Original Research Article

Association of Hypothyroidism with Diabetes Mellitus in Antenatal Women: A Cross Sectional Study

Prerna Jain[1], Nazia Ishrat[2], Imam Bano[3], Sheelu Shafiq Siddique[4], Gul Ar Navi Khan[5]

[1,2]Doctor, Department of Obstetrics & Gynaecology, J.N. Medical College, AMU, Aligarh, [2]Doctor, ORCID No.- 0009-0006-6219-2417, Department of Obstetrics & Gynaecology, J.N. Medical College, AMU, Aligarh, [3]Professor, Department of Obstetrics & Gynaecology, J.N. Medical College, AMU, Aligarhm. [4]Professor, Rajiv Gandhi Centre for Diabetes & Endocrinology, J.N.Medical College, AMU, Aligarh, [5]Doctor, ORCID No.- 0009-0006-7377-2214, Department of Physiology, J.N.Medical College, AMU, Aligarh.

How to cite this article: Prerna Jain, Nazia Ishrat, Imam Bano et. al. Association of Hypothyroidism with Diabetes Mellitus in Antenatal Women: A Cross Sectional Study. Indian Journal of Public Health Research and Development/Volume 15 No. 3, July-September 2024.

Abstract

Introduction: Pregnancy is a state of endocrinal changes and increased metabolic demand. In Western India, the prevalence of gestational diabetes has been reported as 9.5%. Similarly about 10-15% of antenatal women have thyroid dysfunction in 1st half of pregnancy which is hypo or hyperthyroidism.

Objectives: The purpose of this study is to evacuate the association of Hypothyroidism with Diabetes mellitus in antenatal women.

Material and Methods: A cross sectional study was carried out in the Obstetrics & Gynaecology department of Jawaharlal Nehru Medical College, AMU, Aligarh. Total 420 women between 16 to 32 years of age were enrolled in the study after taking consent. All antenatal women were screened for diabetes and thyroid dysfunction in order to determine the prevalence of diabetes and hypothyroidism in pregnancy and to find the association between hypothyroidism and diabetes mellitus.

Result: Among 420 antenatal women screened for diabetes mellitus, 38 (9.05%) were found to be diabetic women and 87 were hypothyroid (20.71%). Out of 38 women diagnosed with diabetes 15 (39.5%) antenatal women were associated with hypothyroidism. Among 382 nondiabetic, 72 (18.8%) women were associated with hypothyroidism. The association of thyroid dysfunction with diabetes mellitus was statistically significant ($p < 0.05$).

Conclusion: Prevalence of diabetes was more or less the same as compared to previous studies while the prevalence of hypothyroidism was much higher than previous studies though the cut off level of serum TSH was low in our study. Thyroid dysfunction hypothyroidism was strongly associated with diabetes mellitus in pregnancy.

Keywords: Antenatal women, Diabetes mellitus, Hypothyroidism

Corresponding Author: Gul Ar Navi Khan, Associate Professor, M.B.B.S, M.D (ORCHID NO- 0009-0006-7377-2214), Department of Physiology, J.N.Medical College, Faculty of Medicine, AMU, Aligarh, U.P, India.

E-mail: dr.gular@rediffmail.com

Submission date: Aug 14, 2023 **Revision date:** Aug 22, 2023 **Published date:July 4, 2024**

Introduction

Pregnancy is a state of endocrinal changes and increased metabolic demand. India leads the world with the largest number of diabetic subjects earning the dubious distinction of "The diabetes capital of the world". According to the International Diabetes Federation 2015, there were an estimated 199.5 million women with diabetes. By 2030, this number is expected to rise 313.3 million. In Western India, the prevalence of gestational diabetes has been reported as 9.5%.[1] Similarly 10-15% of antenatal women have thyroid dysfunction in 1st half of pregnancy which is hypo or hyperthyroidism[2]. An autoimmune multisystem disorder is thought of association between thyroid dysfunction and diabetes mellitus in antenatal women. Abnormal thyroid hormones have a profound effect on insulin secretion resulting in insulin resistance and glucose intolerance[3].

Diabetes mellitus in pregnancy can lead to excessive weight gain, pregnancy-induced hypertension, preterm labour, preterm premature rupture of membranes, postpartum haemorrhage (PPH), increase caesarean section rate due to fetal distress etc. Fetal complications of diabetes mellitus are respiratory distress syndrome, growth restriction, sudden intrauterine death, stillbirth, preterm birth, macrosomia, fetal hydramnios, congenital anomalies, spontaneous abortion, low Apgar score, metabolic derangements (hypoglycaemia, hypocalcemia, hyperbilirubinemia, polycythemia) etc.

Similarly according to the American Thyroid Association[4] in August 2017, Thyroid hormone is important during pregnancy for normal development of the baby. Two pregnancy-related hormones human chorionic gonadotrophin and estrogen cause an increase in thyroid hormones (1.5 times) level in blood. As HCG is similar to TSH, it mildly stimulates the thyroid gland to produce more thyroid hormones. Increase estrogen produces a high level of thyroid-binding globulin, a protein that transports thyroid hormone in the blood. Maternal complications of thyroid dysfunction are preeclampsia, heart failure, placental abruption, hypertension, death etc. Fetal complications of thyroid dysfunction are preterm delivery, growth restriction, stillbirth, thyrotoxicosis, hypothyroidism, goiter, respiratory distress syndrome, admission to neonatal intensive care unit etc.

Material and Methods

This study was a hospital-based cross-sectional study conducted in Department of Obstetrics and Gynaecology and Rajeev Gandhi Centre for Diabetes and Endocrinology, J. N. Medical College, AMU, Aligarh from February 2018 to October 2019. The study has been passed through the Institutional Ethics Committee. A sample of 420 pregnant women was chosen for the study from Antenatal Care Clinic and Wards and informed written consent was taken. Antenatal women with pre-gestational diabetes, gestational diabetes mellitus diagnosed by 75gm OGTT or history of diabetes mellitus in a previous pregnancy were included in the study. Antenatal women already diagnosed thyroid disease or family history of thyroid disorder, women who had received radiation exposure to head and neck, women taking any medications which affect thyroid function and hormonal profile (estrogens, tamoxifen, anabolic steroids, glucocorticoids, salicylates, diazepam, furosemide, sulfonylureas, anti-inflammatory, anticonvulsants etc.), autoimmune disorder, co-morbid conditions (hepatitis/PCOD/hypertension) were excluded.

In this study, the selected subjects were explained the purpose of the study. A standardized questionnaire was used and details pertaining to their anthropometric, socioeconomic status, menstrual and obstetric history, co-morbid condition, family history, and other relevant information were collected. Glucose levels were assayed in venous plasma by enzyme method known as the **DPEC GOD-POD METHOD (Glucose oxidase peroxidase method)** - is a quantitative determination of glucose in human serum and plasma. The results were interpreted according to the DIPSI (The Diabetes In Pregnancy Study group India) criteria which recommends non fasting OGTT with 75 gm glucose to diagnose GDM, 2-hour plasma glucose cut off ≥140mg/dl.

Thyroid function test that is T3, T4, TSH were measured using ChemiLuminescence ImmunoAssay(CLIA) and ImmunoRadioMetric Assay (RIA and IRMA) technique. The machine used for chemiluminescence was **Beckman Coulter ACCESS 2** (This is a test unit that contains an assay-specific coated bead which serves as a reaction vessel for sample processing) and **PC-RIA.MAS stratec**

machine used for ImmunoRadioMetric Assay. The reference range for TSH in antenatal women -

According to The American Thyroid Association 2011[5]

1st trimester - 0.1 - 2.5 mIU/L

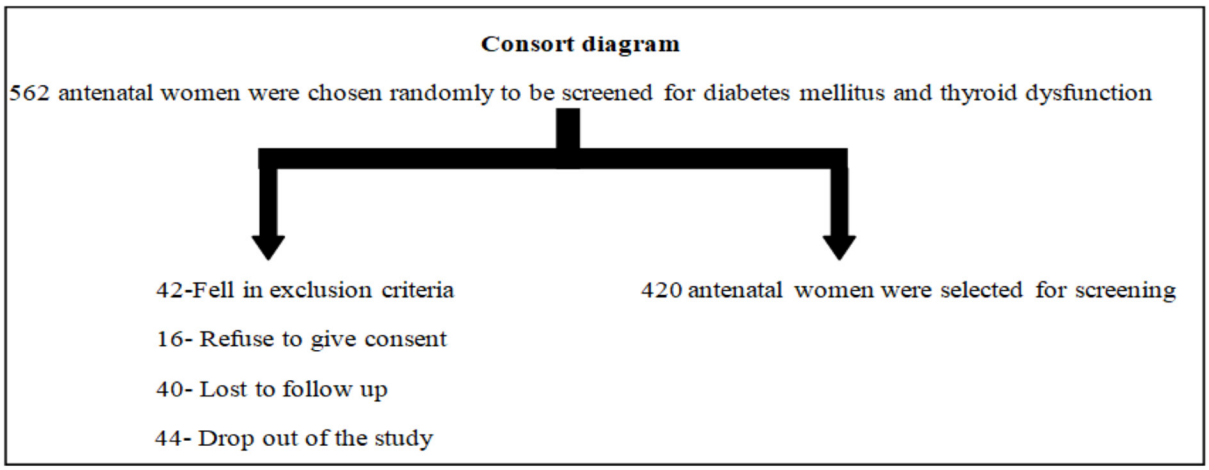
2nd trimester - 0.2 - 3.0 mIU/L

3rd trimester - 0.3 - 3.0 mIU/L

Prevalence of hypothyroidism and diabetes mellitus in antenatal women were estimated. Statistical analysis was done using the SPSS 20 (Statistical Package for Social Science) from windows software. Normal distribution of data was tested by K. S. Test (Kalmogorov - Smirnov) test. Association between hypothyroidism and diabetes mellitus was studied by applying the Chi-square test for qualitative data. Pearson correlation or Spearman correlation, T-test (in 2 groups) and ANOVA (in 3 groups) were applied for quantitative data. In the above statistical tools the probability value, 0.05 was considered as significant level.

Results

Consort diagram



Ultimately, 420 antenatal women were screened for diabetes mellitus according to DIPSI criteria and thyroid function tests (T3, T4, TSH) using chemi luminescence immunoassay (CLIA), radioimmunoassay (RIA) test and immune radiometric assay (IRMA). Women with positive OGTT results were stated as diabetic (cases) and non diabetic (controls) and with deranged thyroid function were stated as hypothyroidism.

Prevalence of diabetes mellitus in study population of was 9.05% and prevalence of hypothyroidism was 87 (20.71%), none was diagnosed with hyperthyroidism.(Table 1)

Table 1: Association of Hypothyroidism with Diabetes Mellitus

OGTT	Total=420	Euthyroid		Hypothyroid	
Diabetic	38	23	60.5%	15	39.5%
Nondiabetic	382	310	81.2%	72	18.8%

P value <0.05 (S), Chi square =8.952, df =1

Out of 38 antenatal women diagnosed with diabetes 15 (39.5%) antenatal women were associated with hypothyroidism. Among nondiabetic 72 (18.8%) out of 382 antenatal women were associated with hypothyroidism. The association of thyroid dysfunction with diabetes mellitus was statistically significant (p <0.05).

Thus our study showed that antenatal women with diabetes mellitus have more incidence of developing hypothyroidism.

Demographic and pregnancy characteristics

Maximum women with diabetes were in the age group between 26-30 years(12.8%), gravida 4(12.8%) followed by gravida 2(12.2%), gestational age between 36-40 weeks (14.9%).

The risk of diabetes in antenatal women was 4 times higher in extremely obese 1/3(33.3%), twice in obese that were 10/56 (17.86%) as compared to normal BMI 17/192 (8.85%). The difference was statistically significant.

Distribution of diabetes among rural/urban and in different socio economic groups was same.

Maximum proportion of women with hypothyroidism was seen in age group between 26-30 years (27.1%), gravida 2(27.0%) followed by gravida 3 (23.5%), gestational age between 36-40 weeks (29.8%) followed by 31-35 weeks (20.3%).

The risk of developing hypothyroidism was twice in extremely obese is 1/3(33.3%), more than twice in obese women 24/56 (42.86%) as compared to women with normal BMI 35/192 (18.23%). The difference was statistically significant between BMI and thyroid status**.**

The incidence of hypothyroidism among rural/ urban and different socio economic classes was comparable and not significant.

Discussion

Prevalence of Diabetes Mellitus- Among 420 antenatal women, 38 women (9.05%) were found to have gestational diabetes mellitus. The following table shows the prevalence of diabetes in different studies.(Table 2)

Table 2: Prevalence of diabetes in different studies

Author	Year	Cut off of blood sugar (mg/dl)	Prevalence
Balaji et al[6]	2011	140	13.4%
Singh et al[7]	2013	140	5.7%
Bhatt AA et al[1]	2015	140	9.5%
Bhavadharini B et al[8]	2016	140	18.5%
Muche et al[9]	2019	140	12.8%
Present study	2018-2019	140	9.05%

The prevalence of diabetes mellitus in antenatal women in our study is quite similar to the study by Bhatt et al 2015. However, all other studies show more prevalence of diabetes mellitus while Singh et al showed less prevalence of diabetes mellitus compared to our study.

Prevalence of thyroid dysfunction

87 women (20.71%) have hypothyroidism while **none have hyperthyroidism**. The following table shows the prevalence of hypothyroidism in different studies.(Table 3)

Table 3: Prevalence of hypothyroidism in different studies

Author	Year	Cut off of TSH level (mIU/L)	Prevalence
Casey et al[10]	2005	2.47	2.5%
Rao et al[11]	2008	0.5-3	4.12%
Shahbazian et al[2]	2013	4	10-15%
Dhanwal D et al[12]	2016	4.5	13.13%
Nancy et al[13]	2018	0.1-2.5	10.8%
Bharti Kalra et al[14]	2018	< 2.5 – 1st tri <3– 2nd – 3rd tri	12.3%
Present study	2018-19	<3 in 2nd -3 rd tri	20.71%

The prevalence of hypothyroidism is quite high in our study as compared to studies done by Casey et al, Rao et al, Shahbazian et al, Dinesh et al, Nancy et al, and Bharti Kalra et al.

The reference range in the present study was taken according to The American Thyroid Association (2011). The high prevalence of subclinical hypothyroidism and overt hypothyroidism was seen in our study may be due to a lower cut off for normal TSH. The cut off used in other studies was higher thus may have missed a number of antenatal women with subclinical hypothyroidism when the pregnancy-specific ranges were applied. As we have seen in this study, the prevalence of hypothyroidism is increased with time, there is need for screening antenatal women for thyroid dysfunction. Therefore, thyroid function tests should be recommended as a routine screening test for all antenatal women.

This study showed that gravidity, gestational age, residency, and socioeconomic status have no statistically significant difference with diabetes mellitus and hypothyroidism in pregnancy. However, the risk of diabetes mellitus increases with an increase in age.

While the risk of diabetes mellitus and hypothyroidism were 2- 4 times increased with obesity. So weight reduction and a healthy lifestyle can decrease the risk of developing diabetes and hypothyroidism in pregnancy.

Association of Hypothyroidism with Diabetes Mellitus in antenatal women

In this study 38 (9.05%) were diagnosed with diabetes mellitus for which 15 (39.5%) were associated with hypothyroidism. While 72(18.8%) out of 382 nondiabetic women were associated with hypothyroidism. The association of hypothyroidism with diabetes mellitus is found to be highly statistically significant ($p < 0.05$).

Parham M et al (2015)[15] in his study found that in patients with GDM, 18 (17.1%) had subclinical hypothyroidism and 11 (10.48%) had clinical hypothyroidism, while among non GDM patients, 7 (6.66%) had subclinical hypothyroidism and 4 (3.81%) had clinical hypothyroidism. Thus concluded that the women with GDM have increased risk of hypothyroidism and the mean serum TSH level in antenatal women with gestational diabetes mellitus was higher than control groups (3.43=-2.06 and 1.74=-1.47 μIU/ml respectively).

Hema Divakar et al in (July 2017)[16], studied the prevalence of hypothyroidism in pregnant women with gestational diabetes mellitus (GDM) as well as the association in between GDM and hypothyroidism in India and found that 38 of 315 (12.1%) subjects were diagnosed with GDM while rest have normal glucose tolerance while 87 out of 251 (34.66%) subjects were diagnosed with hypothyroidism (cut off was 2.5 mIU/L) comparable to our study. Out of 251 subjects for whom TSH and blood glucose data were available only 29 had GDM. Out of 29 subjects with GDM, 24 were hypothyroid. This study tells regarding the dual endocrinopathy of hypothyroidism and GDM in pregnant women

Thus our study shows that antenatal women with diabetes mellitus have more incidence of developing hypothyroidism similar to study by Parham et al 2015 and Hema Divakar et al 2017.

Limitations of this study

As it was a cross-sectional study and women were not followed up till postpartum so we have not evaluated women for the maternal and fetal outcome. Large scale prospective studies are needed to assess the long term complications in women with diabetes mellitus and hypothyroidism.

The thyroid function tests could not be performed in women less than 20 weeks gestation, as screening for gestational diabetes mellitus, was done in women with more than 20 weeks gestation. Studies on a large number of patients, starting with early gestation are needed to detect thyroid dysfunction at an early gestation so that immediate treatment can be started which can prevent the complications of hypothyroidism in antenatal women.

Conclusion

Present study screened antenatal women for diabetes mellitus and hypothyroidism and found that the prevalence of diabetes was more or less the same as compared to previous studies while the prevalence of hypothyroidism was much higher than previous studies though the cut off level of serum TSH was low in our study.

Thyroid dysfunction hypothyroidism was strongly associated with diabetes mellitus in pregnancy. So it is suggested that during antenatal workup, women should be tested for thyroid function as a routine, as we are already screening for diagnosis of diabetes mellitus in pregnancy.

The study showed that gravidity, gestational age, residence, and socioeconomic status have no statistically significant difference with diabetes mellitus and hypothyroidism in pregnancy except for age in diabetes mellitus. So with the increase in age, there are more chances of having diabetes mellitus in pregnancy. Prevalence of diabetes mellitus, hypothyroidism and antithyroid antibodies were 2- 4 times increased with obesity. Weight reduction and a healthy lifestyle can decrease the risk of developing diabetes and hypothyroidism in pregnancy.

Ethics Committee Approval: The study protocol was approved from Institutional Ethical Committee, Faculty of Medicine, AMU, Aligarh. (D.No- 1012/ FM, Dated 13.07.2018)

Informed Consent: Informed consent was taken from all the participants before enrollment in the study.

Conflict of Interest: No conflict of interest was declared by the authors

Financial Disclosure: The authors declared that no financial support was received for the study.

Referances

1. 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 journal of endocrinology and metabolism. 2015 Jul;19(4):507-510
2. Shahbazian H, Shahbazian N, Baniani MR, Yazdanpanah L, Latifi SM. Evaluation of thyroid dysfunction in pregnant women with gestational and pre-gestational diabetes. Pakistan journal of medical sciences. 2013 Apr;29(2):638-641
3. Vitacolonna E, Lapolla A, Di Nenno B, Passante A, Bucci I, Giuliani C, Cerrone D, Capani F, Monaco F, Napolitano G. Gestational diabetes and thyroid autoimmunity. International journal of endocrinology. 2012;2012.
4. Erik K. Alexander, Elizabeth N. Pearce, Gregory A. Brent Rosalind S. Brown, Herbert Chen, Chrysoula Dosiou, William A. Grobman,Peter Laurberg, John H. Lazarus, Susan J. Mandel, Robin P. Peeters, Scott Sullivan. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. American Thyroid Association & Mary Ann Liebert, Inc. Volume 27, Number 3, 2017.
5. The American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum, Stagnaro- Green A, Abalovich M, Alexander E et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011; 21:1081-125.
6. Balaji V, Balaji M, Anjalakshi C, Cynthia A, Arthi T, Seshiah V. Diagnosis of gestational diabetes mellitus in Asian-Indian women. Indian journal of endocrinology and metabolism. 2011 Jul;15(3):187-190.
7. Singh A, Uma B. Incidence of gestational diabetes mellitus and its outcomes in a rural population. J Evol Med Dent Sci. 2013 Apr 1; 2(13):1982-7.
8. Bhavadharini B, Mahalakshmi MM, Anjana RM, Maheswari K, Uma R, Deepa M, Unnikrishnan R, Ranjani H, Pastakia SD, Kayal A, Ninov L. Prevalence of Gestational Diabetes Mellitus in urban and rural Tamil Nadu using IADPSG and WHO 1999 criteria (WINGS 6). Clinical diabetes and endocrinology. 2016 Dec; 2(1):8.
9. Muche AA, Olayemi OO, Gete YK. Prevalence of gestational diabetes mellitus and associated factors among women attending antenatal care at Gondar town public health facilities, Northwest Ethiopia. BMC pregnancy and childbirth. 2019 Dec 1; 19(1):334.
10. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG. Subclinical hypothyroidism and pregnancy outcomes. Obstetrics & Gynecology. 2005 Feb 1;105(2):239-45.
11. Rao V, Lakshmi A, Sadhnani M. Prevalence of hypothyroidism in recurrent pregnancy loss in first trimester. Indian journal of medical sciences. 2008 Sep 1; 62(9):359.
12. Dhanwal DK, Bajaj S, Rajput R, Subramaniam KA, Chowdhury S, Bhandari R, Dharmalingam M, Sahay R, Ganie A, Kotwal N, Shriram U. Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India. Indian journal of endocrinology and metabolism. 2016 May;20(3):387-390.
13. Pillai NS, Bennett J. Prevalence of hypothyroidism amongst pregnant women: a study done in rural set up. Thyroid. 2018;11(3):4: 1586-1591
14. Kalra B, Choudhary M, Thakral M, Kalra S. Prevalence of hypothyroidism in term pregnancies in North India. Indian journal of endocrinology and metabolism. 2018 Jan; 22(1):13-15.
15. Parham M, Asgarani F, Bagherzadeh M, Ebrahimi G, Vafaeimanesh J. Thyroid function in pregnant women with gestational diabetes: Is screening necessary?. Thyroid Research and Practice. 2015 Jan 1;12(1):3-7
16. Divakar H, Singh R, Narayanan P, Kulkarni B, Hegde A. Gestational Diabetes Mellitus, GDM, Hypothyroidism, India, DIPSI, Association. Dual Endocrinopathy-The Nexus between Hyperglycaemia (Gestational Diabetes) and Hypothyroidism among Pregnant Women in India. 2017 Jul 28(96480).