

A comparative study on the growth rate of the thymus and suprarenal glands of human fetuses at different gestational weeks - a graphical analysis.

Rajkumari Ajita¹, G. Tempy Sangma²

¹Associate Professor, Department of Anatomy, Regional Institute of Medical Sciences, Imphal, Manipur, 795004, INDIA.

²Assistant Professor, Department of Anatomy, Regional Institute of Medical Sciences, Imphal, Manipur, 795004, INDIA.

Abstract:

Objective: The present study was conducted to find out a relationship of the growth rate of fetuses, thymus, suprarenal glands (both left and right), thymus weight/body weight ratios and suprarenal glands weight/body weight ratios of human fetuses at different gestational weeks.

Materials and Methods: The study was carried out on 89 (eighty nine) fetuses of different gestational ages ranging from 9 to 40 weeks obtained from the Department of Obstetrics and Gynaecology of Regional Institute of Medical Sciences Hospital, Imphal, India. The gross morphological parameters such as weights of fetus, thymus, suprarenal glands (both left and right) and corresponding organs weight/body weight ratios were noted. Their mean \pm SD values were calculated and measured. The data were statistically and graphically analyzed.

Results: The thymus growth rate from 14 to 40 weeks was found increasing faster as compared to that of left and right suprarenal glands. The growth rate of left suprarenal gland from 22 weeks onwards was also found increasing at a faster rate than that of right suprarenal gland. There was almost a similar gradual growth rate from 22 to 40 week for both left and right suprarenal glands, with the left suprarenal gland increasing at slightly faster rate as compared to right suprarenal gland.

Conclusion: There was a gradual growth rate from 22 to 40 week for both left and right suprarenal glands, with the left suprarenal gland increasing at slightly faster rate when compared to right suprarenal gland. There was a gradual increase in thymus weight/body weight ratio from 20 to 30 gestational weeks and then the ratios remained almost constant upto 40 week and in case of suprarenal weight/body weight ratio, there was a gradual decrease from 22 to 30 week and then became almost constant after 30 weeks. The findings had corroborated and substantiated with the previous findings of different workers and at the same time also contrasted partially as well as moderately with the findings of previous workers.

Key Words: Human fetus, thymus, suprarenal glands, gestational weeks, thymus weight/body weight ratio and suprarenal weight/body weight ratio.

I. Introduction

The human suprarenal gland is a remarkable organ due to its incredible capacity for steroid biosynthesis in utero, and because of its unique morphologic features. Bartolomeo Eustachi, an Italian Anatomist is credited with the first description of the suprarenal gland in 1563-64^[1,2]. The suprarenal glands are two small yellowish bodies, flat anteroposteriorly, situated immediately antero superior to each superior renal pole. The right gland is an irregular tetrahedron, whereas the left gland is semilunar and usually larger and superior in level. Each in adults measures about 50 mm vertically, 30 mm transversely, and 10 mm in the antero posterior dimensions, weighing about 5 gm^[3]. At birth, the suprarenal gland is relatively of large size and forms about one-third of the weight of the kidney^[4]. The adrenal glands are named for their location relative to the kidneys. The term "adrenal" comes from ad- (Latin, "near") and renes (Latin, "kidney")^[5]. Similarly, "suprarenal", as termed by Jean Riolan the Younger in 1629 is derived from the Latin supra (Latin: "above") and renes (Latin: kidney). One of the most recognized works on the adrenal glands came in 1855 with the publication of "On the Constitutional and Local Effects of Disease of the Suprarenal Capsule" by the English physician Thomas Addison. Edward Calvin Kendall, Philip Hench and Tadeusz Reichstein were awarded the 1950 Nobel Prize in Physiology or Medicine for their discoveries on the structure and effects of the adrenal hormones^[6].

The suprarenal glands are endocrine glands that produce a variety of hormones including adrenaline and the steroids aldosterone and cortisol^[7]. They are found above the kidneys. Each gland has an outer cortex which produces steroid hormones and an inner medulla. The adrenal cortex itself is divided into

three zones: zona glomerulosa, the zona fasciculata and the zona reticularis^[8]. The adrenal cortex produces three main types of steroid hormones: mineralocorticoids, glucocorticoids, and androgens. The suprarenal gland is composed of two heterogeneous types of tissue. In the center is the adrenal medulla, which produces adrenaline and noradrenaline and releases them into the bloodstream, as part of the sympathetic nervous system. Surrounding the medulla is the cortex, which produces a variety of steroid hormones. These tissues come from different embryological precursors and have distinct prenatal development paths. The cortex of the adrenal gland is derived from mesoderm, whereas the medulla is derived from the neural crest, which is of ectodermal origin^[9]. The suprarenal gland in a newborn baby are much larger as a proportion of the body size than in an adult. The glands weigh about 1 gm at birth^[10] and develop to an adult weight of about 4 gm each^[11]. In a fetus, the glands are first detectable after the sixth week of development^[9]. At 25 weeks, the adult suprarenal gland/cortex zone develops and is responsible for the primary synthesis of steroids during the early postnatal weeks^[12].

The thymus is a primary central lymphoid organ pinkish-gray in colour, soft, and lobulated on its surfaces and a key regulator of the immune system, and is responsible for cellular immunity of the body. It is a bilobed structure divided into lobules by the connective tissue septae that is composed of collagenous connective tissue fibers. Each lobule is consisted of a cortex and a medulla. After fat infiltration replacing the parenchyma as the age advances, its colour becomes yellowish^[13]. At birth, it weighs about 15 gm^[14]. The relative rate of growth of the embryo/fetus is about 15% per day on the 25th day and declined progressively thereafter; the absolute rate of growth is the greatest at about the 240th day^[15]. Boyd E^[16] mentioned that in general, the fluctuations in the weight of the thymus at any age period were concomitant with fluctuations in the body weight.

Over the past years, the relative comparison of growth rate of the thymus and suprarenal glands in human fetuses have been a subject matter of keen interest with the Anatomists working mainly with the human fetuses. In the present study, the weights of the suprarenal glands and thymus were measured and graphical analysis was conducted to find out relationship between the growth rate of suprarenal glands and thymus with reference to gestational weeks. Therefore, an attempt was made to determine the relative growth rate of fetal suprarenal glands with reference to thymus at different gestational weeks. The study will establish the gross development of suprarenal glands and thymus in human fetuses in Manipuri population of the North Eastern States, India. As the relevant existing literatures are found limited and not adequate, the present study attempts to compare the relative growth rate of suprarenal glands and thymus of human fetuses at different gestational weeks.

II. Materials And Methods

Eighty nine human fetuses (40 males and 49 females) of different age groups ranging from 9 to 40 gestational weeks were procured from the Department of Obstetrics and Gynaecology of Regional Institute of Medical Sciences (RIMS) Hospital, Imphal, Manipur for the study with the permission of the Medical Superintendent. These fetuses were the products of terminated pregnancies, spontaneous, medical abortion and stillbirths. Those fetuses from multiple pregnancies, macerated and malformed fetuses were excluded from the study. Only the fetuses with normal obstetrical history and free from detectable abnormality were taken into consideration for the study. Approval of the Institutional Ethics Committee was obtained to conduct the present study.

The fetuses so obtained were examined for their respective crown-rump (CR) length with the help of osteometric board and measuring tap, and body weights by electronic weighing machine. The gestational age of the fetus was determined by its crown-rump length and from obstetrical history. Thereafter, they were fixed in 10% formalin for 10 days. Then the fetuses were subjected to dissection. The sterno-clavicular joints were disarticulated and costal cartilages were cut. Thus the entire thoracic cavity was opened and lower part of the neck was also dissected for complete exposure of the thymus gland in its natural location for proper recording. In case of suprarenal glands, the incisions were given on the subcostal margins extending downwards to the anterior superior iliac spine on both sides and then to the pubic symphysis. The abdominal viscera were exposed. The small intestine along with the stomach, the larger intestines were removed. The positions, shape, size of the suprarenal gland as well as that of thymus in situ were noted. Then, these two glands were then examined and their weights recorded with the help of electronic weighing machine. Particulars of the sex, gestational week, CR length, body weights of the fetuses and location and weights of the thymus and suprarenal glands were then noted down. All the data were then analysed and represented graphically and appropriate statistical analysis was performed. The data of weights of body and the thymus, suprarenal glands, the thymus/body weight ratios and the suprarenal gland/body weight ratios of the fetuses were prepared as group mean values \pm standard deviation.

III. Results And Observations

The weights of the fetuses and their corresponding thymuses were recorded. The results of the mean weights of the fetuses, thymus weights, thymus weight/body weight ratios, suprarenal weights (of both left and right) and suprarenal weight/body weight ratios (9 to 40 gestational weeks) along with standard deviation values have been calculated and summarized. Since no significant sex difference was observed in the body, thymus and suprarenal weights in the present study, the data of both sexes were combined. All these values were presented in Table given below:

TABLE:
Mean weight of the fetus, thymus, thymus weight/body weight ratio, suprarenal weights (both left & right) and suprarenal weight/body weight ratio at different gestational weeks:

Age in weeks	No. of fetuses	Mean weights of fetuses ± S.D. (in gm)	Thymus		Suprarenal		Mean Suprarenal Wt./Body Wt. Ratio ± SD
			Mean Thymus weights ± S.D. (in gm)	Mean Thymus Wt./Body Wt. Ratio ± SD (in gm)	Mean Suprarenal weights ± S.D. (in gm)	Mean Suprarenal weights ± S.D. (in gm)	
					Left	Right	
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
9	3	13.62 ± 0.12583	0.0113 ± 0.00153	0.00083 ± 0.000104252	0.01700 ± 0.00265	0.01433 ± 0.00231	0.00115 ± 0.000190995
10	4	14.74 ± 0.37053	0.0233 ± 0.00330	0.00158 ± 0.000252385	0.02975 ± 0.01081	0.02400 ± 0.00829	0.00182 ± 0.000631641
12	4	36.12 ± 0.17397	0.0488 ± 0.00330	0.00135 ± 8.60357E-05	0.04100 ± 0.00183	0.03500 ± 0.00294	0.00105 ± 6.68848E-05
13	3	58.20 ± 0.32787	0.1267 ± 0.00153	0.00218 ± 2.66708E-05	0.06833 ± 0.00153	0.05933 ± 0.00603	0.00110 ± 5.76157E-05
14	4	78.03 ± 0.18484	0.2085 ± 0.00129	0.00267 ± 2.14619E-05	0.08850 ± 0.00289	0.07850 ± 0.01025	0.00107 ± 8.54925E-05
15	5	153.65 ± 0.48071	0.3262 ± 0.00526	0.00212 ± 0.000950836	0.10020 ± 0.00581	0.08880 ± 0.01038	0.00061 ± 4.87908E-05
16	4	205.78 ± 0.62318	0.5400 ± 0.00183	0.00262 ± 2.43851E-06	0.14700 ± 0.00337	0.13350 ± 0.00806	0.00068 ± 2.20774E-05
18	4	331.59 ± 0.38219	0.7265 ± 0.00351	0.00219 ± 8.33739E-06	0.25975 ± 0.00222	0.24350 ± 0.00597	0.00076 ± 1.07756E-05
20	4	510.68 ± 0.73054	0.9738 ± 0.00299	0.00191 ± 3.4734E-06	0.46650 ± 0.00436	0.44800 ± 0.00668	0.00090 ± 1.01139E-05
22	5	693.17 ± 0.75631	1.4886 ± 0.00986	0.00215 ± 1.21273E-05	1.16580 ± 0.00676	1.11700 ± 0.02660	0.00165 ± 2.1981E-05
24	4	860.18 ± 0.92395	1.9310 ± 0.02945	0.00224 ± 3.23969E-05	1.40875 ± 0.01377	1.36625 ± 0.04090	0.00161 ± 2.94955E-05
26	5	1177.36 ± 0.57444	2.7314 ± 0.05015	0.00232 ± 4.30667E-05	1.53500 ± 0.04637	1.48500 ± 0.04569	0.00128 ± 3.64877E-05
28	5	1460.84 ± 0.75198	3.5688 ± 0.01893	0.00244 ± 1.30665E-05	1.68300 ± 0.04481	1.59600 ± 0.09896	0.00112 ± 4.78956E-05
30	4	1715.63 ± 0.70891	4.2245 ± 0.01943	0.00246 ± 1.09906E-05	1.80625 ± 0.03750	1.71250 ± 0.09260	0.00103 ± 3.27229E-05
31	4	1950.81 ± 0.91321	4.5000 ± 0.09229	0.00231 ± 4.69625E-05	1.95125 ± 0.04871	1.84750 ± 0.05500	0.00097 ± 2.13411E-05
32	5	2115.76 ± 0.35275	5.1314 ± 0.03905	0.00243 ± 1.85023E-05	1.98200 ± 0.01987	1.89400 ± 0.02702	0.00092 ± 8.81326E-06
33	4	2381.23 ± 0.54237	5.8513 ± 0.06981	0.00246 ± 2.97486E-05	2.02075 ± 0.01729	1.96625 ± 0.04171	0.00084 ± 1.10629E-05
34	5	2520.66 ± 0.90428	6.1482 ± 0.03152	0.00244 ± 1.24724E-05	2.28160 ± 0.03133	2.19260 ± 0.03790	0.00089 ± 1.05088E-05
35	4	2780.34 ± 0.58077	6.8300 ± 0.11482	0.00246 ± 4.14171E-05	2.53000 ± 0.05115	2.43325 ± 0.05446	0.00089 ± 1.85925E-05
36	5	2951.01 ± 0.59588	7.2798 ± 0.05823	0.00247 ± 1.96255E-05	2.62500 ± 0.04848	2.52700 ± 0.08822	0.00087 ± 2.1645E-05
38	4	3158.45 ± 0.53582	7.9608 ± 0.05221	0.00252 ± 1.68461E-05	2.79500 ± 0.00816	2.65500 ± 0.10512	0.00086 ± 1.70958E-05
40	4	3260.40 ± 1.73397	8.0863 ± 0.11940	0.00248 ± 3.63177E-05	3.18375 ± 0.02394	3.09125 ± 0.06263	0.00096 ± 1.2924E-05

All mean values are statistically significant at 0.05 level : p < 0.05

The mean weight values of the human fetuses, thymus, suprarenal (left) and suprarenal (right), thymus weight/body weight ratios and suprarenal weight/body weight ratios were plotted in the following graphs and

the comparative growth rate of fetus, thymus, suprarenal and their corresponding organ weight/body weight ratios with reference to different gestational weeks are explained clearly in the graphs shown below:

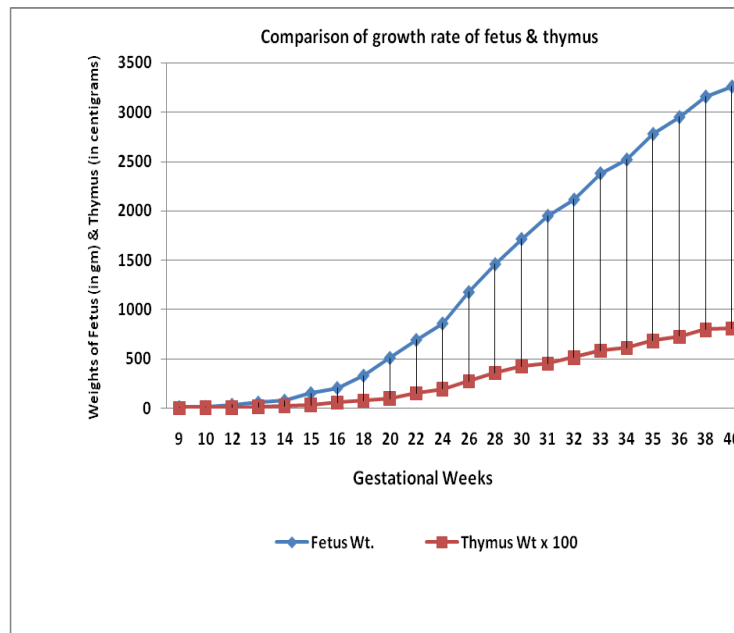


Fig.1: Graph showing the relative growth rate of fetus and thymus weights in human fetuses with increase in gestational weeks. (Weights of thymus are shown in centigrams)

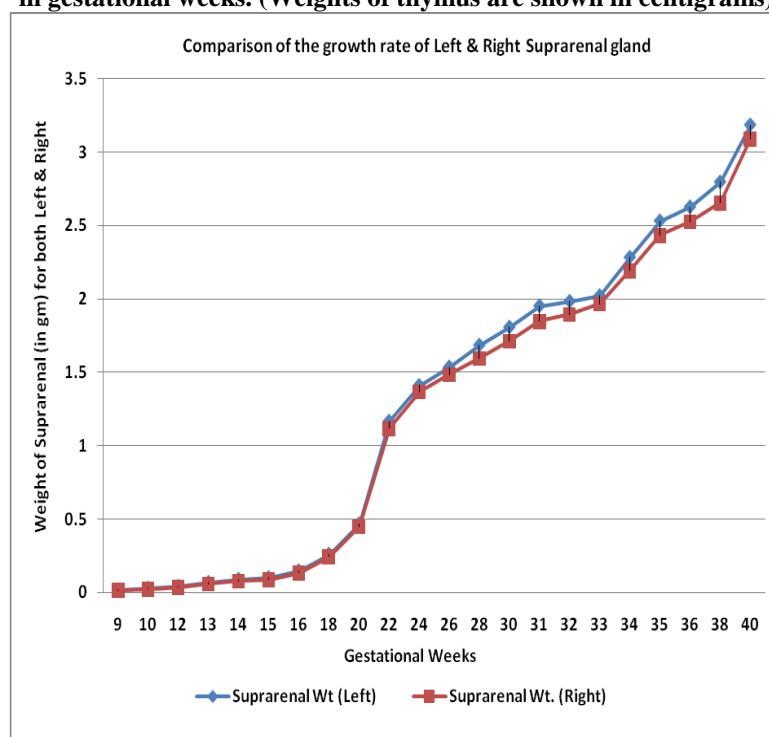


Fig.2: Comparative growth rate of left suprarenal and right suprarenal of human fetus with increase in gestational weeks.

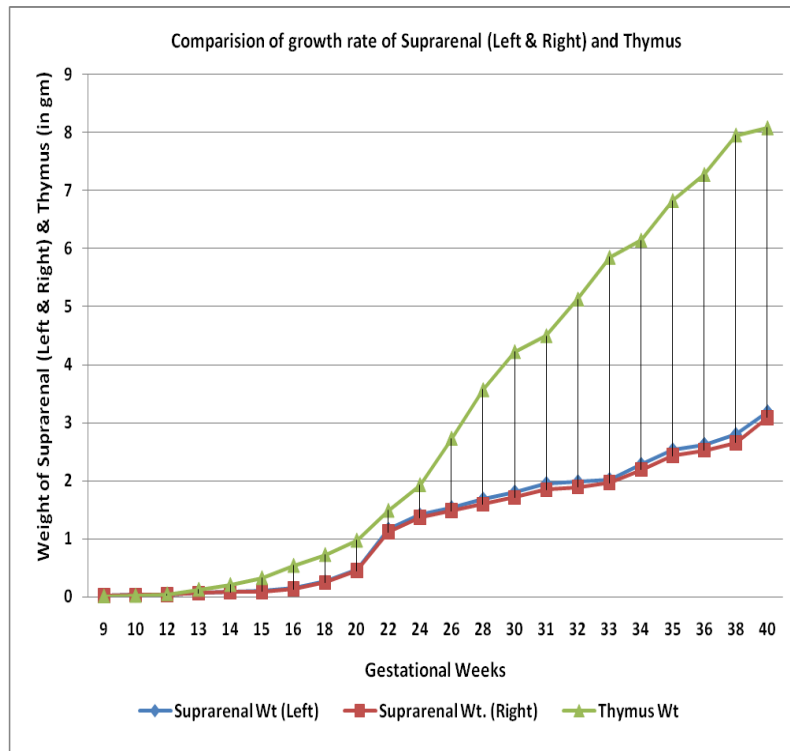


Fig.3: Comparative growth rate of left suprarenal, right suprarenal and thymus weights of human fetus with increase in gestational weeks.

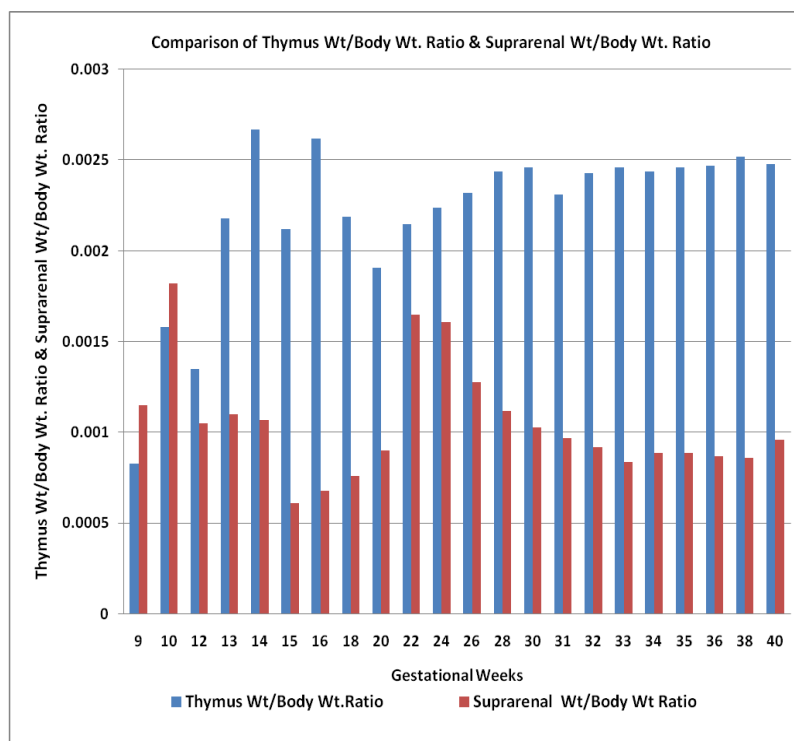


Fig.4: Bar diagram showing the trend of the thymus weight/body weight ratio and suprarenal weight/body weight ratio of human fetus with increase in gestational weeks.

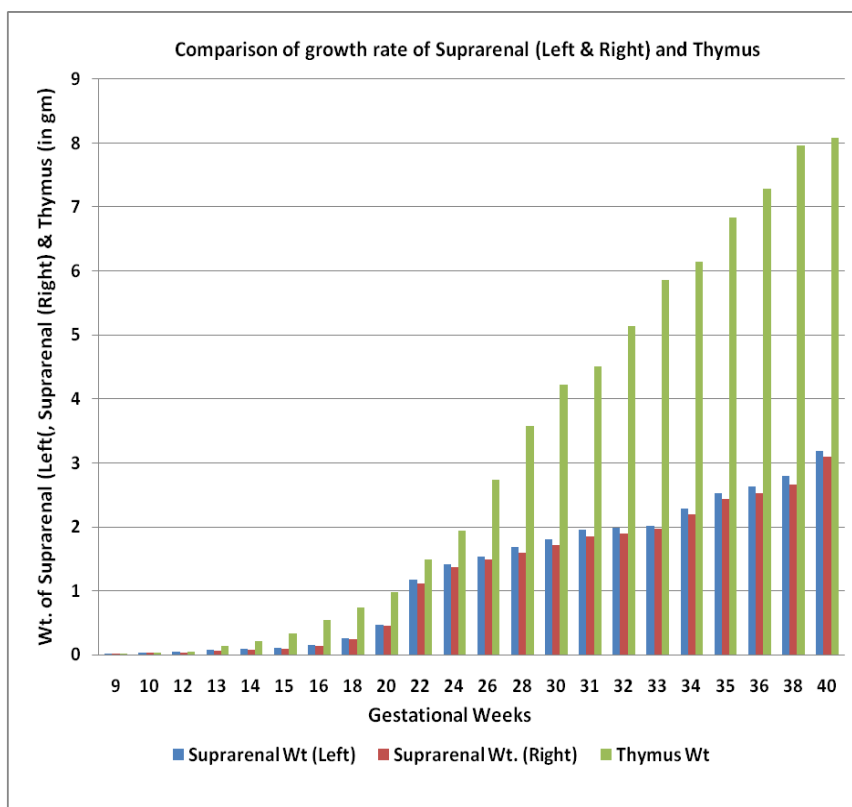


Fig.5: Bar diagram showing the growth rate of suprarenal weight (left), suprarenal weight (right) and thymus weight of human fetus with increase in gestational weeks.

II. Discussion

Studies on comparative works on the growth rate of thymus and suprarenal glands of human fetuses at different gestational weeks have already been conducted by many workers and some significant and interesting findings have also been reported and many more workers are reportedly working on this subject matter. Discussion of the present study focused mainly upon the following sub-headings in the background of the available literatures in the field.

Comparative growth rate of left suprarenal and right suprarenal of human fetuses with increase in gestational weeks:

The growth rate of left suprarenal gland from 22 gestational week onwards was at a slightly faster rate as compared to that of right suprarenal gland (**Fig.2**) and this finding is found in conformity with the finding of Ekholm E and Niemineva K^[17], who reported that the left suprarenal gland was larger in 61.1% of the cases they studied and the right in 26.6 %. Gaillard DA et al^[18] reported that the suprarenal weights increased from 0.2 to 1.5 gm during the 13 to 15 gestational weeks. The left suprarenal was significantly heavier than the right for the same gestational age. Whereas, in the present study, the suprarenal weights increase from 0.2 to 1.5 gm was observed from 13 to 25 gestational weeks, which is somewhat different from the findings of Gaillard DA et al^[18]. This discrepancy may perhaps be attributed due to the difference in the size and samples of the fetuses collected in these two different studies. However, the weights of the left suprarenal glands were found heavier from 24 gestational weeks onwards till 40 week (**Fig.2**). Yet, in another study conducted by Carr BR and Casey ML^[19], it was reported that there was little increase in suprarenal weights between 6 and 12 gestational weeks. Thereafter, the rate of increase in suprarenal weight was rapid. Whereas, in the present study, the growth rate of suprarenal glands increases gradually from 12 to 16 gestational weeks and then increases slightly faster from 16 to 20 weeks. Then, the growth rate is found to be quite rapid upto 22 gestational weeks as can be seen from **Fig. 2**. Thus, our findings are found almost in consistent with the findings of Carr BR and Casey ML^[19].

Comparative growth rate of left suprarenal, right suprarenal and thymus weights of human fetus with increase in gestational weeks:

As can be seen from **Fig.3**, the growth rate of left, right suprarenal glands and thymus was found almost negligible and very insignificant upto 14 week. The thymus growth rate from 14 to 40 gestational weeks was at much faster rate as compared to that of left and right suprarenal glands. There was a gradual growth rate

from 15 to 20 week in case of suprarenal glands, then a moderately steep increase from 20 to 22 week. Thereafter, there is almost a similar gradual growth rate from 22 to 40 week for both left and right adrenal glands, with the left suprarenal gland increasing at slightly faster rate as compared to right suprarenal gland (Fig.3).

Comparison of the growth trend of the thymus weight/body weight ratio and suprarenal weight/body weight ratio of human fetus with increase in gestational weeks:

When compared the thymus weight/body weight ratio with reference to the suprarenal weight/body weight ratio, it was observed that there was a steep rise at 10, 14 and 16 week, then a gradual fall from 16 to 20 week, thereafter a gradual increase from 20 to 30 week and then a fall at 31 week and finally the ratios remained almost constant upto 40 week in respect of thymus weight/body weight ratio (Fig.4). Whereas, G. Mitropoulos et al^[20] in their study reported that the thymus weight/body weight ratio increased from 20 to 30 weeks and then became almost constant. That is, our findings are almost in conformity with the findings of G. Mitropoulos et al^[20] as supported by the graph in Fig.4.

As regards the trend for suprarenal weight/body weight ratio, it was observed that a steep increase from 9 to 10 week, then a steep fall from 10 to 12 week followed by almost a horizontal change upto 14 week and a moderately steep fall upto 15 week, then a gradual increase from 15 to 20 week and a gradual decrease from 22 to 30 week and then became almost constant after 30 gestational weeks, which is also found to be in conformity with the findings of G. Mitropoulos et al^[20] as can be seen from Fig.4.

In our present study, the thymus weight/body weight ratio from 30 to 40 gestational weeks was found to be about 0.0025 and the suprarenal weight/body weight from 30 to 40 gestational weeks was found to be about 0.001 (Fig.4), whereas in the study conducted by G. Mitropoulos et al^[20], it was found to be 0.004 (for thymus) and 0.003 (for suprarenal) respectively. This discrepancy might perhaps be due to the difference of the larger size of the fetuses of the Australian population when compared to the fetuses of Manipuri population of North Eastern States, India, where the general size and weight/height of the Manipuri population are found much smaller and shorter. In their study conducted by G. Mitropoulos et al^[20], it was reported that the thymus are relatively small at 20 gestational weeks, but then showed a striking and unparallel acceleration from 20 to 30 gestational weeks and this finding is supported by the present study as can be seen from Fig.4.

Comparison of the growth rate of suprarenal weight (left), suprarenal weight (right) and thymus weight of human fetus with increase in gestational weeks:

As can be seen from Fig.5, the growth rate of left, right suprarenal glands and thymus was found almost negligible and very insignificant upto 13 week. The thymus growth rate from 13 to 40 weeks was at much faster rate as compared to that of left and right suprarenal glands. There is a gradual growth rate of thymus from 15 to 20 week, then a gradually steep rise from 20 to 40 week. However, there is almost a similar gradual growth rate from 22 to 40 week for both left and right suprarenal glands, with the left suprarenal gland increasing at slightly faster rate as compared to right suprarenal gland (Fig.5).

Some of the limitations of the present study are that this study could have been done with a much larger sample size, as the larger sample size would have improved the spectrum of the findings. Another small and probable limitation is that there might be some inadvertent mistakes, which may have been committed unintentionally by the workers while measuring the weights of fetuses, thymus and suprarenal glands by the electronic weighing machines despite the maximum care taken by the workers.

III. Conclusion

The present study revealed that the thymus growth rate from 14 to 40 weeks was at much faster rate as compared to that of left and right suprarenal glands and there is a gradual growth rate from 22 to 40 week for both left and right suprarenal glands, with the left suprarenal gland increasing at slightly faster rate as compared to right suprarenal gland and these findings are in conformity with the findings of Ekholm E and Niemieneva K^[17]. The study also revealed that there is a gradual increase in thymus weight/body weight ratio from 20 to 30 gestational weeks and then the ratios remain almost constant upto 40 week and in case of suprarenal weight/body weight ratio, there is a gradual decrease from 22 to 30 week and then became almost constant after 30 gestational weeks, the findings of which are almost in conformity with the findings reported by G. Mitropoulos et al^[20].

Another interesting finding of the present study which contrasted the findings of G. Mitropoulos et al^[20] is the discrepancy observed in the thymus weight/body weight ratio as well as in the suprarenal weight/body weight ratio observed from 30 to 40 gestational weeks and the reasons for this discrepancy have been explained clearly under the "Discussion" heading.

Thus, the findings had corroborated and substantiated with the previous findings of different workers and at the same time also contrasted partially as well as moderately with the findings of previous workers as discussed above. This study highlights the need for further research and investigation in the field in the near future. Lastly, we do recommend that the Anatomists should conduct more challenging research. Further studies using larger sample size should be encouraged to strengthen the existing literatures and research data.

Acknowledgement:

The authors express their special thanks to Shri T. Ranjit Singh for computer typing the whole of this original research article.

Conflict Of Interest

The authors declare that there is no conflict of interest in the present study.

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