



ULTASONOGRAPHIC EVALUATION OF THYROID GLAND DURING PREGNANCY: COMPARISON AMONG TRIMESTERS.

Dr. Sudipta Saha

Assistant Professor, Dept. of Radiodiagnosis, IPGME&R, Kolkata.

Dr. Bijaya Lakshmi Gayari*

M.D Radiodiagnosis, Senior Resident, Dept of Radiodiagnosis, IPGME&R, Kolkata *Corresponding Author

Dr. Koushik Mandal

M.D Radiodiagnosis

ABSTRACT

Pregnancy is a period that is associated with an increase in the size of thyroid gland and change in thyroid hormone levels. This occurs due to hormonal changes in pregnancy and also related to iodine intake. In the present study, we have tried to evaluate the changes in thyroid gland and its blood flow using ultrasonography.

KEYWORDS :

INTRODUCTION

During pregnancy, thyroid physiology undergoes several changes in order to adapt to the metabolic and hormonal modifications experienced by maternal organism. Thyroid volume and thyroid vascularisation appear to increase as thyroid hormone production need to be higher in pregnancy. Several factors influence the size of the thyroid gland. There is no definite information available about some of the factors or the complex ways in which they affect the thyroid gland. The thyroid volume is higher in males in comparison to females and there is a correlation between lean body mass, body mass index and thyroid volume. The size and shape of the thyroid gland may alter remarkably with age, gender, physiological condition, race and geographical location. Presumably, in females, thyroid size may be affected by sex hormones during pregnancy and menstruation. The alteration in maternal thyroid function during gestation are intricate and as yet incompletely understood. Historically, there has been a widely held belief that the thyroid increases in size during pregnancy. According to the older literature, the thyroid gland shows some degree of enlargement during gestation, notably in areas of low environmental iodine. In some older reports investigators claimed a relationship between thyroid gland enlargement and pregnancy (Brander and Kivisaan, 1989, Lona et al. 1985, Prout, 1975)⁵. While India has become iodine sufficient after two decades of salt iodisation, there is no informative data for thyroid function and size of healthy pregnant women in this country. It is therefore crucial for evaluation of the morphological changes undergone by the maternal thyroid gland during the three trimesters of pregnancy.

AIMS AND OBJECTIVES

- To determine the thyroid gland volume in first, second and third trimester of pregnancy by ultrasonography,
- To see the changes in vascularity of thyroid gland in different trimesters of pregnancy,
- To see the echotexture of the thyroid gland
- To see any abnormal calcification and nodule of the thyroid gland in different trimesters of pregnancy.

MATERIALS AND METHODS

STUDY AREA

Gynaecology and Obstetrics OPD, SSKM & H and SSKM & H Department of Radio diagnosis.

STUDY POPULATION

Patients attending GOPD for routine antenatal check up will be selected as cases satisfying inclusion and exclusion criteria.

STUDY PERIOD

One year (from June 2015 to June 2016).

SAMPLE SIZE

Total 80 patients will be taken, 20 patients from each trimester. Written consent will be taken from each patient, and studied according to proforma.

SAMPLE DESIGN

The sample to be designed according to the below mentioned criteria-

- Inclusion criteria :-** All patients with confirmed pregnancy (UPT +ve).
- Exclusion criteria :-** Those on LT4 therapy.

Known other autoimmune diseases.

Pregnant mother on antithyroid drug.

Pregnant mother with enlarge thyroid.

STUDY TOOLS :-

- Proforma to note patients' details.
- US machine Philips HD7 with Probes, Broadband 7 to 15 MHz curved linear array transducer with selectable frequency and electronic focus.

PARAMETERS TO BE STUDIED:-

The following morphological parameters will be studied by USG-

- Assessment of thyroid volume
- vascularity
- echogenicity
- Calcification
- Nodularity

STUDY TECHNIQUES:-

The patient is typically examined in supine position with the neck extended. A small pad may be placed under the neck to provide better exposure of the neck, particularly in patients with a short, stocky habitus. The thyroid gland must be examined thoroughly in both transverse and longitudinal planes. Imaging of the lower pole can be enhanced by asking the patient to swallow, which momentarily raises the thyroid gland in the neck. The entire gland including the isthmus must be examined. The examination must also extend laterally to include the regions of the carotid artery and jugular vein in order to identify enlarged jugular chain lymph nodes,

superiorly to visualise submandibular adenopathy and inferiorly to define any pathologic supraclavicular lymph nodes. Real time imaging of thyroid is performed using both gray-scale and colour Doppler techniques. The imaging characteristics of the gland (viz. size, shape, margins, echogenicity, contents, nodules, calcification and vascular pattern) should be identified.

STUDY PROCEDURES :-

- Institutional Ethical Committee clearance will be taken before proceeding with the study.
- Case selection will be done as per sample design and inclusion-exclusion criteria.
- Informed written consent from the patient will be taken in his/her language.
- USG of thyroid gland in pregnant mother in 1st, 2nd, 3rd trimester.
- Results will be tabulated and data will be analyzed using standard methods.

PLAN FOR ANALYSIS OF DATA :-

Standard statistical methods

RESULTS & ANALYSIS

Frequencies

Statistics		
Age of the patient in Years		
N	Valid	80
	Missing	0
Mean		24.89
Median		25.00
Std. Deviation		4.207
Minimum		17
Maximum		34

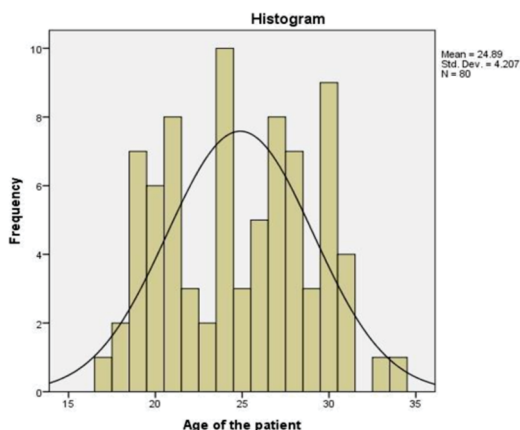


Figure 1- Showing age distribution of study population.

Frequencies		
Statistics		
Weight in Kg		
N	Valid	80
	Missing	0
Mean		56.30
Median		56.75
Std. Deviation		10.828
Minimum		34
Maximum		81

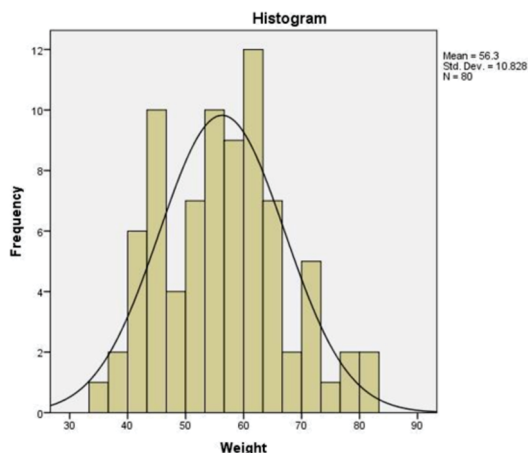


Figure – 2

Fig – 2 showing weight distribution of the study population -- showing it almost normally distributed

Frequencies		
Statistics		
Height in Cm		
N	Valid	80
	Missing	0
Mean		153.84
Median		154.00
Std. Deviation		5.397
Minimum		142
Maximum		166

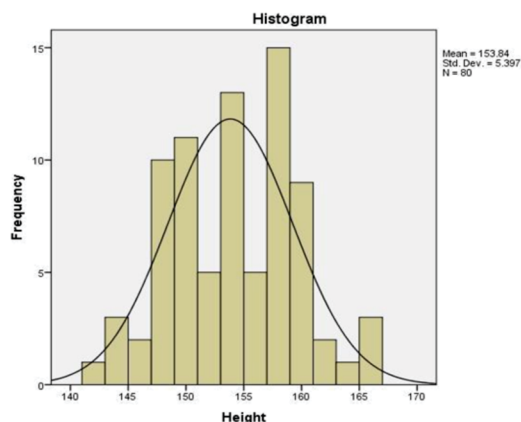


Figure – 3

Figure – 3 shows height distribution of the study population, which is almost normally distributed

Frequencies		
Statistics		
BMI in Kg/sq m		
N	Valid	80
	Missing	0
Mean		23.7811
Median		24.1094
Std. Deviation		4.37474
Minimum		14.72
Maximum		34.72

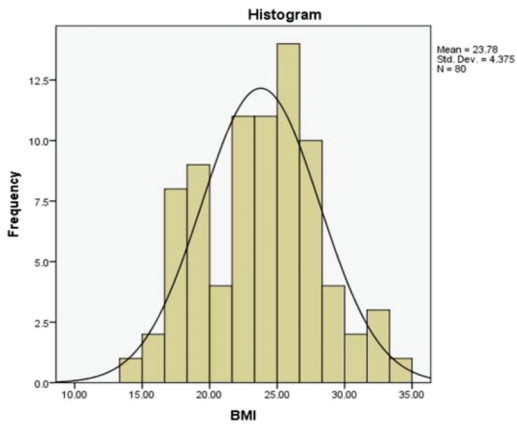


Figure - 4

Fig - 4 shows BMI of the study population which is almost normally distributed

Frequencies

	Frequency	Percent
First Trimester	23	28.8
Second Trimester	31	38.8
Third Trimester	26	32.5
Total	80	100.0

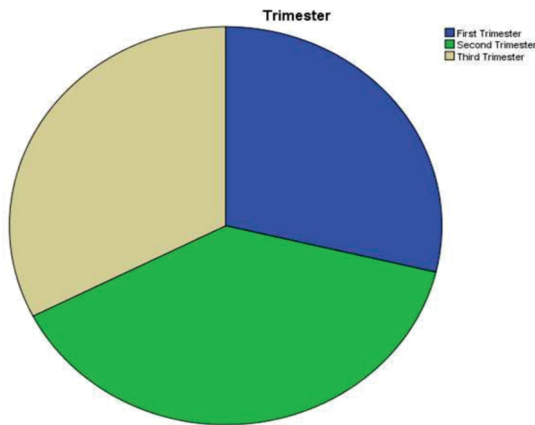


Fig - 5 showing Pie diagram of the study population in three different trimesters

Means Plots

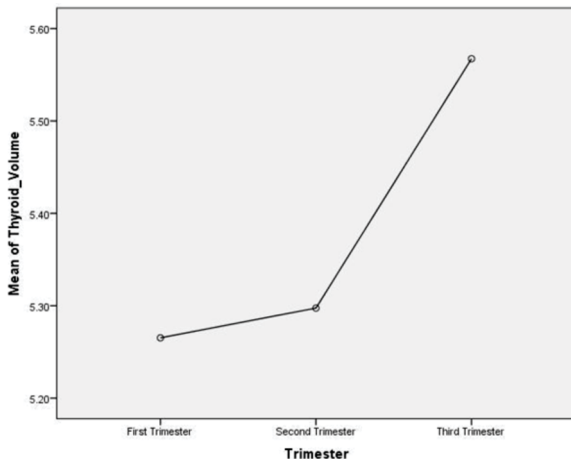


Figure - 6 Mean Line diagram showing mean thyroid volume in three different trimesters

T-Test

		Group Statistics and Independent sample T test				
	Trimester	N	Mean	Std. Deviation	T test	P value
Thyroid Volume	First Trimester	23	5.2652	1.15486	0.095	0.925
	Second Trimester	31	5.2974	1.29081		

Figure - 7

Independent Sample Student T-test shows that mean thyroid volume increases from first trimester to second trimester

		Group Statistics and Independent sample T test				
	Trimester	N	Mean	Std. Deviation	T test	P value
Thyroid Volume	Second Trimester	31	5.2974	1.29081	0.798	0.479
	Third Trimester	26	5.5673	1.24749		

Figure - 8

Independent Sample Student T - test shows that mean thyroid volume increases from second trimester to third trimester

Mean Plot of volume of Right Thyroid Lobe in different

Trimester:

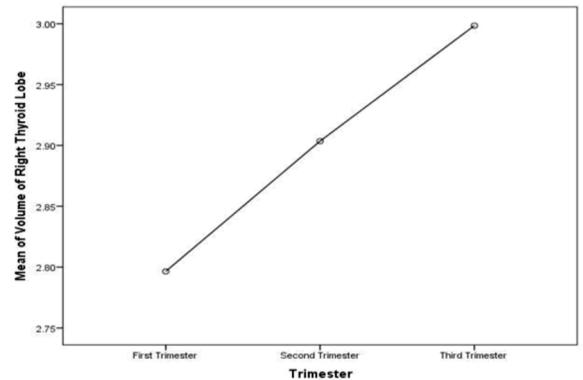


Figure - 9

Figure - 9 shows mean volume of Rt. lobe of thyroid gland in different trimesters. It shows that mean volume of Rt. Thyroid lobe is gradually increasing from 1st trimester to 3rd trimester.

T-Test

		Group Statistics and Independent sample T test				
	Trimester	N	Mean	Std. Deviation	T test	P value
Volume of Right Lobe of Thyroid	First Trimester	23	2.7965	0.64584	0.601	0.550
	Second Trimester	31	2.9035	0.64774		

Figure -10

Independent one way T-test shows there is increase in mean volume of Rt. Lobe of Thyroid from 1st trimester to 2nd trimester

	Group Statistics and Independent sample T test					
	Trimester	N	Mean	Std. Deviation	T test	P value
Volume of Right Lobe of Thyroid	Second Trimester	31	2.9035	0.64774	0.533	0.596
	Third Trimester	26	2.9985	0.69610		

Figure –11

Figure –11 Shows independent Sample T-test shows that there is increase in mean volume of right lobe of thyroid from 2nd trimester to 3rd trimester.

Mean Plot of volume of Left Thyroid Lobe in different

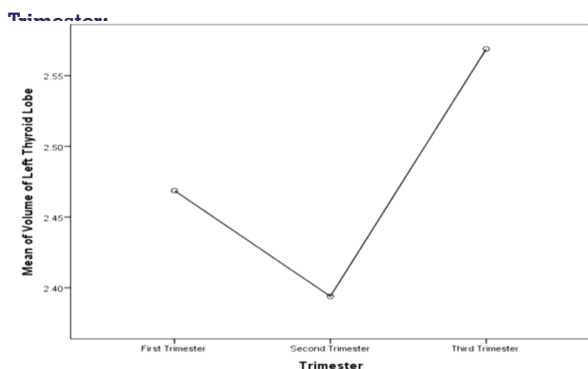


Figure –12

Figure –12 Shows mean volume of Lt. lobe of thyroid gland in different trimesters. It shows that there is decrease in mean volume in 2nd trimester and again increase in mean volume in 3rd trimester.

T-Test

	Group Statistics and Independent sample T test					
	Trimester	N	Mean	Std. Deviation	T test	P value
Volume of Left Lobe of Thyroid	First Trimester	23	2.4687	0.64906	0.370	0.713
	Second Trimester	31	2.3939	0.79163		

Figure –13 Independent Sample T-test shows that there is decrease in mean volume of Lt. lobe of thyroid from 1st trimester to 2nd trimester.

	Group Statistics and Independent sample T test					
	Trimester	N	Mean	Std. Deviation	T test	P value
Volume of Left Lobe of Thyroid	Second Trimester	31	2.3939	0.79163	0.841	0.404
	Third Trimester	26	2.5688	0.77168		

Figure –14

Independent Sample T-test shows that there is increase in mean volume of Lt. lobe of thyroid from 2nd trimester to 3rd trimester.

Difference of Mean and SD of Right and Left Thyroid lobe in

First Trimester:

Statistics^a

	Volume of Right Thyroid Lobe	Volume of Left Thyroid Lobe
Valid	23	23
N		
Missing	0	0
Mean	2.7965	2.4687
Median	2.9200	2.4800
Std. Deviation	.64584	.64906
Minimum	1.48	1.48
Maximum	4.77	3.74

α. Trimester = First Trimester

Figure –15

Figure –15 Shows Difference of mean & SD of Rt. & Lt. thyroid lobe in 1st trimester

T-Test

	Group Statistics and Independent sample T test					
	Lobe of Thyroid	N	Mean	Std. Deviation	T test	P value
First Trimester	Right	23	2.7965	0.64584	1.71692	0.093
	Left	23	2.4687	0.64906		

Figure 16- Independent Sample T-test shows mean volume of Rt. lobe in 1st trimester(2.7965c.c.) is greater than Lt. lobe (2.4678 c.c.)

Difference of Mean and SD of Right and Left Thyroid lobe in

Second Trimester:

Statistics^a

	Volume of Right Thyroid Lobe	Volume of Left Thyroid Lobe
Valid	31	31
N		
Missing	0	0
Mean	2.9035	2.3939
Median	2.8400	2.2400
Std. Deviation	.64778	.79163
Minimum	1.81	1.11
Maximum	4.80	4.25

α. Trimester = Second Trimester

Figure –17

Shows Difference of mean & SD of Rt. & Lt. thyroid lobe in 2nd trimester.

T-Test

	Group Statistics and Independent sample T test					
	Lobe of Thyroid	N	Mean	Std. Deviation	T test	P value
Second Trimester	Right	31	2.9035	0.64778	2.77385	0.007
	Left	31	2.3939	0.79163		

Figure –18

Independent Sample T-test shows that mean volume of Rt. lobe in 2nd trimester (2.9035cc) is greater than mean volume of Lt. lobe (2.3939 c.c.).

Difference of Mean and SD of Right and Left Thyroid lobe in

Third Trimester:

Statistics^a

	Volume of Right Thyroid Lobe	Volume of Left Thyroid Lobe
Valid	26	26
N		
Missing	0	0
Mean	2.9985	2.5688
Median	2.9950	2.4950
Std. Deviation	.69610	.77168
Minimum	1.71	1.24
Maximum	4.77	4.35

a. Trimester = Third Trimester

Figure -19

Shows Difference of mean & SD of Rt. & Lt. thyroid lobe in 3rd trimester.

T-Test

Group Statistics and Independent sample T test						
	Lobe of Thyroid	N	Mean	Std. Deviation	T test	P value
Third Trimester	Right	26	2.9985	0.69610	2.02096	0.044
	Left	26	2.5866	0.77168		

Figure 20-

Independent Sample student T-test shows that mean volume of Rt. lobe of thyroid in 3rd trimester (2.9985 c.c.) is greater than mean volume of Lt.

Mean difference of Right and Left thyroid lobe in different trimester:

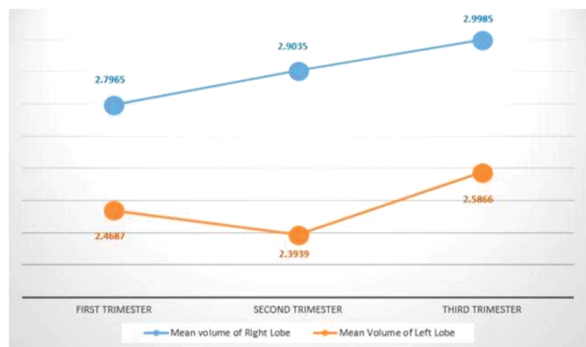


Figure -21

Shows Difference in mean volume of Rt. & Lt. thyroid lobes in different trimesters.

One way ANOVA

		Sum of Squares	df	Mean Square	F	P value
Rt_SV	Between Groups	.058	2	.029	.001	.999
	Within Groups	3585.991	77	46.571		
	Total	3586.050	79			

Rt_DV	Between Groups	2.619	2	1.310	.090	.914
	Within Groups	1121.734	77	14.568		
	Total	1124.354	79			
Rt_SD	Between Groups	.037	2	.019	.139	.871
	Within Groups	10.357	77	.135		
	Total	10.395	79			
Rt_PI	Between Groups	.007	2	.004	.069	.933
	Within Groups	3.959	77	.051		
	Total	3.966	79			
Rt_RI	Between Groups	.008	2	.004	.523	.595
	Within Groups	.577	77	.007		
	Total	.585	79			

ANOVA

Figure - 22

One way ANOVA shows that though Rt ITA Systolic Velocity, Diastolic Velocity, S/D ratio, PI and RI change between trimesters. (ITA – Inferior Thyroid Artery)

Post Hoc Tests

Dependent Variable	(I) Trimester	(J) Trimester	Mean Difference (I-J)	Std. Error	P value
Rt_SV	First Trimester	Second Trimester	.02146	1.87807	0.999
	Second Trimester	Third Trimester	.04535	1.81480	0.988
Rt_DV	First Trimester	Second Trimester	.16288	1.05039	.987
	Second Trimester	Third Trimester	-.42895	1.01501	.906
Rt_SD	First Trimester	Second Trimester	-.05029	.10093	.872
	Second Trimester	Third Trimester	.03636	.09753	.926
Rt_PI	First Trimester	Second Trimester	.01741	.06240	.958
	Second Trimester	Third Trimester	.00583	.06030	.995
Rt_RI	First Trimester	Second Trimester	.00820	.02382	.937
	Second Trimester	Third Trimester	.01640	.02302	.757

Figure - 23

Tukey HSD Post Hoc Tests also confirm that Rt ITA Systolic Velocity, Diastolic Velocity, S/D ratio, PI and RI change between first to second and second to third trimester.[ITA – Inferior Thyroid Artery]

Means Plots

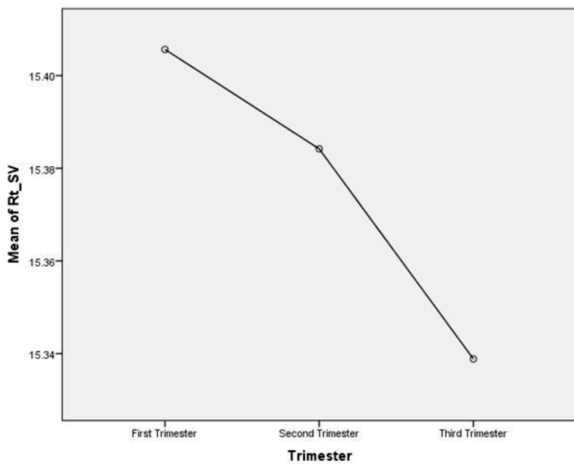


Figure – 24

It illustrates mean systolic velocity of right inferior thyroid artery decreases with increasing trimester.

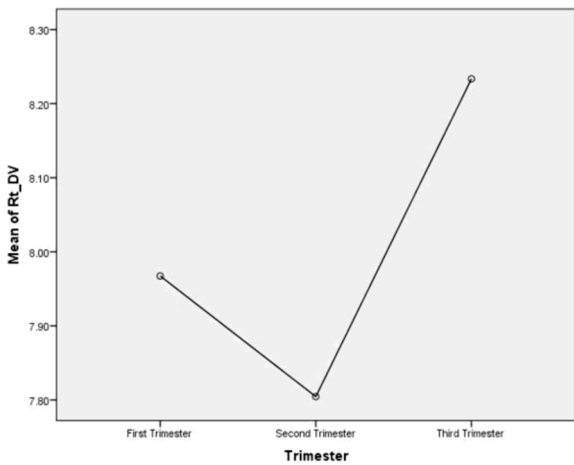


Figure – 25

It illustrates that mean diastolic velocity of right inferior thyroid artery decreases from 1st to 2nd trimester and increases from 2nd to 3rd trimester

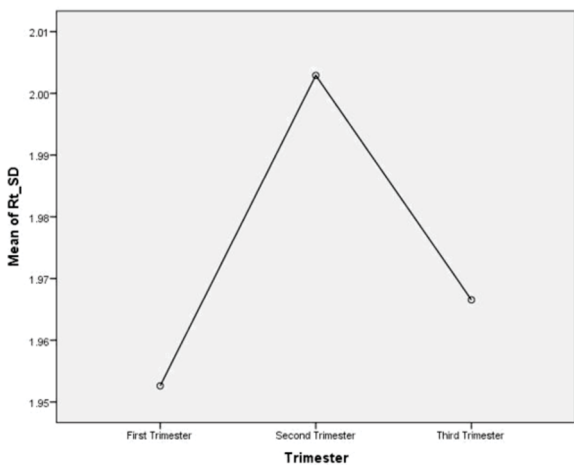


Figure 26

It illustrates increase in S/D ratio from 1st to 2nd trimester, however increase in S/D ratio from 2nd to 3rd trimester.

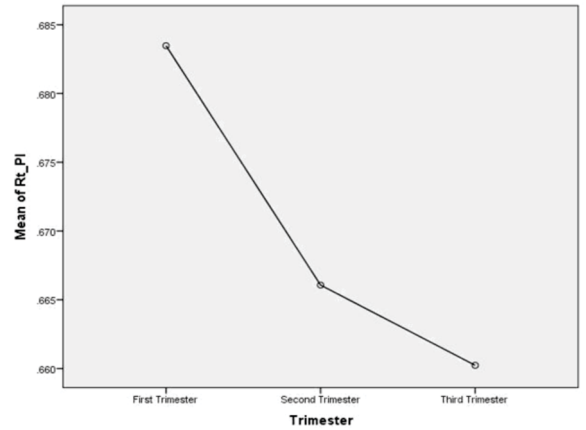


Figure 27

It illustrates decrease in PI of right inferior thyroid artery from 1st trimester to 3rd trimester.

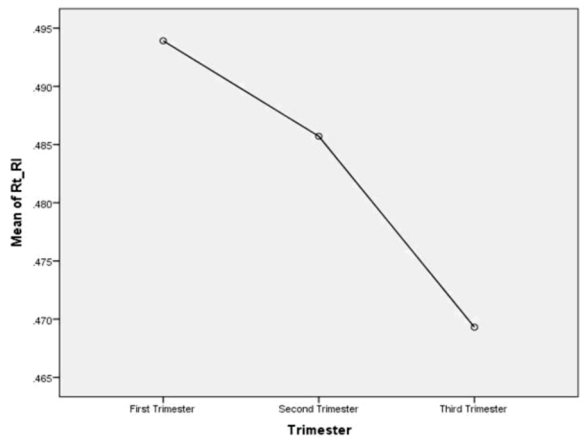


Figure – 28

It illustrates decrease of RI of right inferior thyroid artery from 1st trimester to 3rd trimester.

One way ANOVA

		Sum of Squares	Df	Mean Square	F	P value
Lt_SV	Between Groups	16.722	2	8.361	.310	.734
	Within Groups	2074.777	77	26.945		
	Total	2091.499	79			
Lt_DV	Between Groups	26.755	2	13.378	1.417	.249
	Within Groups	726.956	77	9.441		
	Total	753.711	79			
Lt_SD	Between Groups	1.170	2	.585	2.490	.090
	Within Groups	18.095	77	.235		
	Total	19.265	79			
Lt_PI	Between Groups	.186	2	.093	1.979	.145
	Within Groups	3.624	77	.047		
	Total	3.811	79			
Lt_RI	Between Groups	.048	2	.024	2.593	.081
	Within Groups	.720	77	.009		
	Total	.769	79			

ANOVA

Figure – 29

One way ANOVA shows that Lt. ITA Systolic Velocity, Diastolic Velocity, S/D ratio, PI and RI change between trimesters. (ITA – Inferior Thyroid Artery)

Post Hoc Tests

Dependent Variable	(I) Trimester	(J) Trimester	Mean Difference (I-J)	Std. Error	P value
Lt_SV	First Trimester	Second Trimester	-1.11217	1.42854	.717
	Second Trimester	Third Trimester	.62269	1.38042	.894
Lt_DV	First Trimester	Second Trimester	-1.03171	.84559	.445
	Second Trimester	Third Trimester	-.41127	.81711	.870
Lt_SD	First Trimester	Second Trimester	.15820	.13341	.465
	Second Trimester	Third Trimester	.15138	.12891	.472
Lt_PI	First Trimester	Second Trimester	.04988	.05971	.682
	Second Trimester	Third Trimester	.07227	.05769	.426
Lt_RI	First Trimester	Second Trimester	.02380	.02661	.645
	Second Trimester	Third Trimester	.03820	.02572	.303

Multiple Comparisons

Tukey HSD

Figure – 30

Tukey HSD Post Hoc Tests also confirms that Lt. ITA Systolic Velocity, Diastolic Velocity, S/D ratio, PI and RI change between first to second and second to third trimester. [ITA – Inferior Thyroid Artery]

Means Plots

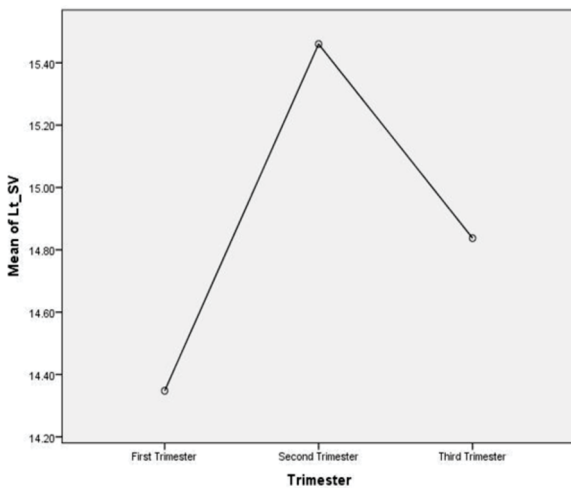


Figure – 31

It illustrates increase in systolic velocity of left inferior thyroid artery from 1st trimester to 2nd trimester and slight decrease from 2nd trimester to 3rd trimester.

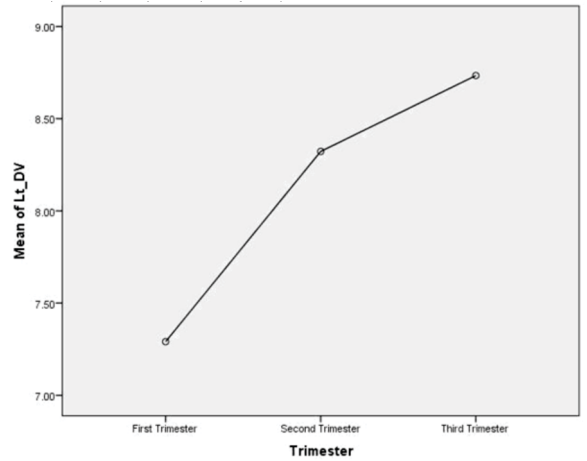


Figure 32

It illustrates increase in diastolic velocity of left inferior thyroid artery from 1st trimester to 3rd trimester.

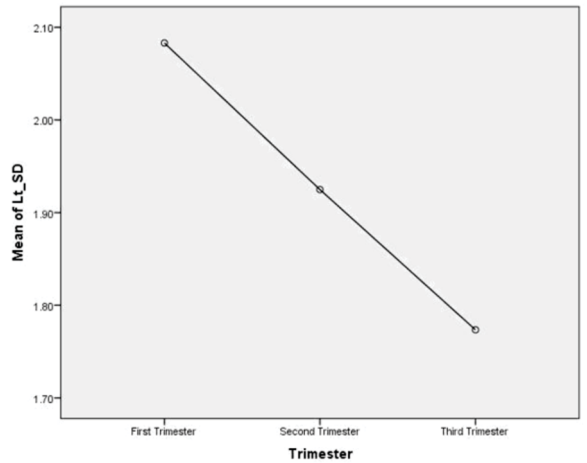


Figure 33

It illustrates decrease in S/D ratio of left inferior thyroid artery from 1st trimester to 3rd trimester.

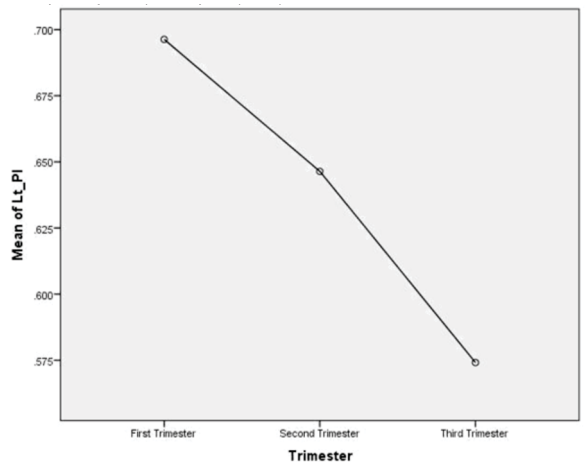


Figure 34

It illustrates decrease in PI of left inferior thyroid artery from 1st trimester to 3rd trimester.

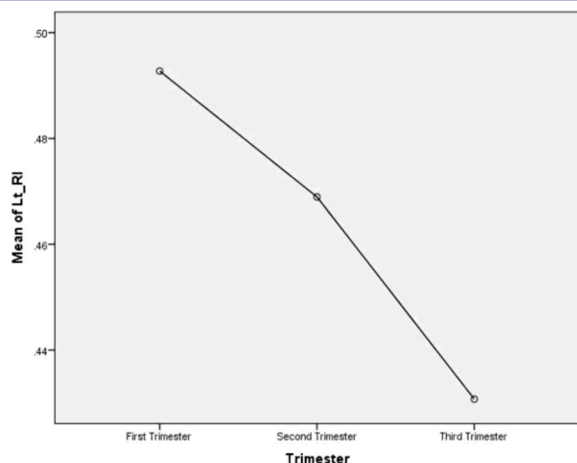


Figure – 35

It illustrates decrease in RI of left inferior thyroid artery from 1st trimester to 3rd trimester.

SUMMARY

- In our study, 80 healthy pregnant women in three different trimesters are included.
- The study population are aged between 17 yrs to 34 yrs. Among these 11 are below 20 yrs, 63 are between 20 yrs – 30 yrs. and 6 are above 30 yrs of age with mean age being 24.89 years and std. deviation being +/-4.207.
- All the study population are weighing between 34 Kg to 81 kg. The mean weight is 56.30 kg and std. deviation is +/-10.828kg.
- Height of all study population are between 142 cm to 166 cm. with mean 153.84 cm. and std. deviation +/-5.397 cm.
- BMI of all the pregnant females are between 14.72 kg/sqm. to 34.72 kg/sqm. The mean is 23.78 kg/sqm and std. deviation is +/-4.37474.
- Among the study population 28.8% is of first trimester, 38.8% is of second trimester and 32.5% is of third trimester.
- The mean thyroid volume of 23 first trimester pregnant females is 5.2652 c.c., std. deviation +/-1.15486 that of 31 second trimester pregnant females is 5.2974, std. deviation +/-1.29081 and that of 26 third trimester pregnant females is 5.5673 c.c., std. deviation +/-1.24749.
- The mean volume of right lobe among 31 second trimester pregnant females is 2.9035 c.c., std. deviation 0.64774, mean volume of left lobe among 31 second trimester pregnant females is 2.3939 c.c., std. deviation 0.79613.
- The mean volume of right lobe among 26 third trimester pregnant female is 5.5673 c.c., std. deviation 1.24749, mean volume of left lobe among 26 third trimester pregnant female is 2.9985 c.c., std. deviation 0.69610.
- From our study, we found that there is small increase in thyroid gland volume from first trimester to second trimester and from second trimester to third trimester.
- Also, from our study we found statistically significant difference in volume between right and left lobe of thyroid gland in second and third trimester pregnancy as reflected by their corresponding P values (<0.05) shown in the respective figures. (Figure 17-20). The right lobe is larger than left lobe in second and third trimester which is statistically significant. This finding is in agreement with previous studies done among the Caucasians and the Chinese.^{53,54,55}
- Out of 80 pregnant females we have examined, 35 females already have done thyroid function test at the time of examination. All the 35 female were euthyroid.
- Among the study population, we found homogeneous echotexture of thyroid gland among all the 80 study

population. We did not find any heterogeneous or abnormal echotexture of the gland

- There is change in vascularity of the thyroid gland of all 80 study population.
- Although there is slight decrease in systolic velocity of ITA, however there is significant increase in diastolic velocity of ITA from 2nd to 3rd trimester, resulting in significant decrease in PI and RI. [ITA–Inferior Thyroid Artery].
- We have not found any abnormal calcification of the thyroid gland of all the study population.
- However, during our study, we have found small cystic nodules of varying sizes in the gland in 8(10%) pregnant females among 80 females. Among these 4(5%) in the first trimester, 3(3.75%) in the second trimester and 1 (1.25%) in the third trimester. Among these 8 females bilateral tiny cyst of the thyroid gland is found in 2 females, one each in first and second trimester. Rest of the thyroid have cystic nodules in single lobe only.

CONCLUSION

- From our study, we may conclude —
- Ultrasonographically, volume of thyroid gland increases as pregnancy advances. And moreover we observed statistically significant difference in volume between right and left lobes in second and third trimesters. Right lobe is larger than left lobe in second and third trimesters.
- Vascularity of the gland changes during pregnancy. There is increase in diastolic flow resulting in decreased PI and RI with increasing trimester of pregnancy.
- However there is no significant change in echotexture of the gland on gray scale imaging among three trimesters.

REFERENCES:

- Marine D & Kimball OP Prevention of simple goitre in man. Journal of the American Medical Association 1921 77 1068–1072.
- Hinton JW. Significance of thyroid enlargement during pregnancy. American Journal of Obstetrics and Gynecology 1927 13 204–209.
- Freedberg IM, Hamolsky MW & Freedberg AS. The thyroid gland in pregnancy. New England Journal of Medicine 1957 256 505–510.
- Glinoe D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocrine Reviews 1997 18 404–433.
- Brander A, Kivissari L. Ultrasonography of the thyroid during pregnancy. J Clin Ultrasound 17: 403-406, 1989.
- Harjeet A, Sahni D, Indar J, Aggarwal AK (2004) Shape, measurements and weight of the thyroid gland in northwest Indians. Surg Radiol Anat, 26: 91–95.
- Hegedus L, Perrild H, Poulsen LR, Andersen JR, Holm B, Schnohr P, Jensen G, Hansen JM (1983) The determination of thyroid volume by ultrasound and its relationship to body weight, age and sex in normal subjects. J Clin Endocrinol Metab, 56: 260–263.
- Parshin VS, Tarasova GP et al (1999) Ultrasound screening in diagnosis of thyroid diseases. Methodical aspects and efficacy. Visulizaciya v clinicke 14–15:1–8 (Article in Russian).
- Van Isselt JW, de Klerk JM, van Rijk PP, van Gils APG, Polman LJ, Kamphuis C et al. Comparison of methods for thyroid volume estimation in patients with Graves' disease. Eur Nucl Med Mol Imaging 2003; 30: 525–31.
- Ruggieri M, Fumarola A, Straniero A, Maiuolo A, Coletta I, Veltri A et al. The estimation of the thyroid volume before surgery: an important prerequisite for minimally invasive thyroidectomy. Langenbecks Arch Surg 2008; 393: 721–4.
- Ghervan C. Thyroid and parathyroid ultrasound. Med Ultrason 2011; 13: 80–4.
- Gomez JM, Maravall FJ, Gomez N, Guma A, Soler J. Determinants of thyroid volume as measured by ultrasonography in healthy adults randomly selected. Clin Endocrinol (Oxf) 2000; 53: 629–34.
- Markova NV (2001) Value of ultrasound angiography in diagnosis of typical thyroid diseases. PhD thesis. Moscow (Book in Russian).
- (a) Lelyuk VG, Lelyuk SE (2007) Some methodological aspects of complex ultrasound examination of the thyroid gland. Moscow (Book in Russian).
- (b) Lelyuk VG, Lelyuk SE (2007b) Ultrasound angiography. Real time, Moscow (Book in Russian).
- CROOKS, J, ABOUL-KHAIR, S, A, TURNBULL, A, C. & HYTTEN, F, E. (1964) The incidence of goitre during pregnancy. Lancet, ii, 334.
- CROOKS, J, TULLOCH, M, I., TURNBULL, A, C., DAVIDSON, D, SKULASON, P & SNAEDAL, G. (1967). Comparative incidence of goitre in pregnancy in Iceland & Scotland. Lancet, ii, 625.
- Burrow, G. N. (1975), The thyroid in pregnancy. Medical clinics of North America, 59 No(5), 1089.
- Burrow, G. N. (1978), hyper thyroidism during pregnancy. New England journal of Medicine, 289, 150.
- CHAN, V, Parascaides, C. A. & HALE, J. F. (1975) Assessment of thyroid function during pregnancy. British Journal of Obstetrics & Gynaecology, 82, 137.
- DOWLING, J, T., APPLETON, W, G. & NICOLOFF, J, T. (1967) Thyroxine turnover during human pregnancy, Journal of Clinical Endocrinology and Metabolism, 27, 1749.

21. Smyth PPA, Hetherington AM, Ryan R & O'Herlihy C. Alterations in iodine status and thyroid volume during pregnancy. In *The Thyroid and Pregnancy*, pp 55–58. Eds C Beckers & D Reinwein. Stuttgart: Schattauer, 1991.
22. Beckers C & Delange F. Iodine deficiency. In *Endemic Goiter and Endemic Cretinism*, pp 199–217. Eds JB Stanbury & BS Hetzel. New York: Wiley, 1980.
23. Thilly CH, Delange F & Stanbury JB. Epidemiologic surveys in endemic goiter and cretinism. In *Endemic Goiter and Endemic Cretinism*, pp 157–179. Eds JB Stanbury & BS Hetzel. New York: Wiley, 1980.
24. Berghout A, Wiersinga WM, Smits NJ & Touber JL. The value of thyroid volume measured by ultrasonography in the diagnosis of goitre. *Clinical Endocrinology* 1988;28:409–414.
25. Rasmussen SN & Hjorth L. Determination of thyroid volume by ultrasonic scanning. *Journal of Clinical Ultrasound* 1974;2:143–147.
26. Hegedus L, Perrild H, Poulsen LR, Andersen JR, Holm C, Schohr P, Jensen GR & Hansen JM. The determination of thyroid volume by ultrasound and its relation to bodyweight, age and sex in normal subjects. *Journal of Clinical Endocrinology and Metabolism* 1983;56:260–263.
27. Berghout A, Wiersinga WM, Smits NJ & Touber JL. Determinants of thyroid volume as measured by ultrasonography in healthy adults in a non-iodine deficient area. *Clinical Endocrinology* 1987;26:273–280.
28. Stoffer RP, Koeneke IA, Chesky VE & Hellwig CA. The thyroid in pregnancy. *American Journal of Obstetrics and Gynecology* 1957;74:300–308.
29. Crooks J, Aboul-Khair SA, Turnbull AC & Hytten FE. The incidence of goitre during pregnancy. *Lancet* 1964;2:334–336.
30. Crooks J, Tulloch MI, Turnbull AC, Davidsson D, Skulason T & Snaedal G. Comparative incidence of goitre in pregnancy in Iceland and Scotland. *Lancet* 1967;2:625–627.
31. Levy RP, Newman DM, Rejali LS & Barford DAG. The myth of goiter in pregnancy. *American Journal of Obstetrics and Gynecology* 1980;137:701–703.
32. Long RK, Felice ME & Hollingsworth DR. Goiter in pregnant teenagers. *American Journal of Obstetrics and Gynecology* 1985;152:670–674.
33. Bauch K, Meng W, Ulrich FE, Grosse E, Kempe R, Schonemann F, Sterzel G, Seitz W, Mockel G, Weber A, Tiller R, Rockel A, Dempe A & Seige K. Thyroid status during pregnancy and postpartum in regions of iodine deficiency and endemic goiter. *Endocrinologica Experimentalis* 1986;20:67–77.
34. Brander A & Kivisaari L. Ultrasonography of the thyroid during pregnancy. *Journal of Clinical Ultrasound* 1989;17:403–406.
35. Rasmussen NG, Hornnes PJ & Hegedus L. Ultrasonically determined thyroid size in pregnancy and postpartum: the goitrogenic effect of pregnancy. *American Journal of Obstetrics and Gynecology* 1989;160:1216–1220.
36. Romano R, Jannini EA, Pepe M, Grimaldi A, Olivieri M, Spennati P, Cappa F & D'Armiento M. The effects of iodophylaxis on thyroid size during pregnancy. *American Journal of Obstetrics and Gynecology* 1991;164:482–485.
37. Pedersen KM, Laurberg P, Iversen E, Knudsen PR, Gregersen HE, Rasmussen OS, Larsen KR, Eriksen GM & Johannesen PL. Amelioration of some pregnancy-associated variations in thyroid function by iodine supplementation. *Journal of Clinical Endocrinology and Metabolism* 1993;77:1078–1083.
38. Berghout A, Endert E, Ross A, Hogerzeil H, Smits NJ & Wiersinga WM. Thyroid function and thyroid size in normal pregnant women living in an iodine replete area. *Clinical Endocrinology* 1994;41:375–379.
39. Glinoe D, De Nayer P, Bourdoux P, Lemone M, Robyn C, Van Steirteghem A, Kinthaert J & Lejeune B. Regulation of maternal thyroid during pregnancy. *Journal of Clinical Endocrinology and Metabolism* 1990;71:276–287.
40. Smyth PPA, Hetherington AM, Ryan R & O'Herlihy C. Alterations in iodine status and thyroid volume during pregnancy. In *The Thyroid and Pregnancy*, pp 55–58. Eds C Beckers & D Reinwein. Stuttgart: Schattauer, 1991.
41. Glinoe D, De Nayer P, DeLange F, Lemone M, Toppet V, Spehl M, Grun JP, Kinthaert J & Lejeune B. A randomized trial for the treatment of mild iodine deficiency during pregnancy: maternal and neonatal effects. *Journal of Clinical Endocrinology and Metabolism* 1995;80:258–269.
42. Nelson M, Wickus G, Caplan RH & Beguin EA. Thyroid gland size in pregnancy. An ultrasound and clinical study. *Journal of Reproductive Medicine* 1987;32:888–890.
43. Report of the subcommittee for the study of endemic goitre and iodine deficiency of the European Thyroid Association. Goitre and iodine deficiency in Europe. *Lancet* 1985;1:289–292.
44. BRANDER A, KIVISAARI L. Ultrasonography of the thyroid during pregnancy. *J Clin Ultrasound* 1989;17:403-6.
45. STOFFER RP, KOENEKE IA, CHESKY VE, HELLWIG CA. The thyroid in pregnancy. *Am J Obstet Gynecol* 1957;74:300-8.
46. CROOKS J, TULLOCH MI et al. Comparative incidence of goitre in pregnancy in Iceland and Scotland. *Lancet* 1967;2:625-7.
47. LEVY RP, NEWMAN DM, REJALI LS, BARFORD DAG. The myth of goiter in pregnancy. *Am J Obstet Gynecol* 1980;137:701-3.
48. BERGHOUT A, ENDERT E, ROSS A et al. Thyroid function and thyroid size in normal pregnant women living in an iodine replete area. *Clin Endocrinol* 1994;41:375-9.
49. RASMUSSEN NG, HORNES PJ, HEGEDUS L. Ultrasonographically determined thyroid size in pregnancy and post partum: the goitrogenic effect of pregnancy. *Am J Obstet Gynecol* 1989;160:1216-20.
50. PEDERSEN KM, LAURBERG P, IVERSEN E et al. Amelioration of some pregnancy-associated variations in thyroid function by iodine supplementation. *J Clin Endocrinol Metab* 1993;77:1078-83.
51. GLINOER D, NAYAR De P, LANGE De F et al. A randomized trial for the treatment of mild iodine deficiency during pregnancy: maternal and neonatal effects. *J Clin Endocrinol Metab* 1995;80:258-69.
52. KUSIZ et al. Endemskoga uvostij odnoprofilaksa u Hrvatskoj. In: KUSIZ et al., eds. *Guavost u Hrvatskoj*. Zagreb: HAZU, 2000.
53. Tahir, A, Ahidjo, and H. Yusuph, "Ultrasonic assessment of thyroid gland size in Maiduguri, Nigeria," *The West African Journal of Ultrasound*, vol. 3, no. 1, pp. 26–31, 2001
54. Y. L. Hsiao and T. C. Chang "Ultrasound evaluation of thyroid abnormalities and volume in Chinese adults without palpable thyroid glands," *Journal of the Formosan Medical Association*, vol. 93, no. 2, pp. 140–144, 1994.
55. P. Langer, "Normal thyroid size versus goiter—post-mortem thyroid weight and ultrasonographic volumetry versus physical examination," *Endocrinologica Experimentalis*, vol. 23, no. 2, pp. 67–76, 1989.