(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 5, Page No: 939-948
September-October 2022

IJMSCR

Genetic And Dietary Influences On The Occurrence Of Gestational Diabetes In Different Trimesters During Pregnancy -An Observational Study

Dr.Vasuki. R[1], Dr. Dharmarajan. P[2*], Dr.Vijaya .S[3], Dr. Periyandavar. I[4], Dr. Pushpa Saravanan[5], Dr. Jeyapackiam[6]

[1,5,6]Assistant Professor, [2,3]Director, [4]Professor Of Biochemistry,
[1,4,5,6]Department Of Diabetology, [2]Institute Of Diabetology, [3]Institute Of Obstetrics And Gynaecology Mmc, Chennai

***Corresponding Author:**
Dr. Dharmarajan. P
Director, Institute Of Diabetology, Mmc, Chennai

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background: The increasing prevalence of glucose intolerance during pregnancy causes both maternal and fetal complications. Studies are needed to assess the correlation of different risk factors with the development of glucose intolerance in different trimesters.

Aim: The study aims to correlate hereditary and dietary risk factors with the development of gestational diabetes among urban women in a tertiary care center.

Methodology: 150 antenatal mothers diagnosed with glucose intolerance for the first time in pregnancy were interviewed with a questionnaire for family history of diabetes, pre-pregnancy, and pregnancy dietary practices.

Results: The mean age of mothers was 28.2 years.43 % were Primi and 20% were detected in the first trimester.79% had a family history of diabetes. The odds of a family history of diabetes influencing the occurrence of glucose intolerance in the first trimester was 9.67 times higher than in other trimesters ($p<0.01$).100% of mothers with diabetes in both parents ($p<0.01$) and 82% of mothers with diabetes in the maternal lineage ($p<0.05$) were detected early in pregnancy. Among mothers without a family history of Diabetes 56% had increased simple sugar intake, 41.4% had red meat intake and 47% had fried food intake.

Conclusion: Family history of diabetes plays a significant role in the development of gestational diabetes. Diabetes in maternal lineage significantly influences the onset of glucose intolerance early in pregnancy. Pre pregnancy and pregnancy dietary factors may also play a role.

Keywords: Gestational Diabetes, Family history of diabetes, Dietary factors, Maternal and Paternal lineage, Glucose intolerance.

Introduction

Gestational diabetes mellitus was traditionally defined as “any form of glucose intolerance occurring or first detected during pregnancy”.[1] In 2013, WHO classified glucose intolerance in pregnancy as “diabetes in pregnancy” and “Gestational Diabetes Mellitus”. In 2017, American Diabetes Association included “glucose intolerance detected in 2nd and 3rd trimesters” as Gestational Diabetes mellitus and “glucose intolerance detected in 1st trimester” as Pre Gestational Diabetes. Irrespective of the nomenclature used hyperglycemia in pregnancy is harmful to both mother and fetus in all trimesters.[2]The prevalence of gestational diabetes mellitus (GDM) is increasing exponentially in consonance with the increasing prevalence of Diabetes. Globally, the prevalence of Gestational diabetes mellitus varies between 1-and 28 % based on several risk factors like maternal age, race, ethnicity, screening methods, etc.[3]Nationally, the

prevalence of GDM varies between 3.8 -and 17.9 % in various studies conducted in India [4,5,6] In Tamilnadu, the prevalence of GDM is as high as 17.8% in the urban population, 13.85 % in semi-urban, and 9.9 % in the rural population.[7] The rising prevalence of gestational diabetes has made it a Public health problem in India. Any degree of Glucose intolerance in the mother has adverse effects on both maternal and fetal outcomes. Hyperglycemia in pregnancy has been associated with an increased risk of abortions, gestational hypertension, pre-eclampsia, and cesarean sections including the development of T2DM in the future.[8] The fetal complications include neonatal hypoglycemia, hypocalcemia, Respiratory distress syndrome, macrosomia at birth, and a higher risk of metabolic abnormalities in the future. [9,10]Though the traditional risk factors are ethnicity, increasing maternal age, family history of diabetes, obesity, and modern lifestyle, the correlation and significance of each risk factor with the development of glucose intolerance are largely unknown. Pre Pregnancy dietary factors may also play a role since the prevalence shows variations between rural and urban populations and among intra urban populations.

Methodology

This is a cross-sectional observational study conducted in the Institute of Diabetology, Rajiv Gandhi Government General Hospital, Chennai, and Tamilnadu, India. Pregnant women who attended our ante-natal clinics were subjected to an oral glucose tolerance test at their first antenatal visit with 75 gms of glucose. Following guidelines of the National Health Mission, Ministry of Health and Family Welfare, Government of India, a 2-hour post glucose venous sample value ≥140 mg/dl was taken as diagnostic of Gestational diabetes.[11] Women who had normal venous blood glucose values in the first trimester were subjected to another oral glucose tolerance test between 24 -28 weeks and again at 32-34 weeks. These mothers were followed up with Fasting and Post Prandial venous Blood glucose tests till delivery. Risk factors for developing glucose intolerance were identified by a detailed interview using a questionnaire along with the clinical examination and laboratory investigations. The woman's pre-pregnancy BMI was taken for classifying obesity status. The following were the inclusion and exclusion criteria. Inclusion criteria: 1. Pregnant women aged between 18-and 45 years who developed glucose intolerance with 75 grams of glucose in any trimester. Exclusion criteria: 1. Pregnant women aged between 18-and 45 years who have already been diagnosed to have T1DM or T2DM before pregnancy. 2. Pregnant women with recurrent GDM. The complete clinical profile of mothers developing glucose intolerance during pregnancy was noted. The features included age, parity, educational status, family history of diabetes in both maternal and paternal lineage of the pregnant woman, presence or absence of markers of Insulin resistance like obesity, Acanthosis, Polycystic ovarian disease, and dietary habits. A detailed history of pre-pregnancy and pregnancy dietary habits were noted with emphasis on intake of simple sugars, consumption of red meat and processed meat, and intake of fried foods. Informed consent was obtained from all mothers before starting the study. Ethical committee approval was obtained from the Institutional Ethics committee. All the variables were analyzed statistically using SPSS software and Chi-square tables.

Results: Totally, 150 pregnant women diagnosed with gestational diabetes for the first time were included in the study. The mean age of the mothers was 28.2 years. 29 % of mothers were graduates and 42% had completed higher secondary school.

Table 1: Patient Characteristics

1. MATERNAL AGE	Less than 20 yrs	4
	20-29 yrs	88
	30-39 yrs	57
	>=40 yrs	1

2. GRAVIDA	Primi	65
	Second gravida	55
	3 or more	30
3.TRIMESTER	First trimester	30
	Second trimester	73
	Third trimester	47
4. EDUCATION	Primary	2
	High school	42
	Higher secondary	63
	Graduate	43
5. FAMILY HISTORY	Present	119
	Absent	31
6. RED MEAT INTAKE>3 DAYS/WEEK	Present	43
	Absent	107
7. INCREASED INTAKE OF SIMPLE SUGARS	Present	87
	Absent	63
8. FRIED FOODS INTAKE >3 DAYS/WEEK	Present	69
	Absent	81
9. OBESITY	Present	69
	Absent	81

Figure 1 Parity Of Mothers In The Study

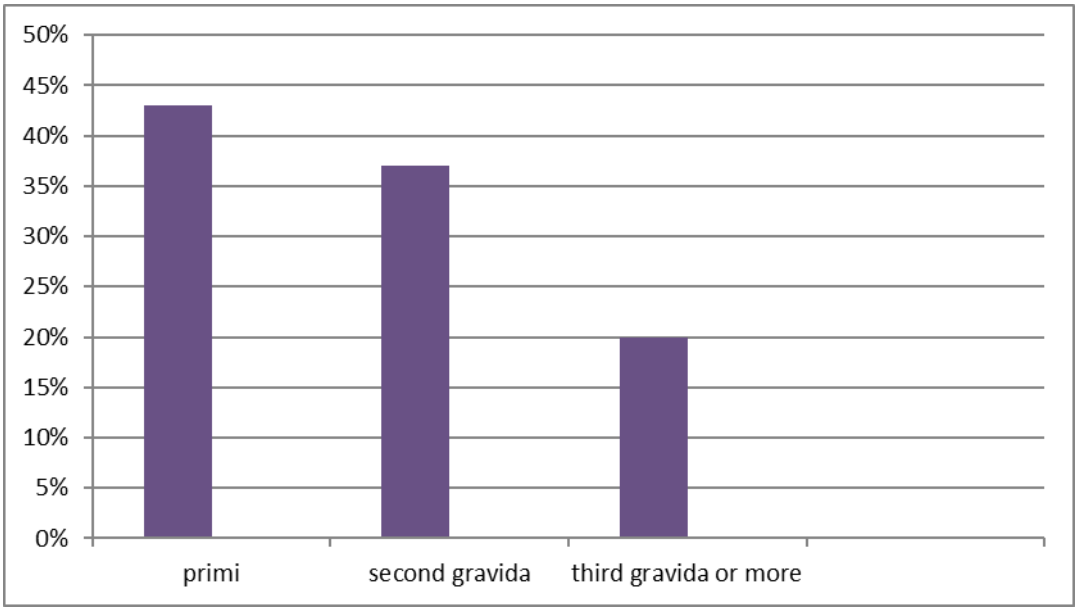


FIGURE :1 Among the 150 pregnant women, 65 (43 %) were Primi, 55 (37%) were second gravid and 30 (20%) were 3rd gravida or more

Figure 2 Diagnosis Of Glucose Intolerance According To Trimester

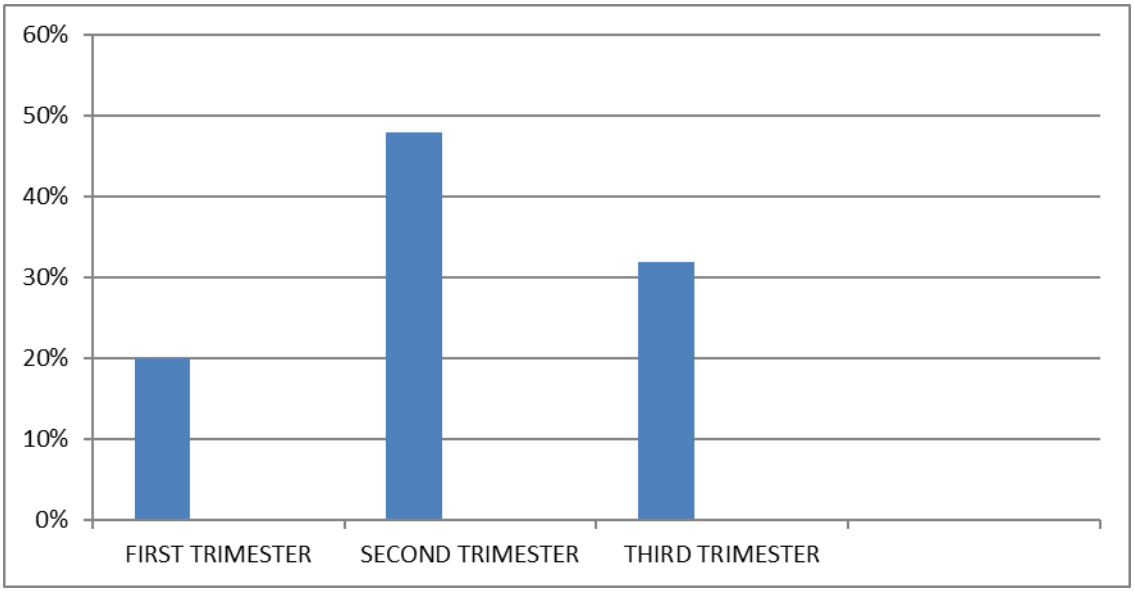


FIGURE:2 Among the 150 mothers, 30 (20 %) were diagnosed in the first trimester, 73 (49 %) were diagnosed in the second trimester and 47 (31 %) were diagnosed in the third trimester.

Figure 1 Family History Of Diabetes And GDM

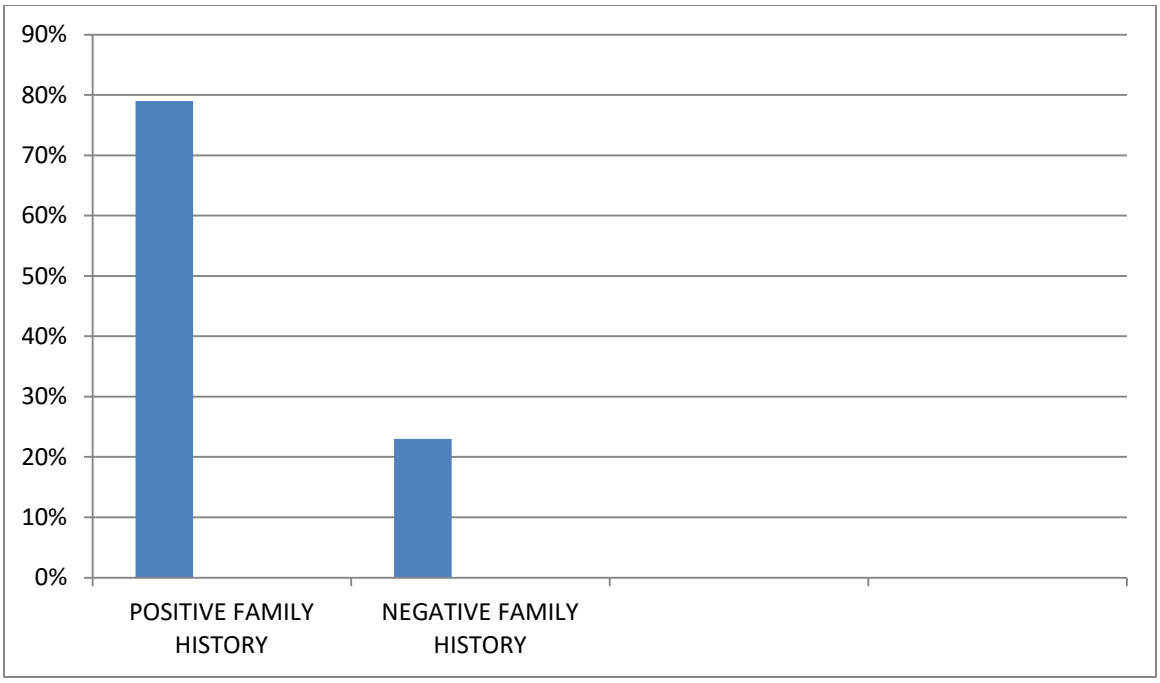


FIGURE :3 Out of 150 mothers who developed glucose intolerance during pregnancy, 119 (79 %) had a family history of diabetes.96 .7 % (n=29) of women who were diagnosed in the first trimester had a family history of Diabetes while 81% (n=59) of women diagnosed in the second trimester had a family history of Diabetes. Only 66 %(n=31) of mothers diagnosed in the third trimester had family h/o Diabetes. Family history of diabetes in a first-degree relative was found to be a significant risk factor using the Chi-square test at **p=0.005.**

TABLE2: Chi-square table for family history of diabetes ABOUT trimester

Onset	Family H/o Present	Family H/O absent	Chi-square value	p-value
First trimester	29 (96.7%)	1(3.3%)	10.725	0.005 **
Second trimester	59 (80.8%)	14 (19.2%)		
Third trimester	31 (66.0%)	16 (34.0%)		

**** - Significance at p<0.01**

TABLE:2 The odds of Family H/o diabetes influencing the occurrence of Glucose Intolerance in the First trimester was 9.67 times higher in comparison to the occurrence of Glucose Intolerance in other trimesters **(p<0.01)**

Figure:4 Family history of diabetes and diagnosis in first trimester

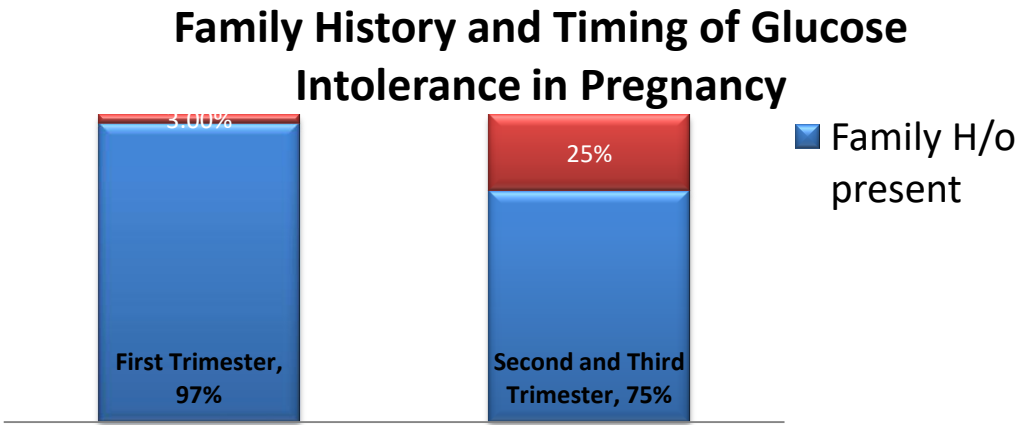


FIGURE:4 If both first and second trimesters are taken together and compared with the third trimester, 85.4 % of mothers who were diagnosed in the first and second trimester had a positive family history**. (p= 0.006).**

TABLE 3: Chi-Square Table For Both The Parents Of Mother Having Diabetes And Trimester Risk

Onset	Both parents Have diabetes	Others	Chi-square value	p-value
First trimester	14 (46.7%)	16(53.3%)	33.853	0.006**
Second trimester	13 (17.8%)	60 (82.2%)		
Third trimester	0 (0.0%)	47 (100.0%)		

**** - Significance at p<0.01**

All pregnant women (100%) whose both parents were diabetic were diagnosed to have gestational diabetes in the first and second trimesters (**p<0.01**). 82 % (p=0.014: **<0.05**) of mothers who had positive family history on their maternal side were diagnosed in the first and second trimesters while only 41 % (p= 0.398) of mothers who had positive paternal family history were diagnosed to have GDM in the first and second trimester.

Figure 2 Parental History Of Diabetes And Timing Of Glucose Intolerance In Pregnancy

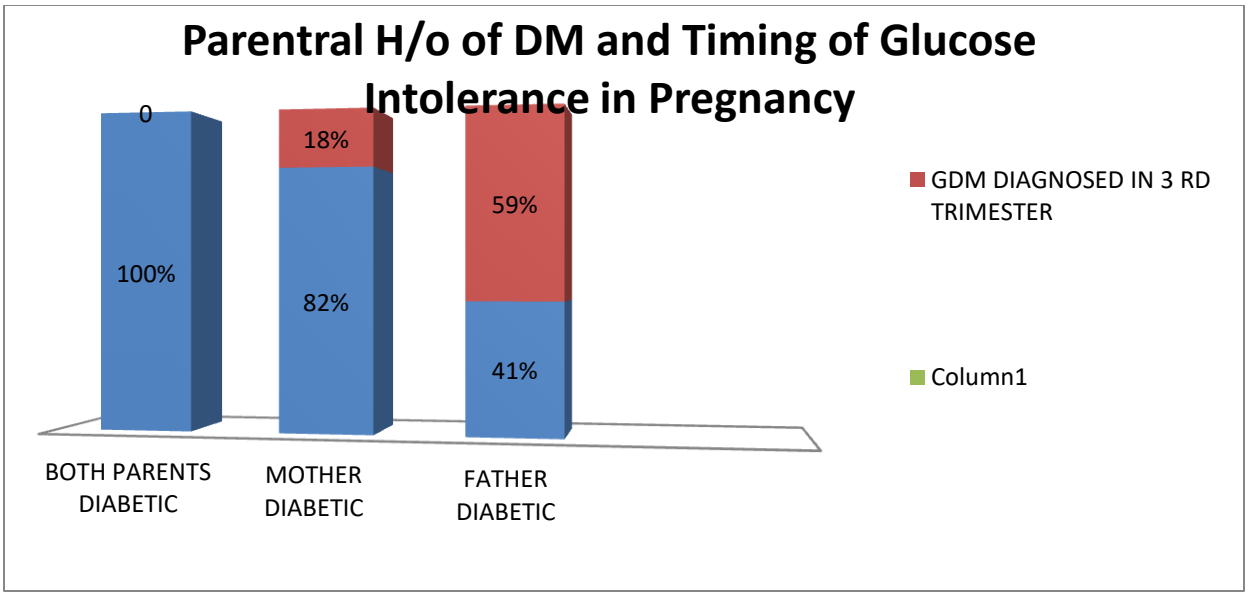
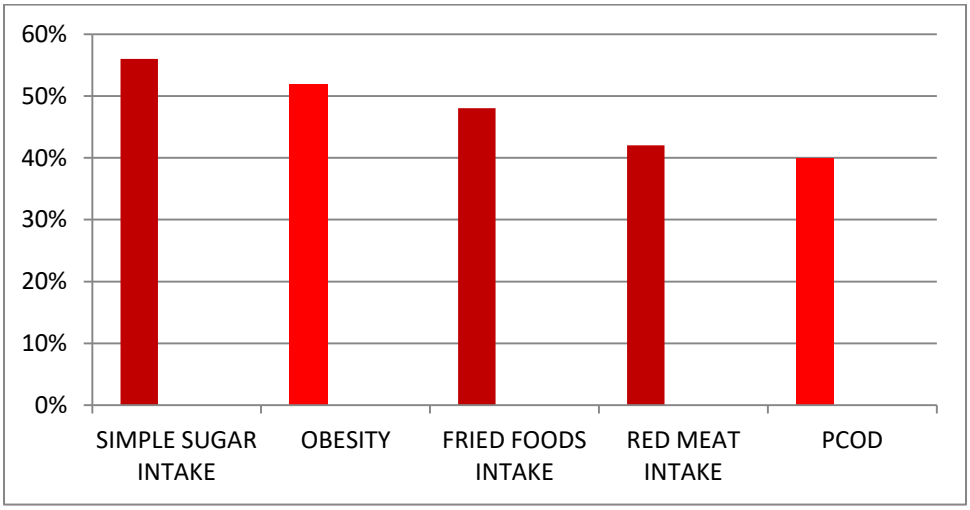


FIGURE:5 58 % of mothers had increased intake of simple sugars. 29 % of mothers had a regular intake of red meat and 46 % had a regular intake of fried foods. 46 % of patients were obese and 16 % had h/o PCOD. Among mothers who did not have family h/o of DM, 56% had h/o simple sugar intake, 41.4 % had h/o of red meat, 52 % were obese, 47 % had fried food intake and 40 % had PCOD.

Figure 6 Influence Of Environmental Factors On Pregnant Mothers With No Family History Of Diabetes



Discussion:

Unrecognized and untreated glucose intolerance during pregnancy has been shown to have major influences on both fetal and maternal outcomes. Gestational diabetes is increasing in prevalence both in urban and rural areas of India. Although there are studies that show familial clustering and hereditary influence on the development of GDM, the correlation of hereditary factors with trimester-wise development of gestational diabetes was largely unknown. The present study is possibly the first of its kind to correlate hereditary risk factors with the time of onset of glucose intolerance across the three trimesters during the period of gestation. Similarly, ours is one of the few studies that has analyzed the risk of diabetes in the maternal and paternal lineage of the pregnant mother for the development of GDM. In our study, 49 % of mothers were detected with glucose intolerance in the second trimester and 31 % were detected in the third trimester. This is by the

classical definition of gestational diabetes more than 20 weeks of gestation.[12] However, 20% of mothers were detected to have hyperglycemia in the first trimester itself. This is slightly higher compared to previous studies showing first-trimester prevalence between 10-18%.[13,14] The high prevalence detected during the first trimester in our study and earlier studies emphasize the importance of early screening for Gestational diabetes during pregnancy. In our study, more Primi gravida (43%) developed hyperglycemia in pregnancy when compared to second or third gravida. This is in contrast to previous studies which showed that the risk of Gestational diabetes increases with parity.[15] In our study, 79% of pregnant women had family h/o diabetes. If we divide trimesters, it is seen that majority of women (96.7%) who developed Glucose intolerance in the first trimester had family h/o diabetes which was statistically significant($p<0.01$). Similarly more than three-fourths of women (85%) diagnosed in the second trimester had diabetes in their family. Our study shows that there is a strong influence of genetic factors in the development of hyperglycemia early in pregnancy. Di Cianni, Volpe L, et al, Yang H, Wei Y, et al and Shirazian et al have shown in previous studies that family h/o diabetes in a first-degree relative is a risk factor that significantly influences glucose intolerance in pregnancy.[16, 17, 18] However, most of the studies done so far have not analyzed the correlation of hereditary risk factors with individual trimesters. In our study, we have shown that the influence of family h/o diabetes on the risk of glucose intolerance is higher in the first and second trimesters than in the third trimester. ($p=0.006$) Tabak AG, Tamas G, et al and Harder et al have shown in their studies that a family history of diabetes in the maternal lineage of the pregnant woman is a significant risk factor for hyperglycemia in pregnancy.[19,20]In our study we have shown that abnormal glucose tolerance developed in early trimesters if a pregnant woman's both parents had diabetes ($p<0.01$) or if the woman's mother had diabetes ($p<0.05$), The present study too shows a significant influence from the maternal lineage of the pregnant woman rather than paternal lineage in causing glucose intolerance early in pregnancy in the first and second trimesters. The following environmental factors were studied and taken for analysis namely obesity, PCOD, increased intake of simple sugars, red meat and processed meat, and fried foods. Maternal obesity is a well-known traditional risk factor for hyperglycemia in pregnancy. Several studies have supported the strong association between maternal obesity and gestational diabetes.[21,22]Our study identified obesity in 52% and PCOD in 47% of pregnant women who did not have family h/o diabetes but still developed glucose intolerance although it was not statistically significant.Pregnancy is a state of Insulin resistance and the inability of beta cells to compensate for this resistance leads to hyperglycemia. Obesity itself being Insulin resistant state further aggravates Insulin resistance in pregnancy and increases the risk of beta-cell dysfunction.[23]T2DM is largely considered a lifestyle disease and several studies have highlighted the influence of dietary habits on T2DM. GDM, being the forerunner of T2DM, can be considered a state influenced by dietary factors. We examined the association between pre-pregnancy and pregnancy dietary habits and the development of glucose intolerance in pregnancy. In our study, we found that among the pregnant women who did not have a family history of diabetes yet developed GDM, 56% had increased intake of simple sugars, 41.4 % had red meat intake more than thrice a week and 40% had fried food intake thrice a week. Though statistically found to be not significant due to the small sample size, our observations are in line with studies from different parts of the world which have highlighted the influence of pre-pregnancy and pregnancy diet on gestational diabetes risk. In the past 2 decades, several studies have highlighted the increased risk of gestational diabetes with the consumption of processed meat. Amelia Mari - Sanchis et al have demonstrated from the SUN cohort that total meat intake, red meat, and processed meat intake correlated significantly with gestational diabetes risk with odds ratios of 1.67, 2.37, and 2.01 respectively.[24] Recently R.Deepa et al from India have shown that red meat intake more than thrice a week significantly correlates with the risk of gestational diabetes with an adjusted RR of 2.1. [25]A few other studies to echo this observation.[26] The American heart association suggests limiting free sugar intake to 150 calories (approximately 9 teaspoons) in men and 100 calories (approximately 6 teaspoons) in women. [27] Similarly, a 2015 WHO advisory suggests limiting free sugar intake to less than 10 % of total calories in adults and children. However, studies have shown that simple sugar

consumption by adults is far higher than recommended. Catherine E Cioffi et al observed that added sugar intake by pregnant American women was higher than nonpregnant women.[28] Liwei Chen et al demonstrated that increased pre-pregnancy consumption of sugar-sweetened beverages was associated with an enhanced risk of GDM with a RR of 1.22.[29] A similar study from the SUN project cohort also demonstrated that sugar-sweetened beverages increased the risk of GDM[30]Similarly calorie-dense foods and high saturated fat intake have been associated with hyperglycemia risk in pregnancy.[31,32]Gestational Glucose Intolerance is a result of the failure of beta cells to compensate for the insulin resistance of pregnancy. The failure of beta cells may be related to hereditary factors and age that are nonmodifiable superimposed by calorie-dense nutrition causing glucolipotoxicity.

Conclusion: The prevalence of glucose intolerance in pregnancy is increasing in Primi mothers and early trimesters. Our study shows that the presence of diabetes in the maternal lineage of the pregnant woman statistically influences the development of hyperglycemia early in pregnancy. Similarly higher intake of red meat, simple sugars, and fried foods have been observed in GDM women without a family history. Our observations are similar to studies done worldwide.

Limitations: The major limitation is that it is a single-center observational study. Large multicentre case-control and cohort studies are needed to further analyze the risks of hyperglycemia in pregnancy.

References:

1. Metzer BE, Coustan DR. Summary and recommendations of the fourth international workshop conference on Gestational Diabetes Mellitus: the organizing committee. *Diabetes Care* 21:B161-B167,1998.
2. World Health Organization study group: Prevention of diabetes mellitus. Geneva, World Health org.,1980(Tech.Resp.Ser., no.844).
3. A.Jiwani, E.Marsielle, N.Lohse, P.Damm, M.Hod and J.G.Kahn, Gestational diabetes mellitus: results from a survey of country prevalence and practices, *The Journal of maternal-fetal and neonatal Medicine*, Vol. 25, no.6, pp,600-610,2012.
4. Raja MW, Baba TA, Hanga AJ, Bilquees S, Rasheed S, Haq IU et al., A study to estimate the prevalence of gestational diabetes mellitus in n urban block of Kashmir valley(North India).*Int J Med Sci Public health*,2014;3:191-5
5. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB , Green A .Gestational diabetes mellitus in India. *J Assoc Physician India*, 2004;52:707-11
6. Bhatt AA, Dhore PB, Purandare VB, Sayyad MG, Mandal MK, Unnikrishnan AG.Gestational diabetes mellitus in rural population of western India – results of a community survey.*Indian J Endocrinol Metab* 2015;19:507-10
7. Seshiah V, Balaji V, Balaji MS,Paneerselvam A ,Arthi T, Thamizharasi M etal.Prevalence of gestational diabetes mellitus in SouthIndia (Tamil Nadu) a community-based study. *J Assoc Physicians India*,2008;56:329-33.
8. HAPO study co-operative research group, B.E.Metzer, L.P.Lowe, et al., Hyperglycemia and adverse pregnancy outcomes, *The New England Journal of Medicine*, Vol.358, no.19, pp. 1991-2002,2008
9. O.Langer, Y.Yogev, O.Most and E.M.J.Xenakis, Gestational diabetes: consequences of not treating, *American Journal of Obstetrics and Gynecology*, Vol. 192,no.4, pp. 989-997,2005.
10. T.D.Clausen, E.R.Mathiesen, T.Hansen, et al., High prevalence of type 2 diabetes and pre-diabetes in adult offspring of women with gestational diabetes mellitus or type 1 diabetes, *Diabetes Care*, Vol.31, no.2,pp.340-346,2008
11. Diagnosis and management of Gestational diabetes mellitus : Technical and Operational guidelines; Maternal health division; Ministry of health and Family welfare ; Government of India; February 2018.
12. Classification and Diagnosis of Diabetes: Standards of medical care in diabetes -2018; *Diabetes Care*,2018;41(Suppl.1):S13-S27
13. Irafat Ara Begum; Gestational diabetes mellitus in primigravida of Bangladesh in different trimesters; *International journal of biology;* Vol 6, no:3; 2014
14. V.Seshiah et al., Gestational diabetes mellitus manifests in all trimesters of pregnancy; *Diabetes research and clinical practice,* 77,482-484.
15. Rajput M , Bairwa M, Rajput R. Prevalence of gestational diabetes in rural Haryana : A

community based study. *Indian journal of Endocrinol Metab* 2014;18:350-4
16. Di Cianni G ,Volpe L et al., Prevalence and risk factors for gestational diabetes assessed by universal screening; *Diabetes Res Clin Pract* ,2003;62;131-7
17. Yang H, Wei Y et al., China national GDM survey working group. Risk factors for gestational mellitus in Chinese women : a prospective study of 16286 pregnant women in china. *Diabet Med*.2009; 26:1099-104.
18. Shirazian N ,Emdadi R et al., Screening for gestational diabetes ; usefulness of clinical risk factors. *Arch Gynecol Obstet* ; 2009;26:1099-104.
19. Tabak AG ,Tamas G et al., The effect of paternal and maternal history of diabetes mellitus on the development of gestational diabetes mellitus. *J Endocrinol Invest* 2009;32:606-610
20. Harder T , Franke K ,Kohlhoff R ,Plagemann A. Maternal and paternal family history of diabetes in women with gestational diabetes or Insulin dependent diabetes mellitus type 1.*Gynecol Obstet Invest* 2001;51:160-164
21. Susan Y Chu ,William M Callanghan et al., Maternal obesity and risk of gestational diabetes mellitus ;*Diabetes Care* , 2007 Aug ;30(8):2070-6
22. Da Yao, Qingchang, Yu Hong Zhao et al., Relationship between maternal central obesity and the risk of gestational diabetes mellitus : A systematic review and meta analysis of cohort studies; *Journal of diabetes research* ;2020; article id 6303820
23. Jasmine F Plows, Joanna L Stanley et al., The pathophysiology of gestational diabetes mellitus ;*Int.J.Mol.Sci* 2018,19,3342.
24. Amelia Mari –Sanchis,Ginette Diaz-Jurado et al., Association between pre pregnancy consumption of meat ,Iron intake and the risk of gestational diabetes :theSUN project*; Eur.J.Nutr.* 2018 Apr;57(3):939-949
25. R.Deepa,Melissa Glenda Lewis et al., Food habits in pregnancy and its association with gestational diabetes :results from a prospective cohort study in public hospitals of urban India ; *BMC Nutrition* ; 2020 Nov 19:6(1):63
26. Bao W,Bowers K ,Tobias DK,Hu FB,Zhang C. Prepregnancy dietary protein intake, major dietary protein sources and the risk of gestational diabetes mellitus : a prospective cohort study. *Diabetes Care*.2013 ; 36(7):2001-8
27. Johnson RK,Appel LJ, Brands M et al., Dietary sugar intake and cardiovascular health: a scientific statement from the American Heart Association. *Circulation*. 2009 ;120:1011-20
28. Catherine E Cioffi , Janet Figueroa et al., Added sugar intake among pregnant women in the United States:National health and nutrition examination survey 2003-2012; *J Acad Nutr Diet* .2018. May;118(5):886-895.
29. Liwei Chen , Frank B.Hu, Cuilin Zhang et al., Prospective study of pre gravid sugar sweetened beverage consumption and the risk of gestational diabetes mellitus. *Diabetes Care* 2009 Dec;32(12):2236-41
30. Mikel Donazar –Ezcurra , Cristina Lopez –Del Burgo et al.,Softdrink consumption and gestational diabetes risk in the SUN project.*Clin Nutr* ; Apr ;37(2):638-645
31. S.Bo , G.Menato, A.Lezo et al., Dietary fat and gestational hyperglycemia ; *Diabetologia* 2001;44:972-978
32. Danielle A J M Schoenaker , Gita D Mishra et al.,The role of energy , nutrients, foods and dietary patterns in the development of gestational diabetes mellitus. A systematic review of observational studies.*Diabetes Care* ,2016 Jan ;39(1):16-23