

**A STUDY ON THE EFFECTS OF GESTATIONAL
DIABETES MELLITUS AND OBESITY ON
PREGNANCY OUTCOMES IN RELATION WITH
THE MICROSTRUCTURAL ALTERATIONS OF
THE PLACENTA**

A THESIS

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SUMMARY AND CONCLUSION

Obesity complicating GDM may compound the metabolic and vascular derangements seen in GDM resulting in poorer pregnancy outcomes and alterations in the structure of the placenta at macroscopic, microscopic, morphometric and biochemical levels. The study was carried out on 95 pregnant women who were grouped into three categories, namely normal BMI and GDM mothers as lean GDM group (LG), obese BMI and GDM mothers as obese GDM group (OG), and the normal BMI normoglycaemic group as control (CL). The WHO guidelines for BMI classification for Asians as recommended by the Indian Health Ministry were used to classify subjects. Their pregnancy outcomes, placental changes, lipid peroxidation levels and the association of pregnancy outcomes with placental changes were analysed. Our results show that the obese group had significantly greater adverse outcomes as compared to control group. The significant pregnancy outcomes that were noticed are the increase in pre-dates and increased risk of LSCS in OG group. There were no statistically significant adverse foetal effects in any of the groups. There was no difference in birth weight across groups. The increased BMI does complicate the outcomes of the OG group.

Morphology of placenta from GDM groups were heavier and were increased in volume, surface area with increased diameter, thickness, number of maternal cotyledons, and had more irregularly shaped placentae as compared to controls. Placental weight and volume were increased in OG group as compared to LG group. Umbilical cord insertion were seen in the LG and OG groups as compared to controls. The significant histopathological changes seen in the GDM placentae were the increased syncytial knots and the fibrinoid necrosis. Fibrosis of the villi was increased in OG placentae while calcification was increased in the LG group placentae.

Morphometric analysis showed a significant increase in the volume of the intermediate and terminal villi in the LG and OG groups. The percentage composition of the foetal capillaries was increased in the terminal villi of the LG group and the harmonic mean thickness of the villous membrane was decreased in the LG group. The

Uniformity Index was increased in the OG group. The diameter of the terminal villi was decreased in the LG group and it was increased in the OG group as compared to control. CD34 immunohistochemistry showed increased reactivity in both the LG and OG groups as compared to the CL group. There were regions of the placenta of LG and OG group where terminal villi showed reduced CD34 staining. Ki67 immunostaining in LG and OG group did not show increased or decreased staining intensity as compared to CL, but the reactivity in GDM placentae was localized more to the endothelial cells, than to both trophoblasts and endothelium in the CL groups.

GDM has been associated with changes in the placenta, which might be either adaptive or degenerative in nature. The study findings showed that the changes in the lean GDM group were more conducive to maintain placental efficiency. In comparison, though the obese GDM group showed the presence of adaptive placental changes, they were impaired to an extent as seen by the microscopic and morphometric changes.

The results showed that while the pregnancy outcomes of the LG group were comparable with that of the control group, the OG group showed more adverse outcomes as compared to the control group. The immediate adverse pregnancy effects seen in obese group was the increase in pre-dates and the LSCS deliveries. The macroscopic, microscopic, morphometric and immunohistochemical changes may be interpreted as attempts to adapt to the altered metabolic and vascular environment in GDM. Increased degenerative microstructural changes seen in OG can be explained by the added oxidative stress of obesity upon the metabolically and vascularly deranged placenta of GDM. Differences in lipid peroxidation levels across groups were not significant, but show a weak positive correlation with BMI.

The Foeto-placental ratio was decreased in the OG group as compared to controls. While the FPR and terminal villous diameter showed moderate positive correlation with BMI, the placental weight, volume, mean placental thickness, lipid peroxidase activity, HPF score and uniformity index showed weak positive correlation with BMI.

Even though significant association of BMI with adverse pregnancy outcome was not evident, significantly higher adverse pregnancy outcomes were seen in the OG group. The macroscopic, microscopic, morphometric parameters, lipid peroxidation and FPR showed statistically significant weak to moderate correlation with BMI. Despite the multifactorial nature of obesity and GDM and the multiple biochemical

mechanisms involved, the placental changes seen in lean GDM group were more adaptive in nature and hence they compensate for the pathologic insult in lean GDM than in the obese GDM group. We conclude that increased pre-pregnancy BMI significantly impacts the pregnancy outcome in the obese group unfavorably. The maintenance of pre-pregnancy body weight and optimal glycaemic control are conducive to better pregnancy outcomes.