

**Details of the Project sanctioned under the Human Resource Development scheme of
Department of Health Research**

1. **Project Title :** Impact of Gestational Diabetes Mellitus (GDM) on Feto-Placental Vascular Function
2. **Category of fellowship:** Young Scientist in Newer Areas of Research (Category-A)
3. **PI (Name & Address) :** Dr. R. Nirupama
Research Scientist
SASTRA University, Thanjavur-613 401
4. **Qualifications :** M.Sc., Ph.D
5. **Mentor or Co.PI (Name & Address) :** Dr. Srinivasan Vedantham M.S., Ph.D
Senior Assistant Professor
School of Chemical and Biotechnology
SASTRA University, Thanjavur-613 401
6. **Duration of the project :** 3 years
7. **Broad area of Research:** Biotechnology
7.1 Sub Area
8. **Summary of the Project:** (Give in about 300 words)

GDM, first diagnosed in pregnancy, affects 6-17% of pregnant women in India. In addition to increased pregnancy risks to mother and fetus, 30-50% of these women go on to have GDM in the next pregnancy and within 5-10 years develop Type 2 diabetes. The offspring is not spared. Beyond macrosomia and risk of congenital malformations, they have an increased risk of developing obesity and high blood pressure in childhood, metabolic disturbances in adolescence, Type 2 diabetes and cardiovascular diseases in adulthood. The mechanistic reason behind this, the *in-utero* perturbation needs urgent attention. The functioning of the placenta dictates fetal well-being. Few previous studies have shown that feto-placental endothelial dysfunction; alteration in vascular reactivity, increased vascular leakage and angiogenesis, are predominant changes which directly affect fetal growth and vascular function and may be behind the later cardiovascular dysfunction. One of the key regulators of vascular function is the angiogenic/permeability factor: vascular endothelial growth factor (VEGF). Increased angiogenesis, endothelial dysfunction together with increased leakage are reported to be related to increased levels of VEGF. VEGF is major regulator of angiogenesis which plays a major role in the vasculogenesis and angiogenesis during pregnancy. Any alteration in the expression and function of VEGF, its receptors and its target molecules may play a role in the occurrence and severity of the vascular dysfunction in GDM. Hence the present proposal aims at investigating the different angiogenic markers, namely VEGF and its isoforms, VEGF receptors and the mechanism behind *in - utero* perturbation in umbilical vein, plasma and cord blood of normal and GDM mothers. Proposal also tries to address the mechanism

of vascular dysfunction in primary HUVEC isolated from both normal and GDM umbilical cords.

9. Objectives of the Proposal:

1. To measure the markers of endothelial dysfunction, angiogenesis and vascular permeability in umbilical cord, plasma and cord blood of normal and GDM mothers.
2. To correlate the markers of endothelial dysfunction, angiogenesis and vascular permeability to GDM.
3. To study the mechanism behind fetoplacental vascular dysfunction in the umbilical vein endothelial cells isolated from umbilical cord of normal and GDM mothers post-delivery.

10. Innovations in the project: (Give in about 100 words)

To our knowledge the proposed study is the first of its kind to be performed in the Indian population. The study focuses on the role of VEGF and its isoforms (VEGF-A165b & VEGFA165a) which are known to be altered in endothelial dysfunction and thus affecting the vascular permeability of the placenta. Except for a few studies at the international level where increased levels of VEGF have been reported in GDM, the role of VEGF receptors and sFlt-1 has not been investigated. The proposed study will help to unravel the mechanisms behind the fetoplacental vascular dysfunction and thus aid in the development of novel therapeutic and management strategies for maternal and child health well-being.

11. Significance of the outcome of the project: (Give in about 150 words)

Identification of the proangiogenic and anti-angiogenic factor would serve as a biomarker in the vascular complications of GDM. Our study could change the way we predict pregnancy outcomes in GDM and will lead to identification of potential targets for therapeutic management.

12. Relevance in Public Health:

GDM is an under-estimated threat to maternal and child health both, during pregnancy. In India alone 6 million women are affected by hyperglycemia in pregnancy. In GDM perinatal outcomes such as macrosomia & fetal hypoglycemia requires neonatal care. Offspring have elevated risk for long-term complications: cardiovascular disease, obesity and diabetes. Clinical care of the mother may extend beyond the pregnancy, 30-50% of women go on to have GDM in the next pregnancy and within 5-10 years these women tend to develop Type 2 diabetes. The burden of disease for the individual and the health services now and in future makes this a top national health priority. The molecular markers identified will have early diagnostic and prognostic value for the clinicians and policy makers could focus on GDM to improve the health of women and future generations. Knowledge of VEGF dependent mechanisms in placental impairment will aid novel therapeutic and management strategies. Our proposal addresses an important national health priority; the outcomes would suggest prevention strategies to protect the fetus and mother.

Signature of the Fellow /Faculty