



Screening for First Trimester's Hyperglycemia in High and Low Risk Pregnancy: A Prospective Cohort Study

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Abstract

Introduction: Hyperglycemia increases the risk of delivering a large for gestational age poor adaptation of the newborn. The aim of this work was to detect cases of hyperglycemia in pregnancy (HIP) as early as possible; this gives the chance to initiate treatment early to achieve euglycemic state during the critical period of organogenesis. **Methods:** This prospective cohort study carried out on 218 pregnant ladies during their first trimester who were tested for the presence of hyperglycemia. They were divided into two groups: high risk women: (n=96) and low-risk women: (n=122) **Results:** Fasting blood glucose (FBG), first hour postprandial, 2nd hour postprandial and glycated hemoglobin (HbA1c) in the first and second visit were significantly higher in high risk than low risk ($P<0.05$). Ten out of those 13 women, blood glucose level could be controlled on diet control and exercise and 3 cases only needed metformin to be added to the regimen all of them were in the high-risk group. FBG and 2hr postprandial were significantly higher in first visit than second visit ($P<0.05$).

Conclusions: Testing for hyperglycemia early in pregnancy could detect cases in both low and high-risk women, this gives the opportunity to interfere earlier in the critical period of organogenesis which is aimed to improve maternal and fetal outcome.

Keywords: First Trimester, Hyperglycemia, High and Low Risk, Pregnancy

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Introduction:

Glucose intolerance is the commonest medical disorder complicating pregnancy.⁽¹⁾ The name Diabetes in Pregnancy (DIP) is preferred if blood glucose levels are high enough to be compatible with the diagnosis of diabetes outside of pregnancy. DIP commonly represents undetected diabetes mellitus that is discovered during pregnancy for the first time and commonly referred to as gestational diabetes mellitus (GDM).⁽²⁾ Hyperglycemia increases the risk of delivering a large for gestational age newborn (LGA) and related complications such as operative delivery, birth trauma and the poor adaptation of the newborn. Maternal risks of GDM include also polyhydramnios, preeclampsia, premature delivery, prolonged labor, uterine atony, postpartum hemorrhage, infection and progression of retinopathy which are the global causes of maternal morbidity and mortality.⁽³⁾

Fetal risks include spontaneous abortion, intrauterine death, stillbirth, congenital malformation, shoulder dystocia, birth injuries, neonatal hypoglycemia and infant respiratory distress syndrome.⁽³⁾

Approximately fifty percent of women who have GDM are at risk of developing type 2 diabetes in later life.⁽⁴⁾ Hence screening, early identification and early management still is very important^[5]. Long-term clinical effects of GDM are major contributors to the burden of non-communicable diseases in most countries.⁽³⁾ Detection of women at higher risk for GDM early in pregnancy also represent a desirable goal as interventions such as diet, medication, and exercise may be implemented earlier in pregnancy and perhaps can reduce later development of GDM or its associated morbidities.⁽⁶⁾ The first trimester is characterized by increased secretion of insulin and improved insulin sensitivity under the effect of elevated maternal estrogen, resulting in an expected drop of glucose concentration at the same time. Early pregnancy shows increased insulin effect ensuring optimal maternal glucose uptake and storage to meet increased energy demands later in pregnancy.⁽³⁾

Unlike changes in glucose homeostasis that occur during early pregnancy, insulin resistance (IR) is elevated 30–70% in the second and third trimester.⁽³⁾ Diagnosis of GDM is most common after the mid second trimester and after an

abnormal glucose challenge test. For an estimated ten percent of patients who have GDM, the diagnosis can be made in the first trimester.⁽⁷⁾

The aim of this study was to detect cases of Hyperglycemia in Pregnancy (HIP) as early as possible; this gives the chance to initiate treatment early to achieve euglycemic state during the critical period of organogenesis. This is expected to optimize fetal as well as maternal outcome.

Patients and Methods:

This prospective cohort study was carried out on 218 pregnant women in their first trimester of pregnancy. Ninety-six women were at high risk to develop gestational diabetes and 122 women were at low risk. All women were below 35 years old. The high-risk group included women who had one or more of the following risk factors:

- gestational diabetes in previous pregnancies
- History of still birth
- History of Macrosomic baby in previous pregnancy
- Women with endocrinopathies like suprarenal, thyroid or pituitary disorders
- Women with auto immune diseases.
- Previous history of preeclampsia.
- Family history of diabetes.
- Previous fetal anomalies.
- History of multifetal gestation.

Low risk group included women pregnant in their first trimester with non of the previous risk factors. The study was done from September 2023 to September 2024 after approval from the Ethical Committee Sohag University Hospitals, Sohag, Egypt. Registration of clinical trials.gov (ID: NCT06064552). An informed written consent was obtained.

All patients were subjected to complete history taking, general, head, neck, abdominal, ultrasonographic examinations, laboratory investigations [fasting blood glucose level (FBG), HbA1C] and ultrasonography.

Gestational age was determined by the date of reliable last menstrual period and using crown rump length measured using ultrasound (by Logic p7 with probe frequency 7-9 HZ). For women in both groups, fasting blood glucose levels were estimated using (a handheld plasma-calibrated glucometer (Care Sens device) after 6-8 hours fasting with good hydration, then one and two hours after receiving their usual meal. Glucose

intolerance was diagnosed if 2 measures exceed the cut off values;(FBS>95mg/dl,1hrpostprandial>140mg/dl,2hrs postprandial >120mg/dl) and for those women HbA1C was estimated and women who were hyperglycemic ,were advised to change their life style .Simple exercise in the form of walking for 30 minutes daily and avoiding excess carbohydrates and sweets in their meals .Signed by their blood sugar was then measured after two weeks .

Results:

Thirteen out of the 218 participants recruited proved to be hyperglycemic at first visit, nine of them in high risk and four in the low-risk group as shown in **table 1**.

FBG, one and two hrs. postprandial were significantly different between the first, second visit and after two weeks of diet control and

exercise. Ten out of those 13 women, blood glucose level could be controlled on diet control and exercise and 3 cases only needed metformin to be added to the regimen all of them were in the high-risk group. Following those cases through the 2nd trimester visit showed significant lowering of their blood glucose measurements. Six of these cases could be controlled by non-pharmacological approach and continued throughout the whole course of pregnancy, while 3 of them required adding metformin after two weeks of initiation of treatment. One of these 3 cases aborted at 14 weeks; one her pregnancy was terminated at 34 weeks because Of severe preeclampsia despite normal blood glucose and HbA1c readings and one completed to term with normal fetal outcome shown in **Table 2**

Table 1: Glycemic state of both groups at first visit.

| Group | Number | Mean G. A | FBS | 1 st hour postprandial | 2 nd hour postprandial | Hyperglycemic ladies | HbA1C |
|-----------|------------|-----------------|-----------------|-----------------------------------|-----------------------------------|----------------------|-----------------|
| High risk | 96 | 9.285 ± 2.722 | 99.702 ± 11.652 | 134.630 ± 22.429 | 130.98 ± 284.711 | 9 % | 6.762 ± 1.7623 |
| Low risk | 122 | 8.742 ± 1.683 | 82.742 ± 9.684 | 103.676 ± 19.823 | 102.716 ± 23.2935 | 4% | 5.7285 ± 1.5188 |
| Total | 218 | P = .255 | P = .012 | P= .009 | P= .035 | 13 cases | P = .025 |

Table 2: Glycemic state in first visit and under non-pharmacological treatment alone or with metformin for hyperglycemic women.

| | First visit (n=13) | After two weeks of diet control and exercise | | Second visits | | P |
|------------------------------------|--------------------|--|---|-------------------------------------|-----------------------------------|---------------|
| | | Controlled (n=10) | Not controlled and need metformin (n=3) | On diet control and exercise (n=10) | After addition of Metformin (n=3) | |
| FBG | 163.712 ±12.35 | 86.712 ±3.352 | 136.873 ±1.71 | 81.742±8.684 | 89.856 ±1.65 | 0.001* |
| 1hr postprandial | 203.640 ±22.22 | 122.640 ±9.22 | 169.736 ±2.25 | 109.673 ±6.82 | 117.861 ±2.76 | 0.001* |
| 2hr postprandial | 173.95 ±21.84 | 113.95 ±8.841 | 152.362 ±1.58 | 105.715 ±5.29 | 109.471 ±1.62 | 0.001* |
| Glycemic state in high risk | | | | | | |
| | First (n=9) visit | Controlled (n=6) | Not controlled and need metformin (n=3) | On diet control and exercise (n=6) | Addition of Metformin (n=3) | |
| FBG | 153.643 ±6.298 | 87.643 ±3.352 | 145.365 ±1.635 | 82.763 ±3.034 | 88.726 ±1.325 | 0.001* |
| 1hr postprandial | 195.841 ±4.541 | 126.830 ±9.22 | 171.236 ±2.335 | 110.321±2.42 | 116.239 ±2.857 | 0.001* |
| 2hr postprandial | 170.302 ±6.952 | 117.52 ±8.841 | 148.321 ±1.361 | 105.642±5.321 | 107.376 ±1.903 | 0.001* |

Data is presented as mean ± SD. *significant as P value <0.05. FBG: Fasting blood glucose.

FBG and 2hr postprandial were significantly higher in first visit than second visit ($P < 0.05$). 1hr postprandial, glycemic state of high-risk women who were euglycemic at the first visit were insignificantly different between first and second visit. **Table 3**

Table 3: Glycemic state of low-risk women during first, second visit and of high-risk women who were euglycemic at the first visit

| | First visit (n=118) | Second visit (n=54) | P |
|---|---------------------|---------------------|--------|
| FBG | 82.742±9.684 | 79.854±12.653 | 0.012* |
| 1hr postprandial | 103.676±19.823 | 103.863±24.768 | 0.727 |
| 2hr postprandial | 102.716±23.2935 | 99.471±12.622 | 0.014* |
| Glycemic state of high-risk women who were euglycemic at the first visit | | | |
| | First visit (n=87) | Second visit (n=56) | |
| FBG | 91.702±7.652 | 88.873±8.735 | 0.264 |
| 1hr postprandial | 130.630±10.429 | 119.716±11.203 | 0.643 |
| 2hr postprandial | 125.98±11.711 | 122.392±9.58 | 0.463 |

Data is presented as mean ± SD. *significant as P value <0.05. FBG: Fasting blood glucose.

Glycemic state of low-risk women was significantly different between first, second visit and after two weeks ($P = 0.001$). **Table 4**

Table 4: Change in glycemic state of low-risk women with hyperglycemia in first visit in response to non-pharmacologic treatment

| | First visit (n=4) | After two weeks | Second visits | P |
|-------------------------|-------------------|---------------------------------|---------------------------------|---------------|
| | | Diet control and exercise (n=4) | Diet control and exercise (n=4) | |
| FBG | 151.642±2.764 | 80.312±.852 | 81.446±.354 | 0.001* |
| 1hr postprandial | 190.753±2.280 | 120.541±.884 | 109.263±.962 | 0.001* |
| 2hr postprandial | 163.053±1.591 | 108.321±.790 | 101.364±.742 | 0.001* |

Data is presented as mean ± SD. *significant as P value <0.05. FBG: Fasting blood glucose.

Discussion

Glucose intolerance is the commonest medical disorder complicating pregnancy.⁽¹⁾ Detection of women at higher risk for GDM early in pregnancy also represent a desirable goal as interventions such as diet, medication, and exercise may be implemented earlier in pregnancy and perhaps can reduce later development of GDM or its associated morbidities.⁽⁶⁾

In the current study, the overall prevalence of Hyperglycemia in both high and low risk cases during the first trimester was about 6% (13 out of 218). high-risk cases contributed to 9 cases (9.4%); while remaining 4 cases (3.3%) were in low-risk group. In a study by Ye, Yunzhen, et al.⁽⁸⁾

found that FPG testing at the initial prenatal visit, followed by a 75-g OGTT at 24 to 28 weeks gestation. There were 807 (3.3%) women who had an FPG of 91.8 to 124.2

mg/dl in early pregnancy. In another study by Yeral et al.⁽⁹⁾ showed that early

identification and treatment of women with GDM is the goal for improving maternal fetal and neonatal outcomes and the 75 g GTT was found to

be a better predictor of GDM than the FPG test and the two-step GTT. The sensitivity of the 75 g GTT was nearly twice that of the FPG test, which had

more false-positive results and thus was less specific than the other two tests. In contrast, in our study, we used FBS by (a handheld plasma-calibrated glucometer) which is cheap, easy and available for all participants. This simple test detected hyperglycemia in 6% of cases which is comparable to the results of the previous two studies.

On the other hand, a higher prevalence in pregnant women was reported in several studies. According to the IDF, globally 20.4 million women of reproductive age (16%) are affected by HIP, of whom 83.6% have GDM; 7.9% have preexisting diabetes; and 8.5% have diabetes first detected during pregnancy (International Diabetes Federation 2018). According to the IDF estimates, MENA region has the highest age-adjusted prevalence of diabetes (12.2%), which is likely to double by the year 2045 (International Diabetes

Federation 2018). These studies included big numbers of participants and conducted on a multicentric basis and comparing their results with ours is unfair.

In our study the high-risk group was 96 cases of whom 9 cases were hyperglycemic in early pregnancy with fasting blood glucose ≥ 95 mg/dl. Six cases were managed by diet control and 3 cases on diet control and metformin. On follow up at 24-28 week one of 3 cases aborted at 14 wks the other case complete with normal pregnancy outcome, the 3rd case had her pregnancy terminated at 34 weeks due to severe preeclampsia despite normal blood glucose reading and normal HbA1C. On the other hand, low risk group (122 cases) of whom 4 cases develop hyperglycemia in early pregnancy all managed by diet control only and normal follow up and complete pregnancy normally. No cases develop GDM in 24-28 wks. So early detection of cases with hyperglycemia in first trimester and management improve fetal and maternal outcome. This is confirmed by a study of Veeraswamy et al. ⁽¹⁰⁾ emphasized the importance of screening all pregnant women for glucose intolerance in the early weeks of pregnancy. This was also emphasized by Cosson et al. ⁽¹¹⁾ who found that treating woman with early fasting hyperglycemia, especially when FPG is ≥ 99 mg/dl, may improve pregnancy outcomes.

The recommendations of this study included that larger epidemiological studies are required for gathering more accurate information about the prevalence of hyperglycemia in early pregnancy. This will help health policy makers in planning effective strategies for early detection and treatment of hyperglycemia.

Conclusions:

Testing for hyperglycemia early in pregnancy could detect cases in both low and high-risk women, this gives the opportunity to interfere earlier in the critical period of organogenesis which is aimed to improve maternal and fetal outcome.

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