, eclampsia are admitted in preeclampsia ward 35 where the ICU ward is where critically ill patients are admitted. The main maternity block is situated close to the theatre block. There are four fully functional theatres. Two for emergencies and two for elective procedures. It is estimated to conduct about 9,000 total deliveries per year

2.2 SAMPLE SIZE AND SELECTION

2.2.1 Sample Size

The sample size was calculated using the prevalence of 25% obtained in a study done by Noubiap et al., 2019 which aimed at determining the burden of hypertensive pregnancy disease in Africa(Noubiap et al., 2019)

Estimated sample size was calculated using the following formula;

N per grp = $(p_0q_0 + p_1q_1) (z_{1-\alpha/2} + z_{1-\beta})^2$

$$\left(p_{1\,-}\,p_{0}\right) ^{2}$$

Where

- N= Sample size
- $p_0 =$ proportion with characteristic in group 1
- $q_0 = (1 p_0)$ proportion without characteristic in group 1
- p_1 = proportion with characteristic in group 2
- $q_1 = (1 p_1)$ proportion without characteristic in group 2
- $z_{(1-\alpha/2)}$ = value of the standard normal distribution corresponding to a significance level of α (1.96 for a 2-sided test at the 0.05 level)
- $Z_{(1-\beta)}$ = value of the standard normal distribution corresponding to the desired level of power (0.84 for a power of 80%, 1.28 for power of 90%)

N per group= $(0.25x0.8) + (0.5x0.5) (1.96+1.28)^2$

$$(0.5-0.25)^2$$

N per group=40

So we had 40 hypertensive pregnant mothers and 40 normotensive pregnant mothers

The minimum of 80pregnant women were included in the study.

Therefore the total number of specimens to be studied in the present study was 80, where 40 placentas from normotensive mothers which was taken as control group and 40 placentas from gestational hypertensive pregnant mothers which was taken as study group.

2.2.2 Sampling technique

Convenient sampling technique was applied; this is also known as availability sampling and is a specific type of non-probability sampling method that relies on data collection from population members who are conveniently available to participate in study.

2.2.3Inclusion criteria:

- 1) Placentas of women who were diagnosed to have pregnancy hypertensive disease.
- Placentas of women who had normal pregnancy with no pregnancy induced hypertension as controls.

2.2.4Exclusion criteria:

- 1) Placentas of women who had other associated condition like gestational diabetes mellitus, hypothyroidism.
- 2) Mothers who had positive VDRL and severe anemia

2.3 VARIABLES

2.3.1 Independent variable

In our study the independent variable was the hypertensive status in pregnancy that is having hypertensive pregnant disease or not having hypertensive pregnant disease.

2.3.2 Dependent variable

In our study the dependent variables which have have been measured are shape of placenta, site of insertion of umbilical cord to the placenta, thickness of placenta, weight of placenta, number of cotyledons, presence of fibrinoid necrosis, presence of syntial knots, presence of calcifications.

Weight of the placenta was obtained by weighing with automatic weighing machine.

Presence of infarctions, presence of syntial knots, presence of calcifications, and presence of fibrinoid necrosis were obtained by histological examination under microscope.

Research assistants

There weretwo research assistants (one nurse and one midwife) who were working in the maternal block and were trained by the principal investigator for one day. The training was entailed to explain the following;

- I. Objectives of the study
- II. How to get consent from the participants by explaining to the pregnant women the aim of the study and having freedom to participate or not to participate in the study
- III. How to get information from ANC card such as previous blood pressure record. This was accomplished by passing through the ANC card on specific areas which are blood pressure record area.
- IV. How to measure blood pressure, whereby blood pressure was measured by automatic blood pressure machine at the left arm of a pregnant woman. Demonstration was done to the Research assistants and then they did it independently in order to assess their practical skills obtained.
- V. How to describe morphological appearance of the placenta that is to be able to describe shape weather ovoid or irregular, site of attachment of the umbilical cord on the placenta, how to measure thickness by calibrated pin, how to measure weight of the placenta by automatic weighing machine.
- VI. How to cut a piece of the delivered placenta and immerse it into a labelled bottle with formalin. This was done by surgical blade.

2.4DATA COLLECTIONMETHODS

During the study period, the information sharing and health sensitization were done. The pregnant women who were met during the course of the study weregiven health education about hypertensive pregnant disease and informed about the study objectives and benefits. The health education was being given throughout the study period to all pregnant women met. Pregnant women who met criteria and recruited in the study were requested to provide written consent and information required documented which aregestational age and hypertensive

15

status that is Hypertensive Pregnant Woman (HPW) and non-hypertensive pregnant woman (NHPW). Then we waited the pregnant women who have consented after delivery their placentas were taken for study. In the labor ward or in the surgical theater their placenta were studied and the gross features which were shape, site of insertion of umbilical cord, weight and thickness were documented and a piece of it was cut and stored in the bottle containing formalin 10% for fixation and other histological procedures were carried out in histological laboratory in Anatomy department. All of these was done by researcher or research assistants.

2.4.1 Blood pressure measurement

In our study we used the British and Irish Hypertension Society (BIHS) and European Society of Hypertension (ESH) recommendations related to BP measurement technique to ensure reliability, we ensured;

- resting for at least five minutes prior to BP measurement.

-sitting upright with the arm supported and the cuff placed at the level of the heart.

- using the appropriately sized cuff.

-deflating the cuff at a rate of 2 mmHg to 3 mmHg.

2.4.1 Collection and gross examination of placenta:-

The placenta with attached membranes and umbilical cord from pregnant women recruited in the study were collected soon after delivery either by normal vaginal delivery or by caesarean section washed in running tap water to clean all blood. Maternal surface was inspected for its completeness, calcification and infarction.

The shape of placenta was ascertained by stretching it flat on the cutting board. Umbilical cord was examined for its site of attachment to the fetal surface. The number of the placental cotyledons were documented. The membranes were cut off the edge of placenta with the knife. The placenta was then weighed in weighing machine calibrated in grams.

Thickness of placenta was measured by piercing a needle through the center at the margin and midway between the center and margin. The average of the three readings was taken as the thickness of the placenta.

Placenta was cut into 2cm vertical sections from maternal to fetal surface to ensure adequate fixation. Sections were collected in tagged containers with 10% Neutral Buffered Formalin (**NBF**) and taken to the department of Anatomy for histological examination.

2.4.2 Light Microscopic examination.

2 cm wedge placental tissue was taken and fixed in cold 10% buffered neutral formalin for 2 weeks. Tissue was thoroughly washed in running tap water before processing. Then the tissues subjected for dehydration with gradual concentrations of 70%, 80%, 90% and absolute alcohol for two hours in each at room temperature. Specimens was then be cleared by passing through two sets of chloroform for three hours each. Paraffin wax embedding wasbe done. 5-7 μ m sections were taken with microtome.

Tissue sections were stained with Hematoxylin & Eosin (H&E).

Histological appearances of terminal villi of placentas were assessed. The terminal villi were counted in each block. Villous counts were made for various morphologic findings, principally trophoblastic basement membrane thickening, syncytial knots, and fibrinoid necrosis.

The results were expressed as percentage incidence for both control and study group

2.5 DATA COLLECTION TOOL.

In our study data collection tool was structured checklist. Itwas made of three main parts. The first part was evaluating the Gestational age of the pregnant woman which was obtained from last normal menstrual period in the Antenatal clinic (ANC) card and getting identification number and categorized her as hypertensive pregnant woman or non-hypertensive pregnant woman.

The second part was determining the gross morphological features of placenta. The third part was determining the histological features of placenta.

2.6 DATA MANAGEMENT AND ANALYSIS

We created identification numbers such as N1 and HTN1 and were used as identities in order to maintain the confidentiality of the study participants. At the end of filling each checklist it was cross checked for completeness and any missing entries was corrected. Data quality check for inconsistence was done on daily bases. Collected data was stored in secure files and locked away only to be accessible by the investigator and authorized personnel. The raw data that was in physical storage was transferred into an electronic form that is in passwordprotected computers for cleaning and data analysis. Accessibility to all storage formats was only under the strict supervision of the investigator whilst ensuring all ethical issues were taken into consideration.

Statistical Package of Social Sciences (SPSS) computer software version 20 was used to analyze the data. Descriptive statistics such as proportions for categorical variables and means for continuous variables wasestimated. Statistical significance of difference between two groups in the aspect of the data that will be expressed in ' means' such as weight of placenta, thickness of placenta, number of cotyledons was calculated by using Students "t" test. A difference between the two groups will be considered to be significant when p<0.05. In the aspect of the data that will be expressed in percentage such as shape of the placenta, site of insertion of umbilical cord, presence of fibrinoid necrosis, presence of syntial knots and presence of villous hypoplasia statistical significance of difference between two groups were calculated by using chi-square test. A difference between two groups were considered to be significant when p<0.05.

2.7 ETHICAL ISSUES

2.7.1 Ethical clearance

Ethical clearance was sought from the MUHAS research and publication committee and the permission to conduct the study was requested from the authority of Muhimbili National Hospital and maternal.

2.7.2Ethical Consideration

Prior to the recruitment of the study participants, the pregnant women eligible for the study wereasked to give a written informed consent for their participation in the study. This was done after explaining the purpose of the study, procedures, and benefits of participating in the study. They were informed that the findings of the study were helpful in increasing awareness on placental impact of the disease particularly with reference to our population. Also knowledge obtained would be a stepping stone towards studying the association of these features with fetal outcomes and maternal outcomes. Pregnant women were given the opportunity to ask questions prior to the consenting and at the end of each data collection session. They were informed of the voluntary nature of participating in the study and that they would opt out at the beginning or at any time during the study without any penalty or loss of any right in the course of her management in the hospital. Confidentiality was ensured through the use of patient registration numbers instead of their names to conceal their identities. Unauthorized individuals were not allowed to access the data that was collected by protecting the data by lock and key.

The pregnant women identified to have hypertensive disorder of pregnancy (HDP) wereinformed about their hypertensive status and got assured that they will get the management appropriate to her condition. The care givers of the appropriate ward wereinformed so as to start or continue with the management of the condition according to the protocol.

The delivered placentas of the pregnant women included in the study were studied grossly in the labor ward or Obstetrics Theater and the information filled on the checklist of the appropriate participants. The section of the placenta was cut using a surgical blade and was immersed in the labelled formalin containing bottle with the registration number of that specific participant and the remaining placenta was sent for incineration in Muhimbili National Hospital so as to ensure proper disposal. The bottles with specimen were locked in the storage container either in the obstetric theater or in labor wards and at the end of each day they were transferred from labor ward or obstetric theater in the specimen container to the histology laboratory in Muhimbili University of Health and Allied Sciences (MUHAS) on foot. All of these was to ensure safety and confidentiality of specimen.

CHAPTER THREE

3.0 RESULTS

In our study, 80 placentae, 40 from normotensive and 40 from hypertensive mothers were used.

3.1 MATERNAL CHARACTERISTICS

The age range of these mothers was between 18 years and 36 years. In both groups the majority of mothers belonged to the age group between 20 years to 30 years that is 70% of normotensive pregnant mothers and 55% of hypertensive pregnant mothers fell in this age group. There was predominance of prim gravida in the hypertensive group that is 67.5% and this difference was statistically significant (p=0.007). In the hypertensive group, 72.5% subjects delivered at pre term in contrast to the normotensive group, 77.5% females delivered at full term. Statistically, a significantly higher number of females delivered preterm in hypertensive group (0.000). Hypertensive group had significantly higher blood pressure with mean systolic blood pressure of 157.65 ± 10.82 mmhg and normotensive group had 121.00±10.04mmhg and the mean weight of the pregnant mothers in each group was approximately the same.

Study parameter	Normotensive group		Hypertensive group	P value	
Mean weight of pregnant women	64.33±7.97		66.08±7.03	0.3	
(kg)	07.35-1.77				
Mean systolic blood					
pressure (mmhg)	121.00±10.04		157.65±10.82	0.000	
Mean diastolic					
blood pressure	76.33±8.45		106.23±8.23	0.000	
(mmhg)					
	N (%)		N (%)		
Age of pregnant	<20	2	4		
woman in years	(5%)		(10%)		
	20 - 30	28	22	0.423	
		(70%)	(55%)		
	>30	10	14		
		(25%)	(35%)		
Gravid status of	prim gravid	14	27		
pregnant woman		(35%)	(67.5%)	0.007	
	Multigravida	26	13		
		(65%)	(32.5%)		
Gestational age at	Preterm (34 to	9	29		
delivery in weeks	36) (22.5%)		(72.5%)		
	Full term (37	31	11	0.000	
	and above)	(77.5%)	(27.5%)		

Table 1 Maternal characteristics betw	een hypertensive and normotensive groun
Table 1. Maternal characteristics betw	een hypertensive and normotensive group

3.2 GROSS MORPHOLOGICAL FEATURES

The irregular shape of the placenta was more predominant in the hypertensive group and it was statistically significant. (p=0.001) The marginal insertion of the umbilical cord was more in hypertensive group and it was statistically significant (p=0.000)

The mean placenta weight, mean placenta thickness and mean number of cotyledons were significantly less in the hypertensive group compared to normotensive group. (p=0.000)

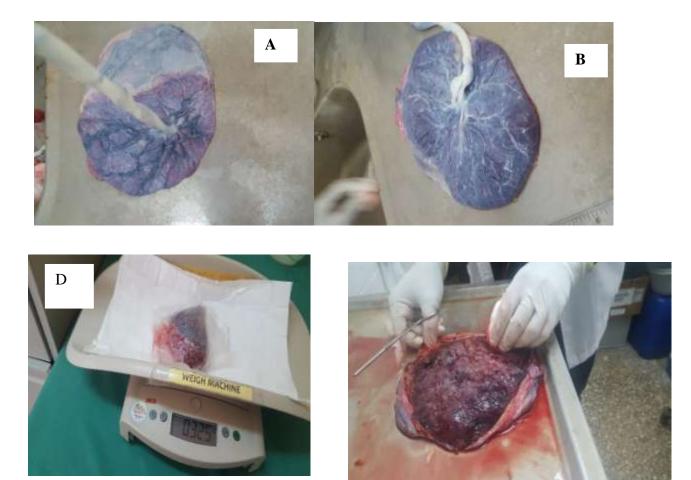


Fig 2: Gross morphological features of the placenta

- A:Placenta with marginal insertion of umbilical cord showing the fetal surface view.
- B: Placenta with central insertion of umbilical cord.
- C: Weighing placenta with weigh machine.
- D: Irregular shaped placenta showing maternal surface

Table 2. Gross morphological features of placenta between hypertensive andnormotensive group

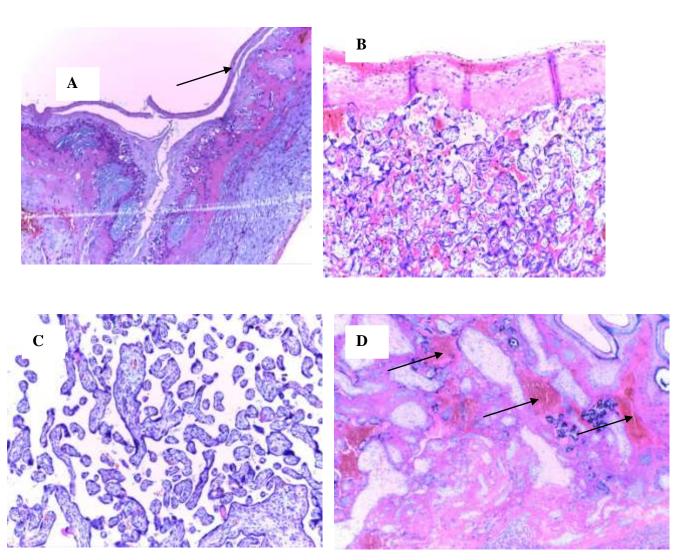
Study parameter	Normotensive group		Hypertensive group	p-value
Mean weight of placenta (kg)	548.13±44.33		398.28±71.1	0.000
Mean thickness of placenta (cm)	3.10±0.15		2.28±0.25	0.000
Mean number of cotyledons	18.50±1.20		16.10±0.87	0.000
	N (%)		N (%)	
Shape of placenta	Ovoid 31 (77.5%)		15 (37.5%)	0.001
	Not ovoid	9 (22.5%)	25 (62.5%)	
Site of insertion of umbilical	Central	34 (85%)	17 (42.5%)	0.000
cord	Not central	6 (15%)	23 (57.5%)	

3.3 HISTOLOGICAL FEATURES OF PLACENTA

Microscopic study of the placenta revealed the presence of fibrinoid necrosis, syntial knots, calcifications and villous hypoplasia in both normotensive and hypertensive group, however these findings were significantly higher in the hypertensive group than in the normotensive group. (P > 0.01)

Table 3. Comparison of placental histological features in hypertensive and normotensive
group

Parameter	Presence/absence	Normotensive		Hypertensive		
		group		group		P value
		N	%	N	%	
Fibrinoid	Present	19	47.5%	32	80.0%	
necrosis	Absent	21	52.5%	8	20.0%	0.005
Syntial knots	Present	24	60.0%	36	90.0%	
	Absent	16	40.0%	4	10.0%	0.004
Calcifications	Present	9	22.5%	27	67.5%	
	Absent	31	77.5%	13	32.5%	0.000
Villous	Present	8	20.0%	26	65.0%	
hypoplasia	Absent	32	80.0%	14	35.0%	0.000

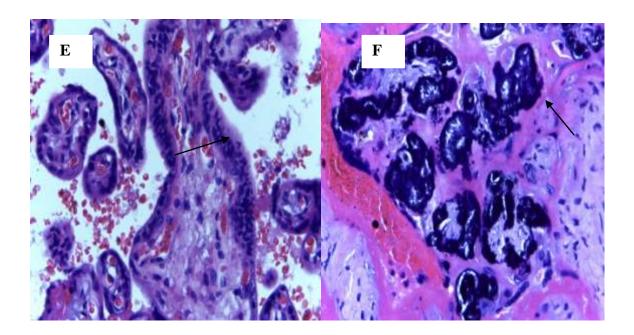




A: Fetal surface of the placenta x 10. It is made of single layered epithelium, the amniotic cells. B: Maternal surface of the human placenta x10 magnification. It is incised by placental septa forming cotyledons.

C: Normal chorionic villi micrographic appearance.

D: Fibrinoid necrosis x 4. There is deposition of fibrin surrounding the crowded chorionic villi.



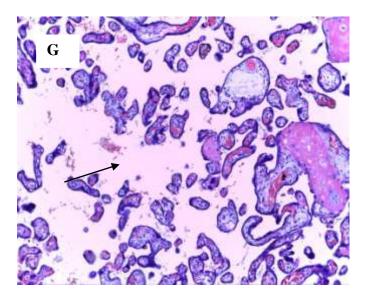


Fig 4: Photomicrographs of the placenta by stained by Haematoxylin and Eosin.

E: Syntial knots x 40. These are recognized as aggregates of snyntiotrophoblastic nuclei.

- F: Placental calcification x40.
- G: Villous hypoplasia, smaller and slender villi with wide intervillous space.

CHAPTER FOUR

4.0 DISCUSSION

Hypertensive disorders of pregnancy exert great impact on the placenta thus affect it morphologically and histologically.

In our study there was predominance of prime gravida in the hypertensive group and was statistically significant with p value=0.007. Prime gravida is one of the etiological factors of hypertensive disorders of pregnancy and this was confirmed in our study since the majority of mothers with hypertensive disorder of pregnancy were prim gravida. This finding is also confirmed by other previous studies(Kambale *et al.*, 2016)(Parmar, Shah and Alamchandani, 2019) Hypertensive group had significantly high blood pressure with mean systolic blood pressure and diastolic blood pressure of 157.65 ± 10.82 mmhg and 106.23 ± 8.23 mmhg respectively. Parmar *et al*, 2019 has reported significantly high blood pressure in the hypertensive group as compared to normotensive just as it was observed in our study (Parmar, Shah and Alamchandani, 2019) Our study revealed that preterm deliveries were significantly high in the hypertensive group as compared to normotensive group. This might be attributed by the vulnerability of mothers with hypertensive disorders of pregnancy to premature delivery that is in some circumstance the pregnant woman should be delivered irrespective of gestation age. This finding in our study is in concordance with other studies(Parmar, Shah and Alamchandani, 2019)

The placental weight is functionally important parameter as it reflects the villous area and fetal metabolism(Communication, 2017) Our study revealed that the mean placental weight in hypertensive group and normotensive group were 548±44.33gm and 393.28±28.71gm respectively. This mean placental weight was significantly less in hypertensive group as compared to normotensive group (p=0.000). These observations correlate well with the previous studies done by various workers(Sankar *et al.*, 2013)(Nag and Vk, 2013)(Goswami and Shah, 2016)(Ashfaq, Janjua and Channa, 2005)(Salmani *et al.*, 2014)(Kambale *et al.*, 2016)(Kartha, Poothiode and P S, 2014). These findings may be attributed by marked reduction in the blood flow in the maternal intervillous space.

Though the placenta adapts well to the hypoxic condition in the hypertensive disorders of pregnancy, these compensatory changes that occur are insufficient. These compensatory changes cause underdevelopment and inadequate placental mass(Sankar *et al.*, 2013). The results obtained from our study revealed that the mean placental weight was more decreased as compared to the previous studies and this may be attributed by genetic and geographical differences.

In our present study mean placenta thickness in the hypertensive group and normotensive group were 3.10±0.15cm and 2.28±0.25cm respectively. Thickness of the placenta was significantly decreased in the hypertensive group as compared to normotensive group (p=0.000). This finding was concordance with previous studies(Communication, 2017)(Chhatwal, Chaudhary and Chauhan, 2018). In our study the mean placental number of cotyledons was 16.10 ± 0.87 in hypertensive group and 18.50 ± 1.20 in normotensive group, so the number of cotyledons was significantly less in hypertensive group. This finding was concordance with findings from other investigators(Goswami and Shah. 2016)(Communication, 2017).

In our study the irregular shape of the placenta and marginal insertion of umbilical cord were statistically more in hypertensive group. Goswami and Shan have reported the same finding(Goswami and Shah, 2016), however Ashafaq *et al*, revealed that the placenta were roughly oval with central attachment of umbilical cord in all groups and this finding may be attributed by small sample size that is 20 placenta from hypertensive group and 20 from normotensive group(Ashfaq, Janjua and Channa, 2005).

In our study microscopic examination of the placenta revealed the presence of fibrinoid necrosis, syntial knots, calcifications and villous hypoplasia in both hypertensive group and normotensive group however they were significantly more in the hypertensive group. Fibrinoid necrosis was seen in 80% and 47.5% in hypertensive and normotensive group respectively. Calcifications noted in 67.5% and 22.5% in hypertensive and normotensive group respectively. Villous hypoplasia was noted in 65% and 20% in hypertensive and normotensive and normotensive group respectively.

A significant increase in fibrinoid necrosis, infarction and villous hypoplasia in placental tissue in the hypertensive group indicates the disturbance in the blood flow. Reduction in blood flow is due to vasculopathies of the spiral arteries, that is maternal vasospasm. These findings were in line with the findings of previous studies(Salmani *et al.*, 2014)(Tateishi *et al.*, 2018)(Goswami and Shah, 2016)(Sankar *et al.*, 2013)(Kartha, Poothiode and P S, 2014). Syntial knots were noted in 90% and 60% in hypertensive group and normotensive group respectively. This finding was significantly higher in hypertensive group as compared to normotensive group. This finding was in line with the observations revealed by other authors(Parmar, Shah and Alamchandani, 2019)(Salmani *et al.*, 2014). This observation may be attributed by reduced blood flow through villi results in stromal fibrosis and thus excess syntial knot formation and thus reflecting placental hypoxia/ischemia.

CONCLUSION

Prim gravida females were among commonly affected group by hypertensive disorders of pregnancy (HDP).Hypertensive disorders of pregnancy (HDP) exert profound impact on placenta. Significant changes in gross morphology have been observed more in hypertensive group.Reduction of weight, numbers of cotyledons and altering its dimensions including shape of placenta and site of insertion of umbilical cord have been observed more significantly in hypertensive group. They induce histological changes including fibrinoid necrosis, calcifications, syntial knots and villous hypoplasia. Thus the pregnant women with pregnancy disorders of pregnancy have increased chance of ischemic damage to the placental tissue along with maldeveloped terminal villi.

RECOMMENDATION

Screening of the pregnant women for the Hypertensive Disorders of Pregnancy (HDP) and proper and effective management of the pregnant women with hypertensive disorder of pregnancy (HDP) is of paramount importance since we have found significantly more placental ischemic lesions which are fibrinoid necrosis and calcifications which threaten the fetal outcomes.

Further studies should be done on the association of the gross and histological features and fetal and maternal outcomes.

REFERENCES

Ashfaq, M., Janjua, M. Z. and Channa, M. A. (2005) 'Effect of gestational diabetes and maternal hypertension on gross morphology of placenta.', *Journal of Ayub Medical College, Abbottabad : JAMC*, 17(1), pp. 44–47.

Avagliano, L. *et al.* (2016) 'Histology of Human Placenta ABSTRACT', pp. 1–15. Available at: www.smgebooks.com.

Bandekar, P. K. and Kale, P. B. (2018) 'Placenta in pregnancy induced hypertension', 7(2), pp. 467–469.

Chhatwal, J., Chaudhary, D. N. and Chauhan, N. (2018) 'Placental changes in hypertensive pregnancy: a comparison with normotensive pregnancy', *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 7(9), p. 3808. doi: 10.18203/2320-1770.ijrcog20183799.

Communication, O. (2017) 'Gross morphological study of placenta in preeclampsia', *Anatomy Journal of Africa*, 6(2), pp. 977-981–981.

Goswami, P. R. and Shah, S. N. (2016) 'Placenta in Normal and Pregnancy Induced Hypertension in Relation to its Clinical Significance : A Gross Study', 4(7), pp. 58–61. doi: 10.17354/ijss/2016/526.

Heazell, A. (2015) 'The placenta and adverse pregnancy outcomes – opening the black box?', *BMC Pregnancy and Childbirth*, 15(S1), pp. 14–15. doi: 10.1186/1471-2393-15-s1-a5.

Huppertz, B. (2008) 'The anatomy of the normal placenta', *Journal of Clinical Pathology*, 61(12), pp. 1296–1302. doi: 10.1136/jcp.2008.055277.

Kambale, T. *et al.* (2016) 'Placental morphology and fetal implications in pregnancies complicated by pregnancy-induced hypertension', *Medical Journal of Dr. D.Y. Patil University*, 9(3), p. 341. doi: 10.4103/0975-2870.182505.

Kartha, S., Poothiode, U. and P S, J. (2014) 'Placental Pathology in Pregnancy Induced Hypertension', *Journal of Evolution of Medical and Dental Sciences*, 3(35), pp. 9272–9278. doi: 10.14260/jemds/2014/3197.

Lilungulu, A. G. (2019) 'The effects of maternal Body Mass Index on placental morphology and foetal birth weight : a study from Dodoma Central Region , Tanzania', (August).

Nag, U. and Vk, C. (2013) 'Morphological changes in placenta of hypertensive pregnant women', 3(2), pp. 3–6.

Noubiap, J. J. *et al.* (2019) 'The burden of hypertensive disorders of pregnancy in Africa: A systematic review and meta-analysis', *Journal of Clinical Hypertension*, 21(4), pp. 479–488. doi: 10.1111/jch.13514.

Parmar, K. M., Shah, G. V and Alamchandani, R. R. (2019) 'Histological evaluation of placenta in hypertensive pregnancies', 7(1), pp. 40–45.

Pembe, A. B. *et al.* (2014) 'Maternal mortality at muhimbili national hospital in Dar-es-Salaam, Tanzania in the year 2011', *BMC Pregnancy and Childbirth*, 14(1), pp. 1–7. doi: 10.1186/1471-2393-14-320.

Salmani, D. *et al.* (2014) 'Study of structural changes in placenta in pregnancy-induced hypertension', *Journal of Natural Science, Biology and Medicine*, 5(2), pp. 352–355. doi: 10.4103/0976-9668.136182.

Sankar, K. D. *et al.* (2013) 'Histomorphological and morphometrical changes of placental terminal villi of normotensive and preeclamptic mothers', *Anatomy & Cell Biology*, 46(4), p. 285. doi: 10.5115/acb.2013.46.4.285.

Shah, S. and Gupta, A. (2019) 'Hypertensive Disorders of Pregnancy', *Cardiology Clinics*, 37(3), pp. 345–354. doi: 10.1016/j.ccl.2019.04.008.

Singh, T. and Singh, T. (2015) 'Hypertensive Disorders in Pregnancy (HDP)', *Clinics in Obstetrics*, pp. 301–301. doi: 10.5005/jp/books/12487_10.

Tateishi, A. *et al.* (2018) 'Histopathological findings of pregnancy-induced hypertension: histopathology of early-onset type reflects two-stage disorder theory', *Virchows Archiv*. Virchows Archiv, 472(4), pp. 635–642. doi: 10.1007/s00428-018-2315-3.

Umesawa, M. and Kobashi, G. (2017) 'Epidemiology of hypertensive disorders in pregnancy: Prevalence, risk factors, predictors and prognosis', *Hypertension Research*. Nature Publishing Group, 40(3), pp. 213–220. doi: 10.1038/hr.2016.126.

Wang, Y. and Zhao, S. (2010) Vascular Biology of the Placenta, Colloquium Series on Integrated Systems Physiology: From Molecule to Function.

APPENDIX

Structured checklist

Part 1: hypertensive status

- 1. Pregnant mother identification number
- 2. Gestational age from the ANC card Weeks
- 3. Previous 2 blood pressure measurements from ANC cardmm/hg,mm/hg
- 4. Current blood pressurehg
- 5. Hypertensive status of the pregnant women(has hypertensive pregnant disease or has no hypertensive pregnant disease)

Part2: gross morphological features

6. Shape of the placenta

1 ovoid

2 not ovoid

- 7. Number of cotyledons in a placenta
- 8. Site of insertion of the umbilical cord

1 central 2 not central

- 9. Thickness of placentacm
- 10. Weight of placentagm

Part 3: histological features

- 11. Presence of villous hypoplasia
- 12. Presence of syntial knots
- 13. Presence of calcifications
- 14. Presence of fibrinoid necrosis



CONSENT FORM-ENGLISHMUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCESDIRECTORATE OF POST GRADUATE STUDIESDEPARTMENT OF ANATOMYINFORMED CONSENT FORMCONSENT TO PARTICIPATE IN A STUDYID NO

Greetings! My name is Dr. Antipas Furaha, a student taking Master of Science in Anatomy at Muhimbili University of Health and Allied Sciences undertaking a research project on comparison of gross morphological and histological features of placenta between hypertensive pregnant mothers and non-hypertensive pregnant mothers attending Muhimbili National Hospital.

Purpose of the study

To compare gross morphological and histological features of the placenta between hypertensive pregnant women and non-hypertensive pregnant women attending Muhimbili National Hospital (MNH).

Confidentiality

All the information obtained from you will be treated with utmost confidentiality. No names are going to be included in the structured checklist. All information collected on these forms will be entered into computers with only identification numbers.

Risks and discomfort

Information from your ANC card would take approximately 5 minutes of your time. Blood Pressure measurement would take less than 5 minutes. No pain will be felt on obtaining the Blood Pressure. There is no danger caused by the testing otherwise to you or your unborn child.

Rights to withdrawal

The participant has right to withdraw from the study, refuse her information from the ANC card to be taken, refuse her placenta to be studied or decline the Blood Pressure(BP) test. No punishment will be given for such decision. However your decision will not affect in any way your rights to care and treatment.

Benefits

The participant will benefit from the study by getting management if found to have Hypertensive Disorder of Pregnancy (HDP)

Who to contact

In case you need more information regarding this study please contact the Principal Investigator Dr. Antipas Furaha of Muhimbili University of Health and Allied Sciences P. O Box 65001, Dar es Salaam. If you have questions about your rights as a participant, you may call +255758469233.

Do you agree? I AgreeI don't agree	2
Ι	Have read the contents of
this form and I agree to participate in this study.	
Signature of the participant	
Signature of the Principal Investigator	
Date	



CONSENT FORM-SWAHILI

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES DIRECTORATE OF POST GRADUATE STUDIES DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

FOMU YA RIDHAA

Namba ya utambulisho _____

Ridhaa ya kushiriki kwenye utafiti

Habari! Jina langu **ni Dr. Antipas Furaha** ambaye ni mwanafunzi wa shahada ya uzamili katika idara ya Anatomy katika Chuo Kikuu Cha Afya na Sayansi ya Afya Muhimbili. Ninafanya utafiti kwa mama wajawazito waliolazwa katika Hospitali ya Muhimbili. Naangalia utofauti wa sifa za nje na sifa zinazoonekana kwa kutumia darubini ya mwanga za kondo la nyuma kati ya mama wajawazito walio na ugonjwa wa kupanda kwa shinikizo la damu unaoambantana na ujauzito na mama wajawazito wasio na tatizo la kupanda kwa shinikizo la damu unaoambatana na ujauzito.

Madhumuni ya utafiti

Naangalia utofauti wa sifa za nje na sifa zinazoonekana kwa kutumia darubini ya mwanga za kondo la nyuma kati ya mama wajawazito walio na ugonjwa wa kupanda kwa shinikizo la damu unaoambantana na ujauzito na mama wajawazito wasio na tatizo la kupanda kwa shinikizo la damu unaoambatana na ujauzito.

Usiri

Majina hayatatumika katika utafiti huu, na matokeo ya utafiti yataingizwa kwenye kompyuta kwa kutumia namba.Hivyo taarifa zote zitakazokusanywa zitakuwa za usiri mkubwa.

Hatari

Kuchukua taarifa kadhaa kutoka kwenye kadi yako ya kliniki itatumia kama dakika tano hivi. Kukupima shinikizo lako la damu itachukua kama dakika tano pia.Hutegemewi kupata madhara yoyote katika kushiriki kwenye utafiti huu. Hautahisi maumivu wakati utakapokua unapimwa shinikizo la damu. Kipimo cha shinikizo la damu hakina athari kwako na kwa mtoto.

Uhalali wa kujitoa

Ushiriki katika utafiti huu ni wa hiari. Endapo utachagua kutoshiriki katika utafiti huu hakuna adhabu yoyote utakayopewa. Uamuzi wako wa kushiriki ama la, hautaadhiri hata kidogo haki yako ya kupata huduma nzuri za afya kama raia.

Faida

Faida utakayopata katika utafiti huu ni kujua kama una ugonjwa wakupanda kwa shinikizo la damu unaotokea wakati wa mimba hivyo kupata matibabu.

Mtu wa kuwasiliana nae

Kwa maswali, maoni au malalamiko wasiliana na mtafiti mkuu **Dk. A ntipas Furaha** wa chuo Kikuu cha Afya na Sayansi ya Afya Muhimbili, S. L. P 65001, Dar es Salaam. Kama una swali kuhusu stahili zako kama mshiriki unaweza kupiga simu +255758469233 Unakubali? Mshiriki amekubali________ Mshiriki hajakubali ________ nimesoma maelezo ya fomu hii. Maswali yangu yamejibiwa . Nakubali kushiriki kwenye utafiti huu. Sahihi ya mshiriki _______

Tarehe ya kusainiwa kwa ridhaa _____