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Review Article

Overview of thyroid gland characteristics in pregnancy using ultrasonography as an assessment tool

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ABSTRACT

Thyroid gland is one of the most common gland affected during pregnancy as it responds to the increased physiological demands of iodine and energy during pregnancy. Any thyroid dysfunction can result in abortion, preterm labor or affects fetal neurodevelopment. Various anthropometric factors or genetic factors apart from iodine intake are known to affect the size of thyroid gland. Changes in thyroid gland morphology can be easily measured using ultrasonography as clinically the enlargement can be labelled as goiter. In this review, we aimed to evaluate the changes in thyroid gland during pregnancy and assess the different factors affecting its size across the various studies as the literature data concerning the thyroid gland enlargement during pregnancy is controversial. Various articles on thyroid volume changes during pregnancy from literature were reviewed along with a cross-sectional observation done in a government hospital setup in India, on 240 patients who were divided into 4 groups of 60 patients each which included non-pregnant females in group 1 and pregnant females in all three trimesters respectively in the rest 3 groups. Thyroid gland morphology and its characteristics such as volume, nodularity, echogenicity and vascularity were measured using high frequency ultrasonography in each group and then compared. Thyroid volume in the third trimester group (7.24±1.16 ml) was found to be significantly greater ($p<0.001$) than in the non-pregnant group (5.44±0.82 ml). BMI was found to be the highest in third trimester group as expected. Even in iodine sufficient areas we found thyroid gland volume to increase during pregnancy from non-pregnant group along with thyroid gland nodularity. Vascularity assessed based on CDFS pattern shows pattern I to be most common. Variation in thyroid gland characteristics between pregnant and non-pregnant controls was found.

Keywords: Thyroid gland, Pregnancy, Ultrasonography

INTRODUCTION

Physiological changes during pregnancy result in alterations in the biochemical and structural parameters of thyroid gland. These changes, though prudent, may at times result in potentially serious outcomes for mother and foetus both, if left untreated.

Pregnancy has a goitrogenic effect on thyroid gland.[1] This effect can be attributed to factors such as increased thyroid hormone production, increased renal iodine excretion, fetal iodine requirements and dietary iodine requirements which are higher in pregnancy than they are for non-pregnant adults. This effect is more pronounced in iodine deficient areas rather than in iodine sufficient area. The increase in size can be probably due to the enhanced thyroid stimulation in iodine deficiency causing enlargement of thyroid gland. Apart from iodine various others factors such as age, weight, gender, BMI (body metabolic index), BSA (body surface area), TSH (thyroid stimulating hormone), smoking and genetic factors impact the size of thyroid gland.[2,3]

The size of the thyroid gland has clinically been determined by visual inspection and palpation. But with clinical method there is high degree of inter-observer

variation and error that may misdiagnose or over diagnose mild variety of goiter. Imaging has long been established as an essential modality in the thyroid gland work up. Ultrasonography is the modality of choice for thyroid assessment in pregnant females being an easily available and radiation free imaging modality. With ultrasonography, size of thyroid gland can be interpreted as thyroid gland volume and any variation in thyroid gland can be assessed on grayscale and color Doppler mode. Different studies have published data regarding thyroid volume in pregnancy and different factors affecting it. This review provides an overview of data available for thyroid volume in pregnant females and factors affecting the changes observed in thyroid volume and compare them with non-pregnant females.

Method

A total of 240 patients who were divided into 4 groups of 60 patients each which included non-pregnant females in group 1 and pregnant females in all three trimesters respectively in rest 3 groups, were studied using high frequency ultrasonography after approval from ethics committee. Thyroid gland ultrasonographical characteristics such as volume, echogenicity, nodularity and vascularity of study groups were observed and thyroid gland volume among non-pregnant and pregnant females was correlated with age, BMI and parity of the females. BMI was measured for every female as weight in kilograms divided by height in meter squared.

Table 1: Author name, year and participants (n) in each group of reviewed literature and in present study.

Author	Year	Sample size (n)	Non-pregnant (n)	1st trimester (n)	2nd trimester (n)	3rd trimester (n)
Brander	1989	57	22	7	28	28
Berghout	1994	10	10	10	10	10
Azizi	2002	931	90	403		
Sultanalieva	2009	1480	-	146	223	211
Kiljanska	2013	62	-	62	62	62
Jaiswal	2013	226	-	226		
Sahin	2014	83	83	83	83	83
Elebrashy	2019	190	40	50	50	50
Vannucchi	2017	155	-	155	155	155
Tuccilli	2017	179	80	7	12	80
Kianpour	2019	441	256	185		
Gao	2020	2139	-	441	1135	563
Guo	2020	2378	2378			
Present study	2022	240	60	60	60	60

Table 2: Mean/median thyroid volume in different trimesters and in non-pregnant groups as per reviewed literature and in present study.

Author	Non-pregnant (ml)	1st trimester (ml)	2nd trimester (ml)	3rd trimester (ml)
Brander	12.2±2.9	11.5±2.3	11.6±1.3	12.6±1.7
Berghout	10.3±5.1	10.6±4.4	9.6±3.8	9.4±3.0 ml
Azizi	7.8±2.8	8.8±3.5	7.0±2.5	7.6±3.3
Sultanalieva	-	6.9	7.5	8.6
Kiljanska	-	11.12	13.0	15.75
Jaiswal	-	7·1±2·6	7·0±2·7	7·0±1·9
Sahin	11.9±6.2301	14.6±9.3301	15.8±9.2301	15.8±9.2301
Elebrashy	7.9±2.5	8.3±3.4	8.7±3.1	8.9±2.2
Vannucchi	-	8.7±2.4	8.8±2.4	9.4±2.4
Tuccilli	7.8	10.36		
Kianpour	6.4±2.1	6±2.5		
Guo	-	9.6	10.1	10.8
Present Study	5.44±0.82	5.85±0.64	6.25±0.67	7.24±1.16

Table 3: Independent predictors for the total thyroid volume in non-pregnant and pregnant groups in present study.

Trimester		Coefficients	P value*	R
Non-pregnant	Age	0.052	0.180	0.364
	BMI	0.167	0.042	
	Parity	0.370	0.367	
1st trimester	Age	0.057	0.299	0.371
	BMI	0.201	0.020	
	Parity	0.063	0.047	
2nd trimester	Age	0.022	0.630	0.36
	BMI	0.185	0.009	
	Parity	0.094	0.046	
3rd trimester	Age	0.049	0.215	0.344
	BMI	0.150	0.013	
	Parity	0.181	0.040	

*P value are considered significant < 0.05.

Thyroid volume was evaluated with high frequency ultrasound with method used as follow: patient lied in supine position with hyperextended neck; high frequency transducer used to insonate both transverse and longitudinal plane. The WHO method described by Brunn et al with an optimised correction factor of 0.479, used a width (cm)×length (cm)×thickness (cm)×0.479 formula for each lobe (ml) and the sum of the volumes of the two lobes are then calculated.[4] Isthmus was not included in the thyroid gland volume. Any change in echogenicity of thyroid gland or any nodule was assessed. The intraparenchymal vascularity was evaluated using colour Doppler. On CDFI the patterns were graded as; pattern 0, absent or minimal flow intraparenchymally; pattern I, intraparenchymal blood flow of uneven distribution; pattern II, mildly increased flow with patchy distribution; pattern III, marked increase in blood flow with diffuse homogeneous distribution.[5]

Literature review of the online databases (Pubmed) was performed to search for articles related to the following inclusion terms: thyroid gland; ultrasonography; pregnant females. This identified a total of 75 articles. After applying the inclusion and exclusion criteria (mentioned below), 13 publications met the criteria and were reviewed as shown in Table 1.

Inclusion criteria

Pregnant females and non-pregnant females of similar age; randomized clinical trials, COHORT studies or case control studies; basic information such as age, gender, grouping of patients, parity, BMI was recorded and counted in detail.

Exclusion criteria

Any pregnant females with any systemic illness; previous history of thyroid disease or thyroid surgery or on antithyroid medications; medical imaging modalities other than ultrasound; subjects less than 18 years of age were excluded.

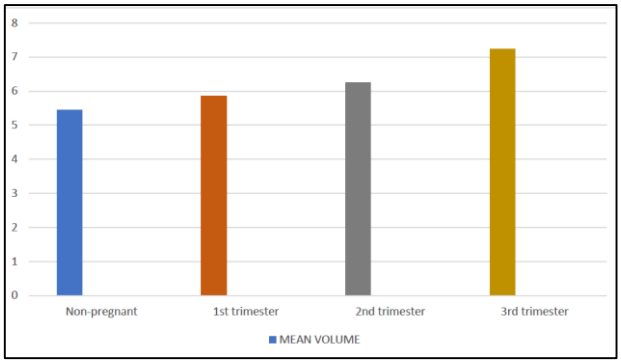

Figure 1: Mean volume of thyroid gland in non-pregnant and in different trimester group.

Thyroid volume

Various metabolic and hormonal changes during pregnancy can result in thyroid gland changes most prominent among them is increase in thyroid volume. As per the studies reviewed, thyroid gland volume was significantly higher in pregnant group than non-pregnant group and 1st trimester group as seen in Table 1.[3,6-10] It was found to be increasing with each trimester with maximum volume found in 3rd trimester. As per some studies, the increase in thyroid volume was significant from non-pregnant status, while in some studies there was a non-significant increase in thyroid volume.[6,7] However, few studies which were done in iodine sufficient areas, have not reported any increase in thyroid volume with the advancement of pregnancy.[11-14] Thyroid volume from the reviewed literature are depicted in Table 2.

As per the study done in department of radio-diagnosis of MGMMC and MYH, Indore (India) we found a significant difference between thyroid volume of non-pregnant group

and pregnant group. Thyroid volume in non-pregnant females was found to be lowest (5.44±0.82 ml) and in 3rd trimester it was highest (7.24±1.16 ml) as shown in Figure 1. A rising trend of thyroid volume with each trimester was found.

The increase in thyroid volume can be attributed to the increase in blood volume and the extracellular fluid during pregnancy causing hyperemia of thyroid gland.[15] It had been established that the increase of thyroid gland volume was more in iodine deficient areas rather than in iodine sufficient areas. An increase in volume of thyroid gland was found to be 12%, to as high as 40% (Ozdikici).[8] In our study we observed a rise of 24% in thyroid volume from non-pregnant females.

Anthropometric factors

Parameters such as age, weight, BSA, BMI, parity, smoking and genetic factors are found to be affecting the thyroid gland volume during pregnancy aside from iodine. Among these, we correlated age, parity and BMI with thyroid gland volume in each group of our study. Some of the reviewed studies also assessed these factors.

Studies have postulated that with the advancement of age there is rise in thyroid volume. However, in the studies evaluated, one study had demonstrated a non-significant positive correlation with age during pregnancy implying that females with older age tend to have higher thyroid volume than their younger counterparts.[6] In few studies there was no correlation of thyroid volume in pregnant females with age.[16,17] We also found a positive correlation of age and thyroid volume though it was insignificant.

Thyroid volume as a function of BMI took into account both height and weight of both pregnant and non-pregnant females. BMI had shown a positive correlation with thyroid volume during pregnancy.[6,16-18] Also, Elbrashy et al in his study showed BMI as an independent factor affecting thyroid gland volume.[6] Similarly, in our study, on applying linear regression analysis BMI was found to the sole independent predictor of thyroid volume as seen.

Another factor that was found to have a positive correlation with thyroid gland volume in our study was parity. This effect can be explained with the continuous adding effects of pregnancy on the thyroid gland of female with each successive pregnancy. However, few studies demonstrated no correlation between parity and thyroid volume.[8] Correlation of age, BMI and parity is depicted in Table 3.

Thyroid nodularity

As per epidemiology, there was high thyroid nodularity noted in women than men both in iodine sufficient or deficient area and also amongst women with higher gravidity. On clinical palpation, the prevalence of nodules was very low whereas on imaging it can be as high as 70%.[19-22] Few studies have researched the prevalence of thyroid nodules in pregnant females and found the it to be ranging from 3% to 27%.[18,23-25] This concluded that with pregnancy there was increase in thyroid nodularity even in iodine sufficient areas. Most common cause can be attributed to the iodine deficiency as in iodine deficient areas the nodularity was found to be as high as 30%.[7] In our study, we found a 12.2% incidence of thyroid nodule with highest incidence in third trimester.

Thyroid echogenicity

Thyroid lobes echogenicity was determined by comparing it with the surrounding adjacent muscles. Brander et al assessed pregnant females for any difference in the echogenicity of thyroid gland and observed no alteration in the echogenicity of thyroid gland in the different trimesters.[3] Similarly, in our study no change was appreciable in the echogenicity of thyroid gland from non-pregnant to pregnant group and also amongst pregnant groups.

Thyroid vascularity

Intraparenchymal thyroid gland vascularity was analysed in the 4 groups using colour Doppler. With the advancement of pregnancy, hyperaemia of thyroid gland occurs resulting in increased vascularity of thyroid gland. However, we found only 11 (6.2%) females during pregnancy with increased intraparenchymal vascularity and in non-pregnant group, CDFS pattern 0 was observed mainly. Most of the females belonged to third trimester group with CDFI pattern II. CDFI pattern III or the inferno pattern was not observed in any pregnant or non-pregnant female. None of the reviewed studies have evaluated the vascularity of thyroid gland but a study done by Fister et al observed a decrease in the intraparenchymal vascularity of thyroid gland in 6 months' postpartum females in comparison to when they were evaluated at 3rd trimester.[26]

CONCLUSION

Thyroid gland continuously keeps on changing its dynamics based on the exigency of body. Pregnancy is one such situation where continuous stimulation of thyroid gland occurs in order to meet the demands of growing foetus increasing the size of thyroid gland. Visual inspection and palpation of thyroid gland are acceptable but ultrasonography is much more precise modality. Most appreciable effect of pregnancy was seen on thyroid gland volume. Reviewed articles had concluded mixed results regarding thyroid gland volume changes during pregnancy. Studies done in iodine sufficient areas observed no change in thyroid gland volume while increase of thyroid gland volume was seen in an iodine deplete area due to continuous thyroid stimulation. However, we found an increase of 24% in thyroid volume from non-pregnant towards the third trimester despite being in an iodine sufficient area proving the goitrogenic effect of pregnancy. A positive association, though

insignificant, between thyroid gland enlargement with the number of previous pregnancies and age of females was found. BMI was found to be a significant parameter affecting thyroid gland size during pregnancy. Pregnancy is associated with an increase in the size of pre-existing thyroid nodules as well as new thyroid nodule formation. No significant change in thyroid gland echogenicity was found but an increase in the intraparenchymal thyroid gland vascularity was observed. The spectrum of changes as documented on ultrasonography of thyroid gland were not pathological, but it definitely provides the proof of change in thyroid characteristics with pregnancy.

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