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Original Research

"To Study the Demographic Profile and Prevalence of Subclinical Hypothyroidism in Antenatal Women: A Cross Sectional Study at Tertiary Care Centre".

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

[1,3,4]Departmnt of Obstetrics & Gynaecology

[2*]Department of Physiology

[5]Rajeev Gandhi Centre for Diabetes & Endocrinology, J N Medical College, AMU, Aligarh

***Corresponding Author-** Gul Ar Navi Khan

*****Department of Physiology, J N Medical College, AMU, Aligarh, U.P (INDIA)
Email- dr.gular@rediffmail.com

Abstract

Introduction-Pregnancy is a state of endocrinal changes and increased metabolic demand. In Western India about 10-15% of antenatal women have thyroid dysfunction in 1st half of pregnancy which is hypo or hyperthyroidism.

Aim and Objective- The purpose of this study was to evaluate the demographic profile & prevalence of subclinical hypothyroidism in antenatal women.

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

Result- Among 420 antenatal women screened 87 were hypothyroid (20.71%) who did not have any feature of hypo or hyperthyroidism, past history of thyroid disease and women already on thyroid treatment. Among all demographic parameters, higher BMI (body mass index) was associated with hypothyroidism.

Conclusion- Prevalence of hypothyroidism was much higher than previous studies though the cut off level of serum TSH (thyroid stimulating hormone) was low in our study. Antenatal screening with serum TSH should be an integral part of antenatal care. Also high BMI (>30) was associated with hypothyroidism, life style modification to maintain normal body weight can help to prevent development of hypothyroidism.

Keywords- Antenatal women, Hypothyroidism, TSH

INTRODUCTION

Pregnancy is a state of endocrinal changes and increased metabolic demand. Thyroid hormone is important during pregnancy for normal development of the baby. Pregnancy markedly affects the thyroid physiology. The concentration of free T4 and free T3 remains unaffected in pregnancy while the concentration of total T3 and T4 is increased during pregnancy due to increase in serum concentration of thyroid binding globulin (TBG), caused by its increase hepatic production and estrogen induced glycosylation [1].

Two pregnancy related hormones human chorionic gonadotrophin (HCG) and estrogen causes increase in thyroid hormones (1.5 times) levels in blood. As HCG is similar to thyroid stimulating hormone (TSH), it mildly stimulates the thyroid gland to produce more thyroid hormones.

According to American Thyroid Association August 2017, in the first trimester there is suppression in the level of TSH which reaches its lowest level with the increase in the serum concentration of HCG at about 12 weeks of gestation. Then TSH increases in the second and third trimester to reach the pre-pregnancy levels in the late third trimester [2].

Therefore, the TSH monitoring at early gestation becomes the gold standard for determining thyroid function during pregnancy. The absolute value of TSH varies in different studies conducted during pregnancy, because they were carried out on different population at different places affected by ethnicity and iodine[1].

Both hypothyroidism and hyperthyroidism in the mother can affect pregnancy outcomes as well as the baby's development. Maternal complications of thyroid dysfunction are preeclampsia, heart failure, placental abruption, hypertension, death etc. Fetal complications of thyroid dysfunction are preterm delivery, growth restriction, still birth, thyrotoxicosis, goitre, respiratory distress syndrome, admission to neonatal intensive care unit etc.

Although there have been a number of studies linking abnormal thyroid function to increased risk of pregnancy complications, universal screening for thyroid disease during pregnancy is still debated.

Subclinical hypothyroidism is defined as a biochemical condition with serum TSH levels above the defined upper limit of reference range with free T4 within the reference range. Other causes of raised serum TSH, past history of thyroid disease and patients already on thyroid treatment are excluded [3].

The prevalence of subclinical hypothyroidism in pregnant women[4] is 2-5%.In an epidemiological study conducted in 9 states prevalence[5]of hypothyroid in Indian pregnant women was 13.13% (Dhanwal et al 2016) [5].

According to the guidelines of The American Thyroid Association 2011[6], the recommended reference range of TSH for antenatal women are 0.1- 2.5 miu/l in first trimester, 0.2 – 3.0 miu/l in 2^{nd} trimester and 0.3 – 3.0 miu/l in 3^{rd} trimester. The American Association of Clinical Endocrinologists uniformly recommended screening only those at risk during pregnancy. This has been still recommended by American College of Obstetrics and Gynecologists. (2017) [7]

The American College of Obstetricians and Gynaecologists (ACOG) 2013 has affirmed high incidence of subclinical hypothyroidism in antenatal women but has not recommended antenatal screening for thyroid dysfunction until further studies are done [8]. Observers have found increase incidence of thyroid dysfunction during pregnancy and they have suggested for routine testing but till now there is no recommendation for screening of thyroid function tests during pregnancy.

So this study was designed to find out prevalence of subclinical hypothyroidism and need for screening thyroid dysfunction in pregnancy.

MATERIAL & METHODS

The present study was a hospital based cross sectional study conducted in Department of Obstetrics and Gynecology and Rajeev Gandhi Centre for diabetes and Endocrinology, J. N. Medical College,

AMU, Aligarh for a period of 18months. The study was approved through the Institutional Ethics Committee. The 420 Antenatal women from antenatal care clinic were enrolled after taking written consent. Antenatal women with already diagnosed thyroid disease or family history of thyroid disorder, taking any medications which affect thyroid function and hormonal profile, with autoimmune disorders, co morbid conditions (hepatitis/PCOD/hypertension) and women who had radiation exposure to head and neck were excluded from study.

Screening for Thyroid dysfunction -
After obtaining the written informed consent, thyroid function test that is T3, T4, TSH were measured using Immuno RadioMetric Assay (RIA and IRMA) technique. The machine used for chemiluminescence was Beckman Coulter ACCESS2 and PC-RIA.MAS stratec machine used for ImmunoRadioMetric Assay. Venous blood sample was drawn irrespective of their fasting state in a plain vaccutainers for evaluation of T3, T4, and TSH.

Reference range for TSH in antenatal women -
According to American Thyroid Association 2011 [6]
1st trimester - 0.1 - 2.5 mIU/L
2nd trimester - 0.2 - 3.0 mIU/L
3rd trimester - 0.3 - 3.0 mIU/L
All the data was presented by percentage. Statistical analysis was done using the SPSS 20 (Statistical Package for Social Science) from windows software and Chi square test was applied.

OBSERVATIONS & RESULTS

The study was conducted in the Department of Obstetrics and Gynaecology in collaboration with Rajeev Gandhi Centre for Diabetes and Endocrinology, JNMC, AMU, Aligarh. 420 antenatal women who reported to the antenatal OPD were selected for the study. All antenatal women were screened for thyroid function tests T3, T4 via radioimmunoassay (RIA) test and TSH via immunoradiometric assay (IRMA). Women with deranged thyroid function were stated as hypo/hyperthyroidism. Study was conducted to find the prevalence of thyroid dysfunction in antenatal women.

Prevalence of Hypothyroidism in Antenatal Women-
Out of 420 antenatal women screened for thyroid dysfunction, the prevalence of hypothyroidism was 20.71% (87 out of 420), no women was diagnosed with hyperthyroidism.(Figure-1)

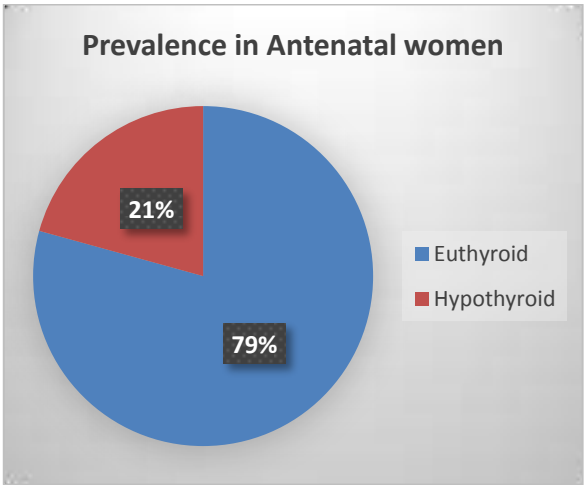

Figure No-1: The Graphical Representation of Prevalence in Antenatal women

Table1 – Age wise distribution in antenatal women with Thyroid Dysfunction

AGE (years)	Total	Euthyroid		Hypothyroid	
	100%	N	%	N	%
16- 20	53	45	84.9	8	15.1
21-25	196	160	81.6	36	18.4
26-30	133	97	72.9	36	27.1
>30	38	31	81.6	7	18.4
Total	420	333	79.28	87	20.71

p value >0.05 (NS), chi square = 5.067, df = 3

As shown in Table 1 – maximum proportion of women with hypothyroidism were seen in the age group between 26-30 years that was 27.1%followed by between 21-25 and >30 years (18.4%).While maximum euthyroid women were in age group 16-20 years (84.9%). The minimum and maximum age of hypothyroid women was 20 years and 38 years respectively. The mean age of euthyroid women was 25.07+_4.25 and hypothyroid women was 25.72 ± 3.9. Hence percentage of women with hypothyroidism increase with increase in age but the result was statistically insignificant. (p>0.05)

Table2- Distribution of antenatal women according to gravidity

Gravida	Total	Euthyroid		Hypothyroid	
	100%	N	%	N	%
G1	156	129	82.7	27	17.3
G2	115	84	73.0	31	27.0
G3	81	62	76.5	19	23.5
G4	47	40	85.1	7	14.9
>=G5	21	18	85.7	3	14.3
Total	420	333	79.28	87	20.71

P value- >0.05 (NS), chi square = 5.700, df = 4

As shown in Table 2 – maximum proportion of hypothyroid women were gravida 2(27.0%), followed by gravida 3 (23.5%) while maximum euthyroid women were primigravida (82.7%) as well as grand multipara (85.7%). The risk of diabetes was found to increase with increase in gravidity. However the association was statistically insignificant. (p >0.05)

Table -3 Distributions of antenatal women according to Gestational Age

Gestation (weeks)	Total	Euthyroid		Hypothyroid	
	100%	N	%	N	%
21-25	61	49	80.3	12	19.7
26-30	184	149	81.0	35	19.0
31-35	128	102	79.7	26	20.3
36-40	47	33	70.2	14	29.8
Total	420	333	79.28	87	20.71

p value >0.05 (NS), chi square = 2.730, df = 3

As shown in Table 3, maximum proportions of hypothyroid women were seen in gestational age between 36-40 weeks that was29.8% followed by 31-35 weeks (20.3%). While maximum number of euthyroid women were seen in gestational age between 21 – 25 weeks (80.3%) and 26-30 weeks (81%). Hence, percentage of women with hypothyroidism was found increased with increase in gestational age, however the result was not statistically significant. (p >0.05)

Table -4 Distributions of antenatal women according to BMI

BMI	Total	Euthyroid		Hypothyroid	
	100%	n	%	N	%
Underweight	112	101	90.2	11	9.8
Normal	192	157	81.8	35	18.2
Overweight	57	41	71.9	16	28.1
Obese	56	32	57.1	24	42.9
Extremely obese	3	2	66.7	1	33.3
Total	420	333	79.28	87	20.71

p- <0.05 (S), chi square – 27.701, df- 4

As shown in Table 4, it was observed that women who were extremely obese and have obese BMI have maximum chance of hypothyroidism that was 33.3% and 42.9% respectively while maximum euthyroid women have normal BMI (81.8%) or were underweight (90.2%). The risk of developing hypothyroidism was twice in extremely obese (33.3%), more than twice in obese women (42.86%) as compared to women with normal BMI (18.23%). This was statistically significant between the two ($p<0.05$)

DISCUSSION

The study was conducted in the Department of Obstetrics and Gynaecology in collaboration with Rajeev Gandhi Centre for Diabetes and Endocrinology, JNMC, AMU, Aligarh for a period of 18months.

Prevalence of thyroid dysfunction, 87 women (20.71%) were hypothyroid while none have hyperthyroidism. The following table shows the prevalence of hypothyroidism in different studies.

Author	Year	Cut off of TSH level	Prevalence
Casey et al[9[	2005	2.47 miu/ml	2.5%
Rao et al[10]	2008	0.5-3 miu/ml	4.12%
Shahbazian et al[11]	2013	4 miu/ml	10-15%
Dhanwal D et al[5]	2016	4.5 miu/ml	13.13%
Nancy et al[12]	2018	0.1-2.5 miu/ml	10.8%
Bharti Kalra et al[13]	2018	< 2.5 miu/ml – 1st tri <3 miu/ml – 2nd – 3rd tri	12.3%
Present study	2018-19	<3 miu/ml in 2nd -3 rd tri	20.71%

The prevalence of hypothyroidism was 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.

Age Distribution

In this study maximum proportion of women with hypothyroidism were seen in age group between 26-30 years that was 27.1% followed by the age group of 21-25 and >30 years (18.4%). While maximum euthyroid women were in the age group of 16-20 years (84.9%). The mean age of euthyroid women was 25.07+_4.25 and hypothyroid women was 25.72 +_ 3.9.

Sahu et al 2010[14]conducted a study in which the mean age in hypothyroidism was 27.2+_4.1 years and in euthyroidism was 25.9+_4 years, comparable to our study.

Eliska Potlukova et al 2012[15] conducted a study in which 857 women (16.4%) were positively screened for hypothyroidism. The average age of women was 31.1 years. The prevalence of hypothyroidism was 5.5 and 5.8% in women aged 30 or older and those under 30 years respectively. There is no statistically significant difference in age found in between hypothyroid and euthyroid women in the present study as well as study conducted by Sahu et al 2010 and Eliska et al 2012.

Gravida status

In the present study maximum proportion of hypothyroid women were gravida 2 that is 27.0%, followed by gravida 3 (23.5%) while maximum euthyroid women were primigravida 82.7% as well as grand multipara (85.7%)

Casey et al[9] 2005 in their study found nulliparity to be 36% in both cases and controls and no statistically significant difference between euthyroid and hypothyroid women in terms of parity.

Sahu et al[14] 2010 who reported the mean parity to be 0.7+_ 0.9 in euthyroid and 0.98+_0.8 in hypothyroid, did not find statistically significant difference in parity of hypothyroid and euthyroid women. There is no statistically significant difference found between the euthyroid and hypothyroid women in terms of gravidity in the present study as well as study conducted by Casey et al 2005 and Sahu et al 2010.

Gestational age

In the present study it was observed that the maximum proportion of hypothyroid women was seen in the gestational age between 36-40 weeks that was 29.8% followed by 31-35 weeks (20.3%). While maximum number of euthyroid women were seen in gestational age between 21 – 25 (80.3%) and 26-30 weeks (81%). In the study by Hong Yang et al2014 [16] observed that the prevalence of overt hypothyroidism or hyperthyroidism was higher in the high risk group than in the non high risk group in the first trimester (0.8% vs 0, p=0.008; 1.6% vs 0.2%, p=0.008, respectively). The prevalence of hypothyroidism was significantly higher in the high risk group than in the non high risk group during the second trimester (1.3% vs 0.5%, p=0.034; 11.6% vs 8.4% p=0.011 respectively). The total prevalence of hypothyroidism or hyperthyroidism and the prevalence of subclinical hypothyroidism or hyperthyroidism were not statistically significant between the high risk and non high risk groups, for either the first or second trimester similar to our study.

Dinesh Dhanwal et alin 2016 [5] found that taking trimester-specific TSH cutoffs of <2.5 mIU/L for the first trimester and <3.0 mIU/L for the second and third trimester as suggested by ATA, the prevalence of hypothyroidism is found to be 44.3%, 32.0%, and 34% women in the first, second, and third trimester, respectively.

In our study we have not screened antenatal women in first trimester. However percentage of women with hypothyroidism was increased with increase in gestational age and the result was not statistically significant

Body Mass Index (BMI)

As shown in our study women who were extremely obese and have obese BMI have maximum chance of hypothyroidism with 33.3% and 42.9% respectively while maximum euthyroid women had normal BMI (81.8%) or were underweight (90.2%). The risk of developing hypothyroidism was twice in extremely obese than in obese women as compared to women with normal BMI that was 18.23% (35 out of 192). The difference was statistically significant between BMI and hypothyroidism ($p<0.05$)

According to Cheng Han et al 2015 [17] (86) BMI $\geq 25\ kg/m^2$ may act as an indicator of hypothyroidism and BMI $\geq 30\ kg/m^2$ was associated with increased risk of hypothyroidism. The prevalence of isolated hypothyroxinemia increased among pregnant women with BMI $> 24\ kg/m^2$. Median serum concentrations of TSH were compared in different BMI groups at the 4th–8th gestational weeks. TSH of normal weight and underweight groups did not exhibit any statistically significant differences. On the other hand, TSH was significantly higher in obese group than that in the overweight group (2.50 mIU/L versus 2.11 mIU/L, $P < 0.008$), and it was also higher in the overweight group than that in the normal group (2.11 mIU/L versus 1.86 mIU/L, $P < 0.001$). A study performed by the other researcher by Collares FM et al2017 [18](101) stated that higher maternal TSH levels were associated with higher prepregnancy BMI (difference: 0.18 kg/m^2 [95% CI: 0.01, 0.36] per SD increase in maternal TSH level) and higher total gestational weight gain

(difference: 0.02 kg/wk [95% CI: 0.01, 0.03] per SD increase in maternal TSH level) .Hence increase in BMI increases the risk of hypothyroidism.

CONCLUSION

In the present study antenatal women were screened for thyroid dysfunction and it was observed that the prevalence of hypothyroidism was much higher than previous studies though the cut off level of serum TSH was low in our study.
Therefore, it is recommended that women undergo routine thyroid function testing as part of their antenatal care, since we are already screening for the diagnosis of diabetes mellitus in pregnancy. It was also observed that that age, gravidity and gestational age has no statistical significant difference with hypothyroidism in pregnancy whereas, prevalence of hypothyroidism was 2- 4 times increased with obesity. Therefore, losing weight and leading a healthy lifestyle can reduce the chance of getting hypothyroidism during pregnancy.

Limitations of the Study

- As it was a cross-sectional study and the women weren't monitored until postpartum, we haven't assessed the women's outcomes for the mother and the fetus. For the purpose of evaluating the long-term problems in hypothyroid women, large-scale prospective studies are required.
- Studies on 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.

Declarations

Ethics Committee Approval- The study protocol was approved from Institutional Ethical Committee, Faculty of Medicine, AMU, Aligarh.

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

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