

# Morphological, morphometric and histological observations in pre and postnatal abnormal human thymuses

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## Abstract

**Introduction:** Very few studies were reported on prenatal and postnatal abnormal thymuses in literature. In the present study, abnormal thymuses were studied for morphological, morphometric and histological features. **Materials and Methods:** A total of 55 thymus glands of both sexes in prenatal and postnatal age groups were collected. Among them 15 prenatal and 02 postnatal thymuses were abnormal. The basis for categorizing as abnormal in prenatal group was bad maternal history in 10 and identifiable foetal abnormalities in 05 cases. In postnatal group, in one case death was due to gas burns and in other due to cerebral malaria. Small bit of tissue from each of the 17 thymus glands were subjected to routine tissue processing, section cutting and haemotoxylin and eosin staining. The sections were observed under binocular microscope. **Results:** The difference in normal and abnormal thymuses and male and females sexes was not significant when tested by  $X^2$  test for proportions. In fetuses of obstructed labor and anencephaly, the thymuses were large in size and heavier than those of normal labor. They presented altered thymic histology. In macerated fetus the weight of thymus is low and also presented altered microscopic picture with irregular cavities. In case of Pre Eclamptic Toxemia, thymus with disturbed architecture and multiple haemorrhages was observed. **Conclusion:** In our study 31% incidence of abnormal thymuses was observed. Among them, those with altered histological features was higher than that reported (1%) in literature.

**Key words:** Anencephaly, Macerated fetus, Pre eclamptic toxemia, obstructed labor.

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## INTRODUCTION

Thymus is one of the primary lymphoid organs of the human body, the bone marrow being the other one. It generates "T" lymphocytes which play an important role in the development of immune system. The gland is most active in puberty and varies in size with age and physiological status. It involutes with advance in age. Its size reduces sharply in malnutrition, infections like

pneumonia and increases in conditions of stress like hypoxia, prolonged labour and during neonatal period. It is normally present in anterior mediastinum behind the sternum, but sometimes ectopic thymic tissues are located in neck region which are to be considered in differential diagnosis especially in pre pubertal population. As limited studies were available in literature on morphological and histological features of thymus in Indian population, this present investigation was carried out as a sample study on prenatal and postnatal age groups for abnormal thymuses. Thymus gland resembles the flowers of thyme plant and appears as warty excrescent. The first case of suffocation due to hypertrophy of the gland was reported by Platter in 1614<sup>1</sup>. Oppenheim proposed an association between myasthenia gravis and thymus<sup>2</sup>. Sauerbruch performed cervical thymectomy<sup>3</sup>. The gland becomes thinner after the age of fifteen although its activity persists into old age<sup>4</sup>. It can be distinguished from surrounding mediastinal fat by the presence of its capsule.<sup>5</sup>

Thymus is prominent in new born than at any time in life.<sup>6</sup> It is one of the earliest to involute after fourteen years of age and this involution seems to be reversible and offers several therapeutic possibilities aimed at improving thymic function in the elders.<sup>7</sup> The thymic activity is influenced by physical state, disease conditions and exposures to chemical substances.<sup>7</sup> Any disturbance in uterine milieu may cause decrease in size. It is maximum in size and heavier than the average in infants who died of anorexia, trauma during labor or immediately after birth. It was smaller in macerated fetuses of comparable weight and in infants who survived only a few days<sup>8</sup>. Appreciable deviation of average weight was associated with certain pathological conditions such as infection, malnutrition, erythroblastosis, anorexia etc.<sup>8</sup> Similarly an increase in size and volume were reported in anencephaly<sup>8</sup>. Vijaya *et al*<sup>9</sup> compared normal thymus and anencephalic thymus and found that anencephalic thymus weighed more than normal one. Mohamed *et al*<sup>10</sup> observed smaller fetal thymuses in pre-eclampsia than those of control. Tooke *et al*<sup>11</sup> stated that prenatal stress associated with P.E.T. and indication for Caesarian section may cause the thymus to shrink. Kendal *et al*<sup>12</sup> reported association between lower weight and lipid thymic weights with long term stressful conditions. They observed higher weights of thymuses in cases of deaths from asphyxia and certain cardiovascular conditions. Boyd<sup>13</sup> observed that thymus involutes in

stress conditions including malnutrition and illness decreasing in weight. Joop van Baarlen *et al*<sup>14</sup> reported that thymus weight was related to duration of acute illness only in prenatal patients and pathologists could estimate the duration of acute disease before death. There are no studies in the literature on morphological, morphometric and histological observations in human abnormal thymuses of a wide age range.

### MATERIALS AND METHODS

Forty five aborted fetal thymus specimens and ten postnatal thymus specimens from Forensic autopsies and anatomy dissection cadavers of S.V.Medical college, Tirupati, Andhra Pradesh were utilized for the present study after approval of Institute ethical committee and informed consent from the next of the deceased. All the physical measurements of thymus namely length, width, weight, location and number of lobes with shape were recorded. Both prenatal and postnatal specimens were further categorized into normal and abnormal specimens. They were categorized as normal if the death was not due to any clinical or pathological condition of the fetus, mother or the adult. Those with presence of such history were categorized as abnormal. Five fetuses with external abnormal features were subjected to detailed fetal autopsy for observing various abnormalities in the organs.

### RESULTS

**Table 1:** Prenatal Thymus Specimens (Age wise and Sex wise Distribution)

Gestational Weeks	Male			Female			Undifferentiated Gonad	Grand Total
	Normal	Abnormal	Total	Normal	Abnormal	Total		
0-16 wks	2	-	2	1	-	1	2	5
>16 wks	13	5	18	12	10	22	-	40
<b>Total</b>	<b>15</b>	<b>5</b>	<b>20</b>	<b>13</b>	<b>10</b>	<b>23</b>	<b>2</b>	<b>45</b>

**Table 2:** Postnatal Thymus Specimens (Age wise and Sex wise)

Age in Years	Male			Female			Total
	Normal	Abnormal	Total	Normal	Abnormal	Total	
0-16	1	-	1	3	-	3	4
>16	3	1	4	1	1	2	6
<b>Total</b>	<b>4</b>	<b>1</b>	<b>5</b>	<b>4</b>	<b>1</b>	<b>5</b>	<b>10</b>

**Table 3:** Origin of Abnormal Specimens of Thymus

Origin of Specimen	No. of Specimens
<b>Maternal History</b>	
1. Pregnancy Induced Hypertension	2
2. Pre Eclamptic Toxoemia	2
3. Cord Prolapse	2
4. Abruptio Placenta	2
5. Polyhydromnios	1
6. Gross Anaemia	1
<b>Fetal Abnormalities</b>	
1. Anencephaly	2

2.	O.E.I.S.Complex	1
3.	Meningocele with Polydactyly	1
4.	Maceration with Ascitis	1

**Table 4:** Morphological and Morphometric Features of Prenatal Abnormal Thymus Gland

Sl. No.	Nature of Abnormality	Age Wk	Sex	Wt. of fetus Kgs.	Thymus Gland						
					Shape	No of lobes	Length cm	Width cm	Thickness cm	Weight gm	Wt. of Thy. x 100/ Wt. of Fetus
1.	Severe P.I.H.	20	M	0.7	Pyramidal	2	2.8	2.0	0.7	1.85	0.26
2.	Polyhydromnia with Mesenteric cyst	22	F	1.2	Pyramidal	2	4.8	4.2	1.7	1.55	0.129
3.	Pre Eclamptic Toxaemia	24	F	0.8	Pyramidal	2	4.4	3.5	1.0	5.1	0.6
4.	Severe P.I.H. Anamia	26	M	1.4	Pyramidal	2	4.3	4.0	0.7	5.7	0.4
5.	Signs of Maceration Hepato splenomegaly Ascitis	28	F	0.85	Pyramidal	2	2.8	3.0	0.4	1.0	0.118
6.	Meningocele, multiple congenital anomalies, club foot, polydactyly	28-30	F	1.5	Pyramidal	4	2.2	2.7	0.3	1.9	0.126
7.	Abruptio placenta	30-32	M	1.0	Pyramidal	3	1.7	2.0	0.6	3.0	0.33
8.	Cord prolapse with footling	32	F	1.1	Pyramidal	2	2.5	4.0	0.8	4.0	0.36
9.	OEIS	32	F	0.8	Pyramidal	2	4.2	3.2	1.0	4.5	0.562
10.	Anencephaly	35	M	2.1	Pyramidal	4	7.0	6.5	1.2	7.8	0.37
11.	PET, foetal bradycardia	36	M	2.3	Pyramidal	2	3.6	3.3	0.6	1.9	0.08
12.	Gross Anaemia of mother	36	F	1.2	Pyramidal	2	4.8	4.2	1.7	4.7	0.395
13.	Anencephaly	38	F	1.2	Pyramidal	2	4.2	2.8	1.0	4.0	0.333
14.	Abruptio Placenta	38	F	2.0	Pyramidal	4	5.2	3.8	1.0	6.4	0.32
15.	Cord Prolapse Shoulder Presentation Obstructed labour	40+	F	3.0	Pyramidal	3	4.5	5.0	0.8	6.1	0.2

**Table 5:** Morphological and morphometric Features of Postnatal Abnormal Thymus Glands

S. No.	Age Yrs.	Sex	Body Wt.	THYMUS GLAND						
				Shape	No. of lobes	Length Cm	Width Cm	Thickness Cm	Weight Gm	Wt. of Thy.x100/ Wt. of adult
1	20	Male	45 kg	Flat	2	9.5	6.5	0.5	17.2	0.038
2	30	Female	50 kg	Flat	2	12.0	6.5	0.8	22.0	0.044

**Table 6:** Comparison between abnormal thymus and normal of same age in the local population by same authors with literature<sup>15</sup>

S.No.	Abnormal/ abnormal	Age wks	Sex	Wt.of fetus kg	Length. of thy.cm	Wid. of thy. cm.	Thicknessof thy. cm	Wt. of thy. gm.	Thy. index
1.	P.E.T (present study)	28	Female	0.8	4.4	3.5	1.0	5.1	0.64
	Normal <sup>15</sup>	28	Male	1.2	3.0	2.8	0.6	2	1.6
	P.E.T <sup>11</sup>	36	Male	2.3	3.6	3.3	0.6	1.9	0.08
	Normal <sup>11</sup>	36	Male	2.6	4.0	6.2	0.6	7.8	0.3
2.	Anencephaly (present study)	35	Male	2.12	7.0	6.5	1.2	7.5	0.35
	Normal <sup>15</sup>	36	Female	1.2	4.0	4.2	1.1	5.4	0.45
3.	Abruptioplacenta (present study)	38	Female	2.0	5.2	3.8	1.0	6.4	0.32
	Normal <sup>15</sup>	38	Female	1.2	4.2	2.8	1.0	4	0.33
	Abruptioplacenta <sup>12</sup>	30-32	Female	1.0	2.1	2.0	0.6	3	0.3
	Normal <sup>12</sup>	32	Female	1.3	5.8	5.2	1.2	12	0.92
4.	Macerated fetus (present study)	28	Female	0.85	2.8	3.0	0.4	1.0	0.12
	Normal <sup>15</sup>	28-30	Female	1.5	2.2	2.7	0.6	1.9	0.126

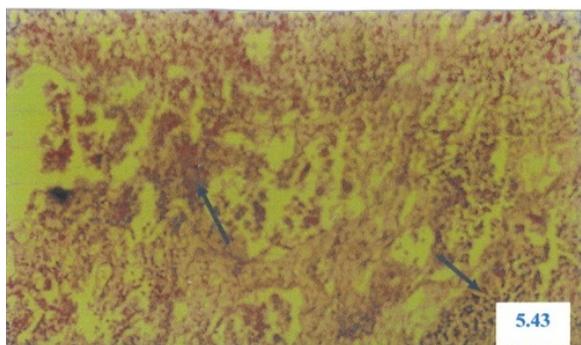


Figure 1

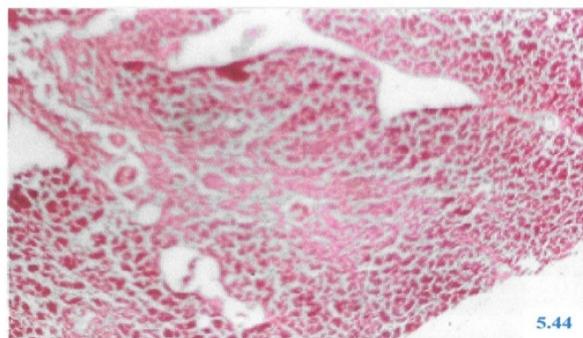


Figure 2

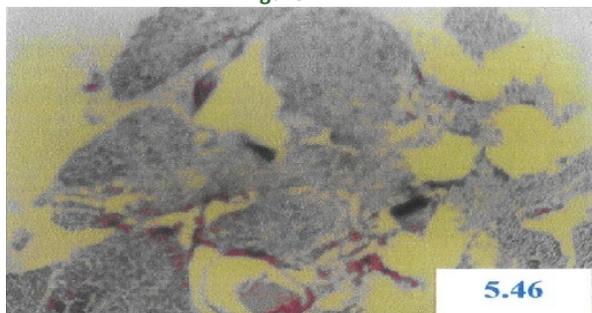


Figure 3

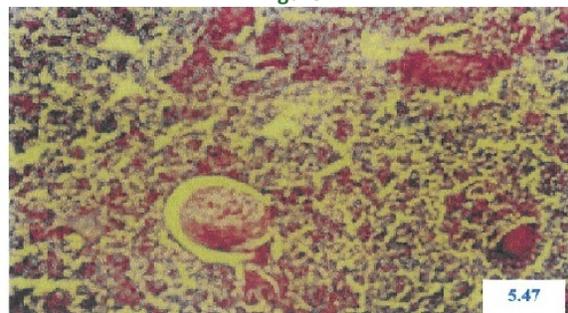


Figure 4

**Legend**

**Figure 1:** Thymus – Pre eclamptic Toxemia (PET) – Cortex and medulla demarcation not seen – Haemorrhages (arrows) X 200.

**Figure 2:** Thymus – Anencephaly – wider cortex increased lobular size X 200.

**Figure 3:** Thymus – macerated foetus wide irregular cavities X 200.

**Figure 4:** Thymus 15 years – Cortico medullary demarcation not seen, increased number of lymphocytes X 200.

All the fifty five thymuses were tabulated in tables 1 and 2 based on sex and age. Among these specimens fifteen were abnormal in prenatal and two in postnatal groups. This difference was not significant when analysed by  $\chi^2$  – test for proportions. Similarly although higher proportions of abnormal thymus glands were observed among the females than in males, the difference was also not significant. Among the 15 abnormal prenatal specimens, 10 were from the mothers with bad obstetric history and rest had external fetal abnormalities such as two cases of anencephaly, one case each of O. E. I. S. (omphalocoel, exstrophy of cloaca, imperforate anus and skeletal abnormalities), meningoceol and macerated foetus with ascitis (Table.3). Among the postnatal, one was a case of death due to gas burns and other a case of cerebral malaria.

The morphological and morphometric features of the prenatal and post natal abnormal thymus glands were presented in Table 4 and 5. Morphological and morphometric parameters of abnormal thymus glands were correlated with the normal thymus glands in the same population reported previously<sup>15</sup> (table.6). In the section of thymus of PET disturbed normal architecture with absence of cortico-medullary demarcation and plenty of haemorrhages were observed (Fig.1). In the

fetuses of Abruption placenta the thymuses were large in size and heavier than those of normal labor and section presented disturbed normal architecture and medullary tissue could not be identified in histological picture.

In Anencephalic fetuses the thymuses were large in size and heavier than those of normal labor with a wider cortex (Fig.2). Thymus in macerated foetus is of less weight, presented lack of characteristic architecture and wide irregular cavities without any cells histologically(Fig. 3). Adult thymus from Road Traffic Accident case presented abnormal weight (54gms) and no demarcation between cortex and medulla being uniformly infiltrated with lymphocytes(Fig.4).

**DISCUSSION AND CONCLUSION**

Among 55 thymuses observed 15(27%) were from those with maternal bad obstetric history or abnormal foetuses. In an earlier study Bale and Sotelo - Avila (1993) reported 34 (1%) abnormal cases in 3226 observed<sup>16</sup>. Shukle *et al.*, in 2004 observed only 90 cases of abnormal thymuses reported in literature since 1901<sup>17</sup>. Higher incidence of abnormal thymuses in this present study may be the basis on which the thymuses were categorized as abnormal. Among the prenatal group all the glands were pyramidal in shape. The two

postnatal abnormal glands were flat. 11 were having 2 lobes, two presented 3 lobes and four with 4 lobes. The categorization of 15 thymuses as abnormal was sustained by subsequent gross and microscopic observations as variations in morphology, morphometry and histological features were observed only in PET,abruption placenta, macerated foetus and anencephalic fetuses (7/15 abnormal foetues). Thus it can be concluded that bad maternal history or even the gross foetal abnormalities may lead to anomalies in the anatomy of thymus gland. In fetuses born due to obstructed labor and anencephaly, the thymuses were large in size and heavier than those of normal labor with altered thymic histological picture. The macerated fetus showed thymus of less weight and altered microscopic picture with irregular cavities. In cases of Pre Eclamptic Toxemia, thymus presented disturbed histologically structure with number of haemorrhages and weighed less when compared with normal labor because of prenatal stress involved<sup>11</sup> and hypothalamo pituitary adrenal axis (HPA)<sup>10</sup> and weighed more as it was death due to asphyxia<sup>12</sup>. In abruption placenta, thymus was larger in size and heavier than that of normal labor but less in weight because there was long term stress conditions<sup>12</sup>. In road traffic accidents the thymus was heavier because of sudden death<sup>12</sup>. Studies involving large number of samples are required to support or refute this inference. The present observations on abnormal thymuses would be helpful for gynecologists and interventional radiologists to prepare for delivery procedures for pregnant ladies.

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