Section: Anatomy

Original Research Article

A STUDY ON HISTOGENESIS OF HUMAN FOETAL ADRENAL CORTEX

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Abstract

Background: To study the histogenesis of the adrenal gland in human foetuses. Microscopically the adult suprarenal gland has two zones cortex and medulla. The cortex is further divided in to zona glomerulosa, zona fasciculata and zona reticularis. These zones are different both functionally as well as morphologically. The aim of this study is to investigate the histological features of foetal suprarenal gland, its development and differentiation mainly the permanent cortex. **Materials and Methods:** 30 foetuses of different gestational ages ranging from 16 weeks to 32 weeks products of terminated pregnancies under Medical Termination of Pregnancy, MTP Act of India, 1971 and stillbirths were collected from the Department of Obstetrics and Gynaecology, Thanjavur Medical College, Thanjavur utilised for the present study with permission from the Institutional Ethical Committee. **Result:** The main mass of the human adrenal gland during foetal period is foetal cor tex, which disappears during the first year of life. By 12 weeks of gestation fetal suprarenal gland is composed of 2 zones namely the permanent cortex and foetal cortex. The capsule was identifiable at 12 weeks of gestation. By 13-36 weeks of gestation, fetal adrenal gland is composed of 3 zones. They are permanent cortex, transitional zone and fetalcortex.after 32 weeks, the fetal cortex starts involuting. **Conclusion:** In the microscopic study of foetal suprarenal gland, two distinct zones could be identified, permanent and fetal cortex. The zona glomerulosa and zona reticularis are developed from permanent cortex. The microstructure of adrenal cortex is very important for the understanding of adrenal disorders and may show lightening on regenerative medicine.

INTRODUCTION

The adrenal gland was described by BartholomaeusEustachius in 1563.[1] Suprarenal glands are the paired endocrine glands situated on upper pole of each kidney. They are flattened bodies, golden yellow in colour, situated retroperitoneally on the posterior abdominal wall, on each side of the vertebral column at the level of 12ththoracic vertebrae.

In late 1800s Arnold and Gottschu (1883) divided the adrenal cortex into 3 Zones.[2]

Starklowa and Wegrzynowski first described a special region of the Cortex in fetal adrenal gland, called fetal cortex.[3]

The permanent adrenal cortex is an active endocrine organ in which most steroidogenic activity is exerted in a specialized cortical compartment known as the fetal zone, a unique feature of fetal adrenals in humans and some higher primates but not in other species such as rodents and sheep.

The adrenals secrete cortisol in response to adrenocorticotropic hormone (ACTH) as early as week 8 of gestation, although the main steroids produced in fetal life are dehydroepiandrosterone (DHEA) and its sulphate (DHEAS), which act as substrates for placental estrogen production.[4]

The main mass of the human adrenal gland during foetal period is foetal cortex, which disappears during the first year of life.[5]

By 12 weeks of gestation fetal suprarenal gland is composed of 2 zones namely the permanent cortex and foetal cortex.

By 13-36 weeks of gestation, fetal adrenal gland is composed of 3 zones. They are permanent cortex, transitional zone and fetal cortex.

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Chromaffin cells start appearing by 10th week of intrauterine life.[6]

The aim of this study is to investigate the histological features of foetal suprarenal gland, its development and differentiation mainly the permanent cortex.

MATERIALS AND METHODS

30 normal fresh fetuses, 14 male and 16 female of different gestational age groups ranging from 12 weeks to 32 weeks collected from Department of Obstetrics and Gynaecology, Thanjavur Medical College, Thanjavur.Ethical committee clearance and informed consent was obtained.The fetuses were products of terminated pregnancies by medical termination of pregnancy under MTP act of India, 1971 and still birth.Foetuses free from gross anatomical abnormality were selected for the study.

the foetuses were dissected and the adrenal gland specimen were subjected to routine histopathological procedures and staining. The stained slides were studied under binocular research light microscope (Magnus) using 4x, 10x, and 40 x objectives and analyzed.

30 foetal suprarenal glands ranging from 12-32 weeks of gestational age were considered and classified into 5 groups. [Table 1]

RESULTS

The appearance of various cortical layers in various gestational age groups were noted, studied and analyzed under the following headings.

- Capsule
- PermanentCortex
- FoetalCortex

Capsule

On light microscopy the capsule was identifiable at 12 weeks of gestation.

At 17 to 20 weeks of Gestational age the capsule is thicker and blood vessels are seen.

At 21 to 25 weeks of gestational age there is no change in the capsule.At 26 to 28 weeks of gestation, well developed capsule, which surrounds the entire gland.

At 29 to 32 weeks of gestation trabeculae extending from the capsule and carries the sinusoidal vessels along with it.

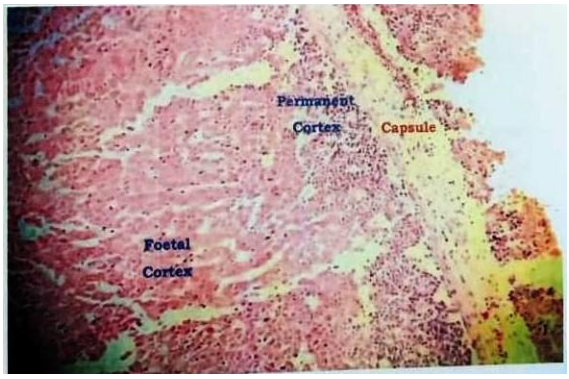

Figure 1: 16 weeks- hematoxylin and eosin- 100 magnification

Permanent cortex

Group I (12 to 16 weeks)

Superficial darkly stained narrow zone was observed.This zone is called as permanent cortex or Definitive cortex.The cells of the permanent cortex are small and basophilic.It occupies 1/10th of the total cortex. [Figure 1]

Group II (17 to 20 weeks)

The cells were widely placed towards the medulla.The cells are arranged in tightly packed columns towards the outer zone of foetal cortex. [Figure 2&3]

Figure 2: 18 weeks- hematoxylin and eosin- 100 magnification

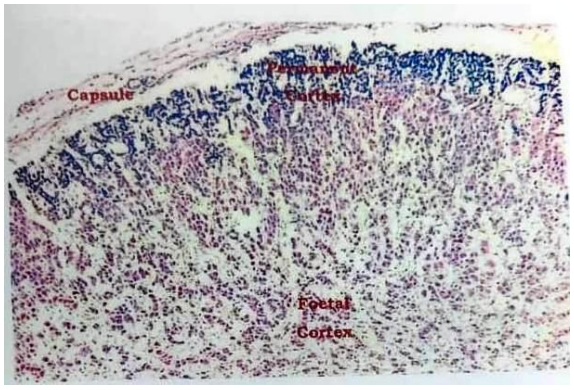

Figure 3: 20 weeks- hematoxylin and eosin- 100 magnification

Group III (21 to 24 weeks)

At the junction between the permanent and foetal zone at some places cords of cells were seen extending from permanent cortex into foetal

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cortex.This zone is referred as transitional zone. [Figure 4]

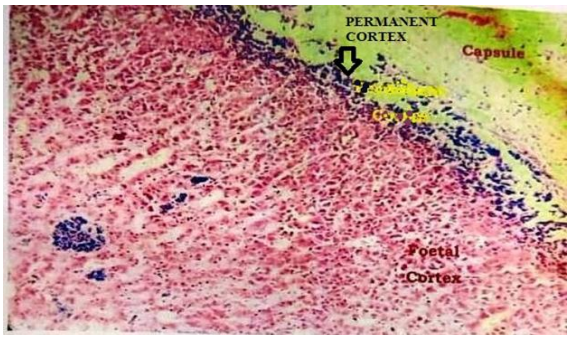

Figure 4: 24 weeks- hematoxylin and eosin- 100 magnification

Group IV (25 to 28 weeks)

The thickness of definitive cortex increases gradually from 25 weeks.It occupies 1/9th of the total cortex. [Figure 5]

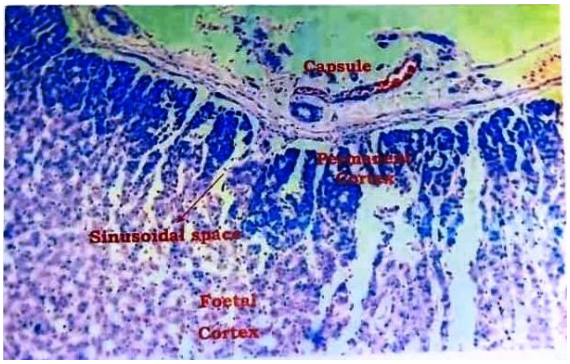

Figure 5: 28 weeks- hematoxylin and eosin- 100 magnification

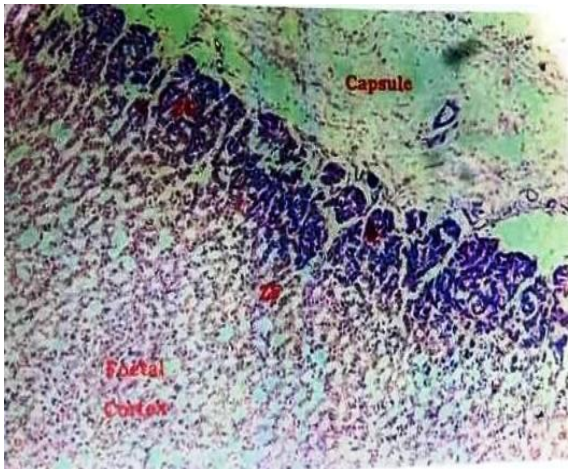

Figure 6: 32 weeks- hematoxylin and eosin- 100 magnification

Group V (29 to 32 weeks)

The cells of permanent cortex are arranged in arched / glomeruli like pattern and the permanent cortex differentiate into 2 layers namely zona glomenulosa and zona fasciculata.It occupies 1/4th total cortex.

Zona fasciculata cells are one or two cell thick.These are arranged in fascicular manner and sinusoidal spaces lies in between them. [Figure 6]

Foetal Cortex

Group I (12 to 16 weeks)

Foetal cortex lies deep to the permanent cortex.Foetal cortical cells are large and eosinophilic and 7 to 8 layers thick.It occupies the 9/10th of the total cortex.

Group II (17 to 20 weeks)

The foetal zone is dominant and composed of large eosinophilic cells.The cells were arranged in fascio reticular pattern and 6 to 7 layers thick.It occupies the 8/9 th of total cortex.

Group III (21 to 24 weeks)

The thickness of foetal cortical cells are starts reducing.

Group IV (25 to 28 weeks)

Foetal cortical cells show marked spongy appearance. This spongy appearance indicates the involution of foetal cortex.

Group V (29 to 32 weeks)

Further reduction of foetal cortical cells was seen.It occupies 3/4th of the total cortex.

During 12 to 16 weeks the foetal suprarenal cortex appeared as 2 layers namely, the permanent cortex and the foetal cortex. The cortex was covered by thin capsule. Medulla was ill defined.

By 22ndweek, the transitional zone appeared between the permanent cortex and the foetal cortex.The cortex was three layered at this stage from periphery to central permanent cortex, transitional zone and foetal cortex.

By 22 to 24 weeks foetal cortex started to reduce. The cells were arranged in 5 to 6 layers with lightly staining eosinophilic appearance.

By 29 to 32 weeks cells of the permanent cortex was arranged in glomeruli/arched like pattern.The cortex was 3 layered namely zona glomerulosa, zona fasciculata and foetal zone.The permanent cortex differentiated into two layers namely zona glomerulosa and zona fasciculata.

The ratio between the permanent cortex and foetal cortex was 1:4. This was maintained in all stages of the development.

The zona reticularis was not yet differentiated until 32 weeks in the present study.

Table 1: Grouping of Foetusesby Gestational Age

Groups	Age in Weeks	No of fetuses
I	12 to 16 weeks	4
II	17 to 20 weeks	7
III	21 to 24 weeks	4
IV	25 to 28 weeks	12
V	29 to 32 weeks	3
Total		30

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Table 2: Observation of different layers in present study

Parameters	Group I 12 to 16 wks	Group II 17 to 20 wks	Group III 21 to 24 wks	Group IV 25 to 28 wks	Group V 29 to 32 wks
Capsule	identifiable	thicker	Thicker and blood vessels are seen	Well developed	Trabeculae extending from it.
Permanent cortex	Narrow zone	Present	Thickness Starts increasing	Markedly increased thickness	Differentiated into ZG and ZF
Foetal cortex	thicker	thicker	Starts reducing	Present but thin	Starts involuting
Transitional zone	absent	absent	present	present	present

DISCUSSION

In the present study, the development of human foetal suprarenal gland is analyzed under the following histological patterns.

Capsule

In the present study the capsule starts appearing at 12th week of gestation as a thin strip and as age advances it increases in thickness.At 16-22 weeks the capsule is thicker and better defined with blood vessels in it.Similar observations were stated by GTN sangma et al (2008). However, the cortex is not encapsulated entirely until later in foetal life.[7]

Throughout the gestational period in our study, it was observed that the vascularity of the gland gradually increased from 9thto 32ndweek.

The study done by khayati et al in 2013 in foetuses of 12thto 28thweek reported that the sinusoidal vessels increase with the gestational age.[8]

The study done by Malleswara et al observed the capsule at 12 weeks of gestation.[9]

Foetal cortex

Rapid growth and changes within the different zones of foetal suprarenal gland is primarily reflection of the growth of the unique foetal zone.

In the present study it was observed that a larger part of cortex was contributed by foetal cortex (i.e., 9/10th) at 12thweek 8/9that 20thweek and 3/4that 32ndweek of gestation.

The study of Benirschke et al (1956) reported that foetal cortex formed 4/5th of adrenal cortex.[9]Miriam (1940) opined that the foetal cortex is 2 to 5 times as wide as true cortex and a few medullary cells are present in groups in the centre of the gland.[10]

The cells of foetal cortex were large polyhedral with eosinophilic cytoplasm and round vesicular nuclei.[11,12]These findings were similar to works done by Benirschke (1956), Turkel and Itabashi (1974) and mesiano and Jaffe (1997), GTN Sangma (2008), Khayatisantram (2013), Mallesware Rao (2015) Kulkarni R (2017).

In the present study it was observed that cells in the outer part of foetal cortex were arranged in the form of longitudinal column separated by capillaries, whereas the cells in the inner part were arranged in the form of a network with sinusoidal spaces in between.Because of this arrangement of foetal cortical cells Uotila (1940) described the foetal cortex of suprarenal gland as fasciculoreticular layer which he found from 7thweek onwards.[13]

In the present study the involution of foetal cortex starts by the 28thof gestation.Whereas keene et al (1927) stated that degeneration of foetal cortex started during lasts 10 weeks of intrauterine life and was completed by the end of 1styear.

Definitive cortex

Throughout the gestational period definitive or permanent forms, a narrow subcapsular zone.These findings were corroborative with the findings of Benirschke (1956), GTN Sangma (2008).They found that definitive cortex is 1/5th of the total adrenal tissue.

MC Intosh (1960) described the outer permanent zone forming only 20% of whole cortex.[14]

In the present study we observed that at the 12th week the definitive cortex forms 1/10th of the adrenal cortex, at 28thweek it is 1/9th and at 32nd week it measured 1/4th.

The cells of definitive cortex are small, polygonal with basophilic cytoplasm and euchromatic nuclei.The findings were similar to that of Benirschke et al (1956), Turkel and Itabashi (1974) and Mesiano and Jaffe (1997).

Bocian - Sobkowaska J et al (1993) have found that the zona glomerulosa and outer part of zona fasciculata begin to form by 20th week of gestation.[15]

The works of mesiano and jaffe (1997) and sangma et al (2008) mentioned that the cells of definitive cortex took the appearance of adult zona glomerulosa in 30thand 28thweek respectively.[16]

According to study by kulkarni the ratio between the permanent and fetal cortex is 1:4.[17]

According to our study the outer zone with dark and deeper stains showed an arc to acini arrangement of cells from 32nd week onwards and differentiated to zona glomerulosa and zona fasciculata.

Transitional zone

Mc Nutt and jone's (1970) reported that the transitional zone appeared between the permanent and foetal zone by 14th week of gestation.[18]

Mesiano and jaffe (1997) described the transitional zone as a zone of finger like columns of cells extending from definitive cortex to foetal cortex.[16]

In present study we found the presence of transitional zone from 21stweek onwards.

CONCLUSION

In the microscopic study of foetal suprarenal gland, three distinct zones could be identified zona glomerulosa, zona fasciculata and foetal zone.The arrangement of cells in the definitive cortex changed

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from the discrete cells and clusters to well-formed glomerulus like pattern in zona glomerulosa layer.In fascicular layer, the cells were arranged in fascicular pattern and sinusoidal spaces lies in between.

The changing pattern of definitive cortex to the foetal cortex with increasing gestational age was 1/10th at 12th week, 1/9th at 28th week and 1/4th at 32nd week of gestation.

Adrenal cortex plays a pivotal role, mainly through steroidogenesis, in the regulation of intrauterine homeostasis and in fetal development and maturation. The steroidogenic activity is characterized by early transient cortisol biosynthesis, and extensive production of dehydroepiandrosterone and its sulfate, precursors of placental estrogen, during most of gestation.

Failure of adrenal function is not compatible with survival. Treatment of all forms of adrenal insufficiency consists of replacement of steroid hormones, e.g. mineralocorticoids and glucocorticoids as soon as the diagnosis is made. This can prevent life-threatening adrenal crisis.[19]

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