(IJRMST) 2023, Vol. No. 15, Jan-Jun **e-ISSN: 2455-5134 p-ISSN: 2455-9059**

Physiological Changes of Thyroid Gland in Pregnancy[1]

***Lalit Narayan Yadav, **Dr. Biren Singh**

**Research Scholar, **Professor*
CMJ University, Shillong, Meghalaya, India

DOI:10.37648/ijrmst.v15i01.006

Received: 28 November 2022; Accepted: 05 January 2023; Published:10 February 2023

ABSTRACT

Women with hypothyroidism who did not take adequate medicine had a three times increased chance of developing preeclampsia. In the group that received inadequate treatment, preterm births and restrictions on the foetus's growth both increased dramatically. In the cohort I looked at, there was not a single incident of placental unexpectedness. It was discovered that the group who received poor treatment had a significantly higher incidence of oligohydramnios. When hypothyroidism is properly managed during pregnancy, pregnancy-related complications such as premature birth, toxaemia, intrauterine growth restriction (IUGR), oligohydramnios, glucose intolerance, preterm labour, low birth weight babies, abruptio placenta, and stillbirth are less likely to occur. Given that this study showed that women with pre-gestational diabetes mellitus frequently have thyroid impairment, it is important to check these women's thyroid function when they are pregnant. Thyroid dysfunction was present in both pregnant women with GDM and healthy pregnant women, but in 27% of them, TPO Ab titers were positive, indicating the need for additional testing for postpartum thyroiditis and dysfunction.

Keywords : *Gestational diabetes-related dysfunction.*

INTRODUCTION

These problems included preterm labour, an irregular birth cycle, and membrane rupture before labour (PROM). TPO-Ab, which may be connected to hyperthyroidism, is present in over 10% of pregnant women in their sixteenth week of pregnancy, while the incidence of TPO antibodies in asymptomatic pregnant women has been estimated to be between 6 and 19%. Thyroid dysfunction is substantially more common in people with type 1 diabetes during pregnancy than in the general population. In fact, some studies have found a connection between type 1 diabetes and thyroid malfunction, with 40% of pregnant women having thyroid dysfunction. Subclinical hypothyroidism is the most common thyroid condition. Other forms of thyroid dysfunction are much less common.**[1]** Clinical and subclinical thyroid hyperthyroidism is an insulin-blocking disease, similar to type 2 diabetes. By alone, this condition would be able to indicate a link between the two infections. According to certain research, prenatal hyperglycemia may affect the hatchling's dynamic T4 to T3 transition or T3 emission. This lends credence to the idea that thyroid problems and diabetes are linked.**[2]**

It was estimated that between 4.7 and 7.4 percent of the population in Iran was affected by GDM (15). 10-15 percent of pregnant women will, throughout the primary half of their pregnancies, be affected negatively by the adverse consequences of thyroid dysfunction . Several studies have shown that women who have GDM had a higher than average prevalence of hypothyroxinemia and higher than average levels of TPO's enemy .

Physiological Changes of Thyroid Gland in Pregnancy

Pregnancy, according to the findings of studies on humans and other creatures, has the potential to alter the normal capability of the thyroid. Physiological alterations to the thyroid occur to a significant degree during pregnancy. During

[1] *How to cite the article:*
Yadav L.N., Singh B., Physiological Changes of Thyroid Gland in Pregnancy; *International Journal of Research in Medical Sciences and Technology*, Jan-Jun 2023, Vol 15, 40-50, DOI: http://doi.org/10.37648/ijrmst.v15i01.007

pregnancy, the size of the thyroid gland can increase anywhere from 20 to 40 percent in regions where there is an inadequate supply of iodine. In countries where there is an adequate supply of iodine, this increase is just 10 percent (ADA et al., 2014). The following are some of the metabolic changes**.[3]**

Increases in Iodine Renal Clearance

As a result of an increase in the glomerular filtration rate, there is an increase in the urine loss of iodine that occurs during pregnancy. This results in iodine shortage and goitre in the mother.

An Increase in Serum Thyroxine Globulin Binding (TBG)

Oestrogen levels rise, which causes thyroxine-restricting globulin (TBG), a protein responsible for carrying thyroid hormone in the blood, to rise (Galofre et al., 2009).

Triiodothyronine (T3) and Thyroxine (T4) Inner-Ring Deiodination Via the Placenta

Type 3 deiodinase, which encourages the development of thyroid chemical fringe digestion and directs "the trans-placental transit of thyroid chemical and iodide" (Landers et al., 2009), is produced by the placenta.

Many endocrine conditions can make pregnancy more challenging. Diabetes is becoming more common, "both in adults and in children in particular," which has increased the number of pregnancies that are complicated by the disease. The most prevalent type of the illness is diabetes, and its incidence is rising**.[4]**

DIAGNOSIS OF GDM

Diabetes in pregnancy study group India (DIPSI) diagnostic criteria, diagnosed based on the 2-hour 75-gram oral glucose tolerance test (OGTT) with a threshold plasma glucose concentration greater than 140 mg/dl at 2-hour, performed in fasting/non-fasting state, regardless of the timing of the last meal.

THYROIDANATOMY

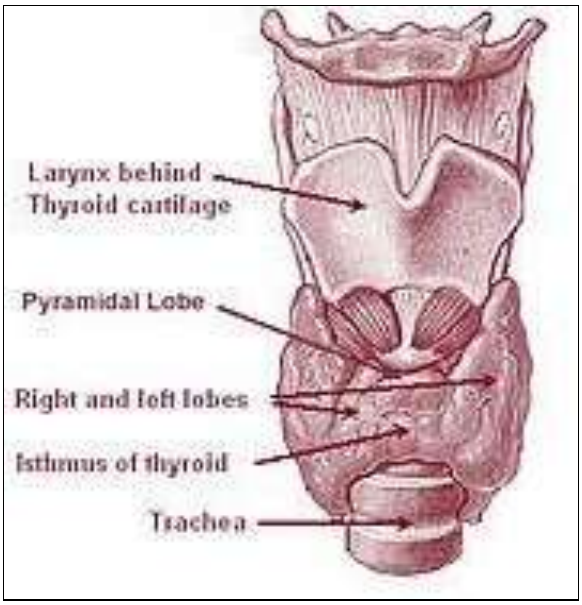

Figure 1

"The thyroid gland resembles a butterfly and is made up of two cone-like projections or wings that are joined by an isthmus. These projections are known as the lobusdexter (right flap) and the lobus sinister (left projection). Each projection has a length of roughly 5 centimetres, a width of approximately 3 centimetres, and a depth of around 2 centimetres. During its journey to the rear of the throat and the sheath that encases the carotid artery, the organ is situated on the front side of the neck. When it travels in this direction, it presses against the larynx and the windpipe and wraps

itself around both of these structures. It begins craniocaudally at the angled line on the thyroid ligament (just beneath the laryngeal noticeable quality, also known as the Throat cartilage'), and it reaches out inadequately to somewhere in the vicinity of the fifth or sixth tracheal ring. This region is known as the inferior tracheal region."**[5].**

When the organ shifts position in relation to the vertebral levels when it is swallowed, it is difficult to determine which line on the organ is higher. This is because it is difficult to decide which line is higher because it is difficult to tell which line is higher. There is a range of prevalence for the presence of a third flap, which is also known as the pyramidal projection of the thyroid organ. This projection can be seen in anywhere from 28 to 55 percent of the population, with the average being 44.3 percent. These percentages are calculated based on the entirety of the population. It has a sloping form and extends from the upper region of the isthmus all the way down to the hyoid bone. Along the way, it travels through the thyroid ligament and the upper part of the isthmus. The foetal thyroid tail, also known as the thyroglossal duct, is the structure that is responsible for the formation of the pyramidal flap. This duct is also known by its other name, the foetal thyroid tail. [6] In some instances, the location is quite remote, or there may be at least two distinct areas that are geographically distinct from one another and are divided from one another by physical barriers. In some contexts, the pyramidal projection could also be referred to "as the Lalouette pyramid." The thyroid gland is encased in a thin sheath of connective tissue known as the capsulagl and ulaethyreoideae. This provides the gland with protection. This sheath can be found surrounding the gland in question. The sheath that surrounds it is made up of two layers: an inner layer and an outer layer. When viewed from an anterior perspective, the pretracheal sash is continuous with the external layer, however when viewed from a posterior lateral perspective, the carotid sheath is continuous with the external layer. The infrahyoid muscles are responsible for covering the organ's anterior surface, while the sternocleidomastoid muscle, which is also known as the sternomastoid muscle, is responsible for covering the organ's horizontal surface. The sternocleidomastoid muscle is made up of these two muscles working together.[**7]**

A thickening of the sash on the back of the organ serves to frame the posterior suspensory tendon of the thyroid organ, which is also known as Berry's tendon. This tendon is located behind the organ. This enlargement of the sash has the purpose of securing the organ to the cricoid and tracheal ligament in addition to the cricopharyngeus muscle that is located on the rear of the organ. Swallowing serves the objective of developing a strong association between the thyroid organ and the hidden windpipe, which is the cause for the formation of the latter. This connection is necessary for the functioning of both the thyroid and the hidden windpipe. This connection is important for the thyroid to function in an appropriate manner. From the side of the projection that is furthest in front, one can gain access to the pyramidal flap in factor degree. This side of the projection is placed in the factor degree. At this stage, the intermittent laryngeal nerve as well as the sub-par thyroid conduit move into close proximity with or fully within the tendon and the tubercle. Alternately, they might be found moving throughout the tendon and the tubercle.

One of the parathyroid glands may be discovered in the area that divides the two layers of the container on each side, while the other one can be found on the rear side of the projections. Both of these glands are placed behind the projections. There is one parathyroid gland on each of the sides.

The presence of the thyroid isthmus, as well as its size and structure, are both subject to change. The thyroid isthmus can also change in size. In addition, the pyramidal flap, which is also referred to as the lobus or the process is pyramidalis, may be absorbed into the thyroid isthmus. Both of these terms refer to the same structure. "The thyroid, which is one of the major endocrine organs, weighs between 2-3 milligrams in children and between 18-60 milligrams in adults, and its size increases during pregnancy. One of the more substantial endocrine organs is the thyroid gland." In children, the thyroid gland normally weighs between 2 and 3 grammes at full development.[8]

When the organ is healthy and working normally in a human being, it is not visible to the naked eye but can be felt as a soft mass. The examination of the thyroid gland is not going to be finished until first we look for any abnormal lumps, and then we measure how big the thyroid is overall.

The primary thyroid supply route is a branch of the outer carotid vein. The subpar thyroid conduit is a branch of the thyrocervical trunk. On occasion, blood is carried to the thyroid gland via the thyroid ima corridor, which expands directly from the subclavian stream. The thyrocervical trunk is comprised of each and every one of these blood veins. Both of these blood vessel blood supply routes are located within the thyrocervical trunk. The thyro-cervical trunk is another name for this particular trunk. The primary thyroid veins empty into the internal jugular vein, whereas the secondary thyroid veins empty into the plexus thyreoideusimpar in the left brachiocephalic vein. Both of these veins are located in the thyroid gland. Both of these types of veins in the thyroid are responsible for the drainage of the venous blood that is produced by the thyroid gland. Both of these processes are carried out in the left brachiocephalic vein. This is the region where they occur.

The pre- and paratracheal lymph hubs, as well as the horizontal deep cervical lymph hubs, are regular channels for the discharge of waste products produced by the lymphatic system. Other regular paths include the deep cervical lymph hubs. Both the conspicuous and the repetitive laryngeal nerves supply the organ with the parasympathetic nerve input that is required for the organ to be able to carry out the activities for which it was designed.

OBJECTIVES OF THE STUDY

1. To the study of inner-ring denomination of triiodothyronine (t3) and thyroxin (t4) by the placenta".

2. To the study of oral glucose tolerance test (ogtt).

MATERIALS AND METHOD

There were 61 pregnant women diagnosed with diabetes who were part of the study group, and there were 35 pregnant women who served as the control group. Measurements were taken of the concentrations of T4, T3, T3RU, FTI, TSH, and Anti TPO Ab in the serum of each participant.

Study approval

"For the sample collection, the appropriate consents were obtained from the pertinent specialists, and authorizations were obtained from the patients for both the meeting and the sample collection. Patients were provided information on the purpose of this research, and prior to any sample collection or meeting, patients were given the opportunity to verbally consent to participate in the study".

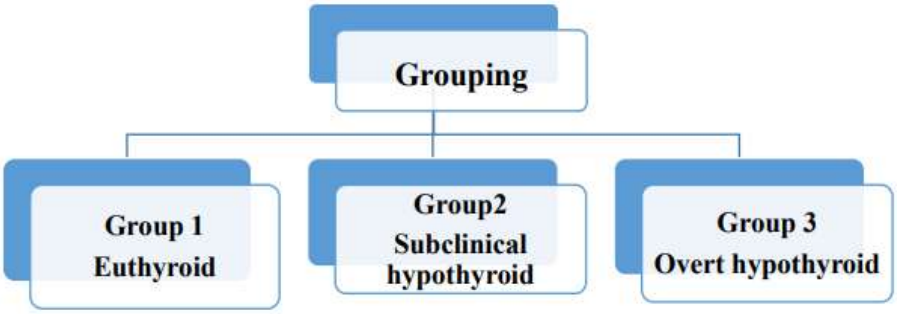

Figure 2

STUDY PROCEDURE

"After a brief period of time, we launched into the assessment work at the CMJ University in Shillong, which is located in Meghalaya. All of the pregnant women aged 18 and older who were present for prenatal care were given information in a language that was understandable to them, either English or Hindi depending on their preference. This information concerned the review convention." **[9]**

The patients who agreed to participate in the review and gave their written informed agreement to do so were recruited for the study.

Details on the participants' demographic profiles, including their age, body mass index (BMI), occupation, and contact information, as well as their whole medical history, were gathered. **[10]**

"Read up members were evaluated for Serum Thyrotropin levels (TSH, FT4) during their first trimester (9 - 13 weeks), based on which they were assembled (Table - 1), cut off qualities were acquired from 'AMERICAN THYROID ASSOCIATION'2017 (Table - 2), and they were followed as of the most recent trimester." Read up members were evaluated for Serum Thyrotropin levels (TSH, FT4) during their first trim During their first trimester, Read up participants had their serum thyrotropin levels (TSH and FT4) checked. Throughout the first trimester, which ranged from nine to thirteen weeks in length, members of Read up had their serum thyrotropin levels monitored.

In accordance with the requirements outlined in the DIPSI recommendations for the evaluation of GDM patients, an oral glucose resilience test was administered to the subjects between the ages of 24 and 28 weeks.

Table 1 TSH cut off values according to American thyroid association guidelines

GROUPS	TSH VALUES	PATIENT CONDITION
GROUP-1	0.1-2.5mU/L	EUTHYROID
GROUP-2	>2.5mU/L	SUBCLINICAL HYPOTHYROID
GROUP-3	>10mU/L	OVERT HYPOTHYROID

Table 2 TSH reference values in different trimesters.

GESTATIONAL AGE	TSH REFERENCE VALUES
FIRST TRIMESTER	0.1-2.5mU/L
SECOND TRIMESTER	0.2-3.0mU/L
THIRD TRIMESTER	0.3-3.0mU/L

Patients who meet the consideration requirements and provide their consent to be reviewed are included in the analysis. The patient's clinical history and the results of any major exams are obtained in accordance with the proforma that has been enclosed. Screening will be performed on all of the patients who are eligible, and their thyroid status will be defined. Patients who are diagnosed with hypothyroidism or who have subclinical hypothyroidism will be monitored until delivery is complete. The clinical progress that has been made as a result of the treatment will be recorded. Sincere investigation will be conducted into the findings of the review**.[11]**

RESULTS

Table 3: Demographic data of the study population.

DEMOGRAPHICS		EUTHYROID	SUBCLINICAL HYPO-THYROID	OVERT HYPO-THYROID
TOTAL PATIENTS N (%)		100(49.02)	78(38.23)	26(12.75)
AGE	± SD	±25.63.9	26.5±4.4	25.3±3.5
	<25 N (%)	43(43)	27(34.6)	11(42.3)
	25-29N(%)	39(39)	29(37.1)	10(38.46)
	30-34N(%)	15(15)	17(21.7)	5(19.23)
	≥35N(%)	3(3)	5(6.14)	0
BMI PRE-PREGNANCY (KG/M2)	±SD	24.4±4.1	25.1±4.3	26.4±3.2
	UNDEWEIGHT N (%)	9(9)	2(2.56)	-
	NORMAL UNDERWEIGHT N(%)	40(40)	29(37.94)	6(23.07)
	OVERWEIGHT N(%)	34(34)	34(43.5)	14(53.54)
	OBESE N(%)	17(17)	13(16.66)	6(23.07)
OCCUPATION N (%)	WORKING	14(14)	16(20.5)	7(26.9)
	HOUSEWIFE	86(86)	62(32.05)	19(73.7)
FAIMLY HISTORY OF DIABETES		18(18)	25(32.05)	8(30.76)
HISTORY OF GDM N (%)		3(3)	4(5.12)	1(3.86)
HISTORY OF PCOD N (%)		6(6)	45(5.12)	2(7.69)
HISTORY OF THYROID N (%)		1(1)	17(21.79)	4(15.38)
HISTORY OF INFERTILITY N (%)		3(3)	3(3.84)	4(15.38)

n- “Number of patients(%)– Percentage”

Table 4 Comparison of the Demographic Factors across the study population

DEMOGRAPHICS		EUTHYROID	SUBCLINICAL HYPO-THYROID	OVERT HYPO-THYROID
TOTAL PATIENTS N (%)		100(49.02)	78(38.23)	26(12.75)
AGE	± SD	±25.63.9	26.5±4.4	25.3±3.5
	<25 N (%)	43(43)	27(34.6)	11(42.3)
	25-29N(%)	39(39)	29(37.1)	10(38.46)
	30-34N(%)	15(15)	17(21.7)	5(19.23)
	≥35N(%)	3(3)	5(6.14)	0
BMI PRE-PREGNANCY (KG/M2)	±SD	24.4±4.1	25.1±4.3	26.4±3.2
	UNDEWEIGHT N (%)	9(9)	2(2.56)	-
	NORMAL UNDERWEIGHT N(%)	40(40)	29(37.94)	6(23.07)
	OVERWEIGHT N(%)	34(34)	34(43.5)	14(53.54)
	OBESE N(%)	17(17)	13(16.66)	6(23.07)
OCCUPATION N (%)	WORKING	14(14)	16(20.5)	7(26.9)
	HOUSEWIFE	86(86)	62(32.05)	19(73.7)
FAIMLY HISTORY OF DIABETES		18(18)	25(32.05)	8(30.76)
HISTORY OF GDM N (%)		3(3)	4(5.12)	1(3.86)
HISTORY OF PCOD N (%)		6(6)	45(5.12)	2(7.69)
HISTORY OF THYROID N (%)		1(1)	17(21.79)	4(15.38)
HISTORY OF INFERTILITY N (%)		3(3)	3(3.84)	4(15.38)

ANOVA (analysis of variance) and Student's t test were used to analyse the data. The statistical significance of the findings was established by examining whether or not the P value was lower than 0.5.

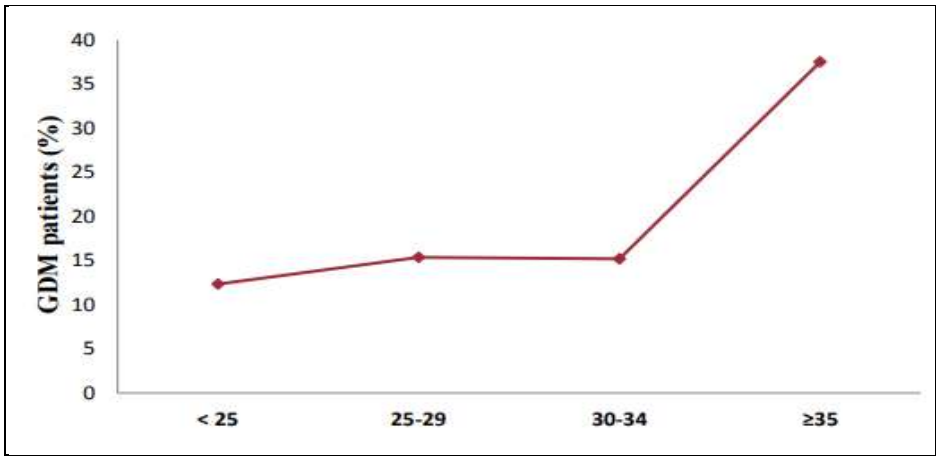

Fig. No. 3: Incidence of GDM in different age group patients

39.75 percent of the entire population was included in the study, and among those persons, 12.34 percent had developed GDM. The participants under the age of 25 accounted for 39.75 percent of the total population. There were 15.38 percent of people in the age range of 25 to 29 who had developed GDM, which accounted for 38.2 percent of the people in the population that was being evaluated for this study. Those between the ages of 30 and 34 made up 18.1 percent of the population that was being researched, and of those persons, 16.21 percent were diagnosed with GDM. Participants in the study accounted for 3.92 percent of the population under the age of 35, and among those people, 37.5 percent acquired GDM.

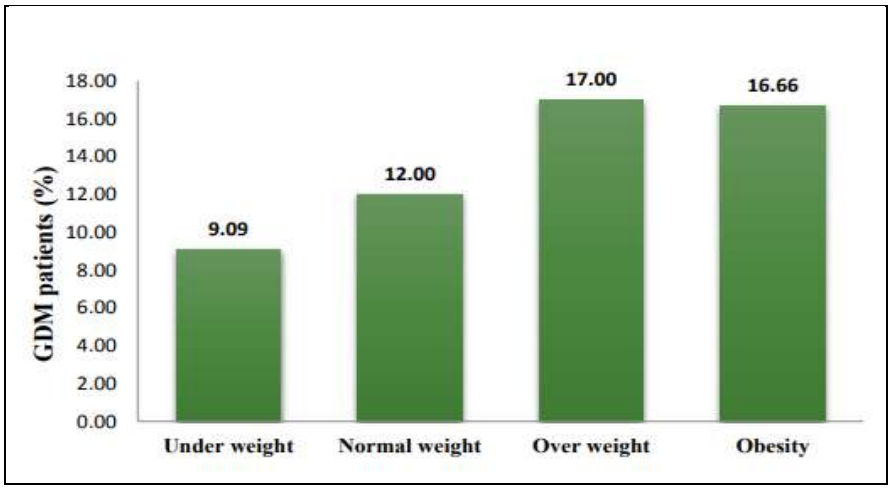

Fig. No. 4 :Incidence of GDM in patients with different BMI

There was a prevalence of type 2 diabetes in this group that was 9.09 percent, and there was a population that was underweight that made up 5.39 percent of the population that was researched. Both of these statistics were found in the population that was examined. There was a prevalence of GDM that was equal to 12 percent among the people in the population who were considered to have a normal weight, which was the equivalent of 36.9 percent of the entire population. The findings of the study indicated that there was a rate of 17.07 percent of people in the population who had GDM and that the proportion of the population that was overweight was 40.19 percent. In the population that was being investigated, the prevalence of obesity was 17.64 percent, and 16.66 percent of those who were obese also had type 2 diabetes.

In the population of people who have normal thyroid function, there is a significant and favourable correlation between the individual's history of childlessness and GDM (0.313). There is a correlation between a person's age and GDM, and this association is positive. Patients who have subclinical hypothyroidism are more likely to have this correlation (0.004). Within the population that has apparent hypothyroidism, there is a correlation between a person's family history of diabetes and their own risk of developing the condition (0.410), a person's family history of polycystic ovary syndrome and their own risk of developing GDM (0.703), and a person's family history of infertility and their own risk of developing GDM (0.592).

Table .5: GDM risk analysis using Odds ratio

Odd Ratio	Value	95%Confidence interval	
		Lower	Upper
Odds Ratio for group (Euthyroid/subclinical)	1.770	0.755	4.151
Odds Ratio for group (Euthyroid/ overt hypothyroid)	1.926	0.604	6.140

Women who have subclinical hypothyroid bunch have a 1.7 times greater likelihood of developing gestational diabetes mellitus when compared to women who have euthyroid bunch. This is because subclinical hypothyroid bunch is associated with an underactive thyroid. This is due to the fact that euthyroid group is connected to functioning thyroid normally. When compared to women who have euthyroid bunch, women who have evident hypothyroid bunch have a 1.9 times greater risk of developing gestational diabetes mellitus during their pregnancies.

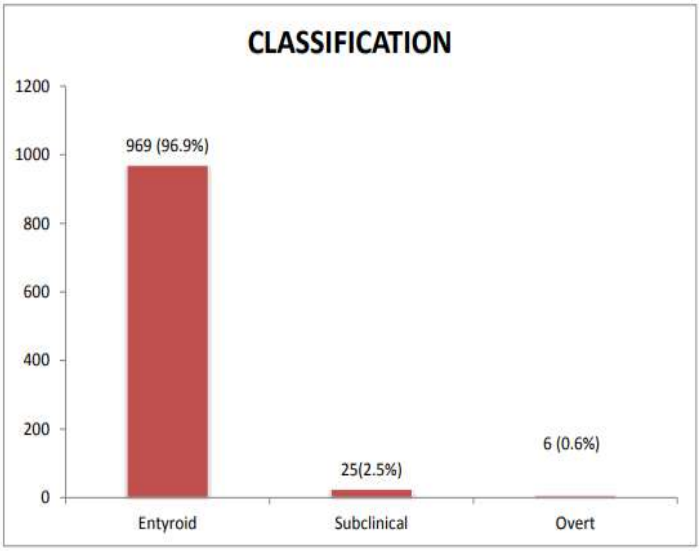

Figure No.5: Classification

Table 6: Classification

CLASSIFICATION	Study	Control	Total	Chisq	P
Eurothyroid	0	969	969(96.9%)	1000	**0.0001**
Subclinical hypothyroid	25	0	25(2.5%)		
Overt hypothyroid	6	0	6(0.6%)		
Total	31	969	1000(100%)		

Table 7: Prevalence

CLASSIFICATION	Frequency
Eurothyroid	969(96.9%)
Subclinical hypothyroid	25(2.5%)
Overt hypothyroid	6(0.6%)
Total	1000(100%)

The prevalence of hypothyroidism in the group that I evaluated is detailed in the table below. I found that 3.1 percent of the patients who had been carefully examined suffered from this condition. The table displays the percentage of patients in this category that have hypothyroidism as their primary diagnosis. 2.5 percent of the people had hypothyroidism at a subclinical level, while 0.6 percent of those people had hypothyroidism at an evident level. Chi square and an extremely significant result for the p-value, which comes in at 0.0001

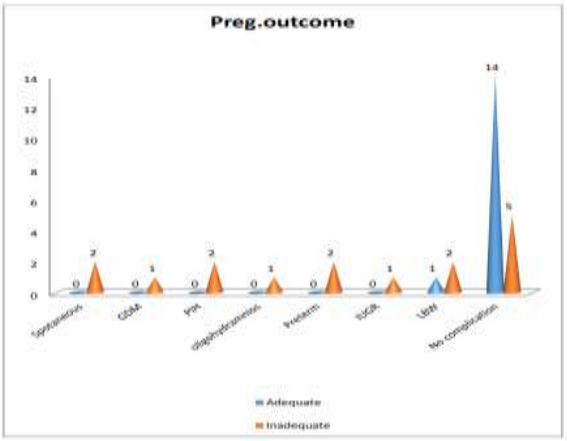

Fig. 6 Pregnancy Outcome

Table 8 Preg. Outcome inadequately treated patients developed complications.

	Adequately traded	Inadequately traded	Total	Chi.sq	P values
Spontaneous abortion	0	2(12.5%)	2	12.57	0.00039
GDM	0	1(6.2%)	1		
PIH	0	2(12.5%)	2		
Oligohydramnios	0	1(6.2%)	1		
Preterm	0	2(12.5%)	2		
IUGR	0	1(6.2%)	1		
LBW	1(6.66%)	2(12.5%)	3		
Total Complications	1(6.6%)	11(68.75%)	12		
No Complication	14(93.33%)	5(31.25%)	19		
Total	**15**	**16**	**31**		

According to the data presented in the table, only 6.66% of patients who received adequate treatment experienced a complication that was characterised by a low birth weight, whereas 68.75% of patients who did not receive adequate treatment encountered complications**. [12]**

CONCLUSION

It is essential to conduct tests to evaluate the thyroid function of patients who are pregnant and have pre-gestational diabetes. This is because women who have pre-gestational diabetes are more prone to suffer from thyroid dysfunction. Individuals diagnosed with GDM have a rate of thyroid dysfunction that is comparable to that of women who are not pregnant and serving as controls. It was discovered that pregnant women with diabetes as well as pregnant women who did not have diabetes had a significant prevalence of positive titers of TPO Ab. The outcomes of this researcher's study indicated that women who had pre-gestational diabetes were more likely to have thyroid dysfunction than women who did not have pre-gestational diabetes. As a consequence of this, it is important to evaluate the thyroid function of these patients while they are pregnant. It was found that women with GDM and normal pregnant women had a similar prevalence of thyroid dysfunction. Nevertheless, 27% of the women with GDM showed a positive titer of TPO Ab, which warrants follow-up for post-partum thyroiditis and dysfunction.

REFERENCES

[1] Global Health Expenditure Database (2013). Geneva World Health Organisation,2012 (apps.who.int/nha/database/DataExplorer Regime.aspx. accessed 7thMarch,2013).

[2] Moosazadeh M, Asemi Z, Lankarani KB, Tabrizi R, MaharloueiN,NaghibzadehTahami A, Yousefzadeh G, Sadeghi R, Khatibi SR, Afshari M, Khodadost M, Akbari M. (13 December 2016), Family history of diabetes and the risk of gestational diabetesmellitus in Iran: A systematic review and meta-analysis. *Diabetes Metab Syndr*; ii: S1871- 4021(16)30239-9.

[3] Kemp HF, Hundal HS, Taylor PM. (4 April 1997), Glucose transport correlates with GLUT2 abundance in rat liver during altered thyroid status. *Mol Cell Endocrinol*; 128(1-2):97-102.

[4] Velayutham K, Selvan SS, Unnikrishnan AG. (Nov-Dec 2015); Prevalence of thyroid dysfunction among young females in a South Indian population. *Indian J EndocrinolMetab*;19(6):781-4.

[5] Bianco A, Stone J, Lynch L, Lapinski R, Berkowitz G, Berkowitz RL. (Jun 1996); Pregnancy outcome at age 40 and older. *Obstet Gynecol*; 87(6):917-22.

[6] Cleary-Goldman J, Malone FD, Vidaver J, Ball RH, Nyberg DA, Comstock CH, SaadeGR, Eddleman KA, Klugman S, Dugoff L, Timor-Tritsch IE, Craigo SD, Carr SR, Wolfe HM, Bianchi DW, D'Alton M; (May 2005); FASTER Consortium. Impact of maternal age on obstetric outcome. *Obstet Gynecol;* 105(5 Pt 1):983-90

[7] Gilbert WM, Nesbitt TS, Danielsen B. (January 1999), Childbearing beyond age 40: pregnancy outcome in 24,032 cases. *Obstet Gynecol*; 93(1):9-14.

[8] Naeye RL. (February 1983); Maternal age, obstetric complications, and the outcome of pregnancy. *Obstet Gynecol*; 61(2):210-6.

[9] Prysak M, Lorenz RP, Kisly A. (January 1995); Pregnancy outcome in nulliparous women 35 years and older. *Obstet Gynecol.*; 85(1):65-70

[10] Ludford I, Scheil W, Tucker G, Grivell R. (June 2012); Pregnancy outcomes for nulliparous women of advanced maternal age in South Australia, 1998-2008. *Aust N Z J ObstetGynaecol*; 52(3):235-41.

[11] Favilli A, Pericoli S, Acanfora MM, Bini V, Di Renzo GC, Gerli S. (August 2012), Pregnancy outcome in women aged 40 years or more. *J Matern Fetal Neonatal Med*; 25(8):1260-3.

[12] Tomar, V. (2022). A Review on Procedure of QSAR Assessment in Organic Compounds As a Measure of Antioxidant Potentiality. *International Journal for Global Academic & Scientific Research*, *1*(1), 7–12. https://doi.org/10.55938/ijgasr.v1i1.2