# Strategic Interventions in the Management of Gestational Diabetes to Reduce Type 2 Diabetes Mellitus in Women in Malaysia

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## INTRODUCTION

According to the Global status report on non-communicable diseases 2010, the prevalence of high blood sugars among adults exceeds 11 % in both males and females in Malaysia. This is the highest among ASEAN countries. This ties up closely with the prevalence of overweight adults in both sexes in the same report, again Malaysians rank highest among ASEAN countries. The burden of diabetes mellitus in Malaysia is estimated to be 12% of the population with a projected figure exceeding 15 % in 2020.[1]

This enormous rise in both obesity and hyperglycaemia in adults is alarming and clear strategies to combat this non-communicable disease is urgently warranted. One such strategy is to relook at the focussed approach of gestational diabetes mellitus (GDM) management currently in vogue in Malaysia, and suggest more effective preventive measures in view of information currently coming to light on both short and long term implications of GDM on both mother and offspring.

Although information on actual prevalence of GDM in Malaysia is lacking, available crude data from hospital births obtained from the National Obstetric Register in 2010 involving 14 major government hospitals was 9.9% with Indians ranking highest followed by Malays and Chinese. Incidence of macrosomia in GDM mothers was double that of non-GDM mothers. A higher caesarean section rate with a threefold increase in shoulder dystocia was also recorded in those with GDM.[2]

## SCREENING, DEFINITIONS AND IMPLICATIONS

The rather loose definition of GDM taken to be 'any form of glucose intolerance detected for the first time in pregnancy' includes all types of undetected diabetes mellitus (DM), i.e., pre-existing unknown Type 1 and 2 DM and glucose intolerance detected in the second half of pregnancy which is clearly related to the antagonistic effect of pregnancy hormones. Insulin sensitivity declines with increasing gestational age. Insulin resistance is greater as the pregnancy advances and it worsens with maternal obesity and weight gain in pregnancy.

Hence 'GDM' in its current definition encompasses, in a majority of cases, 'true GDM' and unrecognised Type 1 and 2 DM. Persistence of glucose intolerance postpartum is indicative of Type 2 DM in most instances. Current views address the definition of GDM as being too broad and are inadequate to highlight the need for more stringent interventions in reducing the burden of Type 2 DM which develops in the future. Clearly, there is a need to extend the management of women who have demonstrated glucose intolerance during pregnancy at any time beyond the conventional postpartum care of six weeks in view of better understanding of the condition. The label 'GDM' is better replaced by 'Hyperglycaemia of Pregnancy' or 'Bradyglycemia' in view of persistence of glucose levels in the blood which is harmful to the growing foetus and surviving offspring and contributes to cardio-metabolic effects in the mother in later years. When glucose intolerance of any degree is demonstrated in pregnancy, one should exploit this 'window of opportunity' to improve extended post-delivery care through simple interventions like lifestyle changes, diet modification and weight reduction after childbirth through personal health education. This sets the stage for better woman empowerment for delaying the onset of Type 2 DM to a further two to three decades. Empowerment through patient education with regimented diet modification and exercise is cheap and effective and removes the paternalistic approach to care of GDM that appears to prevail in current health care in Malaysia.[3]

## WINDOW OF OPPORTUNITY FOR STRATEGIC INTERVENTIONS

Current estimates are that GDM as defined by accepted definition, occurring in the second half of pregnancy probably exceeds 85% of all forms of 'hyperglycaemia of pregnancy'. The two main issues with this form of GDM is macrosomia in the foetus and its consequences, i.e., shoulder dystocia, increased caesarean section, neonatal admissions to Special Care Nursery and preeclampsia. Hyperglycaemia in the mother is easily controlled with medical nutrition therapy with or without antidiabetic medication. New National Guidelines on managing GDM is being drafted by the Ministry of Health Malaysia (MOH). Blood sugar levels in this category of GDM fall rapidly after delivery to normal. Currently, a screening test in the form of oral glucose tolerance test is in order for these patients after 6 weeks of delivery and if this is normal, no further treatment is required. This approach is no longer valid with new

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information that mandates the need for prolonged care of such patients and their off springs. Extended lifelong lifestyle changes with medical nutrition therapy should be adopted and included in this yet to be published National Management Guidelines.

The criteria for diagnosis of GDM based on the O'Sullivan and Mahan or Carpenter and Coustan cut-off thresholds prevailed for decades based on risk factors. More recently, universal screening has been adopted by the American College of Obstetricians and Gynaecologists in view of the increased prevalence of GDM, obesity and/or a first degree relative with Type 2 DM. Universal screening has both ethical and cost - benefit issues to be evaluated. In 2010, the International Association of Diabetes and Pregnancy Study Group (IADPSG) redefined the categories of GDM as 'overt' when glucose intolerance is clearly apparent in early pregnancy and 'GDM' as those women showing glucose intolerance in the second half pregnancy.[4]

This categorisation alerts attending physicians to be more stringent in caring for individuals, especially those in the 'overt' group so as to reduce adverse obstetric events. Further, the risk of developing Type 2 DM could be anticipated in the 'overt' group much earlier than the latter in postnatal life. Observational data shows that women who were diagnosed with GDM in the first half of pregnancy, were obese and required insulin therapy during pregnancy, have a higher risk of Type 2 DM. Overall, women with GDM have a seven fold increased risk of later Type 2 DM. Chinese women who had prior GDM were significantly at an increased risk of developing Type 2 DM at a rate of 1.6% per year. It is now becoming clearer to conceive that any form of GDM indicates undiagnosed Type 2 DM and this concept should be capitalised as a window of opportunity to introduce intervention measures in the immediate postpartum period and long after the birth of the child. The IADPSG appears to place greater importance in using the new cut points in screening measures to help identify more cases for early management so as to avert adverse events in the foetus based on the HAPO (Hyperglycemia and Adverse Pregnancy Outcomes) study. The HAPO study found an increased risk of adverse pregnancy and neonatal outcomes even when maternal blood glucose levels were mildly deranged.[5, 6, 7]

A Finnish Birth Cohort study, though old, associates the untoward effect obesity has on Type 2 DM. Concomitant presence of maternal overweight status and GDM resulted in an increased risk of Type 2 DM (Hazard Ratio (HR 47.24).[8] Pre-pregnancy overweight without GDM had a greater risk than women with GDM and normal weight (HR 12.63 vs, 10.61).[9]

## PATHOPHYSIOLOGICAL PRINCIPLES

Adopting the IADPSG consensus in screening for women at risk early at the time of booking has merits in Malaysia in view of the exponential increase in the incidence of GDM and Type 2 DM over the years. Those without known risk factors are advised screening at 24-28 weeks. All those with GDM should continue to be screened 6-12 weeks postpartum with standard oral glucose tolerance tests and this screening is advised to be extended every 3 years together with lifestyle interventions. Practice change would also be required in the form of intensive diet modification and physical exercise with a limited role for advising metformin as a preventive measure.[10]

There is now convincing evidence to indicate that the offspring of diabetic mothers not only suffer short term morbidity but run the risk of developing DM together with other non-communicable diseases like coronary heart disease and dyslipidaemia. Three factors appear to contribute to foetal macrosomia, i.e., GDM, obesity and excess gestational weight gain. The Modified Pederson's Hypothesis still holds as a plausible theory for these foetal consequences. Apart from hyperglycaemia of GDM, insulin resistance and chronic low grade inflammation in GDM creates a maternal environment that contributes immensely to adverse foetal outcomes. David Barker and his colleagues alluded to 'fetal origin of adult disease'. Current research supports the view that placental transcriptome is target for altered environment seen in GDM. Insulin resistance also promotes maternal hypertriglycedemia.[11, 12, 13]

Apart from intrapartum complications of macrosomia, stillbirth and metabolic complications seen in the immediate postpartum period, GDM has a direct effect on off-springs with childhood overweight and obesity as two common outcomes. This effect is even more apparent when mothers have pre-gestational DM and obesity.

When overweight children were compared in mothers with or without GDM, overweight children in early adolescence were higher in the former (9.7% vs, 6.6. %).[14] Type 2 DM in the offspring aged between 10-22 years of age has been shown to be independently associated with both diabetes in the mother and obesity (Odds Ratio (OR) 5.7; 95% CI 2.4-13.4 and OR 2.8; 95% CI 1.5-5.2 respectively).[15]

Both pre-pregnancy overweight and maternal diabetes have been implicated in worsened cardiovascular risk profile in offsprings. The basis of cardiovascular and renal disease as possible long term outcomes in these off springs have been shown in studies on Prima Indians. Endothelial dysfunction, oxidative stress and chronic inflammatory responses are ongoing events that sets the pace for such non communicable diseases as a result of a 'hyperglycaemic environment'. A series of metabolic aberrations appear as a response to overproduction of free radicals that sets in motion 'metabolic programming' in the foetus which may explain the resulting long term effects on cardiovascular and endocrine systems in offspring in later life. There is now evidence that shortened telomeres seen in offspring of maternal diabetes is associated with increased risk of cardio-metabolic diseases in adulthood.[16, 17, 18, 19]

## STOPPING THE MALAYSIAN EPIDEMIC CALLED DIABETES MELLITUS

There is clearly a need for a review of current strategies in management of GDM. Focussed conventional management during the intrapartum and immediate postpartum is not adequate to stop mothers from developing recurrence of

GDM and long term overt diabetes mellitus and other cardio-metabolic disorders. There is a need to detect 'bradyglycemia' early in pregnancy, preferably pre-conceptually! Excessive weight gain in pregnancy is avoided though a regimen of diet modification and physical exercise. Medical nutrition therapy during pregnancy is better adopted as a lifelong strategy. As pregnancy presents an ideal and unique opportunity for strategic interventions including empowerment of woman, family physicians and carers need to exploit this window of opportunity. Family screening and childcare screening are extensions to these strategies that could be adopted as a health policy.

There is an urgent need for longitudinal evaluation of all GDM mothers and their offspring, overweight woman and those who gain excessive weight during pregnancy. Cheap and cost effective measures like lifestyle modifications can be effective tools for containing this impending epidemic. The dictum 'any form of hyperglycaemia or bradyglycemia in pregnancy is harmful' should be upheld in improving pregnancy outcomes. Care is necessarily continued after delivery based on the principles enshrined under 'Development Origin of Health and Disease (DOHaD)'. Epigenetic mechanisms are affected in-utero and childhood and pose health problems like cardio-metabolic derangement in future in addition to the development of diabetes mellitus. The 'bradyglycemic effect of GDM 'poses threats to not only the index pregnancy and offspring but also to future generations.

## CONCLUSION

GDM is closely related to Type 2 DM and impacts adversely on both mother and offspring. Pre-conceptual counselling provides opportunities for effective screening in risk mothers and optimisation of metabolic aberrations and BMI and would be an ideal strategy. The narrow focus at point of care of GDM conventionally adopted is not sufficient for containing this epidemic. Addressing maternal weight gain and weight retention after birth are vital for good health. Medical nutrition therapy and intensive physical exercise are cost effective measures that should be on going throughout pregnancy and long after. Empowerment of woman to be better informed patients and empowerment of nurses to sustain longitudinal management with involvement of support groups can contribute to cheap yet effective preventive measures in early development of Type 2 DM.

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