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Comparison of ultrasonographic and Doppler mapping of the intervillous circulation in normal and abnormal early pregnancies

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Abstract
There has been increased in studying the development of Intervillous circulation during early pregnancy gestation, made possible by the availability of using transvaginal ultrasound and transvaginal colour Doppler imaging.
Objectives: To assess the value of transvaginal ultrasonography and transvaginal colour Doppler imaging in characterizing the Intervillous circulation in normal and abnormal pregnancy.
Design: cross-sectional study.
Setting: AL-Elwiya Maternity Teaching Hospital, Baghdad-Iraq.
Main outcome measures: Comparison of detection of the moving echoes in the Intervillous circulation with grey-scale and colour Doppler imaging in normal and abnormal early pregnancies.
Subject and Methods: 162 pregnant women fulfilled the criteria for the inclusion in this study were evaluating for diagnosis and fate of pregnancy. All of the pregnant women were subjected to transvaginal ultrasound and transvaginal colour Doppler imaging examination only once time by using 5-MHz curve liner transvaginal probe, with pulsed colour and power Doppler facilities and real time grey-scale ultrasound were used to evaluate the placenta anatomy and to detect the moving echoes inside the Intervillous space at peripheral and central areas. 67 pregnant women has been subjected to both above examinations at 7-9 weeks, 53 of total 162 at 10-11 weeks and the rest 42 at 12-14 weeks of pregnancy.
Results: the overall degree of agreement between the two investigations was good. A significant different distribution of blood flow was found between normal and abnormal pregnancies at 7 to 9 weeks and 10 to 11 weeks but not at 12 to 14 weeks. There is no difference in the use of the transvaginal ultrasound and transvaginal colour Doppler imaging regarding the efficiency of the equipment but it remain dependable on the efficiency of the sonographist.
Conclusion: we concluded from this study the beneficial use of the transvaginal ultrasound or transvaginal colour Doppler imaging in estimating the state or the conditions of the placenta in early pregnancy and the results of these examinations may give an idea to some extents about the fate of the pregnancy. Early prediction of pregnancy that ended with abortion during the first trimester for any reason (Genetic, Immunological, Infectious) still represent a big challenge to the clinicians and patients were reflect the many ways for substantiation the pregnancy like Aspirin, Progesterone derivatives. This study shows that simple methods are useful for the prediction of the fate of the pregnancy that liable for abortion.

Keywords: Intervillous circulation, transvaginal ultrasound (grey-scale), transvaginal colour Doppler ultrasound, fate of the pregnancy

1. Introduction
Development of maternal-fetal circulation: The primary function of the placenta is the effective transmission of nutrient substances to the fetus. Fetal growth may be affected by changes in the mateno- placenta- fetal transport of nutrients, energy producing substrates and oxygen. An understanding of the development of the placenta and its role in utero- placental dysfunction is required in order to study the effects of utero-placental dysfunction. The functional anatomy of the materno-fetal circulation is characterized by profound haemodynamic changes in the uterine and fetal circulations in early pregnancy. The initial development of maternal fetal circulation is of interest due to the controversy of the development of the Intervillous circulation. The implantation of the blastocyst in the endometrium enables the proliferation of the trophoblast and its differentiation into two layers, the cytotrophoblast and the syncytiotrophoblast. The syncytiotrophoblast develop lacunae, which allows nutritive fluid known as embryotrophy to pass to the embryonic disc by diffusion. Syncytiotrophoblast Lacunae unite to form an interconnecting lacunars network, this network enables the flow of maternal blood thus establishing a primitive uteroplacental circulation providing nutritive substances and removing 'metabolic waste products. The lacunar network is the primordia of the Intervillous spaces of the placenta. The trophoblast cells migrate through the decidua and into the myometrium. When the trophoblast cells contact the opening of a spiral artery they enter the Lumina of the artery where they form intraluminal plugs. Endovascular trophoblast cells replace the endothelium of the spiral arteries. The spiral artery media is then invaded resulting in the destruction of the medial elastic, muscular and neural tissue and the incorporation of trophoblast cells in the vessel wall. Eventually the endovascular trophoblastic cells change their phenotype to resemble the endothelial cells that they replaced [1]. These intravascular changes create a low resistance arteriolar vascular system, which allow a dramatic increase in blood supply to the developing fetus. The trophoblastic plugs are thought to act as valves and restrict the flow velocity of the spiral arteries in order not to damage the developing placental membrane [2], the early placental growth develops in a hypoxic environment [3].

The Successful development of the placenta. depends upon the formation of low impedance uteroplacental circulation. This is dependent upon the successful Invasion of trophoblast to transform the maternal intra-myometrial portion of the spiral arterioles to create a low resistance arteriolar vascular system. Early Placental development occurs in a low oxygen environment, which is known to stimulate trophoblast proliferation and inhibit trophoblast invasion [3]. The hypoxic environment also promotes the development of branching vasculogenesis through the up-regulation of vascular endothelial growth factors. Later in the pregnancy, at about 10-12 weeks' gestation, true Intervillous circulation is established and there is an increase in placental PO_2 Levels. This increase in PO_2 levels triggers the trophoblast to change from a proliferative state within hypoxic cell columns to an invasive extravillous trophoblast that is responsible for the secondary wave of trophoblastic invasion of the maternal spiral arterioles [3]. The secondary invasion is responsible for the establishment of a high flow, low impedance uteroplacental circulation. After 11-12 weeks of pregnancy the primary chorionic villi develop and begin to branch to form secondary chorionic villi. These villi are lined with mesenchymal cells, which differentiate into arteriocapillary networks. The development of vascular networks signals the formation of tertiary stem villi that will over time develop into the mature fetal placental circulation. These tertiary stem villi will connect to the developing embryonic cardiovascular system. An effective uteroplacental circulation is effectively established by the fourth week post conception. The maternal blood flows into the Intervillous spaces in funnel shaped spurts. Exchanges occur with the fetal blood across the placental membrane, so the placental membrane consists of fetal tissues and contains four layers; the syncytiotrophoblast, the cytotrophoblast, the connective tissue core of the villous and the endothelium of the fetal capillary artery [1]. Development and pathophysiology of the placental maternal circulation: Continuous circulation of maternal blood through the Intervillous chamber requires progressive adaptation of the individual cotyledon to the blood flow offered to it by the corresponding uteroplacental artery. During the first trimester of pregnancy, the growing embryo and its placenta are completely separated from the maternal circulation [l, 3, 4]. *In vivo* contact transvaginal sonography, hysteroscopy, and examination of chorionic villus sampling materials are unable to detect a real blood flow in the Intervillous spaces before 12 weeks of gestation [1, 2]. The early placenta is bathed by a fluid, possibly composed of maternal plasma and uterine gland secretions [l, 3, 4]. After 12 weeks, the trophoblastic plugs in the spiral arteries, still remaining from the first extravillous trophoblastic wave, no longer obliterate the uteroplacental arteries and real circulation is established [1, 3]. A second wave of endovascular trophoblast migration invades the myometrial segments of the spiral arteries, allowing the progressive dilation of these vessels [4]. By the end of pregnancy, the placenta maternal blood supply is estimated around 600 ml /min. Trophoblast Invasion: Anatomy of trophoblast invasion and the morphological aspects of human trophoblast invasion have been examined in great detail over the last 20 years [6, 7, 8]. Since it is difficult to reliably obtain human material before 4 weeks of gestation, much of our morphological understanding of the earliest phases of trophoblast invasion has been extrapolated from monkey material [9, 10]. Examination of monkey implantation sites has revealed that trophoblast begin to migrate down into the maternal spiral arteries as early as 10 days after fertilization, and at 14 days, many of the spiral arteries beneath the conceptus are totally occluded [10] The specificity of this vascular interaction is revealed by the fact that no such invasion takes place in the veins. Do human trophoblasts behave in the same fashion? This question has been more difficult to answer and addressing it has demanded varied approaches. Hustin and Schaaps [11], using anatomical and ultrasounographic approaches, suggested that there is in fact trophoblast plugging of the maternal spiral arteries and a coincident decrease in maternal perfusion of Intervillous space until 12 weeks of Gestation. Rodesch *et al.* [12] then hypothesized that it is critical that maternal blood flow to the embryo be limited very early in gestation to protect the conceptus from excessively high oxygen levels during critical early stages of differentiation. This concept was supported by Coppens *et al.* [13] whose study of serial ultrasounds on normal pregnant women between 8 and 14 weeks showed no uteroplacental blood flow in the first trimester but a significant increase at approximately 12 weeks, which reached maximal levels at 14 weeks. Burton et al critically examined the Boyd Collection, 12 early-pregnancy hysterectomy specimens ranging from 43 to 130 days of gestation housed in the Department of Anatomy at The University of Cambridge, and showed that there was significant blockage of the maternal spiral arterioles by trophoblasts at points of contact with the Intervillous space between 6 and 8 weeks, but that this blockage was gradually eliminated between 8 and 12 weeks of gestation [14], despite its teleological attractiveness, the first trimester low-flow concept has not been universally accepted [15, 16, 17]. The controversy over this issue, however, seems to have been settled with the use of an advanced oxygen sensing probe. In this issue of The American Journal of Pathology, Jauniaux *et al.* [18] report the direct documentation of a significant increase in placental Intervillous oxygen tension, and hence maternal perfusion of the placenta, between 8 and 12 weeks of gestation. This article also reports that, coincident with this increased perfusion and oxygen tension within the placenta between 8 and 12 weeks, there is a corresponding increase in anti-oxidant systems, including catalase, glutathione peroxidase, and super oxide dismutase, presumably to counteract the oxidative stress of the increased Intervillous perfusion and oxygen tension. If we accept trophoblast plugging and the first trimester low-flow concept, one question remains: how are the first-trimester embryo's nutritional needs met? Hustin and Schaaps [11] suggested that the Intervillous space is bathed by an acellular fluid that could be plasma filtered by the trophoblastic shell. Burton and colleagues [14] have offered another possibility by examining multiple human implantation sites preserved in the Boyd Collection, these investigators noted the presence of dilated endometrial glands below openings to the Intervillous spaces. It is well known that the endometrial glands of early pregnancy are characterized by hypersecretion [19]. Combining these observations, Burton *et al.* [14] have suggested that secretions from the hypersecretory endometrial glands contribute nutrients to the embryo in the first trimester. In confirmation of this hypothesis, these workers noted in several specimen's glandular secretions within the Intervillous spaces near the openings of the gland mouths. Their hypothesis is not unreasonable in light of the fact that other animals, most notably the rabbit and pig, bath their early conceptuses in endometrium-derived fluids, such

as uteroglobin [20, 21] which has also been recently identified in the human [22]. Concomitant with endovascular plugging of the maternal spiral arteries, the processer of trophoblast penetration of the maternal spiral arteries and their conversion to low-resistance channels begins. Pijnenborg *et al.* [23] after examination of many placental bed biopsies from the first and second trimesters, proposed a two-wave hypothesis for trophoblast invasion an initial interstitial invasion in the first trimester followed by endovascular invasion in the second trimester. Matijevic *et al.* [24] using transabdominal colour flow and pulsed Doppler imaging, showed that these changes were complete at around 17 weeks of gestation and that impedance to blood flow is lowest in the uterine arteries in the central area of the placental bed, consistent with the invasive trophoblast. Physiological changes seen in placental bed biopsies in that region [23]. Pijnenborg [23] also made the observation in his study that the interstitial trophoblasts were able to modify the maternal arteries indirectly, presumably via paracrine action, simply by surrounding these vessels.

One possible mediator of this action is nitric oxide [NO], which is capable of markedly vasodilating arteries and arterioles. In support of this concept, Nanaev *et al.* [25] from examination of the guinea pig placental bed, have suggested that [NO] production by invasive trophoblasts may augment maternal vascular dilation before trophoblast penetration. However, Myall *et al.* [26] have recently demonstrated in the human that invasive trophoblasts do not express NO synthase, raising doubts about the role of NO in maternal vascular dilation in the human.

2. Technique

The equipment should be selected according to the sensitivity of the B-mode and Colour Doppler module. The patient, with an empty urinary bladder, is placed in the Lithotomy position. A condom and gel are placed over the head of the vaginal transducer [5-7.5 MHz] and the probe is then introduced gently into the vagina. After visualization of the pelvic anatomy by B-mode and colour Doppler sonography, the colour flow of interest can be explored with Doppler sample volume until the typical spectral waveform is seen. The peak-systolic and end-diastolic frequency shifts can be recorded and A/B ratio, the pourcelot resistance Index [RI] or the pulsatility index can be calculated. On each record, five separate cardiac cycles can be examined and the mean value calculated. The mean duration of the examination is usually no longer than 10 minutes. The spatial peak, temporal average intensity should not exceed l00mW/cm^2. This is the highest limit of insonation energy allowed by the U.S food and drug administration for use in fetal medicine.

2.1. Prediction of abnormal pregnancy

Some authors have already suggested the possibility of using transvaginal colour Doppler ultrasound to assess the uteroplacental circulation from the end of the fourth gestational week [27]. A considerable volume of knowledge has been acquired recently about the normal limits and deviation from normally of Doppler velocimetry during the second half of pregnancy. By contrast there is little information obtained with Doppler ultrasound during the first trimester. Radiological assessment of the maternal-trophoblastic border in hysterectomy patients with pregnancy in situ did not show contrast medium in the Intervillous region before the l2th week. Histological examination of this section detected plugs obliterating the vascular lumen of the uteroplacental arterioles, i.e. spiral arteries in the retro-trophoblastic region [10]. After the l2th week of pregnancy, these arterioles gradually showed free vascular lumen, allowing the identification of the intraplacental blood vessels and uterine arteries. These findings were supported by Jaffe and Woods [28], which studied 46 women from six to 12 weeks of pregnancy and were able to identify Intervillous flow in only one patient, using transvaginal colour Doppler ultrasonography. In another study, some authors studied a group of normal pregnancies from 7 to 12 weeks' Gestational age to evaluate the utility of colour Doppler sonography of the uteroplacental circulation in predicting the outcome of first trimester pregnancies. They described a higher incidence of abortions among pregnancies that showed a greater resistance index (RI) in the retro- trophoblastic region. They also detected blood flow in the Intervillous space between 7 and 12 weeks [29]. By contrast, other authors reported that vascular patterns obtained with colour Doppler ultrasound could not be used to predict adverse gestational result [30]. Normal pregnancies, missed abortions and non-embryonic gestations presented no significant difference in blood flow impedance in the blood vessels of the trophoblastic region [31]. Therefore, there is no enough information presently available on circulatory changes evaluated with Doppler ultrasound during the first trimester of a normal pregnancy that could be associated with gestational prognosis. When comparing features of the placental circulation at different ages on Doppler Imaging, we found that a non-pulsatile signal corresponding to maternal intraplacental blood flow cannot be identified in the Intervillous space of normal pregnancies before 10 to 11 weeks of gestation. By contrast, in complicated early pregnancies, the placenta appears on colour flow mapping to be hyper vascularized well before the end of the first trimester 10-12 Weeks.

3. Materials and methods

3.1. Subjects

The study was conducted on pregnant women (162) attending the Obstetrics and Gynecology Department at Al-Elwiya maternity Teaching Hospital and from private clinic. The study was extended from 1/7/2014 to 1/7/2015.

The pregnant women had been evaluated for the following information:

- Diagnosis of pregnancy is based on the history of amenorrhea and on the last menstrual period. Then confirmed the diagnosis by pregnancy test and abdominal ultrasound in the outpatient clinic.
- Duration of pregnancy (follow up of the pregnancy): The Gestational age of the pregnancy was determined by the initial data of the last menstrual period [LMP], crown-rump length [CRL] up to 14 weeks' gestational age. In those Patients biparietal diameter were used for evaluation the evolution pregnancy.
- Fate of pregnancy: the evolution of the pregnancy was assessed by clinical examination, abdominal ultrasound, transvaginal ultrasound and transvaginal colour Doppler imaging to confirm the viability of the fetus, the fetal death or absence of embryo.
- Criteria for exclusion from the study were as follow:-
- Chronic maternal diseases [pneumopathies, hypertension, autoimmune diseases and diabetics Mellitus].
- Myometrial pathologies, uterine malformations.

- Patients who had undergo surgical intervention through the present gestation.
- Echo graphic embryo malformation.
- Multiple gestation.

3.2. Transvaginal ultrasound and transvaginal colour Doppler imaging examination

Transvaginal ultrasonographic and transvaginal Doppler examinations of the intraplacental circulation were performed to all pregnant women 162 for one time during their pregnancy in 67 pregnant women during 7-9 week, 53 pregnant women during 10-II week, and 42 pregnant women during 12-14 week, by using a 5-7.5 MHz Curvilinear transvaginal probe with pulsed colour and power Doppler facilities. In each Case, the placental insertion of the umbilical cord was located by using colour Doppler mapping. Real-time grey-scale transvaginal ultrasonography was used to evaluate the placental anatomy and detect moving echoes inside the Intervillous space, where the moving echoes detecting at the periphery or at the central of the uertoplacental circulation. In each case, after which colored mapping was carried out in power Doppler mode so that the cursor could be adequately positioned at an angle that varied between 20 and 40 Degree at the area with greatest blood flow. Especially the Intervillous space flow [Moving Echoes inside the Intervillous space] at the peripheral and central area. The presence of Intervillous blood flow [i.e. a continuous flow like inside the placental tissue] was evaluate by using color power Doppler imaging set to the lowest pulse rate frequency to allow a minimum blood flow velocity detectable of 3.7 cm/s for color Doppler and 0.4 cm /s for power Doppler.

3.3. Statistic

The interobserver variability was calculated by using the SPSS program (statistical package of social science, standard version, Version 9.1th, 2012 by SAS. Inst. Inc. Cary. N.C. USA. It included application of the Chi Square test to assess the degree of significance between different variable P [0.05] it also included application of the frequency of the different variables and cross.

4. Results

4.1. The transvaginal ultra sound findings and the transvaginal colour Doppler findings: -

The transvaginal ultrasound [TVUS] findings and the transvaginal colour Doppler imaging [TVCDI] findings were as follow, the TVUS and TVCDI with peripheral flow and without central flow [P +ve, C –ve] 73 (45. 1%), the findings without peripheral flow and with central flow [P -ve, C +ve] 68 (41.9%), the findings of both peripheral and central flow [P and C +ve] 21 (13%) and as shown in Figure (1).

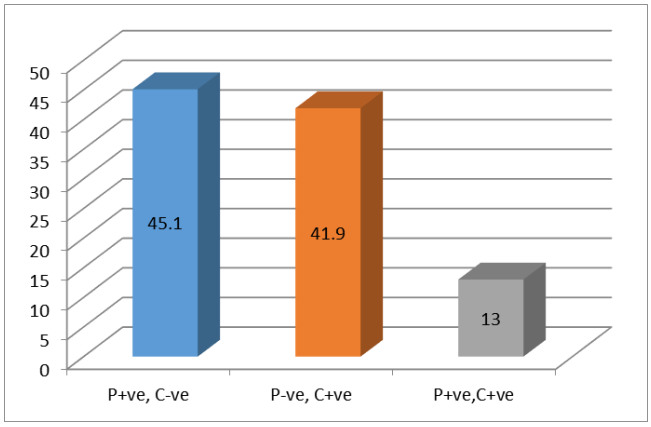

Fig 1: The transvaginal Ultrasound finding, P= peripheral, C= Central.

4. 2. The classification of the pregnant women according to the weeks of pregnancy

Out of the 162 pregnant women, 67 (41.4%) had the TVUS and TVCDI at 9 weeks of their pregnancy, 53 (32.7%) had the TVUS and TVCDI at 10-ll weeks of pregnancy, and the rest 42 (25.9%) had the examinations at 14 weeks of pregnancy as shown in Figure (2).

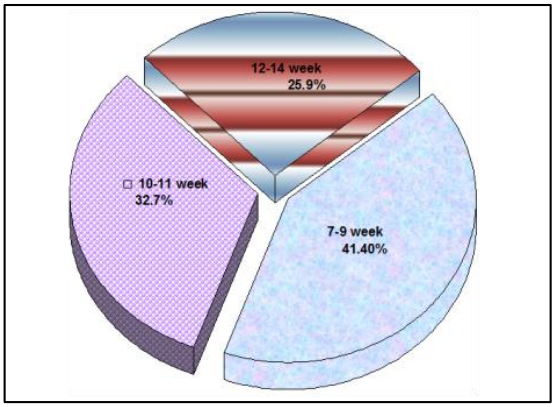

Fig 2: The classification of the pregnant women according to the weeks of pregnancy.

4.3. The relation between the TVUS, TVCDI findings and fate of pregnancy according to weeks of pregnancy: -

4.3.1 At 7-9 week

At 7-9 week of pregnancy, out of 162 pregnant women, 67 (41.4%) pregnant women had the ultra sound and Doppler examination. 39 (58.2%) with [P+ve, C –ve] all of them reached to full term, 28 (41.8%) with [P -ve, C +ve] all of those pregnant women with these findings ended with abortion. was no pregnant woman with both P and C +ve at this period of pregnancy. The result of Chi square that shown in Figure (3, 4) indicate a positive significant association [P = 0.001] between fate of pregnancy and the TVUS and

TVCDI findings at the 7-9 week of pregnancy.
These indicate that in early normal pregnancy (at 7-9week) doing of these examinations [TVUS, TVCDI] whenever the results of the blood flow at the periphery of the circulation indicate normal pregnancy and with less pregnancy complication, while if the results are with central perfusion without peripheral perfusion indicate an abnormal pregnancy and it would end with complication.

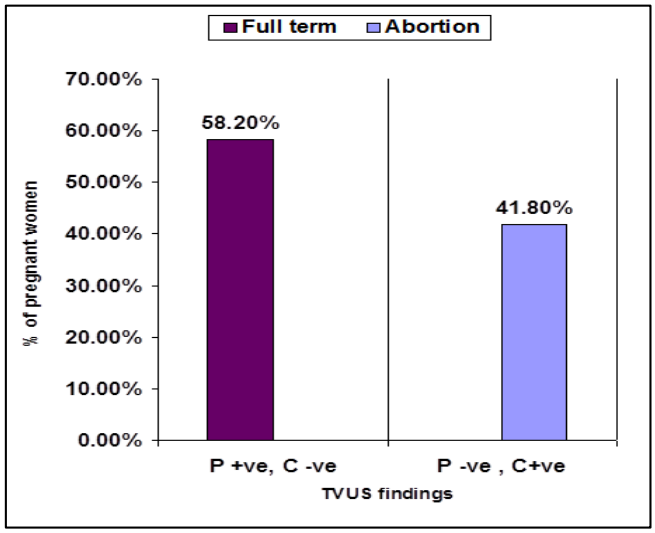

Fig 3: The % of the pregnant women with TVUS findings at 7-9 weeks

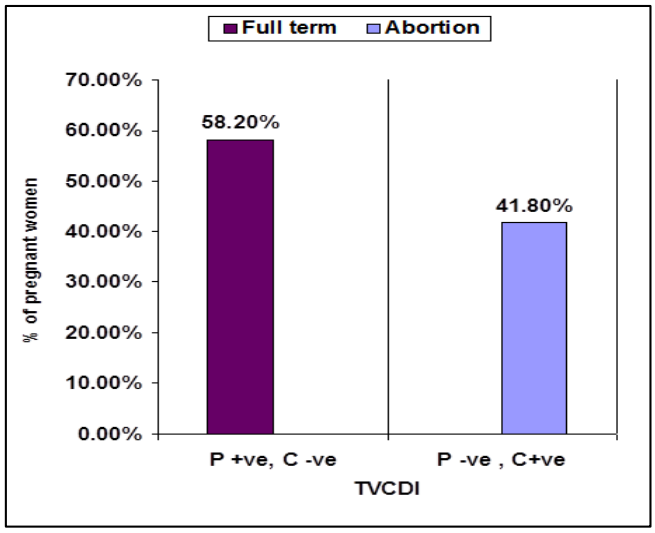

Fig 4: The % of the pregnant women with TVCDI findings at 7-9 weeks

4.3.2. At 10-11 week

At 10-II week of pregnancy, out of 162 pregnant women, 53 (32.7%) pregnant women had TVUS and TVCDI examination. 29 (54.7%) women were with [P +ve, C –ve] all of them reached to full term. 23 (43.4 %) were with [P -ve, C +ve] all of the them ended with abortion. And only one 1.9% with P and C +ve; as the pregnant woman ended with abortion. The result of Chi square that shown in Figure (5, 6) indicate a positive significant association [P = 0.001] between TVUS and TVCDI findings and the fate of pregnancy at the 10-Ilweek of pregnancy.
These indicate that in early normal pregnancy at [10-11 weeks] who had these examinations [TVUS, TVCDI] the results shows that the blood flow at the periphery of the uteroplacental circulation indicate normal pregnancy and it would reach to full term, while if the blood flow is central perfusion without peripheral perfusion indicate an abnormal pregnancy and it would ended with abortion and also indicated that both perfusion central and peripheral start to appear at this period, and this case ended with abortion which indicate that this finding mast be abnormal at this period although the sample is small.

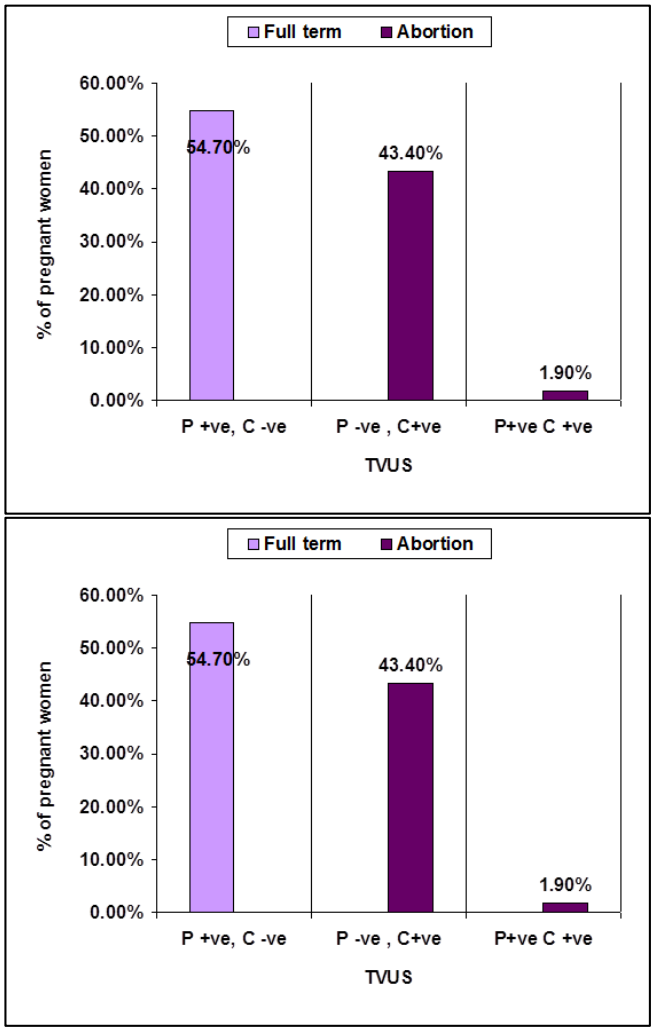

Fig 5: The % of the pregnant women with TVUS findings at 10-11 weeks

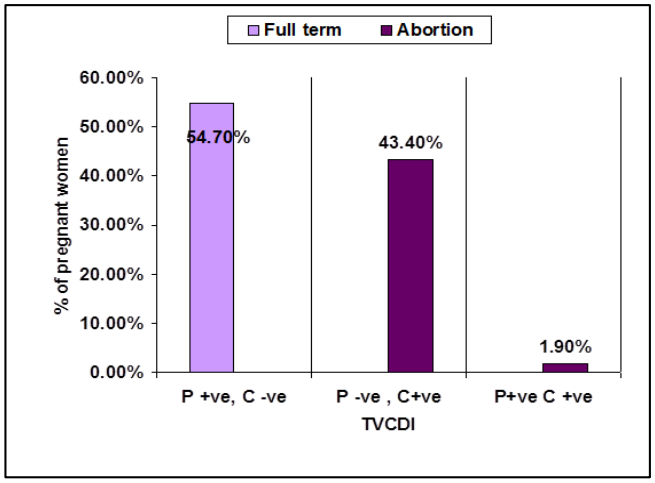

Fig 6: The % of the pregnant women with TVCDI findings at 10-11 weeks

4.3.3. At 12-14 week

At 12-14 week of pregnancy, out of 162 pregnant women, 42 (25.9%) pregnant women had the TVUS and TVCDI examination. 5 (II.9%) of them were with [P +ve and C –ve] and they reached to full term. 17 (40.5 %) of them were with [P-ve and C +ve] and all of them ended with abortion. 20 (47.6%) were with both P and C +ve and all of them reached to full term. The result of Chi square that shown in Figure (7, 8) indicate a positive significant association [P = 0.001] between TVUS and TVCDI findings and the fate of pregnancy at the 12-14 weeks of pregnancy. These indicate that,' the peripheral perfusion with or without central perfusion during this period 12-14 week indicate a normal pregnancy, while central perfusion without peripheral perfusion indicate abnormal pregnancy in this period in addition to other 2 periods [7-9 weeks, and 10-II weeks].

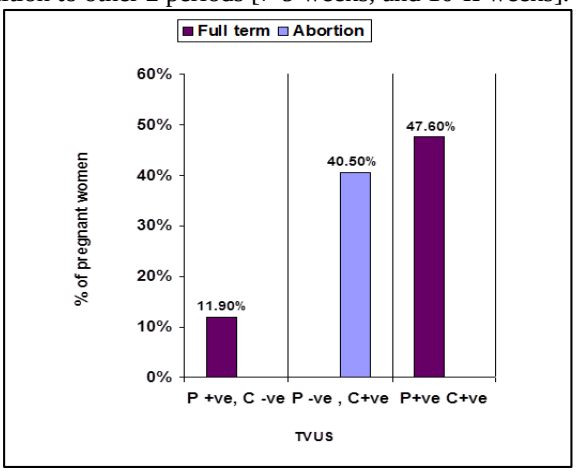

Fig 7: The % of the pregnant women with TVUS findings at 12-14 weeks

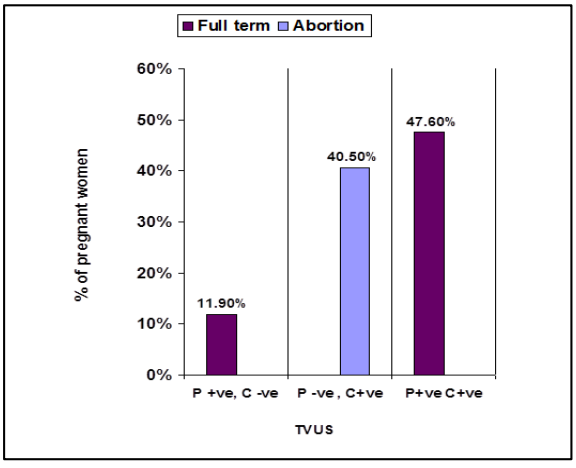

Fig 8: The % of the pregnant women with TVCDI findings at 12-14 weeks

4.4. Pregnant women with fate of the pregnancy

Out of 162 pregnant women, 93 (57.4%) reach to full term pregnancy, and 69 (42.6%) end with abortion. Out of the 69 pregnant women end with abortion 34 (49.3%) with blighted ovum, 24 (34.8%) with missed abortion, and 11 (15.9%) with incomplete abortion. The results of Chi square of the types [P < 0.003] as shown in Figure (10, 11).

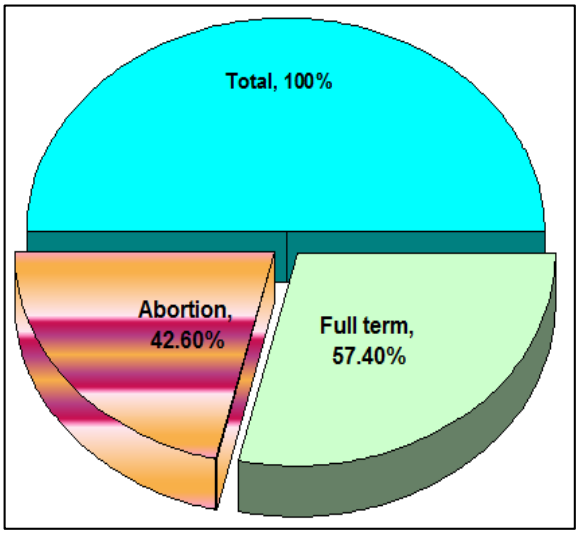

Fig 9: The number of the pregnant with fate of pregnancy

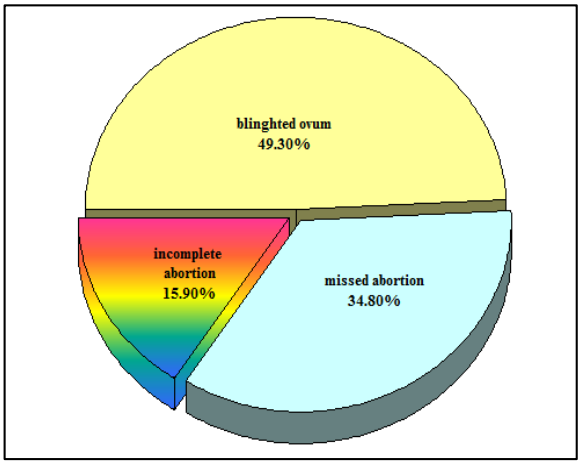

Fig 10: The type of abortions in aborted pregnant women P < 0.003

5. Discussion

There has been increased interest in studying the development of Intervillous circulation during early gestation, made possible by the availability of the technologically advanced equipment and the possibility of studying blood now using transvaginal colour Doppler imaging and transvaginal ultrasound.

The results of our study indicate a significant association between the transvaginal ultrasound [TVUS] and transvaginal colour Doppler imaging [TVCDI] findings and the fate of the pregnancy. Out of 162 pregnant women who did examinations, 73 (45.1%) were with peripheral perfusion +ve and central perfusion -ve [P +ve, C-ve], 68 (42%) with peripheral perfusion -ve and central perfusion +ve [P -ve, C +ve], and 21 (12.9%) with both peripheral and central perfusion +ve [P and C +ve]. The fate in those women with these findings were, all The pregnant women 73 (45.1%), with P +ve, C-ve reached to full term i.e. they had normal pregnancy, while the 68 (42%) with P-ve, C +ve ended with abortion i.e. they had abnormal pregnancy. The 21 (12.9%) women with P and C +ve, 20 (95.2%) reached to full term and only one (4.8%) ended with abortion, also this indicate that, they had normal pregnancy.

These findings agreed with the findings of Rustin and Schaaps [11] who suggested that no real blood circulation in the Intervillous space was present in the initial stages of pregnancy as well as they found that small moving echoes could always be detected in the myometrial vessels in the normal pregnancies but that these moving echoes could only be detected in the placenta in 6% of cases., by contrast, they found slow turbulent movements inside the placenta in 96% of cases of early pregnancy failure. The findings of Rustin and Schaaps [11] were further supported by the results obtained by Jauniaux *et al*. [32] who did not identify Intervillous flow before 12 weeks of gestation in normal pregnancy, although it was observed in women with abortions. as well as Jauniaux *et al*. [32] also concluded that there could be two periods of placental Vascular development during the first trimester of pregnancy: the first period would Last up to the l2th week of gestation when the blood flow does not reach the Intervillous space, blocked by plugs' that obliterate the spiral arterioles. During The second period, starting in the l2th week, the vascular lumen of the spiral arterioles is open and blood reaches the Intervillous space. Later Jauniaux *et al*. [33] suggest that in normal pregnancies, the Intervillous circulation starts in the periphery of the placenta (peripheral), whereas in early pregnancy failures, it is more intense and diffuse throughout the placenta (with central perfusion). In addition, Jauniaux *et al*. [34] founded that, moving echoes were mainly at the periphery of the uteroplacental circulation in the normal pregnancy, and at both the center and the periphery in abnormal pregnancy.

Regarding the results of the examination according to weeks of pregnancy; we found that out of 67 women who did the examination at 7-9 weeks of pregnancy 39 pregnant women with P+ve and C -ve and all of them reached to full term, while the other 28 pregnant women (41.8%) were with P-ve and C +ve ended with abortion. These results indicate that in early normal pregnancy at 7-9week doing of these examinations [TVUS, TVCDI] whenever the results of the blood flow at the periphery of the circulation indicate normal pregnancy and with less pregnancy complication, while if the results are with central perfusion without peripheral perfusion indicate an abnormal pregnancy and it would end with complication. The results of the examination at 10-ll weeks, which show that out of 53 women, 29 (54.7%) pregnant women with P +ve and C-ve and they reached to full term, while the other 23 (43.4%) pregnant women were with P-ve and C +ve ended with abortion and only one (1.9%) women with both central and peripheral perfusions were ended with abortion.

These results also indicate that in early normal pregnancy at l0-11 weeks who had these examinations [TVUS, TVCDI] the results shows that the blood flow at the periphery of the uteroplacental circulation indicate normal pregnancy and it would reach to full term, while if the blood flow is central perfusion without peripheral perfusion indicate an abnormal pregnancy and it would ended with abortion and also indicated that both perfusion central and peripheral start to appear at this period, and this case ended with abortion which indicate that this finding mast be abnormal at this period although the sample is small.

While at 12-14 weeks of pregnancy, the results of 42 women, 5 (11.9%) pregnant women with P +ve and C -ve and all of them reached to full term, while the other 17 (40.5 %) pregnant women with P-ve and C +ve ended with abortion and 20 (47.6 %) women with both central and peripheral perfusion and all of them reached to full term. these results indicate that, the peripheral perfusion with or without central perfusion during this period 12-14 week indicate a normal pregnancy, while central perfusion without peripheral perfusion indicate abnormal pregnancy in this period in addition to other 2 periods [7-9 weeks, and 10-II weeks]. The explanation of these findings, as Jauniaux found that during the first 10 weeks of normal pregnancy, the apical portions of the majority of the uteroplacental vessels are partial obliterated by plugs of invading trophoblast cells, it is hypothesized that these plugs prevent continuous flow of maternal blood into the Intervillous space during this period and therefor the human placenta is not truly hemochorial until the end of the first trimester [35]. On the other hand, Norman and Lodwick [36] found that, in early pregnancy failure the trophoblastic shell is thinner and fragmented and the trophoblastic infiltration of both lumen and endometrial vessels and the deciduas is reduced or absents. Concerning the abnormal fate (abortion) of the abnormal pregnancy, out of 162 pregnant women 69 (42.6%) ended with abortion. 68 (98.6%) of them were with P-ve and C +ve and only one (I.4%) was with P +ve, and C +ve and this woman was at the 10-II weeks of pregnancy period. The type of abortion was: 11 (15.9%), ended with incomplete abortion, 24 (34.8%) ended with missed abortion, and 34 (49.3%) ended with blighted ovum.

These results indicate a significant relation between the examination [TVUS and TVCDI] findings and early pregnancy failure. The explanation for these findings, that the higher significant percent of type of abortion was the abortion with blighted ovum may be due to these types of abortion as they are non-embryonic pregnancy so there is no trophoblastic shell or plugs so there is continuous flow of maternal blood into the Intervillous space as an abnormal utero-placental circulation. But Jauniaux [34] found that, Intervillous blood flow was significantly more frequently with in missed abortion presented with embryonic remnants inside the sac than in those presenting with empty gestational sac.

The results of this study also suggest that the uteroplacental blood flow may be different in missed abortions and non-embryonic gestational sacs than in normal Pregnancies. Women with missed abortions and non-embryonic gestational sacs Frequently showed a facilitated uteroplacental blood flow (central), as indicated by a higher Number of myometrial blood vessels, higher frequency of flow in the Intervillous space and lower vascular impedance, compared with those in normal Pregnancies. Still, the results of this study contribute to the concept that early Intervillous circulation might occur in normal pregnancy and that failed gestations could be associated with a greater uteroplacental blood flow Jauniaux [34].

The results of both examination TVUS and TVCDI was similar, this indicate a similar efficiency of the both equipment in detecting of the early placental circulation as well as detecting abnormal, utero-placental circulation. While Jauniaux [34] founded that the detection of the Intervillous moving echoes by grey-scale imaging significantly more frequently than detection by the colour Doppler imaging. The differences in these finding may be explained on the differences in the types of equipment used in the examination and the resolution in addition to the resolution of the probes used in the examination.

6. Conclusions

We concluded from this study the beneficial use of the transvaginal ultrasound or transvaginal colour Doppler in estimation the state or the conditions of the placenta in early pregnancy especially in the case of presence of abnormal pregnancy and the results of these examinations may give an idea to some extents about the fate of the pregnancy. Also the results of this study indicate that, there is no difference in the use of the transvaginal ultrasound and transvaginal colour Doppler imaging regarding the efficiency of the equipment but it remains dependable on the efficiency of the sonographist. Early prediction of pregnancy that ended with abortion during the first trimester for any reason (Genetic, Immunological, Infectious) still represent a big challenge to the clinicians and patients alike were reflect the many ways for substantiation the pregnancy like Aspirin, progesterone derivatives, and these two simple methods are useful for the prediction of the fate of the pregnancy that liable for abortion. It should be stressed that vaginal ultrasound examination even in early pregnancy is not invasive clinical investigation. This mean it can be a screening test prior to Chorionic Villous Sampling which is associated with 4% abortion, or amniotic fluid sampling in the second trimester, which is associated with 2-3% possibility of abortion, or in recurrent abortion. Early normal color Doppler imaging can avoid unnecessary invasive techniques. The results of this study necessitate further studies to be carried out on the same field for further evaluation of these results.

7. References

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