Introduction

Two-dimensional ultrasound [2D] is in routine use in nearly most hospitals and many physician clinics as it offers a lot of benefits compared to other medical imaging techniques. Ultrasonography offers unique qualities including real-time imaging, physiologic measurement, use of non-ionizing radiation, no known bio-effects in the diagnostic range while being non-invasive. Sonographic image quality has benefited from increasingly sophisticated computer technology **(Schaapas, 1999)**.

2D Ultrasound is basically an axial image and 3D Ultrasound is a volume and 4D Ultrasound is a volume with time and the fifth dimension is how you bring a level of workflow into ultrasound **(Liza Haar, 2015).**

The challenging problem of abnormal placentation has become increasingly clinically significant in obstetric practice, due to the dramatic rise in cesarean deliveries over the past four decades ***(Okada et al., 2007).***

Morbidly-adherent placentas manifest as placenta accreta, increta or percreta, depending on the depth of placental invasion. These conditions present high risk of severe obstetrical

hemorrhage at delivery. The underlying pathology is due to defects in the decidua basalis caused by a variety of insults, such as previous surgery, excessive curettage or infection ***(Milosevic et al., 2009).***

The incidence of morbidly adherent placentas is rising as the frequency of cesarean sections increase. Imaging plays an important role in the antenatal detection of this condition ***(Min-Min Chou et al., 2009).***

In women with placenta previa, the risk of placenta accreta varies from 2% in women younger than 35 years old with no previous caesarean section to 39% in women at or over 35 years of age with two or more caesarean sections. In women with placenta previa, previous caesarean section and advanced maternal age are independent risk factors. In the presence of these risk factors, the obstetrician must have a high index of suspicion for placenta accreta and take appropriate precautions. In particular, this condition must be included in the differential diagnosis in women with previous caesarean sections and anterior placentation ***(Min-Min Chou et al., 2009; Wu et al., 2005).***

Successful management of this potentially catastrophic condition requires early antenatal diagnosis and referral to a tertiary institution where multidisciplinary expertise in

perinatology, anesthesia, diagnostic radiology and blood transfusion services are available. There is therefore a need for reliable antenatal diagnoses, since such a condition, when encountered unexpectedly at delivery, will invariably lead to massive blood loss, multiple complications such as adult respiratory distress syndrome, Sheehan's syndrome, renal failure and death ***(Okada et al., 2007).***

One area in which 3D ultra-sound seems to afford advantages over 2D ultrasound is in the imaging of abnormalities of the placenta, especially when the multislice capability of 3D ultrasound is combined with dynamic assessment of blood flow using power Doppler

Recently considerable success had been found by using 3D tamographic ultrasound imaging (TUI) coupled with power Doppler in the imaging of patients with suspected morbid placentation ***(Silver et al., 2006).***

The development of increasingly sophisticated computer hardware and software tools has advanced to the point that computed tomography- and magnetic resonance imaging (MRI)-like technologies are now incorporated into ultrasonography systems. These new technologies permit, among other things, use of the entire 3D US data set to create a cube that can be sliced and displayed in various ways using intuitive interfaces

and the resulting data can be extracted along a flat plane ***(Silver et al., 2006).***

The TUI mode allows simultaneous display of multiple sequential parallel views of a reference (sagittal, transverse or coronal) plane of an object. The reference plane, the number of images displayed within one screen (1 × 1, 2 × 1, 3 × 2, 4 ×3 or 6× 4), the orientation and rotation of an image, the magnitude of magnification and slice depth and interval (0.5 to 5 mm) can be adjusted according to the region of interest (ROI) ***(Silver et al., 2006).***

The objective of this study is to evaluate the potential of these new techniques for prenatal detection of placental invasion in anterior placenta on scar of previous Cesarean section.

Aim of the Work

To evaluate the potential of the 3 D TUI in diagnosis of morbidly adherent placenta in comparison to 2D grayscale, color Doppler and intraoperative findings.

Null Hypothesis:

There is no difference in diagnosis of placental invasion in anterior placenta on scar of previous Cesarean section by 3D TUI،gray-scale and color doppler techniques.

Research question:

In pregnant women, Does TUI superior in diagnosis of morbidly adherent placenta than Two-Dimensional Ultrasound measurement and color doppler?

Abnormal Placental Adherence

Definition:

Morbidly adherent placenta is a general term that includes placenta accreta, increta, and percreta. Placenta accreta refers to an abnormality of placental implantation in which the anchoring placental villi attach to myometrium rather than decidua, resulting in a morbidly adherent placenta. Placenta increta (chorionic villi penetrate into the myometrium) and placenta percreta (chorionic villi penetrate through the myometrium to the uterine serosa or adjacent organs) are related, but more severe, abnormalities of placental implantation. The pathogenesis is primarily attributed to defective decidualization of the implantation site **(*Tantbirojin et al, 2008)***

In the literature, the term "placenta accreta" may be used to refer to any degree of placental invasion, which is why we prefer the term "abnormal placentation ***(Miller et al., 1997).***

Although there are no studies directly comparing outcomes of these conditions, it is commonly understood that surgical morbidity is related to the degree of placental invasion***(Mehrabadi et al, 2015).***

Incidence:

The marked increase in rate of morbidly adherent placenta has been attributed to the increasing prevalence of cesarean delivery in recent years ***(Mehrabadi et al, 2015).***

The incidence of placenta accreta in Canada was 1 in 695 deliveries in 2009 to 2010

In 1950, placenta accreta was rare, occurring in 1 in 30,000 deliveries in the United States ***(Miller et al., 1997)***.

In a 1977 report, the incidence in the published literature was estimated to be 1 in 7000 deliveries ***(Breen et al., 1977)***.

During the 1980s and 1990s, the incidence markedly increased, reaching 1 in 731 deliveries between 2008 and 2011 in a cohort of over 115,000 deliveries in 25 hospitals in the United States ***(Miller et al., 1997).***

Miller and colleagues reported an incidence of abnormal placentation of 1 in 2510 for a 10-year period at their center ending in 1994 ***(Miller et al., 1997).***

Similarly, Wu and colleagues reported an incidence of 1 in 533 over a 20-year period 1982- 2002 ***(Wu et al., 2005).***

In 2006, the incidence increased to be 1 in 210 deliveries **(Stafford et al, 2008)**.

The marked increase has been attributed to the increasing prevalence of cesarean delivery in recent years. The incidence of placenta accreta in Canada was 1 in 695 deliveries in 2009 to 2010***(Mehrabadi et al, 2015).***

These recent estimates are almost certainly influenced by ascertainment bias and the different criteria used to diagnose abnormal placentation.

Miller and colleagues limited their study to histologically confirmed cases of abnormal placentation on cesarean hysterectomy specimen ***(Miller et al., 1997).***

Risk factors:

Several risk factors for placenta accreta have been reported, including a previous cesarean delivery particularly when accompanied with a coexisting placenta previa, increasing numbers of prior cesarean deliveries increase the risk of placenta accreta ***(Wu et al., 2005).***

Other risk factors include a history of uterine surgery (eg, myomectomy entering the uterine cavity, hysteroscopic removal of intrauterine adhesions, cornual resection of ectopic pregnancy, dilatation and curettage, endometrial ablation), cesarean scar pregnancy, maternal age greater than 35 years, history of pelvic irradiation, and infertility and/or infertility procedures (eg, in vitro fertilization) ***(Roberts and Myatt, 2015).***

Conversely, the increased incidence reported by Wu and colleagues may be a reflection of the broader definition used in the study, which included:

(1) Clinical diagnosis;

(2) Pathological diagnosis;

(3) Difficult manual piecemeal removal if no separation occurred after 20 minutes, despite active management of the third stage; and

(4) Heavy continued bleeding from the implantation site of a well-contracted uterus after placental removal during cesarean delivery.

(Wu et al., 2005).

Pathophysiology:

Abnormalities in the process of trophoblast invasion may result in abnormal placentation. Both the embryonic trophoblast and maternal deciduas produce corticotrophin-relasing hormone (CRH), which promotes implantation. Carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1), which is expressed in extravillous tropho-blasts (EVTs) of normal human placenta, may also function in trophoblast/endometrial interactions ***(Bamberger et al., 2006)***.

Locally produced CRH plays a role in trophoblast invasion, primarily by regulating CEACAM1 expression. CRH inhibits trophoblast invasion by decreasing the expression of

CEACAM1 through CRHR1, an effect that might be involved in the pathophysiology of clinical conditions, such as preeclampsia and placenta accreta ***(Bamberger et al., 2006)***.

The complex development process of implantation involves a series of steps leading to an effective cross-talk between invasive trophoblast cells and the maternal endometrium. This dynamic process requires a precisely coordinated development of a hormonally primed adhesive endometrium and a blastocyst competent to implant. The trophoblast undergoes a number of distinct interactions with the underlying endometrial surface initiated by apposition, which involves close proximity between trophoblast and endometrial epithelium, followed by attachment, and concluded by invasion of trophoblast into the decidualized stroma ***(Bamberger et al., 2006)***.

The hypothalamic neuropeptide corticotrophin-releasing hormone (CRH) is produced in several organs of the female reproductive system, including the endometrial glands, decidualized stroma, and trophoblast. In addition, the gene encoding the CRH receptor type 1 (CRHR1) is expressed in human endometrial and myometrial cells, indicating a local effect of uterine CRH. Indeed, locally produced CRH promotes implantation and maintenance of early pregnancy ***(Bamberger et al., 2006)***.

The trophoblast is the first tissue to differentiate in the mammalian conceptus, and its normal development and specific properties are crucial for both implantation and further survival

of the embryo. Furthermore, the placenta is unique in its ability to proliferate and invade another tissue in a controlled manner. It is not surprising that similarities exist between trophoblast invasion and the invasion of cancer cells. The endometrium restricts trophoblast invasion, whereas the latter is highly invasive when it implants in ectopic sites, such as the peritoneum. Thus, trophoblast invasion is a very interesting model for the study of molecular mechanisms involved in these processes ***(Bamberger et al., 2006)***.

Starting with the initial contact, which is made between the trophoblast and the apical plasma membrane of the endometrial surface epithelial cells, through the invasion of the deciduas and the invasion of decidual vessels with gradual colonization of the arterial wall of the spiral arteries, cellular contacts mediated by cell adhesion molecules are essential. Cell adhesion molecules are important mediators of tissue architecture and cellular polarity and have also been shown to modulate proliferation and differentiation processes ***(Bamberger et al., 2006)***.

The pathogenesis of placenta accreta has been well-characterized microscopically (e.g., poor decidualization with intramyometrial infiltration of the villous tissues) and macroscopically (e.g., prominent uteroplacental neo-vascularizaiton in the region of interest) ***(Tseng et al., 2004)***.

Placental development requires the synergistic effect of angiogenic growth factors and their receptors. Among them,

both Tie-1 (tyrosine kinase with immunoglobulin and epidermal growth factor homology domains) and Tie-2 (tunica internal endothelial cell kinase) receptors have been regarded as specific vascular endothelial markers. However, in humans, their expression is not only limited to the vascular endothelium but also the palcenta; furthermore, their expression is altered in the villous trophoblasts of affected women with recurrent abortion. Therefore, Tie-1 and Tie-2 might be key players in implantation ***(Partanen and Dumont, 1999)***.

Immunohistochemical expression of Tie-2 in the syncytiotrophoblast complicated by placenta accreta was significantly reduced. Ang-2 immunoreactivity in the syncytiotrophoblast of placental villi showed a higher expression in placenta accreta specimens ***(Wulff et al., 2003)***.

The presence of functional Tie-2 receptor in tropho-blast cells demonstrates a specific role for angiopoietins as regulators of trophoblast behavior in placental development. The interactions between Tie-2 and its ligands (Ang-1 and Ang-2) are involved in the well-prepared endometrium, trophoblast invasion, and remodeling of the maternal vasculature during the peri-implantation stage ***(Rowe et al., 2003)***.

Thus, the increased in placental Ang-2 level would result in an overall destabilization of uterine vasculature and then enhance the neovascularized phenomenon found in palcenta accreta ***(Dunk et al., 2000)***.

In placentation, the Ang-1/Tie-2 pathway could promote trophoblast growth, act as a potent chemotactic factor for trophoblasts, and maintain fetoplacental vascular development and stabilization; furthermore, the Ang-2/ Tie-2 pathway could stimulate an increase in trophoblast DNA synthesis and the release of nitrous oxide, and remodel the maternal vasculature. In a variety of invasive, highly vascular malignancies ***(Wulff et al., 2003)***.

In conclusion, it has preliminary findings of increased Ang-2 expression as well as reduction of a special receptor for the ligand, Tie-2, in placentas from pregnancies complicated by placenta accreta. This report demonstrates that life-threatening uteroplacental neovascularization typical of placenta accreta may be correlated with these molecular changes. In addition, that it was acknowledge that decidual defect is still a major contributing factor for the formation of placenta accreta; however, differential expression of Tie-2 and Ang-2 may play an additive or synergistic role ***(Wulff et al., 2003)***.

Human embryo implantation and placentation relay on a series of complex interactions between the trophoblast and the different components of the maternal deciduas. During these morphogenetic processes, trophoblast cells undergo remarkable differentiation allowing them to participatie in distinct functions. Early in the process of placentation, the formation of free-floating villi and anchoring villi directs the differentiation of the trophoblasts along 2 main pathways, namely, the villous and the extravillous one. Although villous trophoblasts display

features of a polarized epithelial cell layer, extra-villous trophoblasts lose their polarization and behave like mesenchymal cells invading the deciduas ***(Kliman and Feinberg, 1990)***.

The pathways involved in the regulation of tropho-blast invasion and migration may be very complex and cAMP may be involved at various steps. Importantly, cAMP was previously found to inhibit trophoblast invasion ***(Kliman and Feinberg, 1990)***.

Placenta Accreta:

Placenta accreta is characterized by lack of intervening decidua which allows direct contact of anchoring villous tissue to underlying myometrium. This leads to excessive invasion, an adherent placenta, and bleeding. The scenario has parallels to tubal pregnancy where the absence of decidua in the fallopian tube is associated with deep invasion of trophoblast into adjacent vessels ***(Roberts and Myatt, 2015)***.

Placental attachment disorders are classified according to the depth of myometrial penetration. In placenta accreta, villi embed on the myometrium in the absence of decidua; in placenta increta, villi embed deeper into myometrium, whereas in placenta percreta, the villi have penetrated through the uterine serosa. Whether the pathology results from lack of