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Study Of High Intensity Breast Feeding And Insulin Sensitivity In Women With Gestational Diabetes Mellitus During Early Postpartum Period.

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ABSTRACT

Gestational Diabetes Mellitus is one of the most common complications in pregnancy causing maternal and fetal complications. Prolonged insulin resistance makes postpartum mothers more susceptible to develop T2DM in future. Lactation improves insulin sensitivity and helps in achieving homeostasis. To determine the effect of High intensity breast feeding in improving insulin sensitivity in GDM mothers. Comparative cross sectional study was conducted for a period of 6 months with 40 subjects with a age limit of 20 to 30 years. 20 were High intensity breast feeding GDM patients as group 1, 20 were non high intensity breast feeding GDM patients as group 2. Fasting plasma Glucose, Insulin and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) were calculated. The mean value of fasting plasma glucose and insulin were 91.5 and 6.71 in group 1 and 116.7 and 9.66 in group 2. Mean value of HOMA-IR in group 1 and group 2 are 1.507 and 2.783 and the difference is statistically significant. Exclusive breast feeding helps in improving insulin sensitivity and glucose oxidation in GDM patients thereby reducing the risk of developing Type 2 Diabetes Mellitus.

Keywords: Gestational Diabetes Mellitus (GDM), Breast feeding, Insulin, HOMA-IR, Type 2 Diabetes Mellitus.

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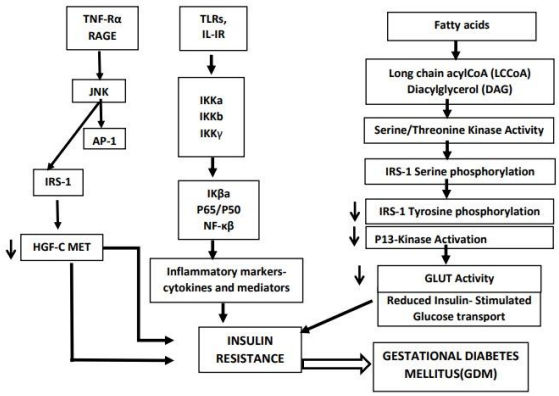
INTRODUCTION

According to International Diabetes Federation, Gestational Diabetes Mellitus (GDM) affects up to 14% of pregnant women worldwide [1]. In India, an estimated 4 million women have GDM [2]. The chances of developing GDM are relatively higher in Indian women as compared to Caucasian women [3]. Asian and African-American women are affected more commonly [4,5]. In India, the prevalence of GDM is not uniformly distributed due to differences in living habitats, socioeconomic levels and diet. In Tamil nadu the prevalence of GDM is 17.8 percent in urban, 13.8 percent in semi- urban, 9.9 percent in rural areas and the prevalence of GDM in Chennai is 16.2 percent [6].

Gestational Diabetes Mellitus is defined as any form of impaired glucose tolerance with onset or first recognition at pregnancy[7,8]. GDM is influenced by genetics, epigenetics and environmental factors. The risk factors for GDM include advanced age (>35 years), obesity (BMI > 25), history of prior neonatal death, prior caesarean section, family history of diabetes, ethnic differences.

Hyperglycaemia develops as a result of pancreatic β-cell dysfunction on a background of prolonged insulin resistance [9]. GDM is due to decreased secretion of insulin and resistance in the peripheral tissues and is not because of defective insulin nor disproportionate secretion of proinsulin or glucagon[10].

Figure1: Pathophysiology Of Insulin Resistance In Gestational Diabetes Mellitus.



Weight gain during pregnancy activates Tumor Necrosis Factor-Rα (TNF-Rα) and Receptor for Advanced Glycation End products (RAGE) which activates the C-Jun-N-terminal kinase (JNK) pathway. JNK forms a complex with Activator Protein (AP-1) and promotes the phosphorylation of Insulin receptor Substrate- 1 (IRS-1) at the serine sites instead of tyrosine site. This leads to negative regulation of IRS/ Insulin receptor complex results in insulin resistance. Metabolic dysregulation also activates ligands for Toll Like Receptor signaling (TLRs) pathways and Interleukin 1R(IL-1R). this induces the translocation of Nuclear factor kappa beta (NF-KB) and forms the Inhibitor of Nuclear Factor KB(IKB) Kinase complex. This leads to activation of various inflammatory markers resulting in insulin resistance [11].

Increased fatty acids and Long chain acyl CoA(LCCoA) and Diacyl glycerol stimulates the serine/ threonine kinase of IRS-1 thereby inhibiting IRS-1 Tyrosine phosphorylation and reduced activation of p13 kinase which results in reduced Glucose transport through GLUT receptors and reduced insulin sensitivity[12].

In normal pregnancy, the glucose level increases as the insulin sensitivity fall so the β-cell undergoes hyperplasia and hypertrophy to meet the increased metabolic needs. After pregnancy, the metabolic requirements decrease; hence β-cell, blood glucose and insulin sensitivity return to normal. During GDM, β-cell fails to compensate for the metabolic requirements and this, along with reduced insulin sensitivity, results in hyperglycemia. After pregnancy, β-cell, blood glucose and insulin sensitivity may return to normal or remain impaired, leading to progression of GDM to T2DM [13].

The study done by Farahvar S. et al. shows that 18.9% of GDM women develop T2DM within nine years, while the incidence of T2DM in non-GDM is only 2% [14]. meta-analysis done by Elpida Vounzoulaki et al., the author compares the progression rates of T2DM in women with GDM and normal Healthy women. It is found that the relative risk for T2DM is ten times higher in women with GDM than healthy women [15].

Pre-pregnancy Body mass index was the major risk factor for abnormal glycemic levels during the postpartum period [16].the BMI of the women decrease or become normal within a few weeks after delivery of the fetus. Failure of the BMI to return to its optimum level in GDM mothers increases the chronicity of insulin resistance and thus favoring the development of T2DM.

Breastfeeding is one of the best ways to improve a woman's health after pregnancy, as it will help to return to a normal metabolic profile and lose the weight gained during pregnancy. Similarly, it benefits the infant by protecting against common childhood infections, reducing the risk of asthma, obesity, and type 2 diabetes. It also improves an infant's cognitive development [17]. pregnancy is also a hyperlipidemic state. Lactation has decreased the risk of hypertension, hyperlipidemia and cardiovascular diseases [18]. Breastfeeding is also protective against reproductive cancers such as breast cancer and ovarian cancer. Women who breastfeed exclusively for a longer duration had a 4.3% reduced risk of developing breast cancer and 28% lower risk of developing ovarian cancer [19].

S F Ehrlich et al. published a study in which he evaluated the association of postpartum weight change with changes in glucose, insulin and homeostasis model assessment of insulin resistance in a subsample of participants from Diet, Exercise and Breastfeeding Intervention. The result of the study showed that modest postpartum weight loss is associated with improvements in glucose metabolism [20]. There is a strong association between breastfeeding and postpartum weight reduction. The findings of weight change at three months and six months show that postpartum weight reduction was significantly higher in mothers who followed exclusive Breastfeeding compared to non-exclusive breast-feeding mothers [21].

Exclusive breastfeeding is the practice whereby an infant receives only breast milk from the mother. WHO recommends that mothers should breastfeed their child exclusively for the first six months and continue breastfeeding along with complementary feeds up to two years [22].

Lactation involves the utilization of lipid from our body stores for milk synthesis. Promoting mothers to increase breastfeeding enhances the lipolysis, diverting glucose to the mammary gland for lactogenesis. Lactation also improves glucose metabolism and insulin sensitivity by increasing glucose disposal rates. The diversion of glucose and lipid into lactogenesis may upregulate the pancreatic β-cell. This upregulation will help in maintaining long term insulin production in women [23].

Gunderson conducted a study estimating 2-h 75-g oral glucose tolerance test (OGTT) at 6-9 weeks after a delivery in women with gestational diabetes mellitus (GDM). The results of the study showed that high-intensity breastfeeding was associated with better fasting glucose levels and lower insulin levels [23] Compared to women who give only formula feed. This shows that exclusive breastfeeding mothers have a significantly low rate of progression from GDM to T2DM.

Extended and exclusive breastfeeding improves metabolism with a significant reduction in fasting glucose level, HOMA-IR, postpartum maternal BMI, triglyceride level and an increase in Insulin Sensitivity Index [24].

Our study tries to find the effect of high intensity breast feeding in reducing the insulin resistance thereby reducing the risk of developing Type 2 DM in women with GDM.

Aim

To determine the effect of high intensity breast feeding in reducing insulin resistance in women with Gestational Diabetes Mellitus during early postpartum.

Objectives

- To estimate and compare fasting plasma glucose and insulin levels in high-Intensity Breastfeeding and Non-high Intensity Breastfeeding GDM women at the early postpartum period.
- To calculate and compare insulin sensitivity through Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) between both the groups

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MATERIALS AND METHODS

After getting approval from the Institutional Ethical committee and informed consent from the lactating women this comparative cross-sectional study was carried out in a tertiary health care hospital for a period of 6 months from May 2022 to October 2022.

Sample size: Total sample size 40 with age limit of 20 to 30 years.

Calculation Of Sample Size:

$$n = (Z\alpha/2 + Z\beta)^2 (p1q1+p2q2) /d^2$$

Zα/2 (power)= 1.96
Zβ (significance)= 0.84
n = 13.06 approximated to 13
for non-response, 50% is added to the sample size**, so n=20 in each group**

Inclusion criteria

GDM Diagnosed lactating mothers attending Pediatric OPD for infant vaccination at six weeks postpartum are included in this study. They were enquired about their breast feeding practice in detail and were divided into two groups based on their breastfeeding practice.

Group 1: exclusively breastfeeding mothers with no additional formula or supplements were categorized as High-intensity breastfeeding women.

Group 2: breastfeeding mothers along with additional formula or supplements were categorized as non-High-intensity breastfeeding women.

Exclusion criteria

- Severe acute illness
- Patients who are currently taking insulin medication to prevent interference in insulin assay.

Methods

Under aseptic precautions blood samples were collected from study population by venipuncture and serum was separated.

Fasting Glucose

Instrument: Fully automated analyzer – Erba XL 640
Method: GOD/POD method (Enzymatic, Endpoint analysis)
Principle: Glucose present in the plasma is oxidized by the enzyme glucose oxidase (GOD) to gluconic acid with the liberation of hydrogen peroxide, which is converted to water and nascent oxygen by the enzyme peroxidase (POD). 4-aminophenazone, an oxygen acceptor, takes up the oxygen and, together with phenol, forms a pink colored chromogen which is measured at 515nm.

Insulin Assay

Instrument: ELISA reader and washer
Method: Enzyme-Linked Immunosorbent assay (ELISA).-
Principle: The wells are coated with a monoclonal antibody with higher activity for insulin. A sandwich complex bound to the well is formed When the samples and controls are incubated in the wells with enzyme conjugate (antibodies linked to horseradish peroxidase). Unbound conjugates are then washed off with wash buffer. The amount of bound peroxidase is proportional to the concentration of the insulin present in the sample. Upon addition of TMB substrate, the intensity of color will develop in proportion to the concentration of insulin in the samples.

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Calculation Of Insulin Sensitivity: HOMA-IR:

HOMA-IR = [fasting plasma insulin (m UI / L) x (fasting plasma glucose (mg/dl)] / 405

RESULTS

Data collection is done using standardized proforma and statistical analysis was done using SPSS20. Two sample t- test was employed for statistical analysis of data. The results are expressed in terms of Mean and Standard Deviation. P value less than 0.5 is taken as significant.

Table 1: Statistical Analysis Of Fasting Glucose, Insulin And HOMA-IR In Group 1 & Group 2.

VARIABLES	GROUP 1 (Mean ± SD)	GROUP 2 (Mean ± SD)	p VALUE
Fasting Glucose	91.5 ± 12.04	116.7 ± 7.59	0.0001*
Fasting Insulin	6.71 ± 1.065	9.66 ± 1.37	0.0001*
HOMA-IR	1.50 ± 0.274	2.783 ± 0.438	0.0001*

*- statistically significant

Mean value of fasting plasma Glucose and Insulin are lower in group 1 than in group 2. HOMA-IR(Insulin Resistance) is lower in group 1when compared to group 2. p value is less than 0.5 which is statistically significant.

Figure 2: Mean Value Of Fasting Glucose In Group 1 & Group 2.

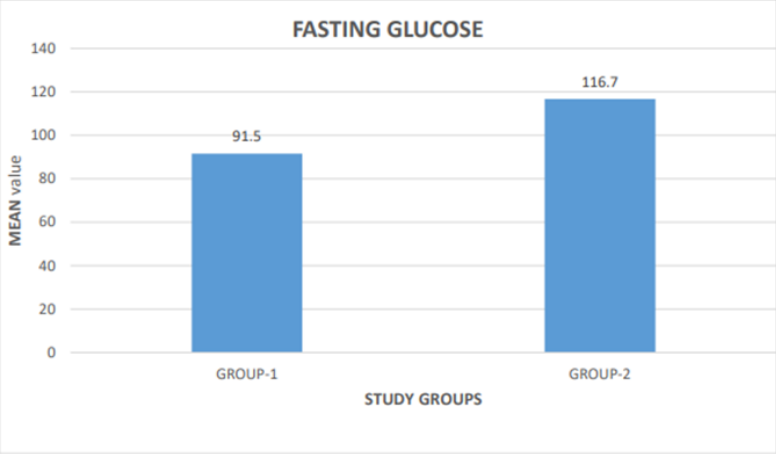

Figure 3: Mean Value Of Fasting Insulin In Group 1 & Group 2.

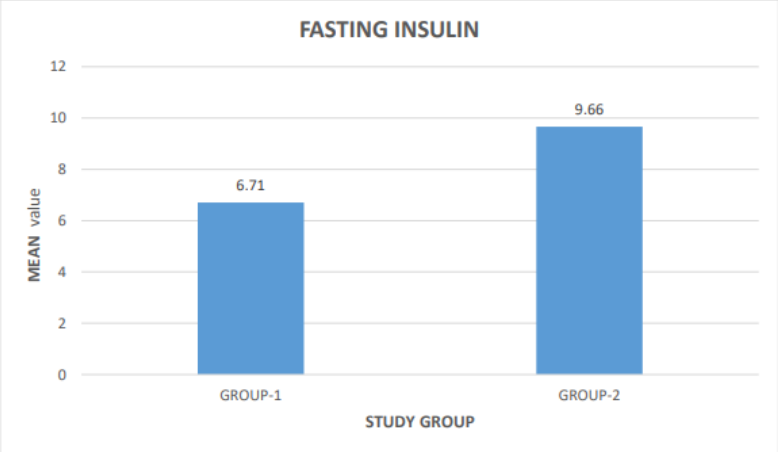

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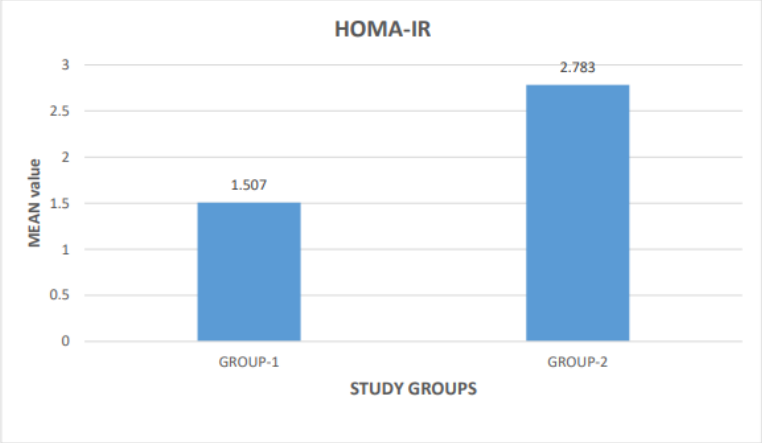
Figure 4: Mean Value Of HOMA-IR In Group 1 & Group 2.



DISCUSSION

The present study finds out the effects of breast feeding in reducing insulin resistance in GDM patients. In our study fasting glucose value in high intensity breast feeding GDM mothers is lower than non-high intensity breast feeding women and the p value is 0.0001 which is statistically significant. The mean value of cases and controls are 91.5 and 116.7This findings are in accordance with the study done by Yasuhi et al. [25].

The mean value of fasting Insulin in group 1 and group 2 are 6.71 and 9.66 and the p value is 0.0001. we have a statistically significant difference in the mean value of HOMA-IR in group 1 & group 2. The mean value of group 1 & group 2 are 1.507 and 2.783. There is a significant variation in insulin sensitivity between high intensity breast feeding women and non-high intensity breast feeding women. High-intensity breast feeders have improved fasting glucose levels and lower insulin values, which are favourable for the glucose metabolism of GDM women during postpartum. Also, HOMA-IR is significantly lower in women who exclusively breastfeed than in women who gave formula milk feed to their infants.

CONCLUSION

Improving glucose metabolism and insulin sensitivity in postpartum period is important to achieve a normal metabolic profile. In this study we found that exclusive breast feeding helps in reducing insulin resistance, increases the glucose utilization in the early postpartum period thereby reducing the risk of developing Type 2 DM in GDM patients. Encouraging high intensity Breast feeding can be used as a primary preventive method to prevent Type 2 DM in GDM patients.

Scope And Limitations

- The study is carried out in the population who visit our tertiary care. Further research may be carried out, which include samples from various geographic regions.
- Follow up of the patients is not done due to the short duration of the study period. Periodic sampling will give a better idea about the impact of breastfeeding on insulin sensitivity from a long-term perspective.
- HOMA-IR is a simple procedure to detect insulin resistance in peripheral tissues. Other insulin sensitivity indices such as QUICKI, Matsuda index, Belfiore index, Cederholm index, Avignon index are other indices of insulin sensitivity and calculation of these indices along with HOMA-IR could give a more accurate value of insulin.

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