



## Development of Metabolic syndrome in Postnatal Women with Gestational Diabetes Mellitus-A Prospective Cohort Study

Authors

**Dr Saravanakumar T V<sup>1</sup>, Dr Nirmala C<sup>2</sup>, Dr Chetana. N<sup>3</sup>**

<sup>1</sup>Associate Professor, Dept. of OBG, Govt. Medical College, Kollam

<sup>2</sup>Professor, Dept. Of OBG, Sree Avittom Thirunal Hospital, Govt. Medical College, Trivandrum

<sup>3</sup>Post Graduate Student, Department Of Obstetrics and Gynaecology, Sree Avittom Thirunal Hospital  
Medical College, Thiruvananthapuram

\*Corresponding Author

**Dr Reji Mohan**

Asst. Professor, Dept. of Reproductive Medicine and Surgery, Sree Avittom Thirunal Hospital, Govt.  
Medical College, Trivandrum, Thiruvananthapuram, India

### Abstract

**Aim:** *To study the incidence of metabolic syndrome in postnatal women with history of gestational diabetes mellitus in the index pregnancy when compared to a women without the history of gestational diabetes mellitus*

*To study the socio-demographic factors affecting the development of metabolic syndrome in postnatal women with history of gestational diabetes mellitus in the index pregnancy*

**Materials and Methods:** *The recruitment of the postnatal women to the study was started after obtaining clearance from the Ethical committee conducted in Sree Avittom Thirunal Hospital, Government Medical College, Thiruvananthapuram and study period was for one year. This was a Prospective cohort study*

**Results:** *In our study we included only women >19 years and <35 years and majority of the women in the GDM group belonged to the age group 26-30 and women in the non GDM group who belonged to 25. In the present study 49.7% of the women in the GDM group belonged to Class IV when compared to 64.6% in the non GDM group also belonged to the same socioeconomic status. Majority of the women belonged to the Hindu religion both in the GDM and the non GDM group.60% of the multipara belonged to the GDM group when compared to 40% of the primipara belonged to the GDM group.24.6% of the patients in the GDM group had a history of gestational hypertension, when compared to 8% of the non GDM group.20% of the women in the GDM group had a past history of GDM in their previous pregnancies.23.4% of the women in the GDM group had a family history of diabetes in father when compared to 5.1% of the non GDM group. Majority of the women in the study did not have any family history of diabetes in the siblings.45.1% of the women belonging to the GDM group had a birth weight between 2.6 to 3.5kg.28% of the women belonging to the GDM group had a pre pregnancy BMI >= 25 when compared to 13.1% of the women in the non GDM group.69% of the women belonging to the GDM group had BMI >= 25 when compared to 48% of the women belonging to the non GDM group. In our study, we included only women >19 yrs and <35 yrs and the percentage of metabolic syndrome was higher in either ends of the range that is 55.6% and 44% respectively. Majority of the subjects were booked at our hospital but the percentage of metabolic syndrome was found to be slightly higher in the referral subjects, p value was 0.4 and it was not*

statistically significant. In our study, the socioeconomic status is classified according to Kuppaswamy classification. The percentage of metabolic syndrome was slightly higher in the class III that is 47.4%. The percentage of metabolic syndrome in Muslim population was slightly higher that is 44.1% when compared to the other religions. In this study, 71.2% of the women with higher order pregnancies that is multiparous women had metabolic syndrome when compared to 28% of the primiparous women and the p value was 0.01 with the relative risk of 1.65 and this association was found to be statistically significant. In the present study, the women with MNT had a metabolic syndrome rate of 39.8% when compared to the women who were not on MNT that is 43.7%. But the other group who were not on MNT was on insulin therapy This association was not statistically significant as the p value was 0.6. Women receiving insulin therapy had a higher incidence of metabolic syndrome that is 63.01% when compared to the women who were not on insulin therapy. The p value was 0.02 with the relative risk being 1.5 and this association was statistically significant. In the present study, the women with the gestational hypertension in this index pregnancy were found to have a higher rate of metabolic syndrome that is 46.5% when compared to the women without history of gestational hypertension. This association is statistically significant with a p value of 0.03 and relative risk of 1.504. Women with history of GDM in their previous pregnancy had a metabolic syndrome rate of 65.7%, when compared to the women without this history and the p value was found to be 0.001 with a relative risk of 1.84 and found to be statistically significant. Majority of the women in the study group did not have any significant past history of illness. Among the study group there were 8 women who had a history of epilepsy and in them the metabolic syndrome rate was found to be 62.5%. But this was not statistically significant as the number of women belonging to this group were very small. 53.4% of the women with the family history of diabetes in mother had metabolic syndrome, p value was 0.02 with a relative risk of 1.49 and was statistically significant. In the present study, the women who delivered > 4 kg babies had a higher rate of metabolic syndrome of 83.3%, when compared to the other women with lesser birth weight. In the present study, 71.4% of the women with the pre-pregnancy BMI >25 had metabolic syndrome whereas only 30.2% of the women with BMI ≤25 had metabolic syndrome. The p value was 0.001 and relative risk of 2.368 and this was statistically significant. In this study 54.5% of the women with postnatal BMI > 25 had metabolic syndrome whereas only 13% women with postnatal BMI < 25 had metabolic syndrome. The p value was 0.001 and relative risk was 4.28 which were statistically significant.

**Conclusions:** The present study was conducted to explore the incidence of metabolic syndrome in the postnatal women with GDM, when compared to a non GDM group and also to study the socio-demographic factors affecting the development of metabolic syndrome in GDM group.

In 2001 metabolic syndrome was noted as a legitimate cardiac risk factor and designated ICD-9 code of 277.7. Women with GDM tend to meet many criteria of metabolic syndrome. A link has been established between metabolic syndrome and GDM. Many view GDM as a pre metabolic syndrome condition. The incidence of metabolic syndrome in postnatal women with GDM attending our hospital is found to be 46.1%. The study was conducted at Sree Avittom Thirunal Hospital, Thiruvananthapuram over a period of one year and involved 175 postnatal women in each in the study and the control groups. The findings of our study were. The women with history of GDM in the index pregnancy had a higher incidence rate of metabolic syndrome, when compared to the non GDM group. Though the study was conducted in an immediate postpartum that is after 6 weeks period, but the study group was compared with a control group which did not show any increased incidence of Metabolic Syndrome. Also a sensitivity analysis was conducted and waist circumference was excluded as criteria as there was significant weight retention 6wks postpartum but the incidence of Metabolic Syndrome was more in the GDM group when compared to non GDM group. This suggests that GDM is an important predictor of metabolic syndrome.

## Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during the current pregnancy<sup>1</sup>. The definition applies regardless of whether

insulin or diet modification is used for treatment, and whether or not the condition persists after pregnancy. It does not recognize the possibility that un-recognised glucose intolerance may have antedated or begun concomitantly with pregnancy.

Women with gestational diabetes are at high risk for future diabetes; 15 to 60 percent will develop type 2 diabetes mellitus within 5 to 15 years of delivery<sup>3</sup>. Therefore, the diagnosis and subsequent management of gestational diabetes after delivery has important implications for the prevention of type 2 diabetes.

The incidence of metabolic syndrome among women with a history of GDM has been shown to range from 6% to 62%<sup>4</sup>. The metabolic syndrome has been defined by the concomitant clustering of central obesity, dysglycemia, hypertension, hypertriglyceridemia, and low high-density lipoprotein (HDL) cholesterol<sup>5</sup>. Currently, controversy exists regarding its underlying etiology, diagnostic criteria, and even its clinical relevance<sup>6</sup>. Although this debate is ongoing, it is nevertheless established that the metabolic syndrome identifies a patient population at high risk for the future development of type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD)<sup>7</sup>.

Gestational diabetes mellitus (GDM) shares some similarity to the metabolic syndrome, in that:

- 1) It too has been the subject of long-standing debate regarding its diagnostic criteria.
- 2) It also identifies patients who are at high risk of developing Type 2 diabetes mellitus and cardiovascular disease in the future<sup>9</sup>.

### Rationale of the Study

The main risk factors for developing type 2 diabetes after a diabetic pregnancy are obesity, hypertension, low HDL, high triglycerides, lack of physical activity and increased maternal age. Thus GDM offers an important opportunity for the development, testing and implementation of clinical strategies for the prevention of metabolic syndrome. Lifestyle behavioral changes including weight reduction and exercise between pregnancies may prevent recession of gestational diabetes mellitus as well as modify onset and severity of type 2 diabetes later in life.

### Aims and Objectives

#### Primary Objective

To study the incidence of metabolic syndrome in postnatal women with history of gestational diabetes mellitus in the index pregnancy when compared to a women without the history of gestational diabetes mellitus.

#### Secondary Objective

To study the socio-demographic factors affecting the development of metabolic syndrome in postnatal women with history of gestational diabetes mellitus in the index pregnancy.

### Materials and Methods

**Study Design:** Prospective cohort study

**Period of Study:** One Year.

#### Study Population

**Study Group:** Women attending the postnatal clinics at 6 weeks with history *GDM*.

**Control group:** Women attending the postnatal clinics at 6 weeks, and during the same period and in whom antenatal period is uneventful.

#### Inclusion Criteria

- 1) Age of the women between 19-35 years.
- 2) Women with history of GDM who was on medical nutritional therapy or insulin therapy during the antenatal period.
- 3) Women willing for follow up after 6 weeks postpartum.

#### Exclusion Criteria

- 1) Age <19 years and >35 years.
- 2) Women with pre-gestational diabetes mellitus.
- 3) Women not willing for follow up.

### Methodology

All the pregnant women attending the antenatal clinics at SAT Hospital Pere routinely screened for Gestational Diabetes Mellitus with Glucose challenge Test (GCT) at 24-28 weeks of gestation followed by a referral for a ^agnostic Oral Glucose Tolerance Test (OGTT) if the screening is abnormal,, bus plasma glucose levels >130mg/dl.) The recruitment of women after an normal glucose challenge test served to enrich the study population. At 6 weeks postpartum

participants returned to the family planning unit for the cardio metabolic characterization and postnatal checkup.

All the women with history of GDM on medical nutritional therapy / Sin therapy which comprised of the study population , and those women uneventful pregnancy which comprised of the control population attending the postnatal clinics at 6 weeks postpartum were interviewed with a detailed questionnaire and data collected.

All the women were subjected to a 75 gram oral glucose tolerance test (fasting levels), serum triglycerides and HDL levels were measured.

Two blood pressures were measured with the women in sitting position left right arm using a standard mercury sphygmomanometer with an appropriate cuff size after at least a 5 minutes rest. The mean of the two blood pressures calculated.

Height: was measured with the stadiometer correct to 0.1 cm. Subjects standing with arms at sides, heels touching the rod with the head held erect

The plane passing through the lower border of orbit and Frankfurt plane parallel.

**Weight:** weighing machine corrected to 0.5kg was used. Machine was necked for zero error prior to each measurement.

**Waist Circumference:** measured at a point midway between costal margin and anterior superior iliac spine using a non stretchable tape and measured in centimeters.

## Observations and Results

### Descriptive Statistics

In the study we included only women >19 years and <35 years. The majority of the women in the GDM group belonged to the age group 26-30, when compared to the women in the non GDM group who belonged to 25. In the present study 49.7% of the women in the GDM group belonged to Class IV when compared to 64.6% in the non GDM group also belonged to the same socioeconomic status. Majority of the women belonged to the Hindu religion both in the GDM and the non GDM group. 60% of the multipara

belonged to the GDM group when compared to 40% of the primipara belonged to the GDM group

### Distribution according to the history of Gestational hypertension

24.6% of the patients in the GDM group had a history of gestational hypertension, when compared to 8% of the non GDM group.

### Distribution according to the family history of diabetes in mother

20% of the women in the GDM group had a past history of GDM in their previous pregnancies

### Distribution of diabetes in father

23.4% of the women in the GDM group had a family history of diabetes in father when compared to 5.1% of the non GDM group.

### Distribution according to the gestational period of Delivery

90.9% of the women in the GDM group had gestational period of delivery >37 wks.

### Distribution according to the weight of the baby

45.1% of the women belonging to the GDM group had a birth weight between 2.6 to 3.5kg.

### Distribution according to pre pregnancy BMI

28% of the women belonging to the GDM group had a pre pregnancy BMI  $\geq 25$  when compared to 13.1% of the women in the non GDM group

### Distribution according to postnatal BMI

69% of the women belonging to the GDM group had BMI  $\geq 25$  when compared to 48% of the women belonging to the non GDM group.

### General Statistics of the Study Group

In our study, we included only women >19 years and <35 years and the percentage of metabolic syndrome was higher in either ends of the range that is 55.6% and 44% respectively. Majority of the subjects were booked at our hospital but the percentage of metabolic syndrome was found to be slightly higher in the referral subjects, p value was 0.4 and it was not statistically significant

In our study, the socioeconomic status is classified according to Kuppuswamy classification. The percentage of metabolic syndrome was slightly higher in the class III that is 47.4%

The percentage of metabolic syndrome in Muslim population was slightly higher that is 44.1% when compared to the other religions.

In the study, 71.2% of the women with higher order pregnancies that is multiparous women had metabolic syndrome when compared to 28% of the primiparous women and the p value was 0.01 with the relative risk of 1.65 and this association was found to be statistically significant

In the present study, the women with MNT had a metabolic syndrome rate of 39.8% when compared to the women who were not on MNT that is 43.7%. But the other group who were not on MNT were on insulin therapy this association was not statistically significant as the p value was 0.6

**Distribution of Metabolic Syndrome in women receiving Insulin Therapy**

Women receiving insulin therapy had a higher incidence of metabolic syndrome that is **63.01%** when compared to the women who were not on insulin therapy. The p value was **0.02** with the relative risk being **1.5** and this association was statistically significant.

**Distribution of Metabolic Syndrome in women with history of Gestational hypertension**

In the present study, the women with the gestational hypertension in this index pregnancy were found to have a higher rate of metabolic syndrome that is 46.5% when compared to the

women without history of gestational hypertension. This association is statistically significant with a p value of 0.03 and relative risk of 1.504.

**Distribution of Metabolic Syndrome in women with history of GDM in the previous pregnancies**

Women with history of GDM in their previous pregnancy had a metabolic syndrome rate of 65.7%, when compared to the women without this history and the p value was found to be 0.001 with a relative risk of 1.84 and found to be statistically significant.

**Distribution of Metabolic Syndrome in relation to history of diabetes in mother**

53.4% of the women with the family history of diabetes in mother had metabolic syndrome, p value was 0.02 with a relative risk of 1.49 and was statistically significant.

Metabolic Syndrome in relation to family history of diabetes in father the association was not found to be statistically significant.

Distribution of Metabolic Syndrome in relation to family history of diabetes in siblings association was also not statistically significant

**Distribution of Metabolic syndrome in relation to weight of the baby**

In the present study, the women who delivered > 4 kg babies had a higher rate of metabolic syndrome of 83.3%, when compared to the other women with lesser birth weight

**Distribution of metabolic syndrome according pre pregnancy Body Mass Index**

Pre pregnancy BMI	Metabolic syndrome				Total	
	Present		Absent		N	%
	N	%	N	%		
≥25	35	71.4	14	28.6	49	100
<25	38	30.2	88	69.8	126	100
Total	73	41.7	102	58.3	175	100

X<sup>2</sup> =24.715 df=1 p= 0.001 Relative Risk =2.368

In the present study, 71.4% of the women with the pre-pregnancy BMI >25 had metabolic syndrome whereas only 30.2% of the women with BMI 25

had metabolic syndrome. The p value was 0.001 and relative risk of 2.368 and this was statistically significant.

**Distribution of metabolic syndrome in relation to postnatal Body Mass Index**

Postnatal BMI	Metabolic syndrome				Total	
	Present		Absent		N	%
	N	%	N	%		
525	66	54.5	55	45.5	121	100
<25	7	13.0	47	87.0	54	100
Total	73	41.7	102	58.3	175	100

$X^2=26.553df=1p=0.001$  Relative Risk=4. **CI =1.069-8.559**

In this study 54.5% of the women with postnatal BMI > 25 had metabolic syndrome whereas only 13% women with postnatal BMI < 25 had metabolic syndrome. The p value was 0.001 and relative risk was 4.28 which were statistically significant.

**Metabolic Syndrome Parameters**

As per NCEP ATP III guidelines, metabolic syndrome is diagnosed with any three of the following

Triglycerides > 150mg / dl

HDL < 50 mg / dl

Systolic BP > 130 mm of Hg

Diastolic BP > 85 mm of Hg

FBS > 110 mg / dl

Waist circumference > 88 cm

**Distribution of Triglyceride levels**

		GDM
Triglyceride	<=150	82 46.9%
	>150	93 53.1%
	Total	175 100.0%

**Distribution of HDL levels**

		GDM
HDL	>50	59 33.7%
	<50	116 66.3%
	Total	175 100.0%

Low HDL level among the subjects were the most striking feature of the study. Among the 175 patients who met the inclusion criteria of the study 116 patients that is 66.3% belonging to GDM group had HDL levels < 50 mg /dl.

**Blood pressure levels**

Distribution of blood pressure

		GDM
BP	Low <= 130/85	122 69.7%
	High >130/85	53 30.3%
	Total	175 100.0%

**Distribution of Fasting Blood Sugar levels**

		GDM
FBS	<110	138 78.9%
	>=110	37 21.1%
	Total	175 100.0%

**Distribution of waist circumference**

		GDM
Waist circumference	<-88	22 12.6%
	>88	153 87.4%
	Total	175 100.0%

**Incidence of Metabolic Syndrome in GDM and non - GDM group**

Metabolic syndrome	GDM		Non GDM		Total	
	N	%	N	%	N	%
Yes	73	41.7	20	11.4	93	26.6
No	102	58.3	155	88.6	257	73.4
Total	175	100	175	100	350	100

$X^2= 41.134 df=1 p= 0.001$

**Sensitivity Analysis**

Because the retention of gestational weight gain could contribute to high rates of central obesity at 6 weeks postpartum we performed a sensitivity analysis wherein we excluded waist

circumference criterion. The incidence of metabolic syndrome was found to be 20.4% in the women with GDM group, when compared to non GDM group where the incidence of metabolic syndrome was 3.4%.

### Incidence of Metabolic syndrome after excluding the waist circumference criteria

Metabolic syndrome	GDM		Non GDM		Total	
	N	%	N	%	N	%
Yes	36	20.6	6	3.4	42	12.0
No	139	79.4	169	96.6	308	88.6
Total	175	100	175	100	350	100

$X^2 = 24.350$   $df=1$   $p= 0.001$  Relative Risk (MS) = 1.899 CI = 1.595-2.261

### Distribution of the components of metabolic syndrome

In this study 53.1% of the women belonging to the GDM group had triglycerides level more than 150mg/dl. 66.3% of the women belonging to the GDM group had a HDL level <50mg/dl. This low HDL level present in the majority of the women with the history of GDM defines an important feature of metabolic syndrome found in our population. By considering the blood pressure levels 30.3% of the women belonging to the GDM group had elevated blood pressure levels >130/85mmHg. 21.1% of the women with the history of GDM had elevated fasting blood sugar levels.

### Socio-demographic and other risk factors effecting the development of metabolic syndrome

#### Age of the women

In our study, we included only women > 19 years and < 35 years and the percentage of metabolic syndrome was higher in either ends of the range that is 55.6% and 44% respectively.

#### Socioeconomic Status

In the present study it was found that the women belonging to the class III had a metabolic syndrome incidence rate of 47.4% when compared to the other classes of socioeconomic status which was consistent with the study conducted by Wamala et al which reported that there was an

increased risk for metabolic syndrome in middle-class women.

#### Parity

The higher order pregnancies were associated with a metabolic syndrome rate of 46.5%. Most previous studies found a modest relationship between higher order births and an increased trend of metabolic syndrome distribution among these women. Our findings are consistent with these results, and show that increasing births results in increased BMI and this may, in part, explain the increase in incidence of metabolic syndrome.

#### Insulin Therapy

Women receiving insulin therapy had a higher rate of metabolic syndrome that is 47.3% when compared to the women who were not on insulin therapy.

History of gestational hypertension in the index pregnancy

In the present study, the women with the gestational hypertension in this index pregnancy were found to have a higher rate of metabolic syndrome that is 46.5% when compared to the women without history of gestational hypertension. This association is statistically significant and observations consistent with the study by Verma et al. in the USA, were systolic and diastolic blood pressure were higher in women with a history of GDM than in controls group.

History of GDM in the previous pregnancies

Women with history of GDM in their previous pregnancy had a metabolic syndrome rate of 46.9%, when compared to the women without this history and the p value was found to be 0.05 and was statistically significant

#### BMI

In the study, women with the history of GDM and metabolic syndrome had significantly higher pre-pregnancy BMI and waist circumference when compared to women with GDM history and no metabolic syndrome.

### Conclusions

The present study was conducted to explore the

incidence of metabolic syndrome in the postnatal women with GDM, when compared to a non GDM group and also to study the socio-demographic factors affecting the development of metabolic syndrome in GDM group.

In 2001 metabolic syndrome was noted as a legitimate cardiac risk factor and designated ICD-9 code of 277.7. Women with GDM tend to meet many criteria of metabolic syndrome. A link has been established between metabolic syndrome and GDM. Many view GDM as a pre metabolic syndrome condition. The incidence of metabolic syndrome in postnatal women with GDM attending our hospital is found to be 46.1%.

The study was conducted at Sree Avittom Thirunal Hospital, Thiruvananthapuram over a period of one year and involved 175 postnatal women in each in the study and the control groups. The findings of our study were the women with history of GDM in the index pregnancy had a higher incidence rate of metabolic syndrome, when compared to the non GDM group. Though the study was conducted in an immediate postpartum that is after 6 weeks period, but the study group was compared with a control group which did not show any increased incidence of Metabolic Syndrome. Also a sensitivity analysis was conducted and waist circumference was excluded as criteria as there was significant weight retention 6wks postpartum but the incidence of Metabolic Syndrome was more in the GDM group when compared to non GDM group. This suggests that GDM is an important predictor of metabolic syndrome

### Limitations

- 1) A major limitation of this study is that, because pre-gravid measurement of cardiovascular risk factors were not performed, it cannot be ascertained whether the observed differences in the incidence rates of the metabolic syndrome between the study group necessarily preceded the pregnancy. Although it is noted, that an earlier cross sectional study reported that

components of the metabolic syndrome were associated with GDM, longitudinal data linking pre-gravid measurements with subsequent GDM are lacking this time.

- 2) The present study had a smaller sample size, when compared to the previous ones and hence, might not be able to detect the minor effect.
- 3) Finally, as this study only examined, women attending the postnatal clinic at one academic institution, there may be difference in the study population characteristics and physician practice styles such that inference may not be drawn across a broader population.
- 4) Despite these limitations, our study demonstrates that women with history of GDM in index pregnancy are at increased risk of metabolic syndrome, when compared to the non GDM group

### Recommendations

- 1) It is advisable to continue the practice of universal screening for GDM, currently practiced in most centres in our country.
- 2) All the patients should be given information and education regarding the nature of the disease and should be motivated for the regular follow up. These women should be emphasized to undergo 75gm GTT, BP recording, BMI calculation and promotion of breast feeding.
- 3) Life style modification including dietary recommendations and regular exercise forms a cost effective and efficient preventing management of Metabolic Syndrome. The adherence to programs of life style change is very poor with high dropout rates. Hence continuing psychological support, motivation, counseling and an extended regular follow up to one year postpartum from the part of clinician is crucial.
- 4) It is advisable for these women to undergo pre-conceptual counseling before the next pregnancy

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