Review Article

A Review of Histomorphological Changes of Placenta in Obese Mothers

Kumar K, Jahan S, Srivastava RK, Praveen T, Sachan A

Abstract: The placenta is a complex fetal organ that fulfills pleiotropic roles during fetal growth. It separates the maternal and fetal circulation, with which it is in contact through different surfaces i.e. the syncytiotrophoblast exposes the placenta to the maternal circulation and the endothelium is in contact with fetal blood. During pregnancy, obese women are at increased risk of metabolic syndrome of pregnancy i.e. gestational diabetes mellitus (GDM) and hypertensive disorders such as preeclampsia. Recent studies have demonstrated a heightened inflammatory response both systemically and locally within the adipose and placental tissue in women with pre-gravid obesity which may play a role in mediating the adverse pregnancy outcomes. This review will focus on evidence from human studies to describe histomorphological changes in placenta during pregnancy in obese patients and to summarize our current knowledge of the implication; this may have short and long-term outcomes for offspring of obese mothers.

Keywords: Placenta; Obese; Mothers; Gestational; Diabetes

INTRODUCTION:

Obesity defined as a body mass index (BMI) >30kg/m^2 has been described as the new worldwide epidemic. As the prevalence of obesity increases, so are the number of women of reproductive age becoming overweight and obese[1].

Obesity is associated with a wide spectrum of obstetric and perinatal complications, including increased risks of hypertensive disorders, gestational diabetes, fetal mortality and morbidity, excessive fetal growth and cesarean delivery.

It is well-accepted that maternal obesity affects fetal development and elevates the risk of offspring disease, but how this happens is unclear. Understanding placental alterations during gestation as a consequence of maternal obesity is critical to understanding the impact of maternal obesity on fetal programming[2].

The placenta is a complex fetal organ that fulfills pleiotropic roles during fetal growth. It separates the maternal and fetal circulation, with which it is in contact through different surfaces i.e. the syncytiotrophoblast exposes the placenta to the maternal circulation and the endothelium is in contact with fetal blood. Because of this unique position, it is exposed to the regulatory influence of hormones, cytokines, growth factors and substrates present in the both circulations and, hence may be affected by changes in any of these. In turn, it can produce molecules that will affect mother and fetus independently[3].

During pregnancy, obese women are at increased risk of metabolic syndrome of pregnancy i.e. gestational diabetes mellitus (GDM) and hypertensive disorders such as preeclampsia[4].

Emerging data from experimental studies in animals and translational studies in humans have suggested that maternal obesity creates an adverse intrauterine environment for the developing fetus, with long term programmed detrimental effects of offspring[5,6].

Recent studies have demonstrated a heightened inflammatory response both systemically and locally within the adipose and placental tissue in women with pre-gravid obesity which may play a role in mediating the adverse pregnancy outcomes.

This review will focus on evidence from human studies to describe histomorphological changes in placenta during pregnancy in obese patients and to summarize our current knowledge of the implication; this may have short and long-term outcomes for offspring of obese mothers.

REVIEW OF LITERATURE:

Swanson LD et al., (2008)[7] mentioned that the placental weight increases with increasing maternal BMI. Normal placental weights have increased over the last decades and this may correlate with increasing maternal obesity.

According to Wallace JM et al., (2012)[8] increased placental weight and placental hypertrophy are more common in obese groups.

Stirrat LI et al., (2014)[9] have stated the following modifications in placentas of obese women, as

Correspondence Address : Kiran Kumar, Deptt. of Anatomy, Rama Medical College, Kanpur

altered placental vascular function, changes in cell turnover and increased maternal inflammatory lesions.

Bar J et al.,(2012)[10] found that the histological examination of placentas from obese women demonstrate significantly higher rate of maternal inflammatory response lesions (consistent with chorioamnionitis) as compared with placenta from a normal-weight control group (43% versus 3.6%).

Robert KA et al., (2011)[11] have revealed a greater degree of muscularity in the vessel walls (p=0.03).

According to Hayward et al., (2013)[12] altered placental vascular function may adversely affect placental oxygen & nutrient transport and subsequently place the foetus at risk.

A study of 1,534 singleton pregnancy placentas, Avagliano L et al., (2011)[13] found that the rate of abnormal spiral arteries modification was increased in women with a BMI>30 (odds ratio [OR] 1.8, 95% confidence interval [CI] 1.1–3.0), and the rate of intrauterine fetal death was significantly increased in abnormal spiral arteries modification (18% versus 2.2%; OR 8.2, 95% CI 3.8–18.0).

Jan Andi Marlin et al., (2009)[14] noticed that placental histological findings represented mainly by the presence of calcifications, thrombotic lesions, fibrinoid or hyaline deposits in optic microscopy are observed significantly higher rate only in groups of women with obesity/excessive weight gain during pregnancy – 63.4% and 50% in diabetes with obese/excessive weight gain.

Olivar C Castejon (2013)[15] studied that obesity associated with hypertension produce severe degenerative changes in stem villi and other placental villi. Peripheric stem villi observed in the intervillous space showed obstructive vessels while others were seen with damage in the endothelial layer. Numerous of them presented occlusive or dilated vessels congestioned by erythrocytes. No thrombosis was observed in these vessels but a hyperplasia of muscular media was noted in the main stems of the villous tree. Although no thrombosis was in stem villi, it could be possible that obstructive lumen of the vessels in the chorionic plate leads to villous stromal changes in the placental villi or in the syncytio by reduction of blood flow. A reduction of blood flow in the intervillous space results in degenerative changes. Zebekakis PE et al., (2005)[16] have mentioned that blood vessels structure is altered in obesity with increase in vessel diameter.

Necrosis of the syncytiotrophoblast is observed with frequency by Olivar C Castejon (2013)[15]. He stated that the features of the syncytio found during obesity associated with hypertension can be due to tissue suffering from severe degenerative changes causing dysfunction of the protective barrier to the fetus. This is in contrast to various published findings in which villous and syncytiotrophoblast area and total nuclear number remain unaffected (Higgin L et al., 2010)[17] although reduced placental proliferation described by Higgins et al., (2013)[18] could be accelerated by this cause. Olivar C Castejon (2013)[15] has discussed that this possibility is evidenced by terminal and more slender branches of the villous tree seen as very fibrotic. Peripheric and more terminal branches of the villous tree were seen as very fibrotic when seen with light microscope.

Olivar C Castejon (2013)[15] observed that the regions of stroma were separated of syncytio by edema. Robert et al., (2011)[11] did not find difference in edema in placenta from obese compared to non-obese woman.

The placencta of numerous stem villi with reticular tissue under the syncytio is indicative of a placenta that is in the 18th week suffering of persistent immaturity (Olivar C Castejon., 2013)[15]. Jan Andi Marlin et al., (2009)[14] have observed that the low arborization showed by an abundance of immature intermediate villi as seen in the results testify a low placental maturity being expression of a low maturation. Roberts et al., (2011)[11] observed there was no difference in villi maturity in placenta from obese compared to non-obese woman.

Filiform terminal villi associated placental villi of different thickness and morphology was noticed by Olivar C Castejon (2013)[15]. Kingdom et al.,(2000)[19] have described that the observation of stem villi with some emptied vessels of erythrocytes indicate that fetus can have problems in to absorb gases and nutrients or that placental villi are with bad perfusion promoting an ambience of hypoxia which break the process of branching angiogenesis resulting in filiform terminal villi. These villi of minimum caliber are atrophied by extensive hypoxic villous damage produced probably by low blood flow in the intervillous space due to obstructive or damaged vessels of stem villi in the chorionic plate. Hargitai et al.,(2004)[20] stated that the ultrasonographic diagnostic of these elements in increased quantity has been enough for immediate termination of pregnancy.

Microvilli of the syncytiotrophoblast have been observed reduced in number (Biagini G et al.,1989)[21], slender and thicker in their extremity when seen with transmission electron microscopy in the baboon (Farley D et al., 2009)[22]. In contrast with that noted by Olivar C Castejon (2013)[15] as irregular or globulous extensions that probably permit a higher nutrient uptake.

Zones of hypercapillarization or chorangiosis were also observed by Olivar C Castejon (2013)[15]. Hypercapillarization of these villi is an adaptative response of the placenta to the reduction of blood flow in the intervillous space. Higgins L et al., (2010)[17], has noted in their study of placental cell turnover identified decreased apoptosis with increasing maternal BMI. This suggests that the lower rates of apoptosis in placentas of large gestational age infants may positively influence placental and fetal growth.

Degenerative changes justify the presence of matrix-type fibrinoid and fibrin-type- fibrinoid that could be involved besides in maternofetal transport processes. Where the thinner syncytio is interrupted by degeneration or by mechanical forces, the gap is immediately filled by fibrin-type fibrinoid resulting from the coagulation cascade. These fibrinoid spots provide an effective transfer route for macromolecules or gases in the maternofetal interchange (Benirscheke K et al., 2000)[23]. It has been hypothesized that maternal obesity results in increased placental nutrient transport to the fetus.

R Hastie et al., (2014)[24] concluded that women with pre-existing obesity or diabetes have decreased placental mitochondrial respiratory chain enzyme activities which may have detrimental consequences on placental function and therefore affects the fetal growth and development. The extent of lipid transfer to the fetus strongly contributes to fetal fat accretion. Human in vivo studies using labeled fatty acids reported a preferential placental fetal transfer of long chain poly unsaturated fatty acids. Although the mechanisms are still uncertain. Knowledge about fatty acids metabolism and adaptations of the placenta in response to obesity are more limited (Gil-Sanchez A et al., 2012; Dube E et al., 2012)[25,26].

Conclusion:

Thus, the review of literature reveals that: (1) The placental histological findings could be an indicator of placental dysfunction. (2) Placental weight and fetal growth are increased. (3) Higher rates of maternal inflammatory lesions and increased muscularity in the vessel wall altered placental vascular function. (4) Abnormal spiral artery modification increases the risk of intrauterine fetal death. (5) Placental alterations remain one important marker of vascular adaptation to maternal metabolic changes. (6) Severe degenerative changes are affecting the structure of placental villi due to obstructed vessels and damage in the endothelial layer results into dysfunction of the protective barrier to the fetus. (7) Presence of calcification, thrombotic lesions, fibrinoid or hyaline deposits in placenta increase in maternal obesity. (8) Also decreased placental mitochondrial respiratory chain enzyme activities may have detrimental consequences on placental function and therefore affects the fetal growth and development. (9) Role of placental fetal transfer of long chain polyunsaturated fatty acids is still to be ascertained. (10) Avoidance of excessive gestational weight gain during pregnancy is important for both mother and fetus.

REFERENCES:

1. Linne Y. Effect of obesity on women's reproduction and complications during pregnancy. Obes Rev. 2004;5(3):137-143.
2. Kim DW1, Young SL2, Grattan DR1, Jasoni CL3 Obesity during pregnancy disrupts placental morphology, cell proliferation, and inflammation in a sex-specific manner across gestation in the mouse. Biol Reprod. 2014 Jun;90(6):130.
3. Khabat A. Ali, Lana S. Salih, Zrar S. Almarzany the role of leptin and insulin hormones in the pregnant women serum infected of diabetic mellitus and its histological structure effects on the placenta and umbilical cord in Erbil city Raf.J.Sci., Vol.23, No.3 pp 38-49,2012.
4. Catalano PM. Management of obesity in pregnancy. Obstet Gynecol. 2007;109:419-433.
5. Li M, Sloboda DM, Vikers MH. Maternal obesity and developmental programming of metabolic disorders in offspring: evidence from animal models. Exp Diabetes Res. 2011;2001:592408.
6. Drake AJ, Reynolds RM. Impact of maternal obesity on offspring obesity and cardiometabolic disease risk. Reproduction. 2010;140(3):387-398.

7. Swanson LD, Bewtra C. Increase in normal placental weights related to increase in maternal body mass index. J Matern Fetal Neonatal Med. 2008;21(2):111-113.
8. Wallace JM, Horgan GW, Bhattacharya S. Placental weight and efficiency in relation to maternal body mass index and the risk of pregnancy complications in women delivering singleton babies. Placenta. 2012;8:611-618.
9. Laura I Stirrat, Rebecca M Reynolds. Effects of maternal obesity on early and long-term outcomes for offspring. Research and Reports in Neonatology 2014:4 pp 43—53.
10. Bar J, Schireiber L, Saruhanov E, Ben-Haroush A, Golan A, Kovo M. Placental histopathological findings in obese and nonobese women with complicated and uncomplicated pregnancies. Arch Gynecol Obstet. 2012;286(6):1343-1347.
11. Roberts KA, Riley SC, Reynolds RM, et al. Placental structure and inflammation in pregnancies associated with obesity. Placenta.2011;32(3):247-254.
12. Hayward CE, Higgins L, Cowley EJ, et al. Chorionic plate arterial function is altered in maternal obesity. Placenta. 2013;34(3):281-287.
13. Avagliano L, Bulfamante GP, Morabito A, Marconi AM. Abnormal spiral artery remodeling in the decidual segment during pregnancy: from histology to clinical correlation. J Clin Pathol. 2011;64(12):1064-1068.
14. Jan Andi Marin, Manuela Russu **et al.** Diabetes, obesity and excessive weight gain and pregnancy outcomes. TMJ 2009;59(2).
15. Olivar C Castejon. A light and scanning electron microscopy study of placental villi associated with obesity and hypertensión. Rev electron biomed / electron j biomed 2013;2:29-36.
16. Zebekakis PE, Nawrot T, Thijs L, Balkestein EJ, van der Heijden-Spek J, Van Bortel, et al.,Obesity is associated with increased arterial stiffness from adolescence until old age. Journal of Hypertension. 2005;23:1839-1846.
17. Higgins L, Mils TA, Greenwood SL, Wareing M, Jones RL, Courley EJ. et al., Maternal Obesity: does placenta cell turnover hold clues the aetiology of aberrant fetal growth?. Reproduction Science. 2010;17: S453.
18. Higgins L, Mills TA, Greenwood SL, Cowley EJ, Sibley CP, Jones RL. Maternal obesity and its effect on placental cell turnover. Journal of Maternal & Fetal Neonatal Medicine. 2013;26:1-6.
19. Kingdom J, Huppertz B, Seaward G, Kaufmann P. Development of the placental villous tree and its consequences for fetal growth. European J ournal of Obstetrics, Gynecology, and Reproductive Biology. 2000;92:.35-43.
20. Hargitai B, Marton T, Cox PM. Examination of the human placenta. Journal of Clinical Pathology. 2004;57: 785-792.
21. Biagini G, Vasi V, Pugnaloni A, Valensise H, Rizzoli R, Miccoli MC, et al., Morphological development of the human placenta in normal and complicated gestation: a quantitative and ultrastructural study. Gynecologic and Obstetrics Investigation. 1989;28: 62-69.
22. Ferley D, Tejero ME, Comuzzie AG, Higgins PB, Cox L, Werner SL, et al. Feto-placental adaptations to maternal obesity in the baboon. Placenta. 2009;30:752-760.
23. Benirschke K, Kaufmann P. Pathology of the human placenta. 4th edition. New York: Springer-Verlag; 2000.
24. R. Hastie, M. Lappas. The effect of pre-existing maternal obesity and diabetes on placental mitochondrial content and electron transport chain activity. Placenta. 35(9), 2014, 673–683
25. Gil-Sánchez A, Koletzko B, Larqué E. Current understanding of placental fatty acid transport. Current Opinion in Clinical Nutrition and Metabolic Care. 2012;15:265-272.
26. Dubé E, Gravel A, Martin C, Desparois G, Moussa I, Ethier-Chiasson M, et al. Modulation of Fatty Acid Transport and Metabolism by Obesity in the Human Full-Term. Biology of the Reproduction. 2012; 87:1-11.