The aim of this study was to assess the association of two panels of candidate genes (A and B) with severe Gestational Diabetes Mellitus (GDM) (2hrBG>11.0mmol/l) in Maltese population [annual Malta incidence is 0.7% of pregnancies at term ~ 25 cases/year (MDA)]. GDM affects ~7% of all pregnancies and is defined as carbohydrate intolerance with onset or first recognition during pregnancy and the prevalence has increased considerably during the last decade concurrently with that of T2DM. Twenty Six probands with past history of severe GDM have been recruited to this study through Gynae-out patient (GOP) Clinic in Mater Dei Hospital, Msida, Malta. All of them had positive family history of T2DM and 75% of them with high waist/hip ratio [>0.85]. Applying a modified SNPplotyping score system with addition of MIF instead of IPF1 and including MTHFR 677C/T, the SNPscore was between 6 and 11, compared to that of Maltese T2DM patients (Ashtar A et al; 2008) in which the SNPscore was between 0 and 8. Maltese neonate DNA Pool of 400 cord samples has been designed constructed and validated for its accuracy in determining allele frequency and used as control group. Using allele specific primers, the frequency of SNPs in Panel B was determined on GDM group and Maltese neonate DNA Pool using Sybergreen mix by quantitative real time PCR (qPCR). Genotype distribution and allelic frequencies were compared between patients and control group. Odds ratios (ORs) and relative risk (RR) with 95% confidence intervals (CI) were calculated for both panels and the results are shown below in table1 and table2.

**Conclusion:** The data of this study showed that there was strong association as well as statistically significant increase in the risk of developing GDM in Maltese GDM cases with a number of SNPs in Panel A (Adrab β2 nt46A→G, FABP2 54G→A, MTHFR677 nt677C→T, IL-6-174G→T, UCP1nt3826A→G, MIF-173G→C) and Panel B (TCF7L2 rs93531, IL6 rs1800795, TNDM rs4828037). These results showed also the link of inflammation to the pathogenesis of GDM and subsequently to T2DM by high Odds ratio and significant relative risk values of inflammatory SNPs (Leptin, IL-6, MIF, MTHFR677C/T and TNDM) in both Panels (A and B). Applying the modified SNPplotyping score system demonstrates more clearly the association of these particular SNPs and increased risk of developing GDM in Maltese population.

**Keywords:** Gestational Diabetes Mellitus (GDM), Type 2 Diabetes Mellitus (T2DM), Genetics, Neonatal DNA Pool, PanelA, PanelB, ASP’s, SNPplotyping score system, quantitative real time PCR (qPCR) and Maltese Diabetic Association (MDA).