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Gestational Diabetes in Undernourished Women of KONKAN Region of State of Maharashtra, India (BKLWHANC-1)

Suvarna Patil[1,*], Netaji Patil[2], Unmesh Santpur[3], Pallavi Bhat[4], Dnyaneshwar Jadhav[4], Omkar Dervankar[4], Charudatta Joglekar[4], Rakesh Hasbe[3], Manisha Patel[3], Vijay Dombale[5], Arvind Yadav[6], Anup Nilawar[6] and Ajit Nandoskar[4]

[1]Department of Medicine, BKL Walawalkar Hospital and Rural Medical College, Sawarde, Taluka-Chiplun, District-Ratnagiri, Maharashtra, India
[2]Department of Radiology, BKL Walawalkar Hospital and Rural Medical College, Sawarde, Taluka- Chiplun, District-Ratnagiri, Maharashtra, India
[3]Department of Obstetrics and Gynaecology, BKL Walawalkar Hospital and Rural Medical College, Sawarde, Taluka-Chiplun, District-Ratnagiri, Maharashtra, India
[4]Regional Centre for Adolescent Health and Nutrition, BKL Walawalkar Hospital and Rural Medical College, Sawarde, Taluka-Chiplun, District-Ratnagiri, Maharashtra, India
[5]Department of Pathology, BKL Walawalkar Hospital and Rural Medical College, Sawarde, Taluka-Chiplun, District-Ratnagiri, Maharashtra, India
[6]Department of Biochemistry, BKL Walawalkar Hospital and Rural Medical College, Sawarde, Taluka-Chiplun, District-Ratnagiri, Maharashtra, India

***Corresponding author:** Suvarna Patil, Medical Director, Department of Medicine, BKL Walawalkar Hospital and Rural Medical College, Sawarde, Taluka-Chiplun, District-Ratnagiri, Maharashtra, India, Tel: +91-2355-264935; Fax: +91-2355-264181; E-mail: dr.suvarnanpatil@gmail.com

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Abstract

Introduction: Offsprings exposed to intrauterine hyperglycaemia are at increased risk of obesity, type 2 diabetes in postnatal life. Little is known about gestational diabetes in KONKAN region of Maharashtra where women are undernourished across all stages of life. We estimated the prevalence of gestational diabetes among pregnant women visiting tertiary care hospital in KONKAN region.

Methods: Between March 2020 and November 2020, 514 pregnant women registered in the antenatal clinic of BKL Walawalkar Hospital in KONKAN region. They underwent oral glucose tolerance test using the protocol set by Maternal & Child Health Division of Government of India.

Results: Five hundred and six women completed oral glucose tolerance test. Mean age, gestation, weight and BMI at registration were 26.7 years, 23.1 weeks, 48.3 kg and 20.5 kg/m^2 respectively. Prevalence of GDM was 20.3% and more than 50% of them were diagnosed before 24 weeks of gestation.

Conclusion: Our results have shown that presence of GDM despite absence of overweight (high BMI). This is the first demonstration of hyperglycemia in pregnancy among undernourished women of KOKAN region. Offspring's exposed to intrauterine hyperglycemia are at increased risk of obesity, type 2 diabetes in postnatal life hence long term implication of GDM in KONKAN can only be understood by systematic, community based study.

Keywords: GDM; Rural; KONKAN; India; Malnutrition; Insulin resistance

List of Abbreviations: BMI: Body Mass Index; GDM: Gestational Diabetes Mellitus; T2DM: Type 2 diabetes Mellitus; IDF: International Diabetes Federation; DOHAD: Developmental Origins of Health and Disease; GOI: Government of India; OGTT: Oral Glucose Tolerance Test; DIPSI: Diabetes in Pregnancy Study Group India; IADPSG: International Association of Diabetes and Pregnancy Study Groups; ADA: American Diabetic Association

Introduction

India is witnessing a rapid rise in prevalence of type 2 diabetes (T2DM). By the year 2030 India will have 101.0 million people with T2DM [1]. This is attributed to rapid nutritional as well as technological transition which has taken place over last 2 decades. Obesity, physical inactivity and increased urbanization have been broadly identified as the major contributing risk factors for the development of T2DM. At the same time hyperglycaemia in pregnancy also known as Gestational Diabetes Mellitus (GDM) is also on the rise. International Diabetes Federation (IDF) in 2018 estimated GDM prevalence of 27.0% in South-East Asia [2] and that of 28.0% in India [3]. It is well-known that maternal nutrition plays crucial role in fetal growth. Maternal under nutrition is associated with reduce offspring size at birth. The Developmental Origins of Health and Disease (DOHAD) concept [4] postulated that maternal under nutrition in pregnancy can influence the long term risk of developing T2DM. On the other hand over nutrition is associated with obesity and diabetes leading to fetal overgrowth. Pedersen proposed that transfer of excess maternal glucose in a diabetic pregnancy stimulates fetal islets to produce fetal hyper insulinemia which leads to macrosomia [5]. According to Freinkel excess supply of maternal macronutrients (lipids and amino acids) together with elevated glucose concentrations affects

the structure and metabolic functions of the fetus, and may result in obesity and diabetes in later life (fuel mediated teratogenesis) [6]. Women who develop GDM are at a higher risk of developing GDM in subsequent pregnancies and developing T2DM in later life [7,8] and her offspring also has risks of obesity and developing T2DM in later life [9]. A recent meta-analysis of 24 studies found increased blood pressure, BMI and glucose in the offspring exposed to GDM in utero [10].There is unanimity among researchers about these risks. But at the same time there is lack of unanimity about criteria to diagnose GDM. Various criteria have been suggested and are used to diagnose GDM [11]. There are also disagreements about gestation of first testing and also frequency of testing. Practical difficulties in implementing testing protocols have also been sighted especially in rural, remote or underdeveloped regions of Asia and Africa [12,13].

GDM prevalence estimates have been reported from many parts of the world. A multinational study involving 12 countries including India reported prevalence of 4.3% [14]. There are many reports from various African countries too [15-18]. There are wide ranging estimates (0% to 41.9%) of GDM prevalence from various regions of India [19-22]. A study in rural area of the state of Maharashtra from where our report comes has shown a prevalence of 9.5% [23]. In a preconceptional micronutrient supplementation trial in the slum areas of metropolitan city of Mumbai, prevalence was 7.3% in the intervention group and 12.4% in control group [24]. Reports from south India showed prevalence estimates of 14%-16% [25,26]. BKL Walawalkar Hospital established in 1996 is located in the Dervan area of the coastal Ratnagiri district of the western Indian state of Maharashtra. It caters to the surrounding community as a tertiary care hospital. It also runs various community programs in village for pregnant mothers, newborns, young children and adolescents with holistic approach. Community program for pregnant women comprises counselling and educational sessions about safe delivery. Importance of hospital delivery is stressed. In addition hospital also provides obstetric services to the community. Approximately 700 women deliver at the hospital every year. Hospital does not have universal screening for diabetes in pregnancy. Women registered in the antenatal clinic undergo testing for GDM only if treating obstetrician thinks of them to be at high risk for diabetes. Criteria to test for GDM kept on changing from time to time. Implementation of whatever protocol was agreed upon faced practical difficulties like ensuring fasting state, prohibiting any food consumption after glucose load. Thus it was becoming very difficult to estimate the prevalence of GDM in our community. In 2018 after recommendation of Diabetes In Pregnancy Study Group India (DIPSI), Maternal & Child Health Division of Government of India (GOI) released new guidelines for GDM diagnosis [27]. The major highlight of these guidelines is the oral glucose tolerance test (OGTT) done in non-fasting state (2 hour post load) as against 3 point OGTT (fasting, 1 hour and 2 hour post load) recommended by International Association of Diabetes and Pregnancy Study Groups (IADPSG). According to DIPSI OGTT is done at 1st antenatal visit to the clinic and a repeated at 24-28 weeks of gestation if earlier test is negative. In March 2020 hospital decided to adopt these guidelines. This manuscript reports the prevalence of GDM in women of Dervan area who were registered in the antenatal clinic of our hospital during March 2020 to November 2020.

Materials and Methods

This was a prospective hospital based study among women attending antenatal clinic. Except known diabetic all other were included. Obstetric history, family history of diabetes was recorded. Gestation of visit to the hospital was calculated based on last menstrual period. Height and weight were recorded for each woman visiting the antenatal clinic. Stunting was defined using WHO criteria [28].

Laboratory methods

Women were administered 75 gm anhydrous glucose after dissolving it in approximately 300 ml water irrespective of whether the pregnant women are in fasting or non-fasting state. Venous blood sample was collected after 120 minutes. Coefficient of variation (CV) for internal low and high control was < 5%. CV using external quality control from Christian Medical College, Vellore, India was <9.2%.

Statistical methods

Continuous data has been presented as mean and standard deviation while categorical data has been presented as percentages. Last menstrual period was used to calculate the gestation at the time of antenatal visit. The SPSS version 25.0 for windows (SPSS Inc, Chicago) was used for statistical analysis. Trend in prevalence of GDM across BMI was tested using chi-square test. P value <0.05 was considered as statistically significant.

Results

Our GDM testing protocol was implemented on all of the women (n=514) newly registered in the antenatal clinic of the hospital between March 2020 and November 2020. Two vomited within 30 minutes and 6 left the hospital premises after glucose load so no blood was collected. Thus 506 women had their oral glucose tolerance test (OGTT) done at least once during our study period.

Table 1 shows the characteristics of women at the time of 1st visit to the antenatal clinic. Women had a mean age of 26.7 y ± 4.0 y height 153.7 cm ± 5.5 cm. More than 50% were primiparous and stunting prevalence was 21%. Mean gestation at 1st visit was 23.1 weeks ± 8.4 weeks, weight 48.3 kg ± 10.0 kg. BMI 20.5 kg/m^2 ± 3.9 kg/m^2 and underweight (BMI ≤ 18.5 kg/m^2) was 35.7%. Overall 267 (52.8%) had their 1st visit before 24 weeks, 75 (14.8%) between 24-28 weeks and 164 (32.4%) after 28 weeks of gestation. Around 5-7% reported the family history of diabetes in parents. Table 2a shows GDM diagnosis details according to gestation. Over all prevalence of GDM was 103 (20.3%). Table 2b shows GDM prevalence according to quartiles of BMI. But the trend for proportions was not significant.

Table 1: Characteristics of women at 1st visit (n=506).

Parameters	Mean ± SD N (%)	Minimum-Maximum
Age (Years)	26.7 ± 4.0	18-40
Primigravida	259 (51.1%)	NA
Multigravida	247 (48.8%)	2-6
Family History of Diabetes Mother	14 (5.0%)	NA
Family History of Diabetes Father	20 (7.2%)	NA
Gestation at registration (weeks)	23.1 ± 8.4	5.9-38.3
<24 weeks	267 (52.8%)	5.9-23.9
24-28 weeks	75 (14.8%)	24.0-28.0
Height (cm)	153.7 ± 5.5	141-172
Stunting	106 (21%)	NA
Weight at registration (kg)	48.3 ± 10.0	28.5-104.4
BMI at first registration (kg/m^2)	20.5 ± 3.9	11.8-38.8
BMI ≤ 18.5 kg/m^2	181(35.7%)	NA

SD: Standard Deviation; BMI: Body Mass Index; NA: Not Applicable
Mean (Standard Deviation) for continuous variables otherwise n (%)

Table 2a: Frequency of GDM and mean weight at various gestational ages.

Gestation at GTT	GTT done	Subjects with 2 hour plasma glucose ≥ 140 mg/dl (n, %)	Weight (kg) at diagnosis Mean ± SD
All	506	103 (20.3%)	48.4 ± 10.1
0-16 weeks	125 (24.7%)	25 (24.3%)	46.0 ± 9.9
16-20 weeks	67 (13.3%)	14 (13.6%)	47.2 ± 8.3
20-24 weeks	75 (14.9%)	13 (12.6%)	48.7 ± 10.0
24-28 weeks	75 (14.8%)	16 (15.5%)	49.6 ± 9.4
>28 weeks	164 (32.4%)	35 (34.0%)	50.0 ± 11.1

SD: Standard Deviation

Table 2b: Prevalence of GDM according to BMI quartiles.

	Q_1(n=126)	Q_2(n=126)	Q_3(n=127)	Q_4(n=127)	P value
Quartile range (min-max)	11.8-17.6	17.65-19.7	19.8-22.9	22.9-38.8	NA
≥ 140 (n, %)	20 (15.9)	18 (14.3)	20 (15.7)	30 (23.6)	0.170

Q_1, Q_2, Q_3, Q_4 are 1st, 2nd, 3rd and 4th quartile respectively.
NA: Not Applicable

Discussion

We have reported GDM prevalence of 20.3% at a tertiary care hospital in rural KONKAN. We used GOI criteria for the diagnosis. The criterion which is based on non-fasting state was laid down by Diabetes in Pregnancy Study Group India (DIPSI) has been subsequently adopted by GOI. The criteria is widely used because of its simplicity but also has faced criticism because of its poor sensitivity when compared to IADPSG and WHO99 criterion [12,29]. Also 35.7% women had BMI below18.5 kg/m^2 at the time of registration. Since the mean gestation at registration is around 23 weeks, the number of women with such a low BMI is likely to be far higher at preconception stage.

Though hospital based, this is the first report on GDM from rural KONKAN. Our estimate of 20.3% is very much similar but on the higher side as that of 16.7% reported recently in the rural area of the north-eastern Indian state of Assam [30]. As per protocol all the women (n=506) were tested on the 1st antenatal visit irrespective of gestation which varied widely as shown in table 1. We were unable to do repeat testing at 24-28 weeks as per protocol on those who had their first visit before 24 weeks. In India there is a cultural practice among pregnant women to migrate to mothers place in the 7th month of pregnancy for delivery. Thus women who underwent 1st testing earlier in pregnancy are very likely to have migrated to their mothers place hence missed the subsequent follow-up. Similarly those who visited in our clinic first time in late gestation are very likely to have moved in to their mother's home for delivery and underwent earlier testing if any at some other clinic. Only 75 (14.8%) women visited 1st time during 24-28 week gestation. This was the major drawback in our data. Very few (n=27, 5.3%) women were able to underwent GTT more than once during pregnancy and none of those were in 24-28 weeks, the most crucial period for GDM diagnosis. But in our data out of total 103 women diagnosed with GDM, >50% (n=52) were diagnosed before 24 weeks of gestation. Early diagnosis of GDM before 24 weeks of gestation has also now been recommended by WHO and DIPSI though American Diabetic Association (ADA) still insists on diagnosis at 24-28 weeks of gestation. Our study subjects come from far away places and they tend to have some food before start of their antenatal investigations (clinical as well as laboratory). Thus we found non fasting OGTT very useful. Causes for low sensitivity of non-fasting OGTT have been reported by Coustan DR, et al. [31]. We did not have data on weight at preconception. Yet we were able to highlight the poor weight across gestation. We have shown earlier [32] that women who delivered in our hospital had a mean weight of 49.1 kg and BMI of 21.4 kg/m^2 at the time of delivery. The women population of KONKAN region is undernourished before pregnancy as well as during pregnancy [32,33]. Twenty one percent women in our data were stunted. Obesity well-known risk factors for GDM which has been described in various studies done mostly in urban settings was almost absent in our population. Another major drawback of our study is the lack of insulin measurements. Risk of early pregnancy impaired insulin secretion in development of GDM has been reported in lean (low BMI) Asian populations from Japan and Bangladesh [34,35]. As per GOI protocol, women with diagnosis of GDM should be managed with diet, OHA, (Oral hypoglycaemic agent) or insulin depending on blood glucose levels and frequent monitoring. Women in our area are poorly educated and majority of them fall under poor socioeconomic status but physically active [36]. They might not be able to recognize hypoglycaemic situation using point of care devices (glucometer) if treated with insulin. Thus strict follow up of the protocol is very difficult. GDM poses risk of developing diabetes to the mother as well as her fetus in later life. It is also linked with cardio metabolic risk. This can be prevented by early screening of GDM during pregnancy irrespective of obesity and presence of other conventional known risk factors. All antenatal mothers including those undernourished should be screened universally for GDM using OGTT. Preconceptional improvement in nutrition will reduce the risk of GDM. Nutritional supplementation during pregnancy is unlikely to have major effect as she is already facing excess nutritional demands for her and fetus. Best way to overcome this obstacle is to initiate nutritional education in her adolescent age. Adolescent nutritional health programmes should be strengthened universally for better pregnancy outcomes.

Conclusion

Thus using a simple protocol though with low sensitivity we have found high prevalence of GDM in our region. Due attention in diagnosis and treatment might benefit mother and her baby in terms of reduced risk of developing T2DM in future. Insulin secretion in early pregnancy in lean women needs to be investigated. Despite some shortcomings our data warrants a systematic, community based study which includes measurements at preconception stage.

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Disclosure of Interest

None of the authors had any financial or personal conflicts of interest associated with this manuscript.

Author's Contribution

Suvarna Patil, Netaji Patil conceptualized the study. Pallavi Bhat, Omkar Dervankar and Ajit Nandoskar design methods. Charudatta

Joglekar wrote the initial draft. Dnyaneshwar Jadhav performed data analysis. Unmesh Santpur, Rakesh Hasabe, Manisha Patel investigated subjects in outpatient clinic. Anup Nilawar, Arvind Yadav, Vijay Dombale provided additional scientific interpretation.

Ethics

Informed and written consent was obtained from all the pregnant women to use the data.

The study was approved by the Institute Ethics Committee of BKL Walawalkar Rural Medical College and Hospital. Our institute ethics committee is registered with the Government of India. Registration code is EC/755/INST/MH/2015/RR-18.

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