Introduction

Placenta accreta is considered a severe pregnancy complication that may be associated with massive and potentially life-threatening intrapartum and postpartum hemorrhage **(Faranesh et al., 2007)**, so it has become one of the most important leading cause of emergency hysterectomy which represents 40–60% of cases **(Daskalakis et al., 2007).**

Maternal morbidity had been reported to occur in up to 60% and mortality in up to 7% of women with placenta accreta **(Sumigama et al., 2007; Eller et al., 2009).** Also the additional potential intraoperative and post operative morbidity were associated with massive blood transfusion, hypovolemai, and infection **(Judson et al., 2008)**.

The exact pathogenesis of placenta accreta is unknown, but the most common theory is the defective decidualization related to previous surgery which allows the placenta to attach directly to the myometrium **(Tantbirojn et al., 2008; Khong, 2008)**.

According to the histopathology, it is divided into three grades: placenta accreta where the chorionic villi are in contact with the myometrium, placenta increta where the chorionic villi invade the myometrium, and placenta percreta where the chorionic villi penetrate the uterine serosa, or even invade adjacent organ most commonly the bladder **(Tan et al., 2007).**

The incidence of placenta accreta has been steadily increasing, mirroring increased rates of caesarean delivery **(Hamilton et al., 2005)**.

In the period of 1982-2002, researchers have reported the incidence of placenta accreta as 1 in 533 deliveries **(Wu et al., 2005)**. In 2006, the incidence increased to be 1 in 210 deliveries **(Stafford and Belfort, 2008)**. The marked increase in incidence has been attributed to the increasing prevalence of cesarean delivery in recent years.

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; Sivan et al., 2010).** The authors of one study found that, in the presence of a placenta previa, the risk of placenta accreta was 3%, 11%, 40%, 61%, and 67% for the first, second, third, fourth, and fifth or greater repeat cesarean deliveries, respectively **(Silver et al., 2006).**

Ultrasound is the recommended first step in the diagnosis **(Doumouchtis and Arulkumaran, 2010)** with sensitivity 77-93 %, specificity 71-97% and PPV 65-88 % **(Chou et al., 2000; Warshak et al., 2006; Zhang et al., 2006; Dwyer et al., 2008 and Esakoff et al., 2011)**.

Color Doppler ultrasound has been suggested to aid in the diagnosis of placenta previa accreta because it highlights abnormal areas of hypervascularity with dilated blood vessels within the placental and uterine tissues **(Lerner et al., 1995; Levine et al., 1997; Chou et al., 2000).**

Color Doppler will show that some of the placental sinuses traverse the uterine wall with turbulent blood flow which extending from the placenta to surrounding tissues, this is very sensitive and correctly identified all patients with accreta and not present in any patient without **(Lerner et al., 1995).**

Several reports have showed that, the use of color Doppler imaging can improve the accuracy of the diagnosis of placenta accreta since the depth of invasion of the placenta into the uterine myometrium or serosa can be more accurately determined, especially in cases where the placenta is located anteriorly **(Twickler et al., 2000; Comstock et al., 2005).**

In this study, we evaluated the vascular morphological manifestations of placenta previa in patients with previous cesarean sections by the transabdominal color Doppler ultrasound, whether accreta or not, then we calculated the sensitivity, specificity, PPV, and NPV for each criterion of the color Doppler ultrasound, and we compared them with the clinical and histopathological results to evaluate their accuracy.

Aim of the Work

The aim of this study is to evaluate the accuracy of color Doppler ultrasound in diagnosis of placenta previa accreta.

The color Doppler criteria suggestive of placenta accreta include:

- Absence of subplacental vascular signals in the areas lacking the peripheral subplacental hypoechoic zone → (A).
- Dilated vascular channels with diffuse lacunar flow pattern scattered throughout the whole placenta and the surrounding myometrial or cervical tissues. High-velocity pulsatile venous-type flow was found in the sonolucent vascular spaces → (D).
- Interphase hypervascularity with abnormal blood vessels linking the placenta to the bladder with high diastolic arterial blood flow → (H).
- Irregular vascular lakes with focal turbulent lacunar flow pattern distributed regionally or focally within the intraparen-chymal placental area → (F).

The Placenta

The placenta is literally the "tree of life." Structurally, the placenta is a hemochorial villous organ. Functionally, the placenta is a highly complex machine: (1) it acts like a lung in the exchange of oxygen and CO2; (2) it works as a digestive system, absorbing all necessary nutrients for fetal development and growth; (3) it functions as a kidney to remove wastes; and (4) it behaves as an immune barrier that protects the growing fetus from antigen attack from the maternal system **(Wang and Zhao, 2010).**

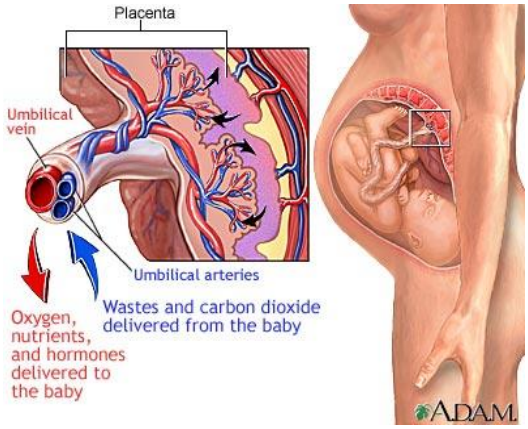

Fig. (1): In the placenta, nutrients, wastes, and gases are exchanged between the mother's blood and the baby's blood. **(www.aviahmidwiferyservices.com)**

The placenta is also an important endocrine organ producing many hormones and growth factors that regulate the course of pregnancy, support and promote fetal growth, and

initiate parturition. However, all these tasks depend on normal vascular development within the placenta itself. Normal placental vascular development ensures a healthy pregnancy outcome, whereas insufficient or abnormal placental vascular development will compromise pregnancy outcomes both of the mother and the fetus. The functional unit of the placenta is the chorionic villus, which contains the layers of syncytiotrophoblasts/cytotrophoblasts, villous stromal, and fetal vascular endothelium that separate maternal blood from the fetal circulation **(Wang and Zhao, 2010).**

Macroscopic appearance:

The expelled placenta is a discoid mass which weighs about 500 gm; its diameter varies from 15-20 cm, and its thickness from 3-4 cm near its center rapidly diminishing towards the periphery. Its fetal or inner surface, which is covered by the amnion is smooth and transparent, so that the mottled appearance of the chorion can be seen through it **(Hibbard, 1989).**

The umbilical cord is usually attached near the center of the fetal surface and the branches of the umbilical vessels radiate out under the amnion from this point, the veins being deeper and larger than the arteries. Beneath the amnion and close to the attachment of the umbilical cord, the remains of the yolk sac can sometimes be identified as a minute sac with a fine thread (a vestige of vitello-intestinal duct) attached to it **(Abramowies et al., 1989).**

The maternal or outer surface is finally irregular in appearance and is mapped out into 15 to 30 areas by a series of fissures or grooves. These areas are the bases of the lobules or cotyledons and from the grooves between them incomplete septa extend into the substance of the placenta **(Boyd and Hamilton, 1970).**

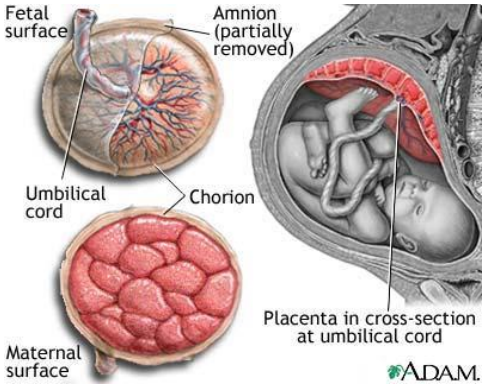

Fig. (2): Placenta in cross section at umbilical cord shows the fetal surface covered partially by amnion and chorion. Also shows the maternal surface exposed in the lower and right corner of the figure. Note the small branches of the uterine artery and the series of grooves. **(www.aviahmidwiferyservices.com)**

Microscopic structure of the mature placenta

The utero-placental unit is composed of both fetal tissue derived from the chorionic sac and maternal tissue derived from the endometrium. In the mature placenta, the fetal aspect is called the chorionic plate, this region carries the fetal chorionic blood vessels, which are branching radials from the umbilical vessels. The maternal aspect of the placenta is called the basal

plate. In between these two regions is the intervillous space which contains the main functional units of the placenta extensively branched and closely packed villous structures containing fetal blood vessels. It is at the terminal regions of these chorionic villi that the large majority of maternal— fetal exchange occurs **(Benirschke et al., 2000).**

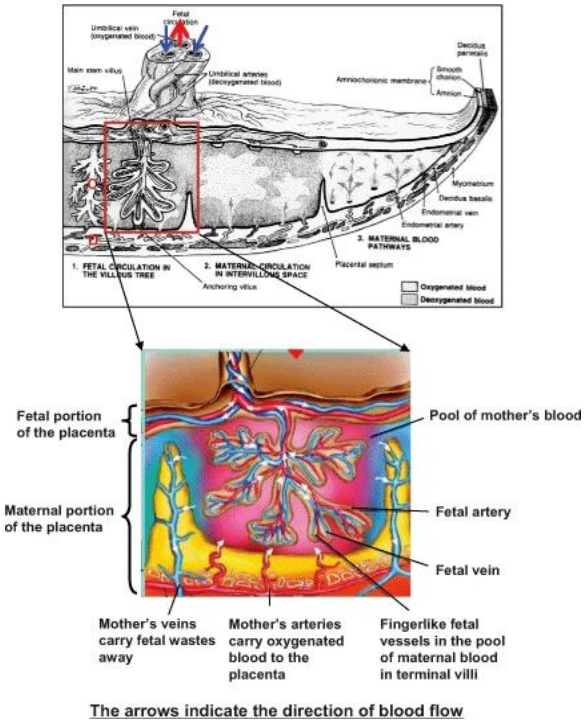

Fig. (3): A schematic drawing of a section through a full–term placenta. Upper panel: (1) The relation of the villous chorion to the decidua basalis (C) and the fetal-placental circulation (D); (2) The maternal blood flows into the intervillous spaces (3) Maternal blood flow pathway. The arrows indicate the direction of the blood flow **(Wang and Zhao, 2010).**

The intervillous space is completely lined with a multinucleated syncytium called the syncytiotrophoblast. Circulating maternal blood enters this space via spiral endometrial arteries, bathes the villi and drains back through endometrial veins. Oxygen-deficient fetal blood passes via two umbilical arteries and the branched chorionic arteries to the extensive arterio—capillary—venous system within the chorionic villi. The well-oxygenated fetal blood in the capillaries returns to the fetus via the various chorionic veins and the single umbilical vein **(Blackburn, 2003).**

The placental membrane

The term placental membrane (sometimes called the placental barrier) refers to the layers of cells that separate the maternal blood in the intervillous space and the fetal blood in the vasculature in the core of the villi **(Moore and Persaud, 2003).**

Initially, the placental membrane is made up of four layers, the maternal facing syncytiotrophoblast, a layer of cytotrophoblast cells, connective tissue of the villus and the endothelium lining the fetal capillaries. By approximately 20 weeks, however, the cytotrophoblast cell layer of many villi becomes attenuated and disappears. Subsequently, in most of the chorionic villi, the membrane consists of three layers and, in some areas, becomes extremely thin such that the

syncytiotrophoblast comes in direct contact with the fetal capillary endothelium **(Moore and Persaud, 2003)**.

The fetal membranes

The fetal membranes contain the fetus throughout the pregnancy and eventually undergo programmed rupture during the first stage of labor **(Bryant-Greenwood, 1998).**

The amnion comprises five distinct layers. The innermost layer is the amniotic epithelium, which is in direct contact with the amniotic fluid on one side and a basement membrane on the other. The other layers consist of the compact layer, the fibroblast layer and the spongy or intermediate layer. The chorion consists of the reticular layer, a basement membrane and the trophoblast cell region, which at term firmly adheres to the maternal decidual tissue. Like the placenta, the fetal membranes play an integral role in fetal development and progression of pregnancy. In addition to autocrine regulatory activities, the membranes secrete substances both into the amniotic fluid, affecting amniotic fluid homeostasis, and towards the uterus, where they may influence maternal cellular physiology. The membranes also play a protective role for the fetus against infection ascending the reproductive tract **(Bryant-Greenwood, 1998).**

Implantation

The period for uterine receptivity for implantation is relatively short. Physiological preparation of the endometrium is modulated by cyclic secretion of 17h-estradiol and progesterone. These hormones regulate growth factors, cytokines and adhesion molecules that alter the endometrial surface and open the implantation window **(Blackburn, 2003).**

Other substances, such as fibronectin, close the window several days later. Prior to attachment to the endometrial epithelium, the zona pellucida surrounding the blastocyst is lost. Immediately after attachment, the trophoblast cell layer of the blastocyst proliferates rapidly and differentiates into an inner cytotrophoblastic layer and an outer multinucleated syncytiotrophoblastic mass. The syncytiotrophoblast extends into the endometrial epithelium and invades the connective tissue **(Boyd and Hamilton, 1970).**

The blastocyst sinks beneath the endometrial surface, which is gradually repaired. Nourishment is obtained from the eroded maternal tissues and lacunar networks form within the syncytiotrophoblast **(Aplin, 2000).**

Maternal blood moves in and out of these networks, thus establishing the uteroplacental circulation. Extensions of proliferating cytotrophoblast cells evaginate into the syncytiotrophoblast in various places. These extensions are the

first stage in the development of the chorionic villi of the placenta **(Moore and Persaud, 2003)**.

The decidual reaction

Decasualization of the endometrial stroma occurs as part of the normal menstrual cycle; however, in the event of pregnancy, decidual changes become more extensive. Glycogen and lipids accumulate in the cytoplasm of the cells causing them to enlarge and take on the appearance of the pale-staining decidual cells. The cellular and vascular changes of the endometrium as the blastocyst implants are referred to as the decidual reaction. The function of the decidua, however, is not certain. Rather than facilitating implantation and trophoblast migration, it has been suggested that the main role of the decidua is to restrain the inherently invasive trophoblast and control its migration **(Loke and King, 1995).** This may be achieved by conversion of the motile invasive trophoblast cells into the static placental bed giant cells.

Trophoblast development

After successful implantation and initiation of placentation, trophoblast cells undergo extensive proliferation and differentiation. There are two main pathways by which trophoblast differentiation may occur, that is, villous and extravillous. By days 13 to 14 of pregnancy, cytotrophoblast cells penetrate the layer of syncytiotrophoblast surrounding the early conceptus to form columns of extravillous cytotrophoblast

cells. These contiguous cells form the cytotrophoblastic shell that is at the interface of the feto-maternal compartments **(Boyd and Hamilton, 1970).** Extravillous trophoblast cells invade the decidua and migrate so that they penetrate and remodel maternal blood vessels in the uterine decidua (endovascular trophoblast). This process produces dilated, compliant uterine arterioles that are unresponsive to maternal vasomotor control. Thus, the maternal blood supply to the placenta is promoted by this process and is, by term, about 30% of the mother's cardiac output, which itself has increased by 30—40% **(Khong et al.,1986).** Trophoblast cells do not invade the decidual veins. Nevertheless, syncytial knots that detach from the chorionic villi into the intervillous space are deported into the maternal circulation via these veins **(Loke and King,1995).**

Extravillous cytotrophoblast cells also invade interstitially (interstitial trophoblast). These invasive cells promote the circumferential expansion of the placental site and recruitment of maternal arterioles; allowing subsequent expansion of the villous region of the placenta below **(Boyd and Hamilton, 1970).** The full thickness of the uterine mucosa to the decidual— myometrial border has been extensively colonised by 8 weeks of pregnancy. Interstitial trophoblast cells become multinucleated and more rounded and form placental bed giant cells as they move deeper into the decidua **(Loke and King,1995).** These cells are regarded as the terminally differentiated end-point of the extravillous pathway.

Extravillous cytotrophoblast cells at the tips of anchoring villi rapidly proliferate to form the cytotrophoblast cell columns. Cells distal in the column subsequently switch from an epithelial to a mesenchymal cell type, facilitating their migration into, and invasion of the decidua and its vasculature. This phenotypic switch is essential for migration of the cells **(Vicovac and Aplin, 1996).** Production and/or secretion of type IV collagenase, matrix metalloproteinases, h glucuronidase, aminopeptidases, cathepsin B, urokinase- type plasminogen activator, urokinase- type plasminogen activator receptor and laminin by the extravillous cytotrophoblast cells enables their infiltration into the decidua by promoting degradation of extracellular matrix **(Morrish et al., 1998).** Insulin-like growth factor may also be involved in this process, as it is abundantly expressed at the invading front **(Han and Carter, 2000),** and induces cytotrophoblast migration in culture **(Hamilton et al., 1998).** Counterbalancing the degradative activity that promotes invasion of the decidual extracellular matrix, extravillous cytotrophoblast cells also secrete plasminogen activator inhibitor and tissue inhibitors of matrix metalloproteinases. These secretory activities appear to be regulated by autocrine and/or paracrine actions of growth factors, particularly, transforming growth factor **(Graham, 1997).**

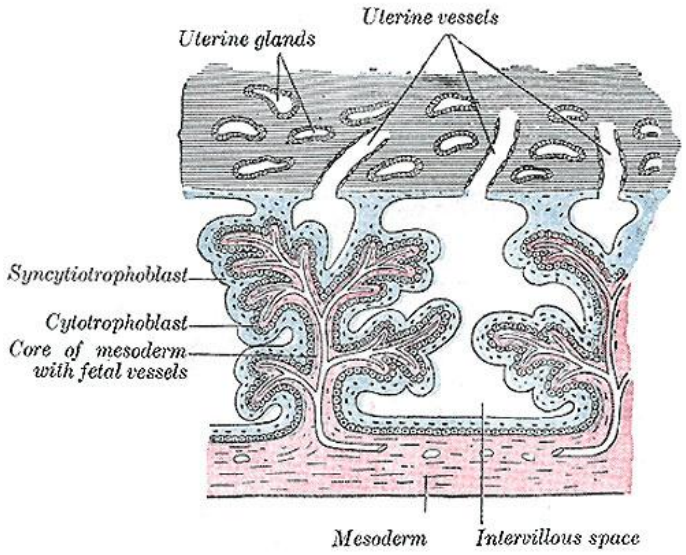

Fig. (4): Section of Chorionic Villi **(www.en.wikipedia.org).**

Villous (non-migratory) cytotrophoblast cells proliferate, differentiate and fuse to form the outer epithelial layer of the chorionic villi, the syncytiotrophobast. The primary villi are formed by evaginations of syncytiotrophoblast with a cytotrophoblast core. Fetal mesenchyme grows into the cytotrophoblast to form the secondary villi and by the third week of gestation fetal capillaries develop within the villous mesenchyme forming the tertiary villi. Initially,chorionic villi are found on the surface of the entire chorion but as the conceptus grows the decidua on the uterine luminal pole (decidua capsularis) atrophies, as does the villi apposed to it. This leaves the definitive placental villi in a discoid region. As gestation progresses the chorionic villi grow and arborise. Exchange takes place in the most part through the terminal villi that project into the intervillous space. It is the tips of villi that