Original Article

# Fetal biometry at the Time of Diagnosis of Gestational Diabetes in Undernourished (low BMI) Mothers from Rural KONKAN Region of Maharashtra, India (BKLWHANC-4)

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**Abstract**

**Background:** To measure fetal biometric parameters and perform oral glucose tolerance test at first antenatal visit in rural undernourished pregnant mothers in a cross sectional study. Compare fetal biometry between mothers diagnosed with gestational diabetes and those with normal glucose tolerance.

**Methods:** Every undernourished pregnant woman at the time of registration in the antenatal clinic underwent oral glucose tolerance test using the protocol set by Ministry of Health and Family Welfare, Government of India. In addition, anthropometric assessment and an ultrasound scan were offered to every woman. Fetal biometric parameters (biparietal diameter, abdominal circumference, femur length and head circumference) were measured. Fetal weight was estimated. All the measures were converted to gestation specific standard deviation scores. Comparison of parameters between mothers with and without gestational diabetes (GDM) was done using t-test. Association between gestational diabetes and fetal biometry was analysed using odds ratios.

**Conclusion:** Our unexpected results of small fetal size along with AC of undernourished pregnant women with gestational diabetes will have clinical implications on treatment of gestational diabetes and fetal outcome in rural India.

**Key words:** Fetal Growth, KONKAN, Gestational Diabetes, Under nutrition

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## Introduction

India is witnessing the escalation in diabetic patients[1-2]. This is mainly attributed to rapid nutrition transition happening over last two decades which has laid to unhealthy diet (over nutrition), increase in obesity. This has also laid to the increase in incidence of gestational diabetes (GDM)[2]. These changes are very much evident in urban India. Though nutrition transition has also intruded into rural parts, yet India is still predominantly a rural country where there is substantial burden of under nutrition, maternal and neonatal mortality[3]. Prevalence of major risk factors (obesity, overweight, physical inactivity) which play crucial role in the development of GDM is still very low in rural settings. There are very few studies exploring the effect of maternal under nutrition in a GDM pregnancy on fetal growth. Prevalence of Low Birth Weight (LBW), early, late childhood and adolescent under nutrition is very high in KONKAN region of the state of Maharashtra, India[4]. According to Developmental origins of Health and Disease (DOHaD) hypothesis these factors increase the risk of adult Non-Communicable Diseases (NCD)[5]. KONKAN area is also witnessing rise in NCD's [3]. BKL Walawalkar Hospital was set up in DERVAN area of rural KONKAN region in 1996. It is a tertiary care referral centre in the region. Recently we concluded a study in our hospital on estimating the prevalence of GDM in rural KONKAN region[6]. In the same study, fetal ultrasound measurements were recorded as a part of antenatal investigations. Fetal overgrowth in abdominal circumference and increase in fetal weight is observed in mothers with GDM which is driven by obesity. But this has never been investigated in undernourished mothers. Its impact on pregnancy outcomes needs to be investigated. We now report the association between GDM in undernourished mothers and fetal ultrasound measurements.

## Materials and Methods

The details of our earlier study to estimate the prevalence of GDM in our region are already reported [6]. The study took place between March 2020 and November 2020. In addition to oral glucose tolerance test (OGTT), the subjects also underwent ultrasound scan and anthropometry measurements. The data on fetal biometric parameters measured was stored in the Microsoft Access database. The study took place during March 2020 to November 2020.

We followed GDM diagnosis protocol laid down by Maternal Health Division, Ministry of Health and Family Welfare, Government of India where pregnant woman undergoes OGTT at her first antenatal visit irrespective of gestation[7]. This enabled us to diagnose GDM in wide range of gestation and record fetal biometry at the time of diagnosis.

### Fetal measurements

Fetal size was measured using ultrasound. Scans were performed by trained radiologists using Philips HD 11 ultrasound scanner. Biparietal diameter (BPD) was measured from the outer table of the proximal calvarium to the inner table of the distal calvarium. Abdominal circumference (AC) was calculated using transverse diameter and anteroposterior diameter. Occipito-frontal diameter (OFD) was measured, and head circumference (HC) was calculated using the formula (BPD+OFD) ×1.62. Femur length (FL) was measured along the long axis of the ossified femoral diaphysis. Sonographic gestation was an average of the predicted ages based on biparietal diameter, head circumference, femur length and abdominal circumference measurements[8]. Ultrasound scans were performed by 2 sonologists. The variation attributable to observers ranged from 0.05% - 0.09% for these measurements. Fetal weight (EFW) was estimated using BPD, HC, AC and FL[9].

### Statistical methods:

Total 506 pregnant women underwent OGTT. Out of theses 312 women had fetal ultrasound measurements. None of the women was diagnosed with any fetal anomaly.

Comparison of basic characteristics between those with and without ultrasound scan was done using t-test. Due to wide spread of gestation of OGTT at registration, we created five groups(0-16 weeks, 16-20 weeks, 20-24 weeks, 24-28 weeks and >28 weeks) of gestation at registration. In each group every fetal biometric measurement was converted to gestation specific standard deviation (SD) score. Independent sample t-test was used to compare fetal biometric parameters between those with and without GDM. In order to see the association of above normal or below

normal fetal biometric parameters with GDM, we created gestation of OGTT specific tertile (1/3rd) of the SD score of each fetal biometric parameter. Thus lowest tertile or lowest 1/3rd of gestation specific SD score of that parameter and similarly highest tertile or uppermost 1/3rd of gestation specific SD score of that parameter represented undernourished/poorly grown and overnourished/over grown foetuses for that parameters respectively. We used middle tertile as a reference and tested the associations with GDM using odds ratios (OR) and 95% confidence intervals (CI). The SPSS version 25.0 for windows (SPSS Inc, Chicago) and STATA 13.0 (STATA Corp, Texas) was used for statistical analysis.

There was no exclusion criteria. It was a sample of convenience. We performed OGTT in every woman who consented. Our subjects come from remote areas and many of them did not wait for ultrasound scans. This has created a selection bias. But our main aim was to generate some cross sectional information on gdm and fetal growth in the region where no prior information is available.

**Ethics:**

At the time of registration, informed and written consent was obtained from all the pregnant women to use the data. Additional permission to analyse the data was granted by Institute Ethics Committee of BKL Walawalkar Rural Medical College and Hospital. Institute ethics committee is registered with the Government of India. Registration code is EC/755/INST/MH/2015/RR-18.

## Results

Overall, 312 subjects had ultrasound scan measurements at the time of registration. Table 1 compares the basic characteristics of the subjects between those with ultrasound scan at the time of OGTT. Those without ultrasound scan had lower gestation at the time of registration. Table 2 compares Z scores of fetal biometric parameters of pregnant women between those without and with GDM. Foetuses of women diagnosed with GDM in early gestation (0-16 weeks) had significantly lower AC (p=0.016), lower FL (p=0.039) and lower fetal weight (p=0.028).Foetuses of mothers diagnosed with GDM at gestation of 16-20 week had significantly lower AC (p=0.028) and lower femur length (p=0.016). Table 2 also shows the association of GDM with fetal biometric parameters. Foetuses of mothers with GDM diagnosed at 0-16 weeks of gestation had higher likelihood of lower AC [OR 7.5, 95% CI 1.46-22.7], lower FL[OR 14.0, 95% CI 1.3-24.5] and lower EFW [OR 4.0, 95% CI: 1.73-21.84. Association with lower AC [ OR 1.61, 95% CI: 1.08-4.37], lower FL [OR 7.6, 95% CI: 1.8-70.1] was also observed in those with diagnosis of GDM at 16-20 weeks of gestation.

**Table 1: Comparison of the basic characteristics of the subjects between those with ultrasound scan and those without at the time of OGTT at registration**

| | USG done (n=312) | USG not done (n=194) | P value |
|---|---|---|---|
| Age (years) | 26.2 | 26.7 | 0.770 |
| Gravida | | | |
| Primi | 148 (49.3%) | 96 (54.2%) | 0.301 |
| Multi | 152 (50.7%) | 81 (45.8%) | |
| Gestation at registration (weeks) | 24.8 | 20.2 | 0.000* |
| Height (cm) | 153.3 | 154.3 | 0.092 |
| Weight (kg)at registration | 48.6 | 47.8 | 0.482 |
| BMI (kg/m$^2$)at registration | 20.7 | 20.3 | 0.339 |

**Table 2: Fetal biometry between normoglycemic and GDM mothers**

| Gestation at diagnosis | Parameters | Normal | GDM | P | OR (95 % CI) for GDM in $Q_1$ ($Q_3$ as reference) | P | OR (95 % CI) for GDM in $Q_2$ ($Q_3$ as reference) | P |
|---|---|---|---|---|---|---|---|---|
| 0-16 weeks | BPD | -0.080 | 0.166 | 0.466 | 0.32 (0.06-1.70) | 0.173 | 0.52 (0.10-2.58) | 0.420 |
| (n=40) | AC | 0.318 | -0.358 | 0.016 | 7.5 (1.46-22.7) | 0.039 | 10.0 (0.65-154.39) | 0.079 |
| Normal n=30 | HC | 0.054 | -0.113 | 0.620 | 1.40 (0.28-7.13) | 0.680 | 0.9 (0.17-4.70) | 0.901 |
| GDM n=10 | FL | 0.157 | -0.352 | 0.039 | 14.0 (1.3-24.5) | 0.011 | 5.33 (0.50-56.2) | 0.135 |
| | EFW | 0.574 | -0.574 | 0.028 | 4.0 (1.73-21.84) | 0.028 | 1.00 (0.04-24.55) | 1.000 |
| 16-20 weeks | BPD | 0.005 | -0.034 | 0.918 | 0.22 (0.02-2.20) | 0.169 | 0.75 (0.14-3.87) | 0.731 |
| (n=61) | AC | 0.473 | -0.064 | 0.028 | 1.61 (1.08-4.37) | 0.022 | - | - |
| Normal n=52 | HC | -0.071 | 0.472 | 0.542 | 1.06 (0.19-5.98) | 0.948 | 0.67 (0.09-4.48) | 0.675 |
| GDM n=9 | FL | 0.117 | -0.774 | 0.016 | 7.6 (1.8-70.1) | 0.045 | 1.00 (0.06-17.18) | 1.000 |
| | EFW | 0.039 | -0.274 | 0.684 | 0.8 (0.5-1.2) | 0.292 | 0.8 (0.58-1.19) | 0.338 |
| 20-24 weeks | BPD | 0.002 | -0.011 | 0.967 | 1.07 (0.22-5.13) | 0.931 | 0.70 (0.13-3.68) | 0.676 |
| (n=56) | AC | -0.056 | 0.229 | 0.398 | 0.67 (0.09-4.54) | 0.677 | 2.46 (0.51-11.79) | 0.252 |
| Normal n=48 | HC | 0.037 | -0.152 | 0.573 | 1.5 (0.29-8.01) | 0.618 | 1.42 (0.27-7.44) | 0.676 |
| GDM n=8 | FL | -0.015 | 0.064 | 0.811 | 1.07 (0.22-5.13) | 0.931 | 0.70 (0.13-3.68) | 0.676 |
| | EFW | -0.062 | 0.186 | 0.716 | 1.00 (0.04-24.54) | 1.00 | 1.00 (0.04-25.54) | 1.000 |
| 24-28 weeks | BPD | -0.0569 | 0.191 | 0.471 | 0.69 (0.13-3.75) | 0.669 | 1.00 (0.20-4.95) | 1.000 |
| (n=48) | AC | -0.081 | 0.274 | 0.300 | 0.38 (0.08-1.93) | 0.238 | 0.24 (0.04-1.43) | 0.102 |
| Normal n=41 | HC | 0.003 | -0.128 | 0.962 | 3.46 (0.32-37.47) | 0.285 | 11.7 (1.23-110.95) | 0.014 |
| GDM n=7 | FL | 0.038 | -0.129 | 0.627 | 0.67 (0.14-3.17) | 0.609 | 0.27 (0.04-1.65) | 0.141 |
| | EFW | -0.020 | 0.768 | 0.834 | 1.14 (0.12-10.38) | 0.906 | 1.00 (0.11-8.94) | 1.000 |
| >28 weeks | BPD | -0.000 | 0.002 | 0.990 | 1.25 (0.37-4.17) | 0.717 | 2.2 (0.71-6.79) | 0.165 |
| (n=107) | AC | -0.006 | 0.023 | 0.895 | 0.43 (0.13-1.43) | 0.164 | 0.87 (0.30-2.47) | 0.789 |
| Normal n=73 | HC | -0.012 | 0.041 | 0.818 | 0.54 (0.17-1.69) | 0.284 | 0.74 (0.25-2.17) | 0.586 |
| GDM n=34 | FL | 0.006 | -0.022 | 0.899 | 1.4 (0.49-4.10) | 0.539 | 0.7 (0.21-2.27) | 0.551 |
| | EFW | -0.010 | 0.036 | 0.842 | 0.69 (0.21-2.27) | 0.550 | 1.12 (0.38-3.35) | 0.832 |

BPD= Biparietal diameter (mm);

AC = Abdominal circumference (mm);

HC= Head Circumference (mm);

FL= Femur Length (mm);

EFW= estimated fetal weight (gm); figures in the normal and GDM columns are means of gestation specific SD scores of respective fetal parameters; $Q_1, Q_2, Q_3$ are tertiles of SD scores of respective parameters; OR: odds ratio; CI: Confidence interval.

## Discussion

We have reported fetal biometry by ultrasound measurements at wide range of gestation on undernourished pregnant women diagnosed with GDM from rural KOKAN region. In almost all the Indian studies on pregnancies with GDM, fetal growth refers to neonatal anthropometric parameters at delivery or outcomes like macrosomia. We have not calculated fetal growth velocity at diagnosis as this was first ultrasound investigation at the time of registration in the antenatal clinic. Most of the reports comparing fetal biometry and growth in GDM and non-GDM pregnancies come from North America and Europe. A recent report from US[10] found larger AC at 24-30 weeks of gestation in mothers with GDM.

A study in UK[11] found higher HC at 12 weeks, higher AC and higher EFW at 16 weeks in GDM mothers. But within ethnicity, fetal measurements were smaller in south Asian mothers with GDM than white European mothers with or without GDM. In another report from UK[12] diagnosis of GDM was preceded by rapid growth in AC between 20 and 28 weeks of gestation. A study in Africa[13] found increased abdominal circumference at 16-18 weeks of gestation. In a report from China [14] BPD, HC and AC were higher at 37-40 weeks in mothers diagnosed with GDM. Larger AC at 29-32 weeks and 37-40 weeks of gestation was also reported in Chinese mothers with GDM[15]. Our data is limited only to fetal biometry at her first antenatal registration visit coupled with OGTT as well as ultrasound scan. Woman in our region come to our hospital from far away villages. In our sample of 506, only 60% had ultrasound scan on the day of OGTT as remaining staying in the remote regions rushed back home. Very rarely they came back to the hospital for subsequent investigations or ultrasound scans. This puts constraints on analysis of fetal growth trajectory. Despite these limitations we would like to highlight the fact that it comes from region with substantial undernutrition (low BMI) [4]. There is little published data from India on fetal ultrasound measurements in mothers diagnosed with GDM. There are some reports about GDM in populations with low BMI[16,17]. Ours is probably first report on fetal biometry in Indian mothers with low BMI diagnosed with GDM. We expected increased fetal abdominal circumference in women with GDM. However, to our surprise all fetal parameters were smaller including abdominal circumference in pregnant women diagnosed with GDM at 0-16 weeks and 16-20 weeks when compared with mothers with normal glucose tolerance in our study. Estimated fetal weight was also lower at diagnosis windows of 0-16 weeks and 16-20 weeks respectively. We were able to find just one study from south Indian city of Chennai where all fetal ultrasound measurements at 20 weeks of gestation except anterior abdominal wall thickness were smaller in pregnant women with GDM[18]. Our findings also resonated with another report from China[19] where Fetal parameters in the lowermost decile had a high risk of GDM at 22-24 weeks of gestation. A review by Newbern et al attributes smallness of fetal parameters to deficiency of placental growth hormone[20], however we do not have any placental measurements in our study. Fetal biometry is affected by fetal nutrition which depends on nutrition of mother. Low fetal parameters can also be ascribed to the intrauterine growth restriction as an effect of GDM[21].

## Conclusion

To summarize we have reported data on fetal biometry at the time of diagnosis of GDM in undernourished Indian mothers across wide range of gestation. Fetal weight, femur length including abdominal circumference were lower in mothers with GDM. This findings are completely opposite from those found in obese mothers with GDM, were fetal parameters are large. This smallness of fetal parameters in undernourished mothers with GDM needs further systematic investigation.

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**Conflict of interest:** None of the authors have any conflict of interest to declare.

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