1.1 Introduction

Hypertension is the most common medical problem encountered during pregnancy, complicating 2-3% of pregnancies. High blood pressure occurs in 6% to 8% of all pregnancies in U.S, about 70% of which are first time pregnancy. In 1998 more than 146.320 cases of preeclampsia alone were diagnoses. (Michael P Carson et al 2015)

Although many pregnant women with high blood pressure have healthy babies without serious problems, the condition can become a major problem for some pregnant women. High blood pressure can be dangerous for both the mother and the fetus. Women with pre-existing, or chronic, high blood pressure are more likely to have certain complications during pregnancy than those with normal blood pressure. The effects of high blood pressure range from mild to severe. High blood pressure can harm the mother's kidneys and other organs, and it can cause low birth weight and early delivery. In the most serious cases, the mother develops preeclampsia - or "toxemia of pregnancy"--which can threaten the lives of both the mother and the fetus. (Bridget Coila 2013)

While having hypertension during pregnancy can often pass uneventfully, it can cause serious health complications for both mother and developing fetus. According to the CDC, hypertension-related problems during pregnancy are among the leading causes of death for expectant mothers. (Robin Madell 2013)

The fetus brain is one of the most important vital organs in the fetus body so, assessment of the fatal cerebral circulation is essential in the better understanding of pathophysology of wide range of the pathological pregnancy and their clinical management. In general, high blood pressure, or hypertension in pregnancy can be chronic or gestational and contributes to the development of placental insufficiency which leads to fetus hypoxemia and early adaptation by increase of blood to the more vital organs like brain and heart and Decreased blood flow to less vital organs so IUGR for the fetus will present and the cerebral arteries tend to become dilated in order to preserve the blood flow to the brain. Obtaining early diagnosis and regular prenatal care is the most important thing we can do for mother and her baby. (MA Zamorski et al 2001)

Doppler ultrasound is now a day's common in the management of pregnancies complicated with hypertension as an indirect assessment of fetal well-being. However, the value of abnormal umbilical artery Doppler results in predicting poor fetal outcome in hypertensive pregnancies which has been studied in most of patients to investigate the relation between abnormal umbilical artery Doppler velocimetry and fetal outcome in hypertensive pregnancies. (Hung et al 2000)

Doppler ultrasound is also one of the most used imaging modalities in obstetric in order to established a precise diagnosis in fetus cerebral circulation flow redistribution. The earliest detectable change in the course of fetus MCA in maternal hypertension is done by Assessment of blood flow resistance which has become a major tool in evaluation of fetal well-being, (Clerici G et al 2002) mainly in fetuses diagnosed with intrauterine growth restriction (IUGR) (Gramellini D et al 2001)

Fetal blood vessel resistance is assessed by determining indirect indexes based on flow velocity as measured by Doppler studies. (Morris RK et al 2012)

Usually in the clinical management for hypertension pregnancy the fetus blood vessels resistances assessed by detecting the flow velocity indexes .however, the vessels resistances strongly affected by the vessels diameter. (Moore KL et al 1999) .Therefore, this study assess the measurement of blood vessel diameter in order to provide a more sensitive tool for assessing resistance in MCA and compared with conventional Doppler velocimetric indexes.

1.2 Problem of the Study:

Pregnancy induced hypertension is associated with significant fetal morbidity and mortality.MCA PI had low specificity in predicting adverse prenatal outcome. As it depicts first a reduction as a mechanism of defense put in worsening cases the PI raises again as a sign of decompensation.

At the moment there is no evidence; based on RCT, that Doppler flow study on fetal MCA improves the management and outcome.

Taking into account the significance of vessel diameter in regulating resistance to flow, we hypothesized that measurement of blood vessel diameter by using color Doppler would help in increasing the specificity in predicting adverse prenatal outcome with conventional Doppler velocimetric techniques.

1.3 Objectives of the Study:

1.3.1General objective:

To assess whether MCA diameter measurement can be increased as early fetus brain adaptation to hypoxemia in hypertensive mothers.

1.3.2 Specific objective:

- To assess the wall diameter of MCA by using color Doppler ultrasound and correlated with the MCA PI index.
- To evaluate blood flow of MCA by calculation Resistive index (RI) = (PSV-EDV)/PSV pulsatility index (PI) = (PSV-EDV)

- To assess blood flow of UA by calculation Resistive index (RI) = (PSV-EDV)/PSV Pulsatility index (PI) = (PSV-EDV)
- To assess the CPR (MCAPI/UAPI).
- To assess the GA and EFW by measuring PPD, HC, AC and FL.

1.4 Significant of the Study:

The applicability of measuring the fetus MCA width in the assessment of IUGR fetus in singleton high risk pregnancy has not been studied to date. Measurement of MCA width can potentially increase the specificity in prediction of brain sparing in CFH with MCA flow resistance.

1.5 Overview of Study:

The study includes five chapters, chapter one is the introduction include introduction, problem statement, objectives, significant of the study. Chapter two includes theoretical background and literature review of previous studies. Chapter three includes materials and methods of the study. Chapter four includes the results of the study. Chapter five includes discussion, conclusion, and recommendations of study.

Literature Review

2.1 Fetus Middle Cerebral Artery:

2.1.1 Anatomy of the MCA:

MCA is the main terminal branch of the internal carotid artery (ICA) and The middle branch from circle of wills that anteriorly, composed of the anterior cerebral arteries (branches of internal carotid artery [ICA] connected by anterior communicating artery); posteriorly, it consists of the two posterior cerebral arteries (branches of basilar artery connected on either side to ICA by posterior communicating artery), which supply the cerebral hemispheres on each side. The MCA arises from the internal carotid and continues into the lateral sulcus where it then branches and projects to many parts of the lateral cerebral cortex. It also supplies blood to the anterior temporal lobes and the insular cortices (Grand .W et al 1999).

MCA conveys approximately 40% of the blood flow volume from the circle of Willis to each cerebral hemisphere. So total of 80% of the blood volume to the brain supplied by MCAS. (Rhoton AL et al 2003)

Most anatomical classification divide the MCA into 4 segments, including M1 (from the ICA to the bifurcation [or trifurcation]), M2 (from the MCA bifurcation to the circular sulcus of the insula), M3 (from the circular sulcus to the superficial aspect of the Sylvian fissure), and M4, which is made up of cortical branches. (Alpers BJ et al 1959)

- **M1 segment:**

Most anatomic studies define the M1 segment as ending where the MCA branches take a right angled turn within the Sylvian fissure; however, the division point of the MCA trunk is considered by most clinicians to be the M1/M2 junction. The MCA most commonly bifurcates but, may also trifurcate or quadfurcate. Branches include lenticulostriate arteries, which supply the anterior commissure, internal capsule, caudate nucleus, putamen, and globuspallidus, and an anterior temporal artery, which supplies the anterior temporal lobe.

- **M2 segment:**

The M2 segment extends from the main division point of the M1 segment, over the insula within the Sylvian fissure, and terminates at the margin of the insula.

- **M3 segment:**

The M3 segment begins at the circular sulcus of the insula and ends at the surface of the Sylvian fissure. This part travels over the surface of the frontal and temporal opercula to reach the external surface of the Sylvian fissure. The M3 and M2 segments give rise to stem arteries from which cortical branches are derived.

- **M4 segment:**

The M4 segment begins at the surface of the Sylvian fissure and extends over the surface of the cerebral hemisphere. Its cortical branches, which supply the frontal, parietal, temporal, and occipital lobes, including the Orbitofrontal, Prefrontal, Precentral, Central, Anterior and posterior parietal, Angular, Temporo-occipital Temporal and Temporopolar branches.

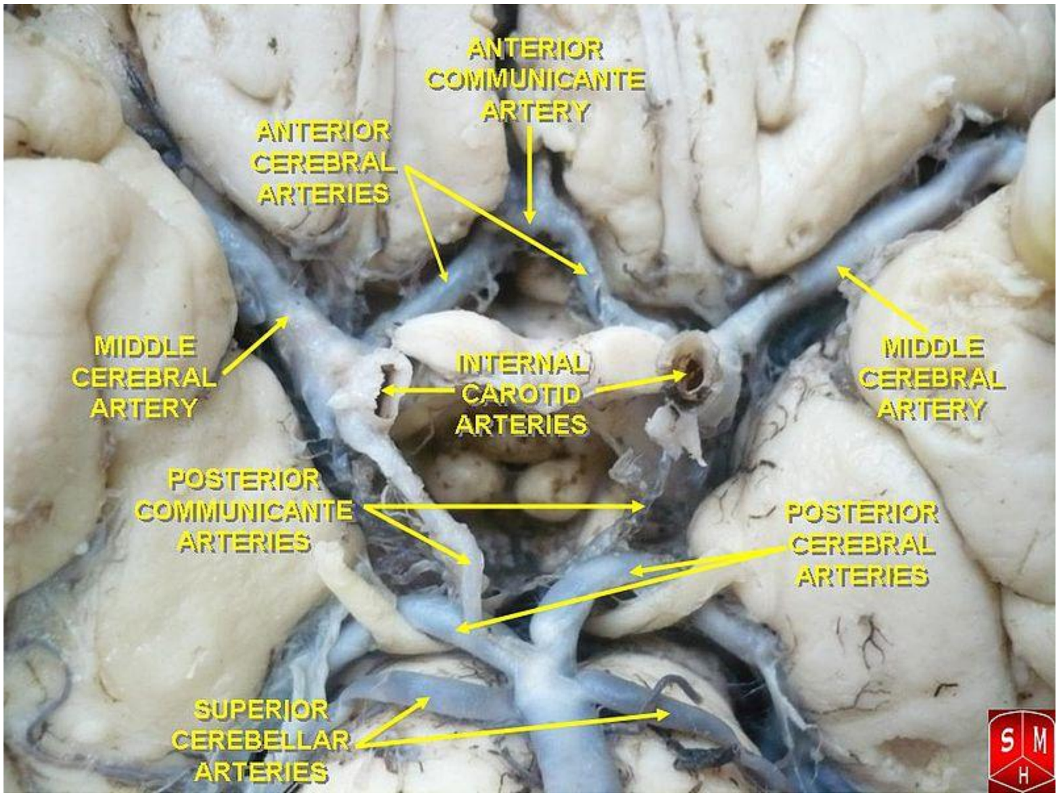


Figure2.1: Anatomy of Middle Cerebral Artery (Moore KL ET AL 1999)

2.1.2 Physiology of the Middle Cerebral Artery:

Middle Cerebral Arteries are known as high resistant blood vessels which supply 80%of the blood flow volume from the circle of Willis to the cerebral hemispheres. During pregnancy the diastolic flow in the MCA is lower than in the umbilical artery , thus the cerebral vascular resistance (PI MCA) is higher than the placental vascular resistance (PI UI), and the cerebroplacental ratio (CPR = PI MCA/PI UI) in a normal pregnancy is greater than one. This index is a very sensitive predictor in (80%) of fetal growth retardation. In case of fetus cerebral circulation flow redistribution in response to hypoxemia mainly from placental insufficiency due to maternal hypertensive complications, the cerebral arteries tend to become dilated in order to preserve the blood flow to the brain, therefore, due to increase in diastolic flow the systolic to diastolic ratio (A/B) will decrease and this indicate fetal hypoxemia. The vasodilatation of the MCA with an increase in diastolic flow and corresponding hyper perfusion is considered pathologic. This phenomena knew as ‘brain-sparing effect ‘which is associated with an abnormal cerebroplacental ratio (<1), however if the fetal hypoxemia persists the diastolic flows will return to a normal level, presumably this reflects terminal decompensation in the setting of acidemia or brain edema. (Werner S et al 2011)

Most of the fetus cerebral hemodynamic studies focused in MCAs as they conveys the most blood flow volume to the fetus brain and it easy to examine by Doppler ultrasound with zero degree between the ultrasound beam and the vessels blood flow. However, they mainly study the blood flow indices as a tool to assess the blood vessel resistance, therefore, become the most used technique in maternal management of prenatal outcome.

2.1.3 Pathology of the Middle Cerebral Artery:

2.1.3.1 Stroke:

Middle cerebral artery (MCA) strokes occur when the MCA or its branches are occluded. With occlusion blood and along with it oxygen and nutrients fail to reach the brain. If blood flow is not restored quickly the affected brain tissue dies leading to permanent neurological injury. (Taussky P et al 2011)

2.1.3.2 Atherosclerosis:

If we break the term down into its components, "athero" is Greek for a gruel or paste, and sclerosis means hardening. This is precisely what is happening in the blood vessels of people with this disease. A paste-like material hardens overtime to form a plaque. The specifics in how and why that paste-like material forms are much more complicated. The paste-like material is composed of several different elements. The first, and perhaps most important element, is low density lipoprotein (i.e. LDL). LDL, or the "bad cholesterol" as it is commonly referred to, is a mixture of lipid (i.e. fat and cholesterol) and protein. These molecules are highly atherogenic, which means that they accelerate the plaque forming process. (Taussky P et al 2011)

2.1.3.3 Aneurysm:

It is a disorder in which weakness in the wall of a cerebral artery causes a localized dilation or ballooning of the blood vessel. This can be because of acquired disease or hereditary factors. The repeated trauma of blood flow against the vessel wall presses against the point of weakness and causes the aneurysm to enlarge. Cerebral aneurysms are classified by size to Small aneurysms have a diameter of less than 15 mm, Larger aneurysms include those classified as large (15 to 25 mm), giant (25 to 50 mm) and super-giant (over 50 mm), by shape to Saccular aneurysms, fusiform aneurysms and Micro aneurysms. Saccular aneurysms are almost always the result of hereditary weakness in blood vessels and typically occur within the arteries of the Circle of Willis, Saccular aneurysms tend to have a lack of tunica mediaand elastic lamina around its dilated location (congenital), with wall of sac made up of thickened hyalinized intima and adventitia .In addition, some parts of the brain vasculature are inherently weak—particularly areas along the Circle of Willis, where small communicating vessels link the main cerebral vessels. These areas are particularly susceptible to saccular aneurysms. Approximately 25% of patients have multiple aneurysms, predominantly when there is familiar pattern. (Bhidayasiri et al 2005)

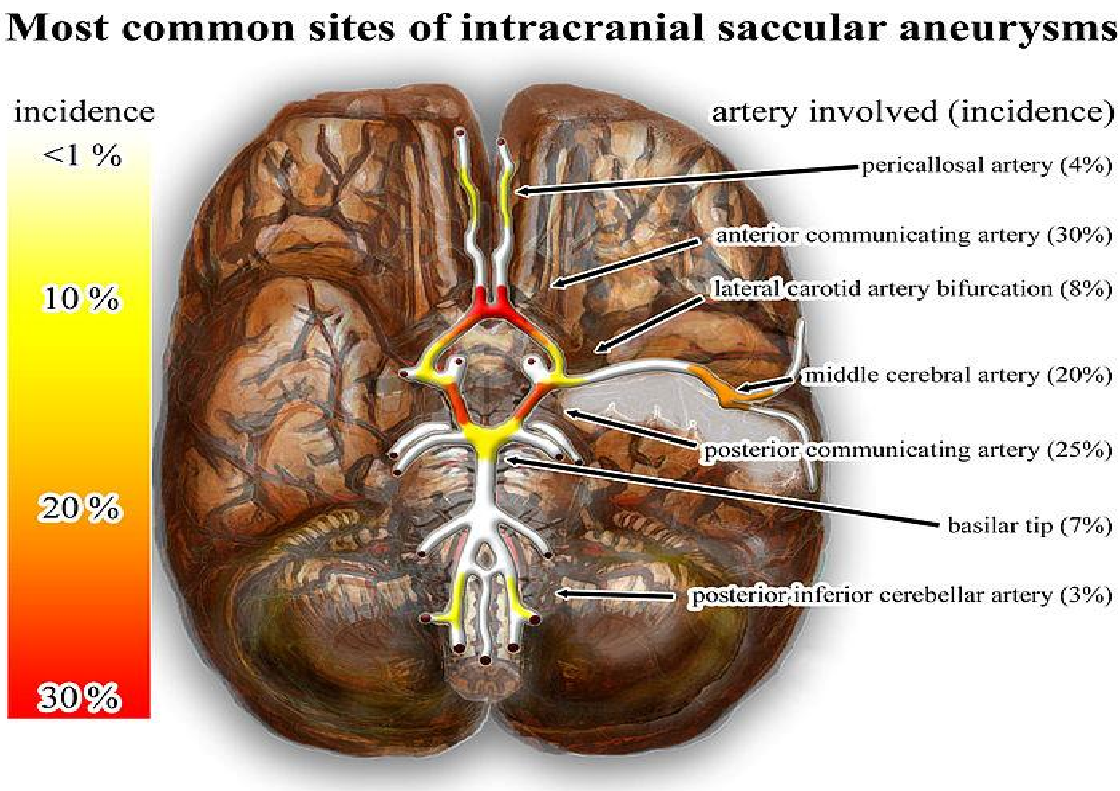


Figure 2.2: The most common sites of intracranial saccular aneurysms

(Haberland et al 2007)

2.2 Pregnancy Hypertension :

High blood pressure, or hypertension, is defined as blood pressure higher than 140/90 mm Hg. Women who have had pre-existing high blood pressure are at higher risk for related complications during pregnancy than those with normal blood pressure. Maternal hypertension is one of the most common causes of placental insufficiency which associated with fetus cerebral circulation distraction as adaptation to Decreased blood flow to the placenta , which increasing the risk of a low birth weight due to reduces in the fetus supply of oxygen and nutrients, Premature delivery and potentially life-threatening complications , which produce Future problems for premature babies include

Learning disabilities, Cerebral palsy, Epilepsy, deafness and blindness. These babies may also be more prone to diabetes or hypertension of their own when they grow older. There are three main types of hypertension during pregnancy:

(A) Chronic hypertension:

If high blood pressure develops before pregnancy, during pregnancy but before 20 weeks or lasts more than 12 weeks after delivery, it's known as chronic hypertension.

(B) Gestational hypertension:

If high blood pressure develops after 20 weeks of pregnancy, it's known as gestational hypertension. Gestational hypertension usually goes away after delivery.

(C) Preeclampsia:

Sometimes chronic hypertension or gestational hypertension leads to preeclampsia, a serious condition characterized by high blood pressure and protein in the urine after 20 weeks of pregnancy. Left untreated, preeclampsia can lead to serious even fatal complications for mother and baby. When preeclampsia causes seizures, the condition is known as eclampsia--the second leading cause of maternal death in the U.S. Preeclampsia is also a leading cause of fetal complications, which include low birth weight, premature birth, and stillbirth. (John c et al 1977)

A fetal condition often associated with maternal hypertension is intrauterine growth restriction (IUGR). Infants who are growth-restricted are in or below the tenth percentile of mean weight for gestation. These small-for-dates infants have a prenatal mortality rate eight times higher than babies who are appropriate for gestational age. They also have a four times greater chance of becoming asphyxic in labor, and their neonatal course is often complicated by hypoglycemia, polycythemia, and hypocalcaemia. Those that survive the neonatal period are subject to higher rates of mental-motor retardation. (Fitzhardinge PM et al 1972) Therefore, it is imperative that this condition be diagnosed as early in pregnancy as possible. Although investigators had limited success in identifying the growth-retarded fetus with hormonal parameters, Stuart Campbell was able to successfully diagnose IUGR with ultrasound. He found that when there was subnormal growth (below the 10^{th} Percentile) of the fetal biparietal diameter (BPD), 82% of these infants were growth retarded at birth. On the other hand, one-fifth of growth-retarded babies did not have a lag in incremental BPD growth. This latter finding is due to the fact that in many cases the fetus has the compensatory ability to spare its brain at the expense of its body when confronted with adverse conditions affecting its supply line. These fetuses have a head-to-body disproportion. (Am J et al 1976)

Intrauterine Growth Restriction divided according to the etiology to two part typically Symmetric IUGR in case of fetal anomalies or infection and typically Asymmetric IUGR in case of placental or maternal diseases. (See figure 2.3)

	Normal	IUGR	
HEAD	NORMAL	NORMAL	SMALL
ABD	NORMAL	SMALL	SMALL
		ASYMMETRIC	SYMMETRIC

Figure 2.3: classification of IUGR according to the etiology

2.3 Doppler Ultrasound:

2.3.1 Doppler physics:

The Doppler phenomenon was first described by Christian Doppler in the 19th century. In its simplified version, this phenomenon is experienced in daily life by all of us. The pitch of the sound of a moving object (e.g. train) is altered when the distance between the observer and the source of sound changes. This change caused by a relative motion between the observer and the object is known as the Doppler shift and is a consequence of the Doppler phenomenon. Accordingly, when the frequency of sound emitted from a stationary source is fixed, and its insonation angle is known, the Doppler shift (i.e. the difference between the emitted and the reflecting frequency) can be calculated, as it is correlated to the velocity of the relative movement between the target and the transducer. This relation is defined by the formula: $f_D = 2f_0 v \cos \theta / c$; where f_D is the Doppler shift, f_0 is the frequency of the transmitted ultrasound, v is the velocity of sound within the tissue. (Burns PN et al 1993)

Doppler ultrasound has been used in almost every medical discipline to study blood flow in diseases where an alteration of this dynamic system is anticipated. Until this development the only way to study circulation was the invasive technique of angiography. With the availability of this technique, it has been possible to study the circulation patterns and their pathologies non-invasively. (Campbell S et al 1971)

The first Doppler ultrasound report using continuous wave assessment of umbilical artery flow was published in 1977 (Fitzgerald 1977). With the same systems, in 1983, Campbell published the assessment of the utero-placental circulation and that high resistance waveforms were obtained in pre-eclampsia (Campbell 1983) (Berkowitz 1988). Subsequently these studies were done with color Doppler and in many centers have become an important screening technique to predict women at risk of pre-eclampsia. (Berkowitz GS et al 1988)

2.3.2 MCA Doppler assessments protocol:

The middle cerebral artery (MCA) has become an important part of the fetal Doppler assessments because it is easier to detect and measure compared with other cerebral vessels and has a high sensitivity in the detection of fetal intrauterine growth restriction (IUGR) and related complications. The Doppler indexes used in most studies were based on variations in flow velocity such as resistance index (RI), pulsatility index (PI), systolic/diastolic ratio(S/D ratio) and peak systolic velocity. (Marsoosi V et al 2012)

In the middle cerebral artery (MCA), lowering of pulsatility index (PI) was indicates placental insufficiency and fetus hypoxemia but the more persist to hypoxemia the pulsatility index will return to normal value. The middle cerebral artery peak systolic velocity (MCA PSV) is increased in IUGR fetuses this increase predict prenatal mortality more accurately than does the MCA PI ,So the above physiological effects explained that MCA PI is abnormal in most IUGR fetuses but subsequently increases and trends toward normalization before delivery or fetal death. Conversely, the MCA PSV progressively increases with advancing gestation in all fetuses and tends to decrease slightly just before fetal biophysical deterioration or fetal demise. Despite this decrease, however, the MCA PSV value remains above the upper limit of normal until a few hours before delivery or fetal demise. In growth-restricted fetuses the disappearance of the brain-sparing effect or presence of reversed MCA flow is a critical event for the fetus and precedes fetal death. (Mari G et al 2007)

For an accurate measurement, the fetal head should be in the transverse plane. The MCA vessels are often found with color or power Doppler ultrasound overlying the anterior wing of the sphenoid bone near the base of the skull. An angle of insonation of $< 15^{o}$ should be used; typically, an angle that approximates zero degrees can be achieved by moving the transducer on the maternal abdomen. Parameters used include fetal MCA pulsatility index (PI) ,fetal MCA peak systolic velocity (PSV) the highest velocity should be recorded ,MCA systolic/diastolic (S/D) ratio a normal fetal MCA S/D ratio should always be higher than the umbilical arterial S/D ratio and cerebroplacental ratio (CPR) ratio of pulsatility index of MCA and umbilical artery should be greater than one. (Henry k et al 2015)

2.3.3 Normal ultrasound characteristic of MCA Doppler waveform indices:

The Middle Cerebral Artery blood flow was evaluated according to their sonography features as following: Doppler Indices (Resistive index, pulsatility index, systolic-to-diastolic ratio, and peak systolic velocity) (figure 2.4). Flow waveform description (absent of –end-diastolic - in first term and decrease-in-end-diastolic-flow in 2end &3rd term of pregnancy) (Figure 2.5).

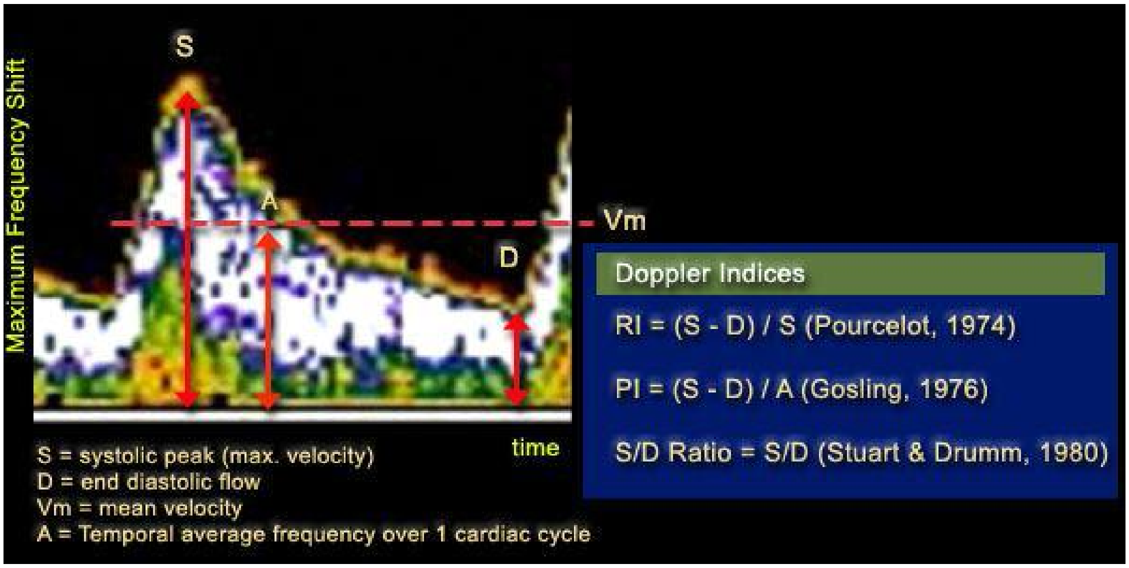
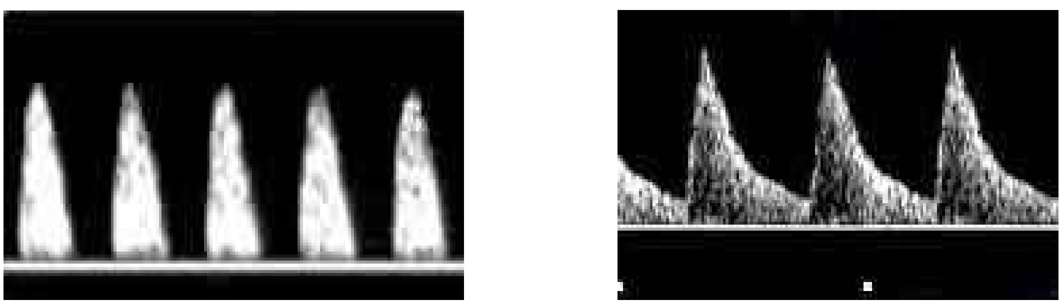


Figure 2.4: Flow velocity indices (Werner S et al 2011)



1st trimester A

2end& 3rd trimester B

Figure 2.5**:** Normal Pregnancy - Development of the Middle Cerebral Artery 1st trimester A &2end& 3rd trimester B (Werner S et al 2011)

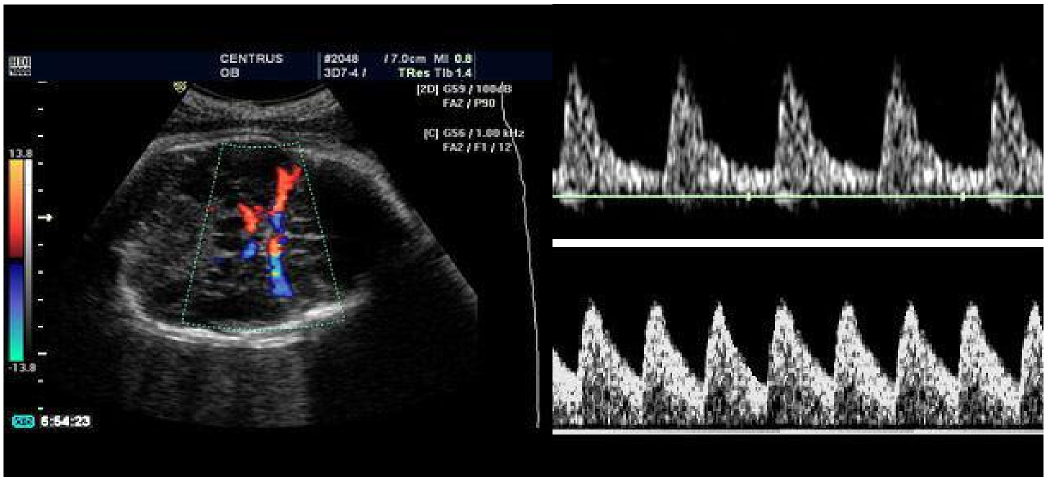


Figure 2.6: Color Doppler examination of the circle of Willis (left). Flow velocity waveforms from the middle cerebral artery in a normal fetus with low diastolic velocities (right, top) and in a growth-restricted fetus with high diastolic velocities (right, bottom). (Werner S et al 2011)

2.4 Previous Studies:

Very few studies went through the Morphometrical and anatomical development of the fetus cerebral arteries and understanding of normal and variable growth.

(Eran Barzilay et al 2014) Study done on the Measurement of middle cerebral artery diameter as a method for assessment of brain sparing in intra-uterine growth-restricted discordant twins. In ten dichorionic–diamniotic twin pairs with weight discordance. Fetal assessment included estimated fetal weight, umbilical artery flow, MCA flow and MCA diameter. Paired statistical analysis was used to compare MCA diameter and MCA pulsatility index (PI) between the discordant twins. Study aimed to determine the utility of middle cerebral artery (MCA) diameter measurement as a tool for evaluating brain sparing effect in intrauterine growth-restricted (IUGR) discordant twins.

Study results were MCA diameter was significantly larger in the smaller twin (mean diameter 3.55 ± 0.26 vs. 2.71 ± 0.22, $P = 0.018$, mean ratio 1.39 ± 0.14).

There was no significant difference in MCA PI values within the twin pairs (mean PI 1.51 ± 0.13vs 1.57 ± 0.07, P = 0.878, mean ratio 0.99 ± 0.11).

(Jerzy Gielecki1et al 2009) Study done in the Morphometric and volumetric analysis of the middle cerebral artery in human fetuses. Conducted on 304 MCAs taken from brains of 152 formalin-fixed human fetuses (83 males and 69 females) from a collection housed at the Department of Anatomy of the University of Warmia and Masuria. Cerebral vessels were injected with a mixture of 30% suspension latex (LBS 3060) and detergent. The mixture was then perfusing into the vessels according to a standard methodology. Three weeks after the infusion, the brains were removed from skulls. The study group consisted of fetuses from both from spontaneous and therapeutic terminations of pregnancy. Specimens were screened for indications of external and internal malformations or abnormalities prior to taking images of cerebral vessels. Fetuses aging between 12-40 weeks in GA were subdivided into seven Gestational Age Range Groups (GARG) encomassing four weeks stage. The fetal age estimation was based on clinical documentation .The somatic developments of the fetuses were determined by crown-rump length, crown-heel length and brain weight measurements. The fetal brain base arteries were carefully dissected under a stereoscopic microscope and digital-images were stored in uncompressed data format. The digital-images of the MCAs were used to compute the average diameter, length, and volume of the MCA using Angio-Analyser 08 software which was specially designed for this study. The study finding that Diameter of M1 segment of the MCA increases approximately 3 times according linear function $y = -0.0705455 + 0.0043678*x$ with r=0.65 from 12 to 40 weeks of gestation. Analysis showed statistically significant differences mean value of M1 segment diameter between all Gestational Age Range Groups. There is no statistically significant difference between diameters of left and right and of M1 segment of MCA in each Gestational Age Range Group.

(Eugeniusz Tarasw1 et al 2007) was study the Measurements of the middle cerebral artery in digital subtraction angiography and MR angiography. Conducted on 114 examinations of cerebral vessels (88 DSA, 26 MRA), included patients in whom the angiographic examinations did not show any pathological lesions. DSA was carried out using a routine protocol applied to examinations of cerebral arteries; MRA was performed with a 1.5 T scanner and the time of flight (TOF) method using the fast gradient echo sequence with RF spoiler- multivolume RF-FAST.The diameter measurements of the internal carotid arteries (ICA) and segments of the MCA and the lengths of MCA segments from the origin to the first ramification and from the origin to the bifurcation. Result in The diameters of ICA and MCA and its upper branch are age and sex dependent, being wider in men than in women and increasing with age.

(Veille JC et al 1993) study done in the longitudinal quantization of middle cerebral artery blood flow in normal human fetuses. Conducted on 20 normal fetuses had color pulsed Doppler ultrasound of the middle cerebral artery. A total of 68 studies were successfully done and are reported. The Doppler sample was placed as parallel to the direction of the vessel flow as possible. All waveforms were recorded on a strip chart at a preset speed of 100 mm/sec. Six Doppler waveforms were digitized for the time velocity integral (area under the curve is equal to time velocity integral) and averaged. Middle cerebral blood flow was obtained by multiplying the time velocity integral of the Doppler curve by the cross-sectional area of the vessel. The combined cardiac output was obtained by adding the right and left ventricular outputs, which were obtained by multiplying the time velocity integrals by the area of the corresponding annuli. Analysis of variance for repeated measurements was used to determine significance. Results in the diameter of the middle cerebral artery, the time velocity integral, and the peak flow velocity of the Doppler waveform increased significantly with advancing gestational age. Blood flow to the middle cerebral artery ranged from 23 ml/min at 19 weeks to 133 ml/min at term. Resistivity index values were not correlated with advancing gestational age. The percent of the cardiac output to one of the two middle cerebral arteries remained constant throughout gestation with a range between 3% and 7%.

Chapter Three

Materials and Methodology

3.1 Materials:

3.1.1 Area of Study

The study took place in radiology department of Gulf Hospital and Alqadi Medical Center in Abu Dhabi. Ultrasound screening units was selected as it is the most suitable place to conduct this research, based on that they receives all pregnant mothers from obstetric clinics, so, I could anticipate a large enough volume of patients to allow for the required study sample size to be obtained within a reasonable period of time .as well as all ultrasound screening units having modern machines.

3.1.2 Study population and duration of study:

The study population consisted of all normal and hypertensive singleton pregnant mothers took apart in ultrasound screening department. A total of 42 uncomplicated singleton pregnancies were used to define the normal range .the study group was made up of 40 singleton hypertensive pregnancies. The indication for referral includes suspected SGA fetus and preclamcia the gestational age at referral varied from 24 to 40 weeks. In time spam from June - October 2015.

3.1.2.1 Inclusion criteria:

Normal singleton pregnancy and hypertensive singleton pregnancy with gestational age rang 24-40 weeks.

3.1.2.2 Exclusion criteria:

Singleton or multiple pregnancies with a major malformation or chromosomal abnormality and maternal diabetes were not included in the study.

3.1.3 Ultrasound machine:

Obstetric ultrasound Examinations were carried out using C5-1MHz curvilinear transducer (iU22ultrasound system .PHILIPS) and C5-1MHz (VolusonE6, GE Healthcare, USA). All ultrasonic assessments were performed by experience single sonographer in each hospital. After delivery data regarding mode of delivery, birth weight and fetus complications were not collected due to many difficulties which can be retrieved by other researcher in future.

3.2 Methodology:

3.2.1 Research design:

Observational analytical design (prospective cohort-study) was applied to this study as it most appropriate design to use.

3.2.1.1 Observational analytical design:

Describe the similarities and differences observed between two or more groups. These are often used when the clinical question is about either exposure to risk factor is associated with an outcome.

3.2.1.2 Prospective cohort-study:

Used to study recruiting groups of people with and without exposure to risk factor then monitor the groups to see how frequently the outcome arise in each group .

3.2.2 Ultrasound technique:

3.2.2.1 Introduction:

In order to perform a good sonographic assessment by Doppler ultrasound in obstetric, scanning experience is one of the most important factors and really the only way to achieve optimum results.

3.2.2.2 Maternal position

During Doppler studies, the mother should lie in a semi recumbent position with a slight lateral tilt. This minimizes the risk of developing supine hypotension syndrome due to inferior venocava compression.

3.2.2.3 Fetus head scanning technique:

Prior to Doppler assessment, routine obstetric ultrasonography was done for each subject using 2D mode to evaluate the fetal growth. by the way UA Doppler measurements examined in segment of free floating part of the cord and detect the flow velocity in vertical plane allows the pulsed Doppler gate to be placed with a minimum angle of insonation .Then Doppler measurements for MCA flow velocity were obtained on the transverse plane, by magnifying the circle of Willies and the MCA for at least 50% of the screen. The MCA vessels are often found with color or power Doppler ultrasound overlying the anterior wing of the sphenoid bone near the base of the skull. The Doppler was set at pulse repetition frequency of 2.4 KHz, normal quality and low wall motion filter. The angle between the ultrasound beam and the direction of blood flow was always less than 20 degree. MCA diameter was measured at the main trunk (M1 segment) of the artery, at the peak systole. The crossbar of the caliper was placed as it converges with the flow ('in-in' measurement).Care was taken to apply minimal pressure to the maternal abdomen with the transducer, to avoid fetal head compression as fetal head compression is associated with alterations of intracranial arterial waveforms. Doppler recordings and measurements were made in the absence of fetal activity or in periods of fetal apnea.

3.2.3 Data collection sheet of study variables:

Data collected by clinical sheet for each fetus in the two groups which include GA, EFW, flow measurements in the AU and the MCA and MCA diameter. The clinical history of last three reading of blood pressure and protein in urine for hypertensive mothers had been taken. Finally tabulated in two separate sheets one for normal maternal and other for hypertensive maternal.

3.2.4 Data analysis:

The software Microsoft office Excel 2010 was utilized for data organization. The cases were divided into six gestational age range groups by three week intervals and classified into two groups according to the presence or absence of maternal hypertension complication.

Analyses were conducted using the social sciences Statistical web site by using simple descriptive statistics such as mean, median and stander deviation for measurable features, quantitative-percentage Structures for qualitative features and calculator statistics using significant tests like Analysis of samples as dependent samples using Wilcoxon signed-rank test, analysis of samples as independent samples using Mann– Whitney U test and the correlation between variables and GA using Pearson’s correlation test. Significance was accepted at $P<0.01$.

3.3 Ethical Considerations:

Ethical clearance was obtained from Sudan University of Science and Technology before the study would initiate. Privacy was insured by represent of patient's identification through a research in number. No personal information concerning the examination was veiled to anyone who was not involved in the study. The results of the study were published only in the form of tables and graphs together with all p-values of all significance test done. Written informed consent was obtained from all pregnant participants prior to the examination.

Chapter Four

Results

4.1Characteristics of the Study Population:

Table 4.1: Baseline characteristics of the study population (n= 82)

	Parameter	Measure	
		Control group (n= 42)	Target group (n=40)
Maternal	Age (median, range)	30.5 (18-41)	31.5 (19-41)
	Chronic HT%	0%	35%
	Gestational HT%	0%	65%
	Protinuria%	0%	17.50%
Fetal	Gestational age (median, range)	33 (26-39)	30 (24-39)
	Fetal weight (median, range)	2181 (876-3742)	1018.5 (157-3461)
	Middle cerebral arterial PI (mean ± SD)	2.16 (±0.45)	1.35 (±0.50)
	Umbilical arterial PI (mean ± SD)	0.94 (±0.15)	1.47 (±0.45)
	Cereberoplasental ratio (mean ± SD)	2.35 (±0.58)	0.98 (±0.48)
	Middle cerebral arterial diameter (mean ± SD)	0.41 (±0.08)	0.52 (±0.42)
	<10% percentile (%)	0%	75%
	>10% percentile (%)	100%	25%

4.2 Age distribution of the study population

Table 4.2: Age distribution of pregnant mothers in the study population

Mothers Age in years	**Control Group**		**Target Group**	
	Total	**%**	**Total**	**%**
<25	7	16.66%	7	17.50%
25-35	27	64.28%	21	52.50%
>35	8	19.06%	12	30.00%
Total	42	100%	40	100%

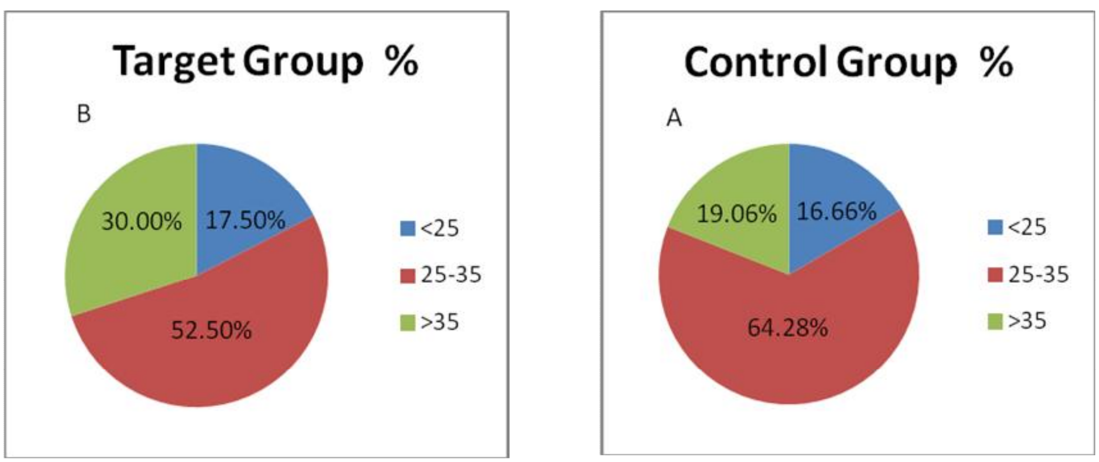


Figure 4.1 : Age distribution in years of control pregnant women (A) & target pregnant women (B) in the study population by %

4.3 Distributions of Types of Maternal Hypertension in Target Group:

Table 4.3: Types of maternal hypertension in target group

Types of HTN	Total	Percentage %
Chronic	14	35%
Gestational	26	65%
Total	**40**	**100%**

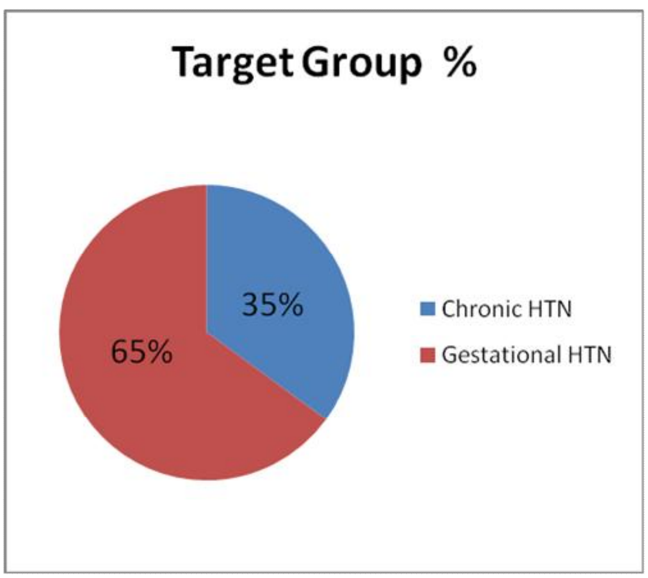
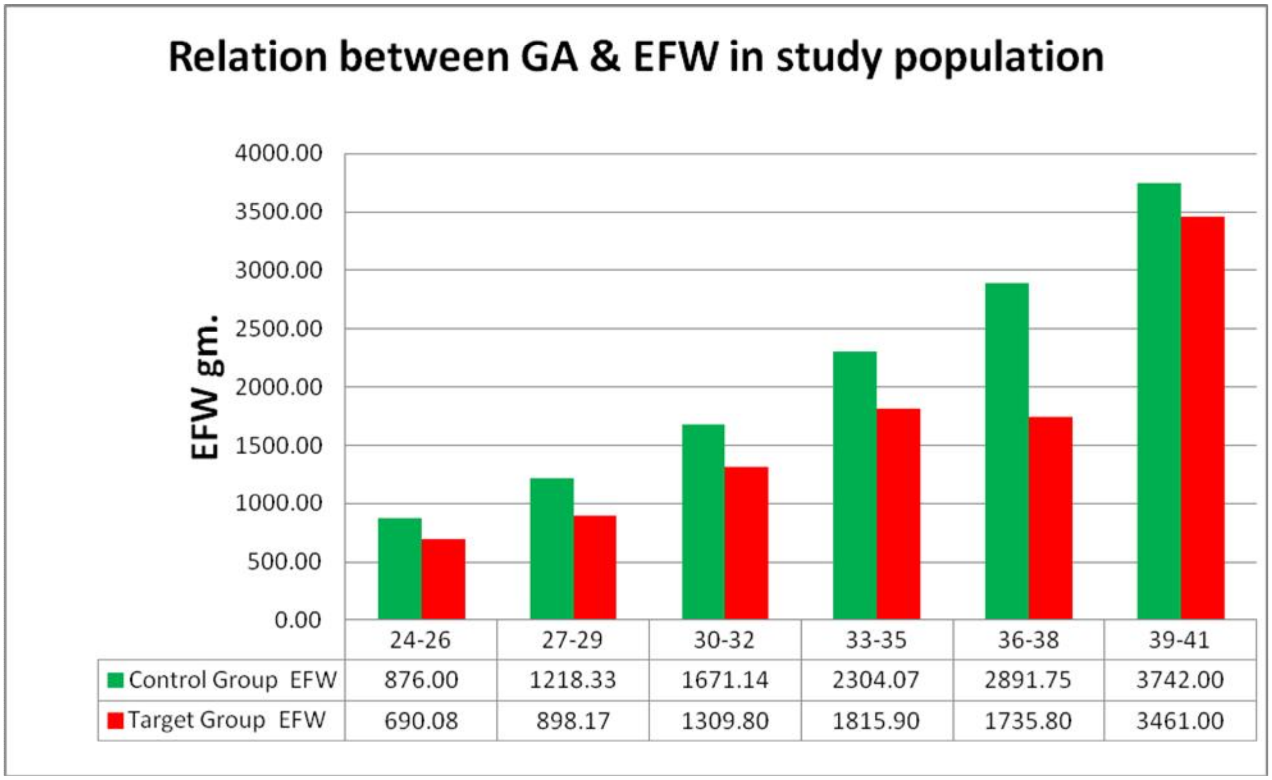


Figure 4.2: Type of maternal HTN in target group by %

4.4 Relation between GA and EFW in study population:

Table 4.4: Ultrasonic data collection of fetus's weight & discordance in study population

GA in weeks	EFW Control Group(gm)	EFW Target Group(gm)	EFW(gm) Differences	EFW discordance %
24-26	876.00	690.08	185.92	21.22%
27-29	1218.33	898.17	320.16	26.28%
30-32	1671.14	1309.80	361.34	21.62%
33-35	2304.07	1815.90	488.17	21.19%
36-38	2891.75	1735.80	1155.95	39.97%
39-41	3742.00	3461.00	281.00	7.51%
Mean	**2117.22**	**1651.79**	**465.42**	**22.97%**



	24-26	27-29	30-32	33-35	36-38	39-41
Control Group EFW	876.00	1218.33	1671.14	2304.07	2891.75	3742.00
Target Group EFW	690.08	898.17	1309.80	1815.90	1735.80	3461.00

Figure 4.3: Relation between GA & EFW in control & target groups

4.5 Relation between GA and MCA PI, Width and CPR in study population:

Table 4.5: Ultrasound Measurements of Fetuses MCA PI, width and CPR in Study Population

GA in weeks	Control Group			Target Group		
	PI	Width(cm)	CP Ratio	PI	Width(cm)	CP Ratio
24-26	2.10	0.37	1.96	1.11	0.61	0.85
27-29	2.60	0.39	2.43	1.22	0.45	0.76
30-32	2.19	0.39	2.23	1.92	0.45	1.32
33-35	2.31	0.42	2.57	1.40	0.48	1.13
36-38	1.68	0.46	2.13	1.36	0.52	0.78
39-41	1.92	0.31	2.53	1.82	0.41	1.96
Mean	**2.13**	**0.39**	**2.31**	**1.47**	**0.49**	**1.13**

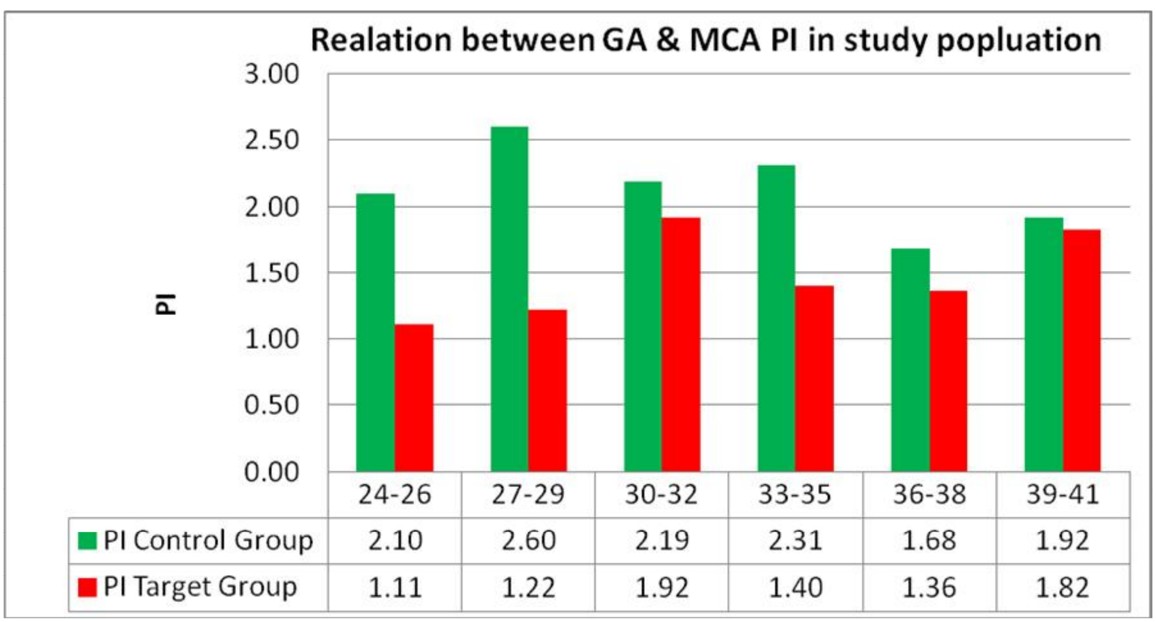


Figure 4.4: Relation between GA and MCA PI in control and target groups

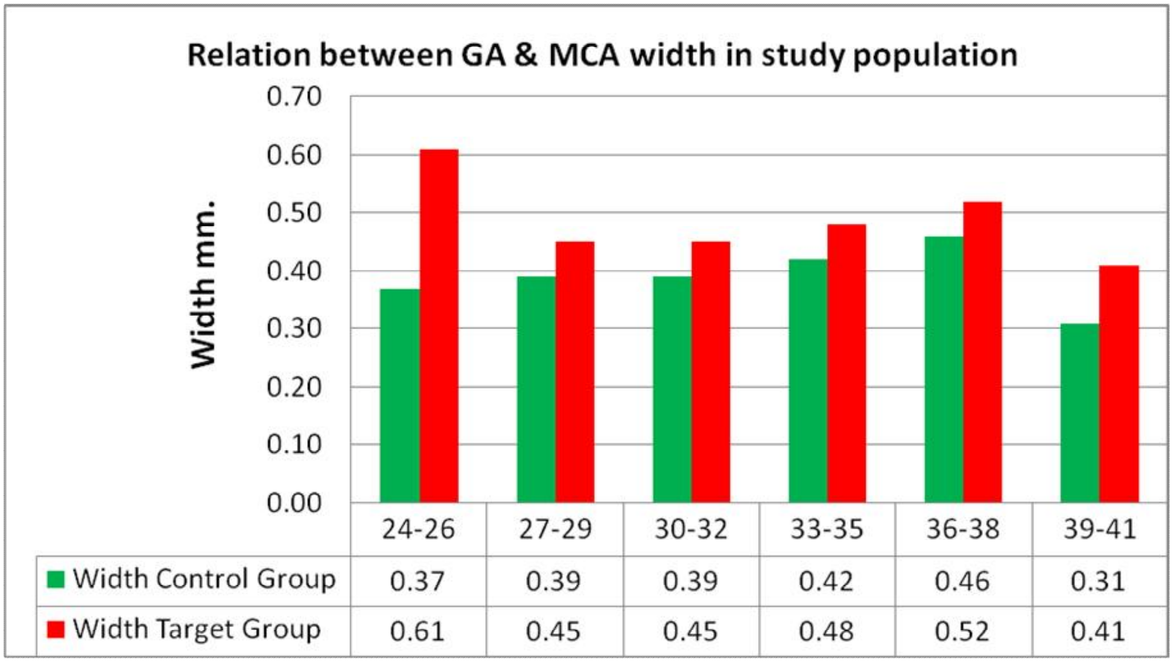


Figure 4.5: Relation between GA and Width in control and target groups

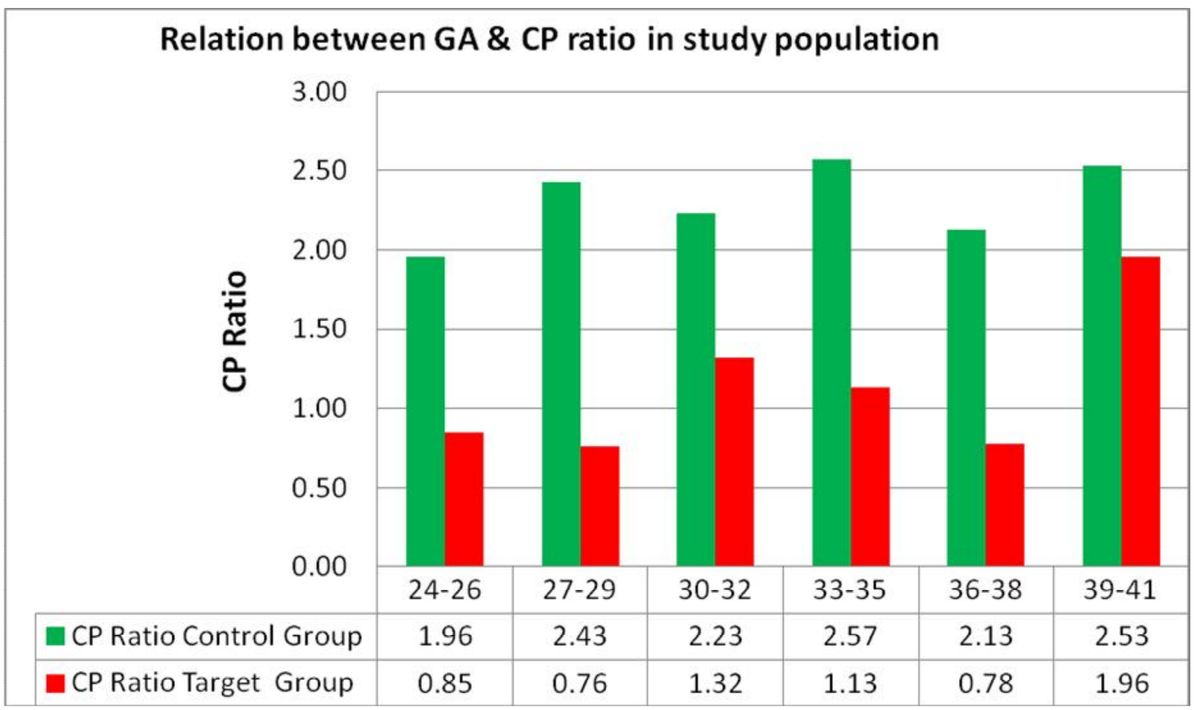


Figure 4.6: Relation between GA and CP ratio in control and target group

4.6 The Mean Ratio of MCA PI and MCA Width for Target/Control Fetus and compression of mean MCAPI and mean MCA Width in study groups:

Table 4.6: Mean target/control fetus ratio of MCA PI and MCA diameter in study population

GA in weeks	Control Group		Target Group		Ratio	
	PI	Width(cm)	PI	Width(cm)	PI	Width
24-26	2.10	0.37	1.11	0.61	0.53	1.65
27-29	2.60	0.39	1.22	0.45	0.47	1.15
30-32	2.19	0.39	1.92	0.45	0.88	1.15
33-35	2.31	0.42	1.40	0.48	0.61	1.14
36-38	1.68	0.46	1.36	0.52	0.81	1.13
39-41	1.92	0.31	1.82	0.41	0.95	1.32
Mean	**2.13**	**0.39**	**1.47**	**0.49**	**0.71**	**1.26**

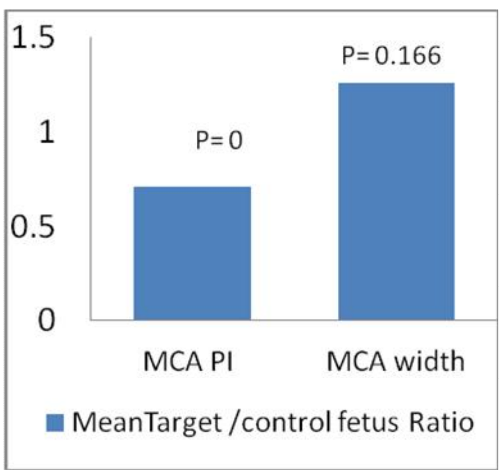


Figure 4.7: Mean target/control ratio of MCA PI and MCA width with pairing. P values represent the results of analysis as dependent samples using Wilcoxon signed-rank test on the actual measurement in each fetus.

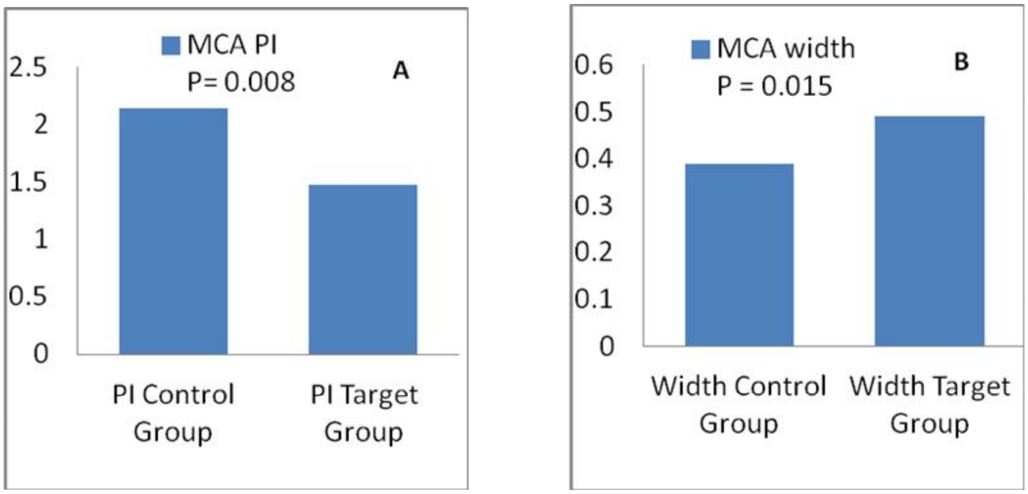


Figure 4.8: comparison of mean MCA PI (A), mean MCA Width (B) without pairing. P value represents the result of analysis as independent samples using Mann-Whitney U test

4.7 The Association and Significant Difference between the MCA PI, MCA Width and GA:

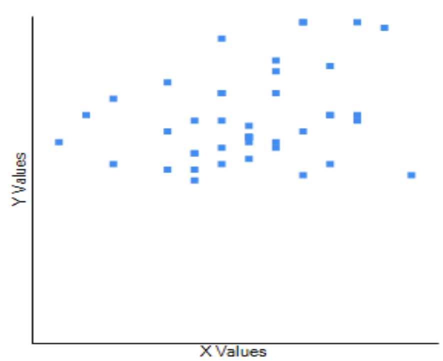


Figure 4.9: Association between GA & diameter in control group (r= -0.369)

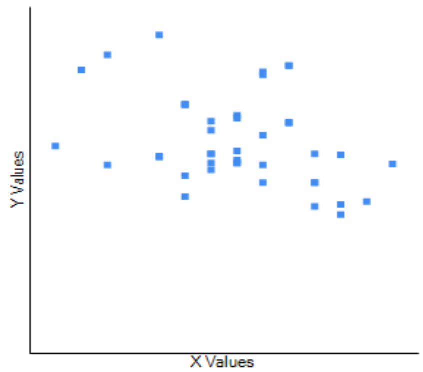


Figure 4.10: Association between GA & PI in control group (r= 0.282)

4.8 The Association and Significant Difference between the MCA PI, MCA Width:

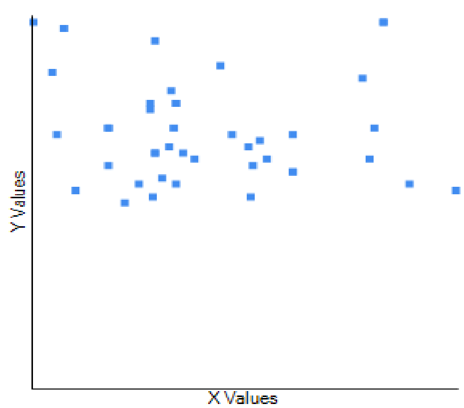


Figure 4.11: Association between Diameter & PI in control group(r= -0.081)

Chapter Five

Discussion, Conclusion and Recommendations

5-1 Discussion:

(Table 4.1) At time of ultrasonic assessment in control group the median maternal age was 30.5 Years(range18-41),the median gestational age was 33 weeks (range 26–39), the median EFW was 2181 gm(range 876-3742) ,the mean MCA PI was 2.16 (± 0.45),the mean UA PI was 0.94 (±0.15),the mean CPR was 2.35 (±0.58),the mean MCA width was 0.41cm (±0.08). In target group the median maternal age was 31.5 Years(range19-41),the median gestational age was 30 weeks (range 24–39), the median EFW was 1018.5gm(range 157-3461) ,the mean MCA PI was 1.35 (± 0.50),the mean UA PI was 1.47 (±0.45),the mean CPR was 0.98 (±0.48),the mean MCA width was 0.52cm (±0.42). In ten cases the percentile was more than 10% and in four cases was less than 5%.

(Table 4.2) and (figure 4.1) Two groups of singleton maternal women were enrolled in this study and the maternal age distribution of the study population (n=82) although maternal age was not objective for this study, it was described to use the information as matter of interest. So it divided into three groups (<25/25-35/>35). Age distribution of pregnant mothers represented that the high percentage of 64.28% in control group and 52.50% in target group fall in the age group (25-35) years which indicated the age effective for pregnancy.

(Table 4.3) and (Figure 4.2) the distribution of maternal hypertension types in target group represented that 14 (35%) had chronic hypertension and 26(65%) had gestational hypertension which more incident in this study.

(Table 4.4) and (Figure 4.3) Ultrasonic data collection of fetus's weight & discordance in this study was shown with the fetuses GA classified into six gestational age range groups by three week intervals, the mean EFW for the control fetus was (2117.22 gm), the mean EFW for target fetus was (165.79gm) with mean discordance was 22.97 %. The relation between the EFW and GA in the study groups gave high difference in EFW at gestational age (36-38) weeks.

(Table 4.5) and (Figures 4.4, 4.5, 4.6) The relation between MCA PI values and GA in control group was show gradually increase in PI values in early term and sudden decrease in midterm between (30-32) weeks and again increase in late term which was approved in previous studies , with completely inversed relation in target group .See (figure 4.4)

The relation between the MCA width and GA in control group was show less value in the early and mid terms and increase in late term between (36-38) weeks, with irregular values within the all gestational age range groups. See (figure 4.5)

The relation between the MCA PI/UAPI ratio and GA in control group was show gradually increase in CPR values in early term and sudden decrease in midterm between (30-32) weeks and again increase in late term which was approved in previous studies, with irregular general decreases in CPR values in all gestational age range groups in target group. See (figure 4.6).

(Table 4.6) and (Figure 4.7and 4.8) The difference in mean target/control ratio of MCA PI result was significant difference at (dependent analysis of MCA PI using Wilcoxon signed-rank test, P = 0.000) (mean PI ratio 0.71), but the difference in mean target/control ratio of MCA width result was insignificant difference at (dependent analysis of width values using Wilcoxon signed-rank test, P = 0.166) (mean width ratio 1.26).

The differences in MCA PI between the target and control fetus was still markedly visible and significant when comparing the two groups as independent samples using Mann–Whitney U test (Figure 4.8A, mean PI 1.47 and 2.13, respectively, P = 0.008). Moreover, the differences in MCA width between the target and control fetus was still markedly visible and insignificant when comparing the two groups as independent samples using Mann–Whitney U test (Figure 4.8 B, mean width 0.49cm and 0.39cm, respectively P = 0.015).

(Figure 4.9 and 4.10) The association between the MCA PI, MCA width and GA for study groups showed negative correlation between PI and GA with (r= - 0.369). And positive correlation between width and GA with (r= 0.282). The P value from r score result in insignificant difference between the two variables and GA. (p=0.101, 0.216 respectively).

(Figure 4.11) The association between the MCA PI and MCA Width in study groups was result in negative correlation (r= - 0.081) and insignificant difference at p value from r score = 0.726.

(E. Barzilay et al 2014) recently assess the MCA diameter as a method for assessment of brain sparing in intra-uterine growth-restricted discordant twins, and they found there was no significant difference in the MCA PI between the large and small fetuses(mean PI 1.51 ± 0.13vs 1.57 ± 0.07at P = 0.878, mean ratio 0.99 ± 0.11). While the MCA diameter was significantly larger in the smaller twin (mean diameter 3.55 ± 0.26 vs. 2.71 ± 0.22, P = 0.018, mean ratio 1.39 ± 0.14). show that measurement of MCA diameter can potentially be used as a tool for assessing resistance. E. Barzilay et al were studied the MCA diameter comparing with MCA PI in discordant twins in normal pregnant women concerning each twin as two groups large and small fetus while this study studied the fetus MCA in hypertensive women comparing with fetuses in normal pregnant women , Their study goal to determine the utility of middle cerebral artery (MCA) diameter measurement as a tool for evaluating brain sparing effect in intrauterine growth-restricted (IUGR) discordant twins while this study goal to assess the fetus MCA in hypertensive women , But if we compare the results of E. Barzilay et al with the results of this study see(appendix), the MCA PI was significantly smaller in target fetus(mean PI 1.47 vs. 2.13, P = 0.008 mean ratio 0.71,P=0.000). While there was insignificant difference in the MCA width (mean width 0.49cm vs. 0.39cm, P = 0.015, mean width ratio 1.26, P = 0.166), the different in values between two studies can be explained by the different group of pregnant mother in this study while their study only on one group of pregnant women Another factor may explained the deferent is E. Barzilay et al studied the twins MCA in inpatients normal maternal women where the status of patients not affect the results unlike this study whereare studied hypertensive maternal whose affect the results .

(Jerzy Gielecki1et al 2009) was performed a study of the Morphometric and volumetric analysis of the middle cerebral artery in human fetuses. The study finding that Diameter of M1 segment of the MCA increases approximately 3 times according linear function(y = −0.0705455 + 0.0043678*x with r=0.65) in gestational age range from (12-40) weeks. Analysis showed statistically significant differences mean value of M1 segment diameter between all Gestational Age Range Groups. There is no statistically significant difference between diameters of left and right and of M1 segment of MCA in each Gestational Age Range Group. Jerzy Gielecki1et al focused on the morphometric measurement while this study focused on both morphometric and volcimetric measurements Their study conducted in152 formalin-fixed human fetusesincluding long gestational age range from (12-40) while this study had conducted in42 alivenormal fetuscompared with 40 unnormal fetusin short gestational age range from (24-40) but if we compare results of goal achieved by Jerzy Gielecki1et al with results of this study (positive correlation between width and GA with (r= 0.282). The P value from r score result in insignificant difference between the width and GA) in gestational age range from (24-40) weeks, we find different between results, taking into account all different factors mentioned previously.

(E. Tarasw1 et al 2007) were performed study in the Measurements of the middle cerebral artery in digital subtraction angiography and MR angiography. Conducted on 114 examinations of cerebral vessels (88 DSA, 26 MRA), included normal adult patients, result in The diameters of ICA and MCA and its upper branch are age and sex dependent, being wider in men than in women and increasing with age. (Mean MCA 2.41±0.82mm) with insignificant differences were stated between age groups, which it was support this study although it was in not in fetuses.

(Veille JC et al 1993) were performed study of the longitudinal quantization of middle cerebral artery blood flow in normal human fetuses. Conducted on 20 normal fetuses had color Doppler ultrasound of the middle cerebral artery. A total of 68 studies were successfully done and are reported, Results in the diameter of the middle cerebral artery, the time velocity integral, and the peak flow velocity of the Doppler waveform increased significantly with advancing gestational age. In this stud the same result noted in control group as it consist of normal fetuses.

Scientific studies about the measurement of arterial sonographic parameters are difficult to compare, because different methods and statistical analysis steps are in use. In fetal studies, confounding variables could be created because of different methods of dividing the experimental/age groups. Other problems could arise in the metering of fetal arteries, as their size is quite small and could be due to inaccuracies in the method used to measure the vessels width. (Mari and Deter 1992) Fetal artery visualization and measuring is possible in ultrasound imaging (USG); but Sonographic methods are complicated and can carry high error levels:

30.40%, ± 1 mm in a vessel of 1.3 mm in diameter in an old GA group. (Noordam et al.1994).

Current vital research uses new imaging techniques like computerized tomography (CT) and magnetic resonance imaging (MRI) in adults to better visualize such structures, but not in fetus.

In this study pregnancies were complicated by maternal hypertension Inadequate cerebral perfusion was associated with decrease neonatal weight with mean EFW (165.79gm). There was significant difference in MCA PI between the target and control fetuses, with negative correlation between MCA PI and GA. and insignificant difference observed in MCA width between the target and control groups however the width increment markedly visible in target group with positive correlation with GA. Negative correlation observed between MCA width and MCA PI with insignificant difference in pregnancies with maternal hypertension.

This study was limited by the small number of patients enrolled and by our inability to determine whether the SGA fetuses were growth restricted because of placental insufficiency. Furthermore, because of the difficulty to fallow up after delivery we could not correlate the increased MCA width with the prenatal outcome. Another issue of concern is the fact that the vessel width was not measure directly but rather by measuring the color Doppler signals. So, variations in color Doppler signal may decrease the accuracy of this measurement. The small sample size and the heterogeneity of our study population regarding gestational age and ultrasound findings such as oligohydraminos and AEDF in umbilical artery are amongst the limitation of our study. Heterogeneity of the patient population may derived from the fact that not all cases of target group necessarily reflect placental insufficiency or may reflect different severity levels of placental insufficiency. It is also important to mention that as this is only a preliminary study of concept and because of the fallow up difficulty, we did not examine the maternal outcome measurement variation. For that purpose, large study, probably focused on singleton pregnancies with outcome correlation should be conducted.

5-2 Conclusion:

The study was show that assessment of fetus MCA PI and width in hypertensive women using Doppler ultrasound resulted in (mean MCA PI 1.35, mean UA PI 1.47, mean width 0.52cm, mean EFW 165.79gm and mean CPR 0.98) which indicated the effectiveness of mother hypertension in the fetus and predicted the intrauterine growth restriction. Although the results are somewhat satisfactory insignificant deference found between MCAPI, width, and GA that affected the specificity of MCA in predicting adverse prenatal outcome. Also the study reveals the efficiency and lack of in MCA width measurement as it can carry high error levels 50%, ± 2 mm in a vessel of 0.23 cm in diameter in an old GA group. This explains why USG is more investigative of the width measurement in relatively big vessels, but in quite small vessels it was more diagnostic of the quantitative blood flow measures.

5.3 Recommendations:

In order to improve the prediction of prenatal outcome for the fetuses in hypertensive pregnant women the researcher strongly recommends to:

1. All hypertension pregnant women in UAE should evaluated by Doppler studies by second trimester and onwards.
2. Create efficient pathways and processes to rapidly identify and evaluate potential IUGR fetuses.
3. Organize IUGR protocol for the high risk pregnancy.
4. More research is needed to determine the long-term health effects of hypertensive disorders in pregnancy and to develop better methods for identifying, diagnosing, and treating women at risk for these conditions.

Suggestions:

- Assessment of the accuracy and sensitivity of color Doppler in measurement of fetus MCA diameter.
- The clinical significance MCA dilatation with the presence of abnormal Doppler indices in IUGR fetuses.
- Nomograms of normal UAE fetal MCA Doppler diameter and equivalence of their pattern with other research.
- Sensitivity of the MCA vasodilatation to detect fetuses in the early stages of increased brain perfusion.