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Histopathological Alternations of Placenta in Pregnancy Women Complicated with Gestational Diabetes

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ABSTRACT

Diabetes mellitus is the metabolic disorder, which affect the pregnant mothers as well as their neonates because of its influence on the placenta, the occurrence of which is continue to increase. By studying the placentae of the gestational diabetic pregnancy and comparing it with the placentae of normal pregnancy, we can recognize the changes that occurs in placenta because of gestational diabetes, such as crowding of villi, increased villous number of immature intermediate villi, decreased terminal villi density, increased terminal villi size, numerous syncytial knots, basement membrane thickening in terminal villi, cytotrophoblast in terminal villi, decreased vascular-syncytial membrane thickness, extravillous fibrinoid, fibrosis, fibrinoid necrosis, stem villi and mature intermediate with indented margin, villi with continuous trophoblastic layer, immature intermediate villi with loose reticular stroma and basement membrane thickening as well as increased of Hofbauer cells population, calcification intracellular as well as extracellular, chorangiosis, thickening of villi vessels, fetal vessel thrombosis, nucleated fetal RBCs, edema in terminal and stem villi and villous edema in mature intermediate and which can affect the neonates.

Keywords: *Placenta, Gestational diabetes, Histopathology.*

INTRODUCTION

The placenta is a highly complex and fascinating organ. During the course of a pregnancy, it acts as the lungs, gut, kidneys, and liver of the fetus. The placenta also has major endocrine actions that modulate maternal physiology and metabolism and provides a safe and protective milieu in which the fetus can develop [1]. When GDM develops, in the maternal tissues, the insulin-dependent glucose uptake is further decreased and hyperglycemia develops. Because the placental transfer of glucose is concentration dependent under conditions of maternal hyperglycemia and placental normal function, there is increased placental transfer of glucose and fetal hyperglycemia and secondary to this alteration, hyperinsulinism develop. Once the umbilical supply of glucose is suddenly arrested after delivery, in the newborn, the remaining hyperinsulinism increases the risk of hypoglycemia [2].

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Histopathologically, gestational diabetes has been associated with increased fibrinoid material, villous edema, and thickening of the basement membrane in trophoblastic cells [3]. Thickness of the endothelial basement membrane, and increase in collagen fibers of villous stroma have been described for GDM placentae [4]. However, the gross and histopathological alterations in gestational diabetes placentae are changeable and even somewhat controversial [5].

Thus, the aim of the present study is to investigate the incidence of histopathological alternations in placentae of gestational diabetes and normal pregnancies at term and preterm gestation in Iraqi women.

MATERIAL AND METHOD

Fresh placentae were obtained from Department of Obstetrics and Gynaecology in three hospitals in Baghdad at the period between 1 December 2016 and 1 may 2017. Two studying groups were analyzed: First group, women with uncomplicated, the group was considered as control group (cases n=34). Second group included women with pregnancies complicated by

gestational diabetes mellitus (cases n=34). The mothers' informed consents were gained according to Local Research Ethics Committee approval in Iraqi Ministry of Health.

Placentae were cut and sampled for histological examination. Two standard samples were taken from the selected lobule of placenta one from the central area and other from the peripheral area. Fresh placental tissue pieces were placed in a labelled clean plastic container containing 10% NBF solution [6]. Tissue samples from placentae after delivery were prepared for histopathological studies according to the methods of [7]. The sections was transferred to glass slides to be stained. Haematoxylin and Eosin staining was accomplished according to Bancroft, *et.al.* (2013). [8]. The sections were examined by compound light microscope (Meijitechno, Japan) with digital camera (Canon, Japan, 18 megapixels). Images were analyzed independently with the help of expert pathologist by Multihead teaching microscope (Genex, USA).

RESULT AND DISCUSSION

Diabetes is metabolic disorder in the world that has the effect on all the organs of the body, including the temporary organ such placenta, thus can have adverse neonatal outcome, and thus is of serious concern [9]. On investigation of placental sections with light microscope, a numerous of histological variations were recognized in the present study. These variations mentioned as follow:

Crowding of villi (Fig.1-A): In the present study, crowding of villi was seen to be increased significantly higher in DM group followed by GDM group then control group which recorded one case. [10] reported that histological anomalies such as presence crowding of villi was more frequently observed in diabetic placenta this finding agreed with our study.

Increased villous number of immature intermediate villi (Fig.1-B): A placental abnormality that has been individually related with an increased risk of stillbirths [11]. Due to defect in placental maturation have been related with chronic fetal hypoxia [12], a larger rate of immature intermediate villi may be revealing of a better preuterine hypoxic environment [13; 14].

Decreased terminal villi density (Fig1-B): Increasing the size of villi especially terminal and immature intermediate villi, gives the false impress of increased terminal villous density [15]. Number of studies reported an association between the frequency of immature villi and insufficient or absent terminal villi in GDM [15; 16].

Increased terminal villi size (Fig1-B): In the current study, terminal villous size significantly increased in both diabetes groups compared to controls. Mayhew (2002)reported that terminal villi size was statistically different in diabetic placentae compared to control[17].

Numerous syncytial knots (Fig1-C): Increased numerous of syncytial knots, bridges and sprouts are called as syncytial knotting or Tenny-Parker changes [18]. In past study, done by Gheorman, *et.al.*2012; as compared with the normal placenta, placentae from pregnant women with diabetes showed an increased incidence syncytial knots[15].

Basement membrane thickening in terminal villi (Fig1-D): This histological change of placenta are mainly due to metabolic disturbances that leads to accumulation of carbohydrate and fat in the placenta. Whereby, this thickening is the consequence of mucopolysaccharide storage [18]. This finding was described in various study, [19] who noticed increasing thickening trophoblastic basement membrane were present in most of the diabetic placenta in comparison of normal women.

Cytotrophoblast in terminal villi (Fig1-D): The absence of cytotrophoblast layer could be due to its obvious mitotic division at the 16th week of gestation to form syncytial trophoblast and become incorporated together as a syncytial layer. This incorporation in one homogeneous layer without basement membranes will manage the transport effectiveness through it to meet the increased metabolic supplies of the developing fetus mainly during the second half of gestation (19th-38th week) [20]. Bentley-Lewis, *et.al.* 2014; found that placental anomalies in GDM including increased cytotrophoblastic[21].

Decreased vasculo-syncytial membrane thickness (Fig1-D): The barrier between maternal and fetal circulation is reduced by the thinning of the vascular-syncytial membrane. This can negatively affect the transplacental transport, metabolism, and oxygen distributing [22]. Decreased vasculo-syncytial formation can be due to the delayed villous maturation that might be the etiology for the improved risk for intrauterine losses in diabetic women [23].

Extravillous fibrinoid between terminal villi (Fig1-E): Increased of extravillous fibrinoid deposits are reflected pathological phenomena and it was frequently inconsistent with normal fetal growth [24].

Fibrinoid in terminal and stem villi (Fig1-E): Stromal fibrosis is descripted abnormal when increased in the stem villi. In diabetic women, there is an increased villous stromal oxygen partial pressure, in the side of insufficient uptake by the fetal capillaries, which prompts the synthesis of collagen [25]. [26] observed increased villous fibrosis in GDM placenta controlled by insulin, but such noticing was not seen in GDM placenta controlled by diet and in control women [23; 27].

Fibrinoid necrosis of stem and terminal villi (Fig1-F): Fibrinoid necrosis was recognized as non-cellular homogenous eosinophilic material within the villi. At places, the fibrinoid material had increased by pushing the basement membrane and pressing the complete villous stroma [18]. Histological pathologies such as the presence of fibrinoid necrosis were detected more repeatedly in GDM [23] placentae compared with the control placenta.

Stem villi with indented margin, continued trophoblastic layer and stroma with respectable cell population (Fig1-G): Dubova, *et.al.* 2011;found to be continued trophoblastic layer and cell population more common in GDM groupcompared to control group and this result consistent with our finding[11]**Basement membrane thickening in immature intermediate villi (Fig1-H):** This thickening of syncytiotrophoblast basement membrane was resulted of a higher degree of nonenzymatic glycosylation or an increased quantity of the prominent type of basal lamina collagen, type IV. As well as higher substances of DNA, phospholipids, triglyceride, and of cholesterol are distinguishing features of placenta in diabetes women [18].

Immature intermediate villi with more loose reticular stroma and increased Hofbauer cells population (Fig1-I): The most often reported alteration in the placenta of diabetic women is the relative immaturity of villous, however a closely best metabolic control in these women [22].

Calcification intracellular as well as extracellular (Fig1-J): In many studies, calcifications observed as intracellular as well as extracellular basophilic deposits after stained with haematoxylin and eosin in the placentae of GDM group [27].

Chorangiosis (Fig1-K): The increased villous chorangiosis probably a response to the relative hypoxemia due to an increase of VEGF expression and the immaturity of the villi, which considered by centrally placed villous capillaries causing in a greater space for oxygen and nutrients to permit from maternal to fetal exchange [28].

Thickening of villi vessels (Fig1-L): Thickness villi vessel walls due to endothelial proliferation and thickening of the basement membrane. As well as it has been observed that increased blood glucose levels prompt oxidative stress (OS) and following variations of the placental architecture [19] principally the vascular properties, which are obvious in diabetic women.

Fetal vessel thrombosis (Fig1-L): This feature was diagnosed when a large fetal stem villous vessel was partly or completely obstructed by a thrombus [29]. The blood vessels in some of the terminal villi showed occulting by thrombus in GDM [13].

Nucleated fetal RBC's (Fig1-M): Tissue hypoxia consequences in increased levels of erythropoietin, which in turn performs to prompt of erythropoiesis and increased numbers of circulating nucleated fetal RBC's. The increased erythropoiesis is maybe due to together an increase in erythropoietin levels and an immediate haemopoietic effect of hyperinsulinaemia [14].

Mature intermediate villi with continuous trophoblastic layer (Fig1-N): This histological feature is evidence of villous immaturity in women with diabetes mellitus [18].

Villous edema (Fig1-N,O,P): The accumulation of fluid in the stroma of placental villi. As hyaluronic acid molecules have the particularity to retain water, it was concluded that, the existence of abnormal deposits of mucopolysaccharides in the stroma of villi can lead to the presence of the true villous edema in placentae of diabetic pregnancies [30].

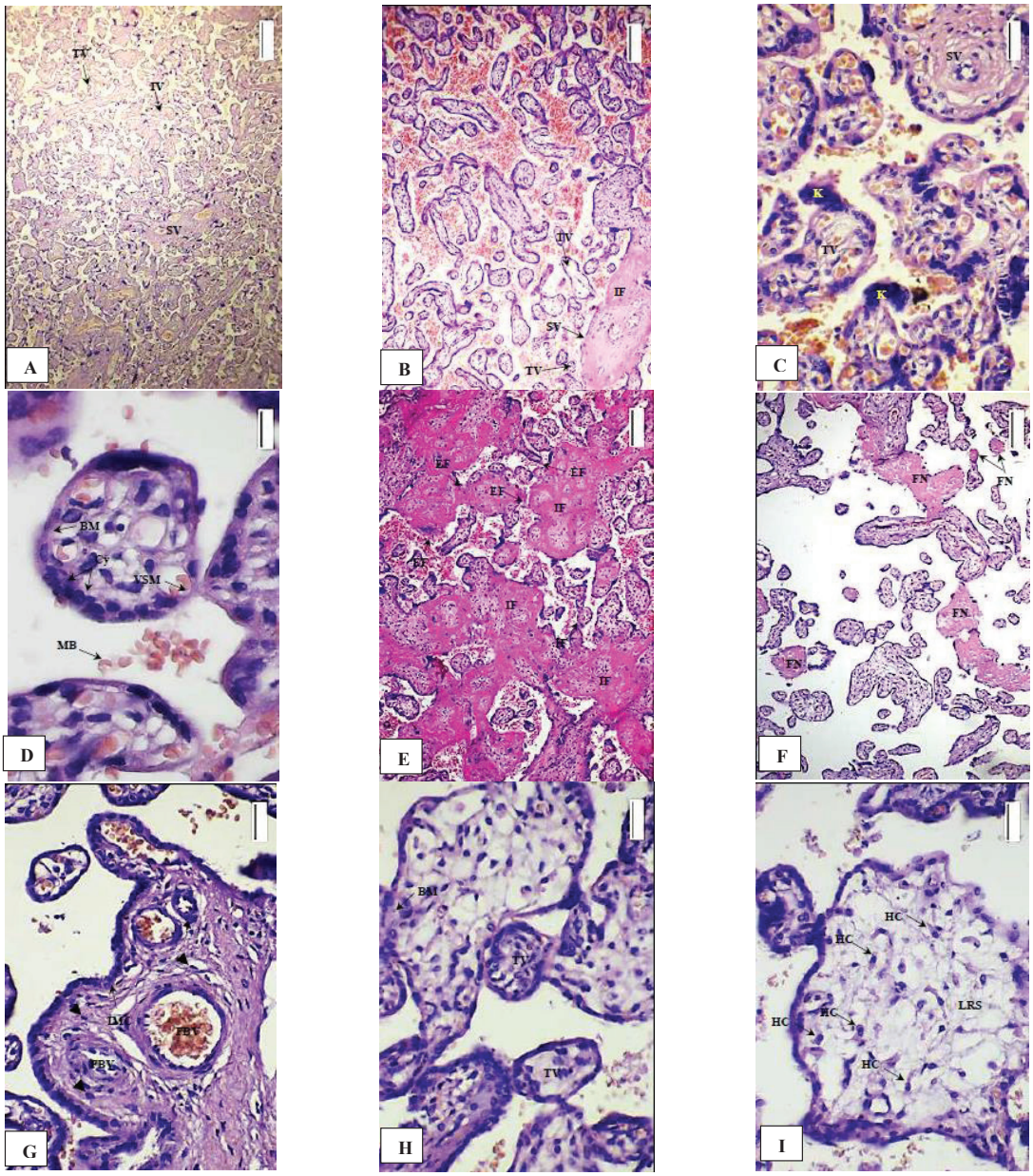

Figure (2): Section of placenta in women complicated with DM showing: A- Crowded villi,(4X); B- Decreased terminal villi density and increased size as well as immature intermediate villi(10X); C- Numerous syncytial knots(40X); D- Basement membrane thickness in terminal villi, more cytotrophoblast and decreased vascular-syncytial membrane thickness in terminal villi(100X); E- Present extravillous fibrinoid between chorionic villi and fibrosis inside terminal and stem villi(10X), F- Present fibrinoid necrosis in terminal and stem villi(40X), G- Stem villi with indented margin, continued trophoblastic layer and stroma with respectable cell population (arrow head) (10X), H- Thickening of syncytiotrophoblast basement membrane in immature intermediate villi(40X), I- Immature intermediate villi with more loose reticular stroma and Hofbauer cells population(40X); stem villous(SV) and mature intermediate villous(MV), immature intermediate villous(IV), terminal villous(TV), fibrinoid necrosis(FN), fibrosis inside(IF) chorionic villi, syncytial knots(K), basement membrane(BM), cytotrophoblast(Cy), vascular-syncytial membrane(VSM), syncytiotrophoblast(Sy), Hofbauer cell(HC), fetal blood vessel(FBV), maternal blood(MB), fetal blood vessel(FBV), trophoblastic layer(IMC), edema(E), loose

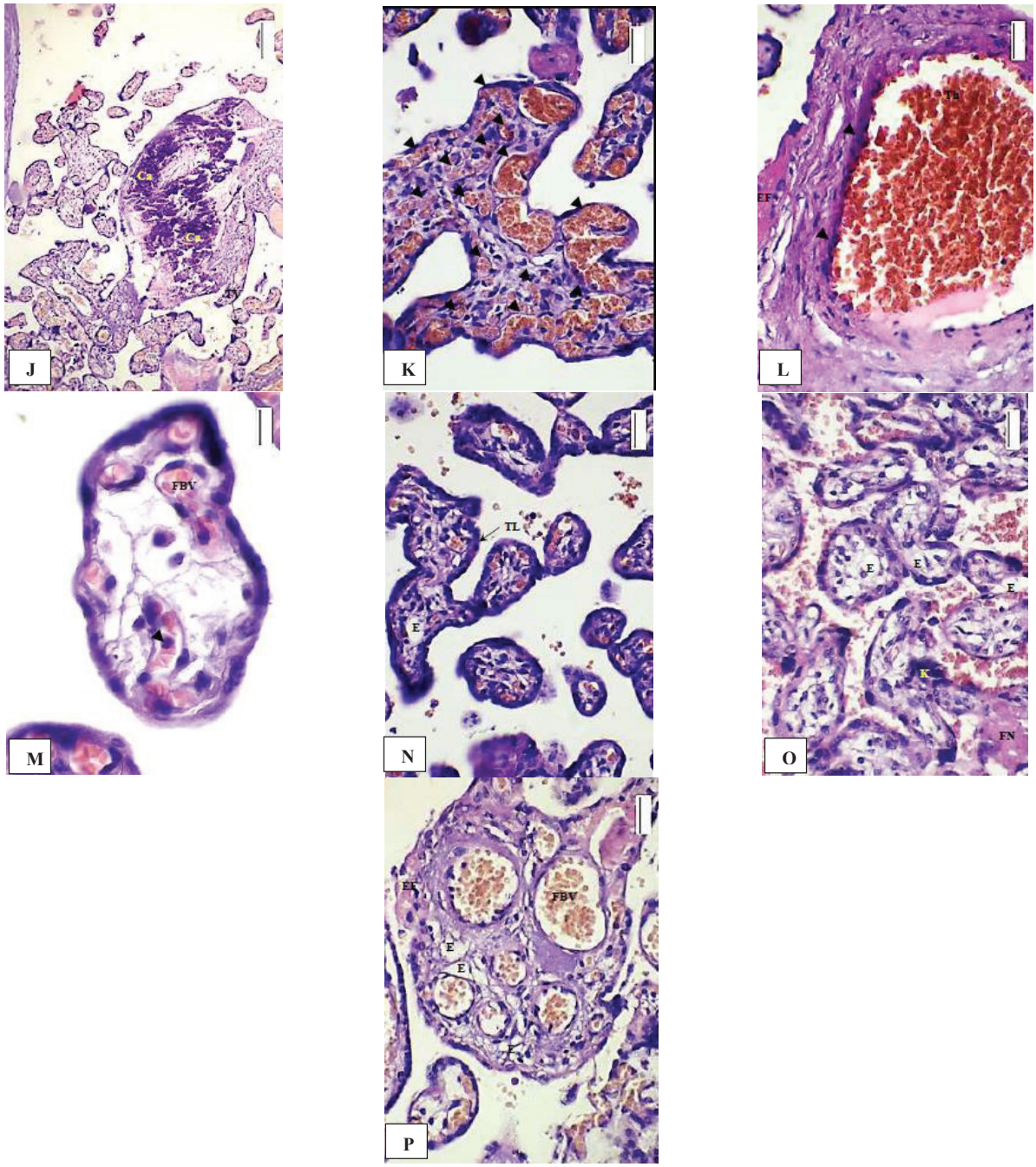

Figure (2): J- Placental calcification(40X); K- Chorangiosis (arrow head)(40X), L- Thickening of villi vessels (arrow head) and vessel thrombosis(40X), M- Present nucleated fetal RBCs(arrow head) (100X), N- Contained mature intermediate villi with continuous trophoblastic layer and edema in mature intermediate(40X), O- Edema in terminal villi(40X), P- Edema in stem villi (40X); calcification(CA), vessel thrombosis(Th), terminal villous(TV), edema(E), extravillous fibrosis, maternal blood(MB), fetal blood vessel(FBV), trophoblastic layer(TL), syncytial knot(K), fibrinoid necrosis(FN), extravillous fibrosis(EF).

Ethical Clearance: The Research Ethical Committee at scientific research by ministry of higher education and scientific research

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