FIGO’s response to the global challenge of hyperglycemia in pregnancy – toward a global consensus

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Introduction

The occurrence of hyperglycemia in pregnancy (HIP) parallels the prevalence of prediabetes, overweight, obesity and type 2 diabetes in a given population. These conditions are on the rise globally also affecting younger people in the reproductive age, thus more women entering pregnancy have risk factors that make them vulnerable to HIP. For example, a recent large population study examined results of fasting capillary plasma glucose (FPG) in 2.1 million women planning pregnancy in China; diabetes and prediabetes was seen in 1.4% and 12.9% women, respectively, and 7.2% were overweight and 1.0% obese [1]. In the developed world and many parts of the developing world high levels of overweight and obesity in the adult population including among women in the reproductive age is an important issue. The high prevalence of maternal obesity drives childhood obesity and creates an inter-generational cycle. According to the WHO data; in 2014, already 41 million children under the age of 5 were overweight or obese and more than half of the world’s adult population was overweight (39%) or obese (13%) [2]. Going forward this obviously has important further ramification on the prevalence of HIP and obesity, as well as pregnancy related costs. During pregnancy the mean total cost of health service utilization for in patient care rises incrementally with higher BMI because of increased risks of maternal morbidity, gestational diabetes mellitus (GDM), a higher risk of operative interventions, and the increased number and duration of maternal and neonatal admissions. It has been estimated that the total cost for overweight and obese pregnant women with GDM during pregnancy and up to two months following delivery increased 23% and 37%, respectively as compared to women with normal BMI [3,4]. Global HIP prevalence rates also depend on ethnicity and ethnic heterogeneity of populations studied as well as on the screening and diagnostic criteria used. The international diabetes federation (IDF) estimates that 1 in 6 live births (16.8%) occur to women with some form of HIP and 16% of these may be due to overt diabetes in pregnancy and rest due to GDM [5].

In the past, most of the attention on gestational diabetes including setting diagnostic cut off values was related to the future risk of type 2 diabetes with scant attention paid to perinatal outcomes particularly among women with the so called ‘mild gestational hyperglycemia’. Studies in the last decade have shown significant association between adverse pregnancy outcomes and levels of maternal glucose considered within the non-diabetic range [6–8]. Also meta-analysis of randomized control trials shows that treatment of gestational hyperglycemia improves pregnancy outcomes [9,10].

The association between maternal plasma glucose and adverse pregnancy outcomes is linear and continuous with no inflection point [6], making it difficult to define clear diagnostic thresholds. The quantum of hyperglycemic exposure in terms of duration and degree are relevant, as is the timing of the onset of exposure in the course of pregnancy. Early exposure during fetal organogenesis and placental development has more severe consequence then later exposure closer to term. Hyperglycemia also adversely affects placental function and its vasculature. Placental dysfunction predisposes the fetus to acute and chronic changes in gas and nutrient exchange – turning the placenta from a ‘fetus protector’ to a potential source of damaging outcome [11]. And finally, the availability and transfer from the mother and utilization by the fetus of other nutrients such as lipids and amino acids are also relevant in determining fetal size and some perinatal, as well as long term outcomes in offsprings of mothers with HIP. The impact of maternal hyperglycemia on the fetus and perinatal outcomes is the sum total of the interplay of these and other variables [12].

Apart from affecting immediate perinatal outcomes, HIP is the most reliable marker of future type 2 diabetes [13] and cardio metabolic disorders in women [14,15]; with a proven possibility of prevention or at least delaying onset by instituting appropriate post-partum lifestyle interventions [8,16,17]. There is also evidence that excessive weight gain between pregnancies especially due to retention of previous pregnancy weight gain is associated with more complications in subsequent pregnancies, including higher risk of stillbirth [18]. Additionally, offsprings of mothers with HIP are at a significantly heightened risk of early onset obesity, type 2 diabetes and cardio-metabolic disorders as a consequence of intrauterine developmental programing [19,20].

Whether good control of HIP helps prevent or reduce these risks is currently unknown and requires further well designed studies. Being born full term and normal weight is undoubtedly a good start; in addition, early life attention to avoid excess weight gain and inculcate healthy eating and physical activity behavior will further help prevent or delay onset of long term consequences.

Identifying and treating women with HIP is therefore logical and clearly relevant, but how to identify and diagnose them?

Should all pregnant women be tested for hyperglycemia in pregnancy?

Globally there are approximately 130 million births annually, 85% of which occur in low and low middle income countries with limited resources. Implementing universal testing on such a large scale is truly a Herculean task. There are no published data on the level of adherence to recommended policies for HIP screening at individual country level. Even within Europe there is considerable diversity reported in the screening strategies and diagnostic criteria used despite high prevalence of obesity in reproductive age women approaching 30% in some countries. Five countries did not have any written screening policy. Among the 28 respondents, the most commonly used diagnostic criteria for GDM are the 2013 WHO Criteria in 67.9%, the 1999 WHO criteria in 10.7%, the European Association for the study of Diabetes Criteria in 7.1% and the Carpenter and Coustan criteria in 7.1%. Of all the national societies advising the use of the 2013 WHO criteria, 52.6% recommended risk factors based screening, 10.5% universal screening in a two-step strategy and 36.8% by one-step approach with a 75 g OGTT [21,22]. Risk factors to
help identify women who could be prioritized for testing have been described [23,24]. Unfortunately as shown in multiple studies, risk factor based screening fails to identify substantial proportion of women [1,25–27], supporting the contention that identification of women with HIP requires testing of all pregnant women [28]. Concerns are expressed particularly from the developed world that universal testing and (consequently) increased diagnosis would place additional logistical and economic challenges to healthcare systems. On the other hand, complex protocols for testing based on risk factors place high demands on healthcare providers and result in lower compliance and missed diagnosis [29].

Should all women be subjected to a 75 g oral glucose tolerance test (OGTT)?

Some professional organizations and countries while accepting universal testing recommend a two-step approach – a 50 g non fasting glucose challenge test (GCT) followed by a 75 g OGTT in women who test positive on initial screening. This reduces the number of OGTTs and ensures that women diagnosed with GDM have ‘significant glucose intolerance’ [12]. However, it does not take into account that the GCT also misses around 25% of cases with OGTT abnormalities and in particular fails to identify women manifesting only fasting hyperglycemia as they do not qualify for the OGTT [12]. Moreover, a significant proportion of women fail to complete the evaluation as they do not turn up for the OGTT [30]. This approach therefore may miss many women with HIP.

Can there be a global consensus on diagnostic cut off values?

While it would be preferable to have uniform global diagnostic cut off values, in view of the continuous linear association between maternal glycaemia and perinatal outcomes any set of diagnostic criteria proposed will need to evolve from a consensus approach, balancing risks and benefits in particular social, ethnic, economic and clinical contexts [31]. Mean glucose values for fasting, 1 h and 2 h 75 g OGTT test based on an acceptable odds ratio of 1.75 for markers of diabetic fetopathy (large for gestational age [LGA], excess fetal adiposity and fetal hyperinsulinemia) in the HAPO study were proposed as diagnostic cut off values by the international association of diabetes in pregnancy study groups (IADPSG) [32]. These cut off values were accepted and endorsed by the WHO [33]. However, LGA and fetal adiposity are not solely dependent on maternal glucose alone as described earlier. For example in using a 2-h glucose cutoff value of 8.5 mmol/L or 153 mg/dl (based on an odds ratio of 1.75 for adverse outcomes derived from HAPO data) as per IADPSG recommendation may not be as efficient in identifying women at risk for fetal overgrowth as those identified by having a 2-h glucose corresponding to a slightly lower odds ratio, e.g. 1.5. The latter corresponds to the older WHO criteria 2 h. value of 7.8 mmol/L or 140 mg/dl. This maybe of importance in the developing countries particularly in South Asia where women are relatively small and a larger baby may pose greater obstetric risk [28]. The use of lower fasting and post-load glucose thresholds to diagnose gestational diabetes in south Asian population maybe appropriate [34].

The FIGO initiative

The recent focus of the international federation of gynecology and obstetrics (FIGO) on HIP, resulting in the release of pragmatic guidelines [28] at the FIGO World Congress in Vancouver in 2015 and the subsequent setting up a working group on HIP is very welcome.

International federation of gynecology and obstetrics demands greater attention on the links between maternal health and non-communicable diseases in the sustainable developmental goals (SDG) agenda; in particular, to gestational hyperglycemia and its propensity to fuel the global diabetes, obesity and cardiovascular disease pandemic. FIGO also asks for public health measures to increase awareness, access, affordability, and acceptance of prevention counseling, and prenatal and postnatal services for women of reproductive age to be prioritized.

Universal screening for hyperglycemia during pregnancy

While the FIGO guidelines are pragmatic and accommodative to the operational, logistical and resource constraints in different parts of the world, its recommendation is very categorical and uncompromising on two issues – as a minimum standard all women should be tested for hyperglycemia during pregnancy and a single step approach should be used for diagnosis. FIGO encourages all countries and its member associations to adapt and promote strategies to ensure this.

With regard to diagnostic criteria FIGO adopts the WHO [32] criteria for diagnosis of diabetes mellitus in pregnancy and adopts the WHO [32] and IADPSG [33] criteria for diagnosis of GDM. Given the operational, logistical and resource constraints in many low-resource countries, other strategies described in the guideline are considered equally acceptable [28].

Post-partum follow-up

Following a pregnancy complicated by GDM, the post-partum period provides an important platform to initiate beneficial health practices for both mother and child to reduce the future burden of obesity, diabetes and cardiovascular diseases. FIGO recommends that obstetricians establish links with family physicians, internists, pediatricians, and other healthcare providers to support postpartum follow-up of mothers with HIP and their children. A follow-up program linked to the child’s vaccination and regular health checkup visits provides an opportunity for continued engagement with the high risk mother child pair.

International research collaboration in HIP

International federation of gynecology and obstetrics also seeks greater international research collaboration to address the knowledge gaps to better understand the links between maternal health and non-communicable diseases and create evidence-based best practice standards for testing, management, and care of women with GDM.

Preventive strategies for the long term sequelae of HIP

The growing burden of diabetes is becoming a major threat to women’s health. Hyperglycemia can impact her whole sexual and reproductive life and beyond, starting from increased frequency of urogenital infections, infertility and difficulty in conception, to early pregnancy loss, to complications during pregnancy, delivery and in the immediate post-partum period, to early onset of type 2 diabetes and higher risk for premature cardiovascular diseases, etc. Gestational hyperglycemia is most often the trigger and
marker of this downward spiral but is also a window of opportunity [35] to provide maternal care services, not only to reduce the traditionally known maternal and perinatal morbidity and mortality indicators, but also for improving health of the women and prevent diabetes, cardiovascular and other chronic diseases through targeted health promotion, and also address transgenerational prevention of several chronic diseases. Thus, with one high-quality intervention related to maternal health service, it is now possible to achieve several cascading objectives with far reaching health and economic benefits. It is about time that health planners and policy makers all over the world pay heed to these recommendations and take appropriate steps to implement the necessary actions.

Disclosure statement

No potential conflict of interest was reported by the authors.

References


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