Journal of the Anatomical Society of India 65 (2016) 75–82

Contents lists available at ScienceDirect

Journal of the Anatomical Society of India

journal homepage: www.elsevier.com/locate/jasi

Original Article

Comparative microanatomy of suprarenal gland of anencephalic and normal fetuses of different gestational age groups

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ARTICLE INFO

Article history:
Received 20 May 2016
Accepted 1 February 2017
Available online 21 February 2017

Keywords:
Suprarenal gland (adrenal gland)
Permanent cortex
Fetal cortex
Medulla

ABSTRACT

Sixty suprarenal glands (both right and left) of different gestational age groups were studied to see the cytoarchitecture of the normal and anencephalic fetuses. The present study was carried out in the Department of Anatomy, Government Medical College & Hospital, Chandigarh. The material for the study consisted of 60 spontaneously aborted human fetal specimens from 12th to 28th weeks of gestational ages (30 – normal fetuses, 30 – anencephalic fetuses). The suprarenal glands were taken from fetal specimens for histological study. The staining was done by hematoxylin and eosin. Histologically, it was observed that suprarenal gland has a superficial narrow zone of darkly stained cells underneath the capsule, which was the permanent cortex and a deeper lighter zone called the fetal cortex. The changes were seen in thickness of capsule, medulla and the layers of the cortex and these layers were compared with the anencephalic suprarenal gland. The study will establish the micro development of suprarenal gland inhuman fetuses in North-West Indian population. The arrangement of cells in the permanent cortex changed from the discrete cells and clusters to well formed glomerulus like structure with increasing gestational period. Fasciculoreticular zone of the fetal cortex decreased in thickness as gestation advanced. The cells were arranged in columns extending deeper into the cortex toward medulla. Sinusoidal vessels increased in number and were 34 μm wide at 11–15 weeks and decreased to 15 μm at >25 weeks gestation. In the medulla, the ganglionic cells were 3–4/field initially which increased to 25–30/field in later gestation period. Few cells showed vacuolization at 11–15 weeks and there was presence of fibrous zone in the medulla consisting of collagen fibers with fibroblasts at >15–20 weeks suggesting early degenerative changes whereas in anencephalic fetuses the medulla was observed to be bulkier as compared to permanent cortex. The fetal cortex was observed till 20 weeks of gestation but after 20 weeks fetal cortex diminished.

1. Introduction

The suprarenal gland plays an important role in survival and maintenance of internal milieu. Its slightest alteration in function can lead to major life threatening consequences. The structure of suprarenal gland undergoes a massive change during its development and growth.[1] In earlier stages fetal cortex grows maximum, followed by regression which paves way for the appearance of adult cortex. In addition, the changes are in the thickness of capsule, permanent cortex and fetal cortex.

Anencephaly is neural tube defect during early embryogenesis in which cranial vault over vertex is defective. It is one of the commonest disorder of neural tube occurring 1 in 1000 human pregnancies associated with failure of endocrine organ development like hypoplastic pituitary, adrenal insufficiency, adrenocortical hypoplasia, etc.

Adrenal cortical atrophy was well known to occur in anencephalic fetuses and may be due to involution of the fetal zone of the fetal cortex as a result of the absence of normal hypothalamic-pituitary function. The major secretory product of the definitive zone is cortisol, and the major product of the fetal zone is dehydroepiandrosterone sulfate (DHAS), which is transformed by the placenta to form several estrogens. In the anencephalic fetus the suprarenal gland has been shown to develop normally until approximately gestation week 20, at which time the fetal zone undergoes premature involution. The definitive zone remains and thus comes to lie close to the medullary tissue. As a result of the decreased fetal zone, the production of DHAS is significantly reduced.[7,8]

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http://dx.doi.org/10.1016/j.jasi.2017.02.007
0003-2778/

Table 1
Grouping of normal and anencephalics fetuses according to gestational age.

Groups	Gestational age	Number of fetuses	
		Normal	Anencephalic
A	11–15 weeks	5	5
B	15–20 weeks	9	12
C	>20–25 weeks	10	9
D	>25 weeks	6	4

Therefore an attempt was made to assess histological changes in suprarenal gland of anencephalic fetuses and its comparison with the normal suprarenal gland in different gestational age groups.

2. Material and method

The material for the study consisted of 60 human fetuses (30 – normal, 30 – anencephalic) ranging from 12th to 28th weeks of gestational ages which were sent by the Department of Obstetrics & Gynaecology, to Department of Anatomy, GMCH, Chd for routine fetal autopsy. Consent for the autopsy and relevant history from the parents was taken. The suprarenal glands were dissected out, removed and fixed in 10% formalin for 72 h. The specimens were divided into four groups according to the gestational age as follows and processed for histological examination. The study was carried out in the Department of Anatomy, Government Medical College & Hospital, Chandigarh (Table 1).

Wedge shaped section was taken from surface to the hilum and paraffin embedding was done. Further 5 μm sections of tissues were processed for hematoxylin and eosin stain, Picosirus red for organization of collagen and reticulin fibers, Singh's modification of Masson–Hamperl argentaffin technique for chromaffin cells, IHC was done via ABC technique. Block was prepared, slides were coated with polylysine and 4 μm sections of tissues were taken on slide, 3 changes of xylene and alcohol was given. Then blocking step with endogenous peroxidase was done, retrieval was done in pressure cooker, primary antibody S-100 (polyclonal rabbit, dako), was put on the slide for sustentacular cells, then secondary antibody (monoclonal mouse, dako) was put. Slides were dipped in hematoxylin, then mounted with DPX.

All the slides were examined under Olympus microscope (proj res cap pro.2.9.0.1.ink) and photodocumentation was done.

3. Results

3.1. Group A (11–15 weeks)

Capsule: In normal suprarenal gland the collagen fibers were compactly arranged initially then the fibers were loosely arranged throughout the periphery measuring on an average 54 ± 3.2 μm (28–59 μm), there was presence of fibroblasts and blood vessels in it.

In anencephalic fetuses the capsule was not well defined and it measured on an average 57 μm (24–62 μm) in the periphery, there was no statistically significant difference between both the capsules (Fig. 1a). In the capsule there was presence of clusters of small rounded cells, with dark single pynotic nucleus and scarce cytoplasm. These clusters of cells were compactly packed, oval in shape, avascular. These cells were known as sympathogonia cells (S) (Fig. 2). In anencephalic suprarenal glands the capsule was made up of dense collagen fibers, blood vessels, fibroblasts, sympathogonia cells (S) (clusters of chromaffin cells).

3.1.1. Permanent cortex

Immediately deep to capsule a superficial strip of dark zone the permanent cortex. Cells in this zone were arranged in U shape/clusters/arched/some extended in short cords in both anencephalic and normal fetus. The cells were round/oval in outline, basophilic, closely packed cells with scanty cytoplasm. The cell cluster comprised of two kinds of cells majority were dark staining with basophilic, scanty cytoplasm interspersed with few light staining smaller cells (Fig. 3).

In anencephalic fetuses in addition to above two cell types variable size aggregates of chromaffin clusters were scattered in permanent cortex. These cells were rounded cells, with single dark pyknotic nucleus and scarce cytoplasm. These aggregates appear as islands (darker) in surrounding as compared to relatively lighter

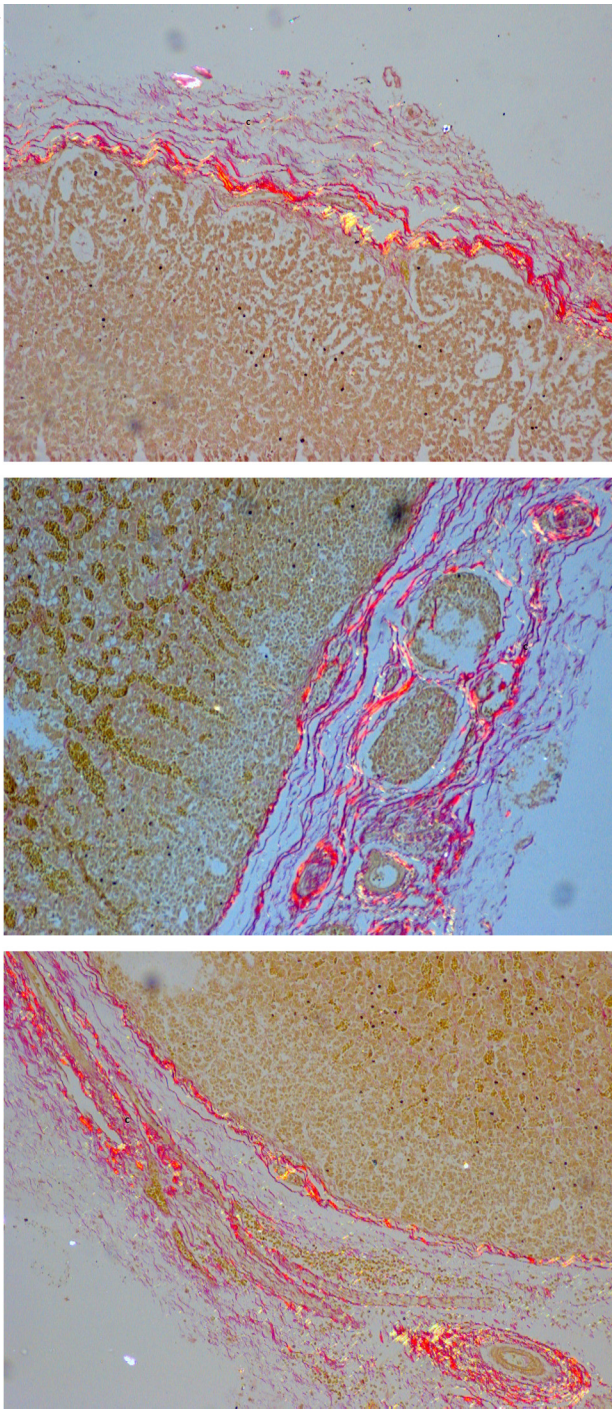

Fig. 1. Arrangement of capsule (C) in anencephalic fetuses gland at 15 weeks (a), 22 weeks (b) and 26 weeks (c) (H&E; ×20).

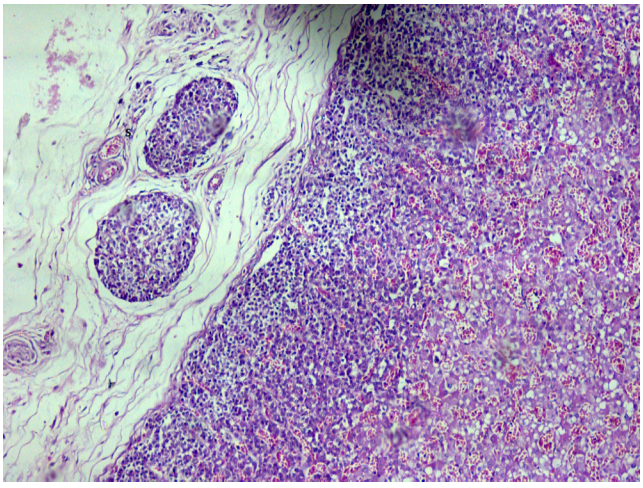

Fig. 2. Presence of cluster of sympathogonia cells (S) in the capsule of anencephalic fetuses at 15 weeks (H&E; ×20).

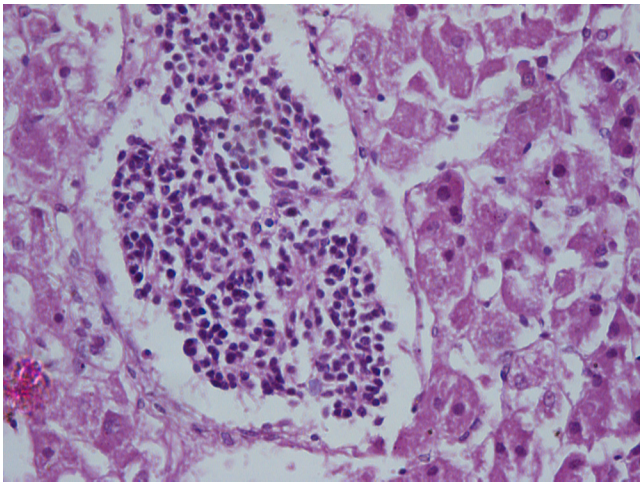

Fig. 4. Sympathogonia cells in cluster at 15 weeks (H&E; ×20).

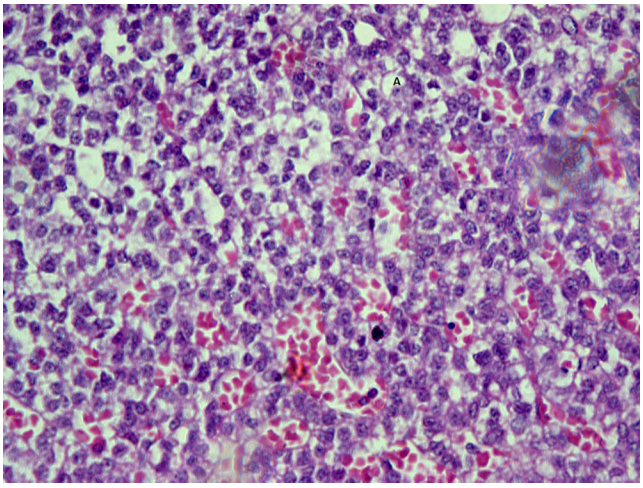

Fig. 3. Cells of permanent cortex round/oval basophilic, closely packed cells with scanty cytoplasm with presence of adipose cells (A) and blood vessels at 12 weeks in normal fetuses.

staining background. These clusters of cells were compactly packed, oval in shape, avascular. The cells in the clusters consisted of basophilic cells these clusters were present directly on the wall of sinusoids. These cells were known as sympathogonia cells (Fig. 4). The average size of clusters was in the range of 120–240 μm, these were 7–8 per field and was present throughout the cortex. Scattered amongst cells of permanent cortex there were aggregates of adipose cells, these cells were lying singly and some were aggregated into groups.

In anencephalic fetuses permanent cortex had lot of capillaries 15–20/field which was more as compared to normal fetuses 4–5/field.

The average thickness of permanent cortex in normal fetuses was 31.36 ± 3.43 μm (range 18.5–32.7 μm) which was less than in anencephalic fetuses 37.78 ± 4.6 μm (range 19–39.4 μm). The difference was not statistically significant (Fig. 5a, Table 2).

3.1.2. Fetal cortex

Deep to the dark zone there was a light zone, the fetal cortex. Cells in this zone were polyhedral with eosinophilic cytoplasm, nuclear chromatin was arranged in irregular clumps the cells were arranged in cords in both the glands (Fig. 6). Fasciculoreticular zone was 6–7 cell layered thick in normal fetuses whereas in anencephalic fetuses the fasciculoreticular zone was 1–2 cell layered thick. This zone was separated by sinusoids. These cells were arranged in columns extending toward the medulla.

But in anencephalic fetuses in this zone we also observed large oval shaped cells, whose nuclear chromatin was basophilic and single or multiple acidophilic cytoplasmic inclusion bodies darkly stained nucleus which was centrally placed, few cells were binucleated. Blood vessels were observed in both the glands (Fig. 5a).

The chromaffin cells which were large epithelioid cells which were arranged in clusters and cords, they contain granules that stained intensely with Singh's modification of argentaffin technique in both the glands (Fig. 7a).

Fetal cortex average thickness in anencephalic fetuses 26 ± 4.6 μm (range 11–26 μm) and 164.4 ± 5.6 μm (range 100–165 μm) in

Table 2
Thickness of permanent cortex is marginally greater in anencephalic fetuses and also showing expansion of medulla in anencephalic fetuses with massive infiltration with sympathogonia cells. Morphometeric measurements of cortex and medulla in normal and anencephalic fetuses (40×).

Groups	Permanent cortex (μm)		*T* test	Medulla (μm)		*T* test
	Normal Mean ± SD, range (mm)	Anencephalic Mean ± SD, range (mm)		Normal Mean ± SD, range (mm)	Anencephalic Mean ± SD, range (mm)	
A	31.36 ± 3.43 (18.5–32.0)	37.78 ± 4.6 (19–39.4)	0.51	54 ± 4.7 (43–57)	74.4 ± 5.6 (63–76)	0.78
B	29.48 ± 4.98 (18.5–35)	48.06 ± 3.56 (19–50)	<0.05	47 ± 3.9 (35–48)	101.7 ± 2.8 (80–102)	<0.05
C	47.57 ± 5.7 (24.0–50)	60.27 ± 4.09 (41–62)	<0.05	33 ± 3.5 (26–35)	178 ± 3.2 (110–179)	<0.05
D	60.48 ± 2.8 (54–63)	74.47 ± 2.60 (52–77.5)	0.67	26 ± 2.4 (22–28)	200 ± 2.3 (90–210)	<0.05

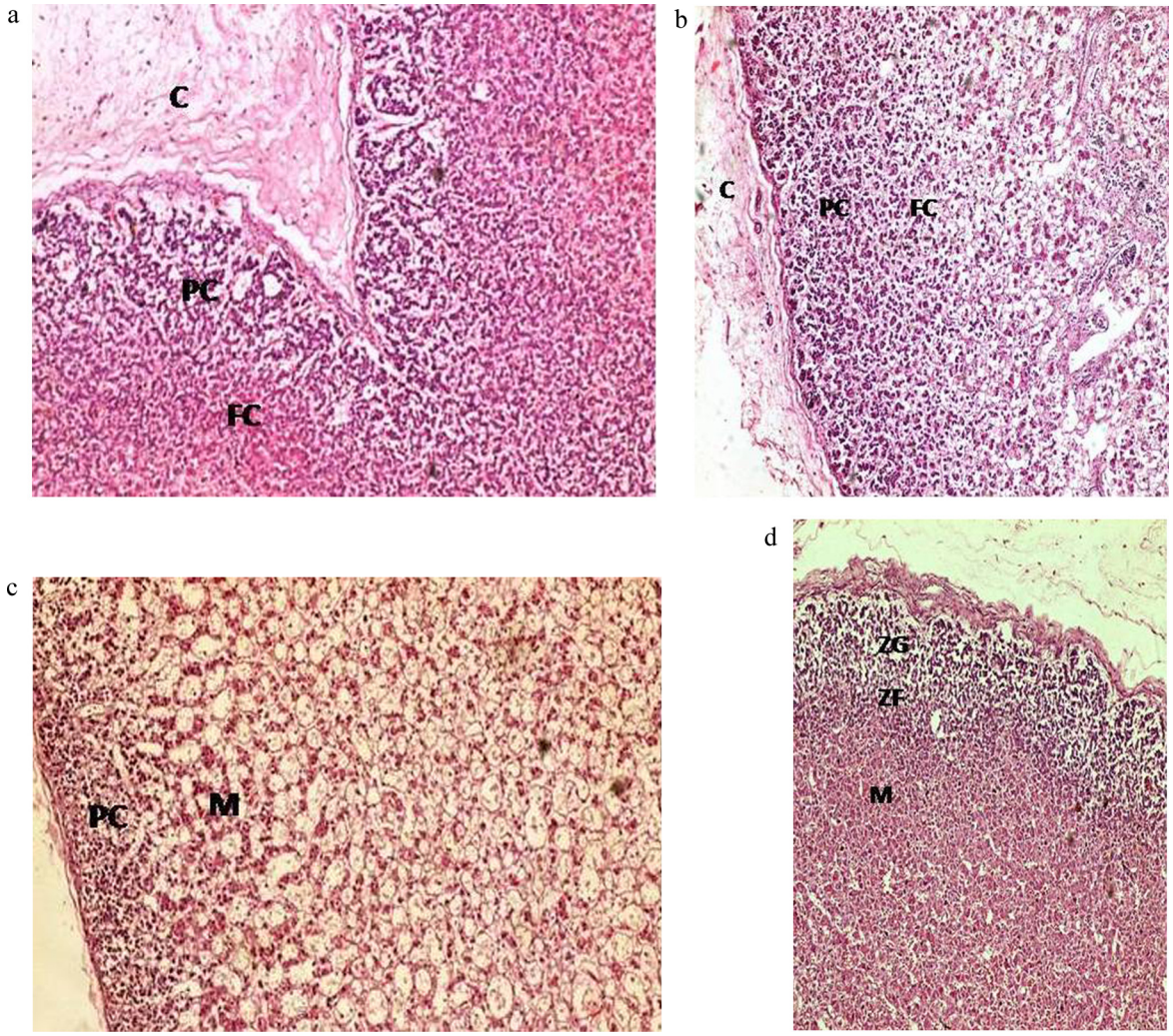

Fig. 5. Permanent cortex (PC) and fetal cortex in (FC) normal fetuses at 14 weeks (a), and 20 weeks (b) in anencephalic at 23 weeks (c) and 26 weeks (d) showing reduction of fetal cortex as gestation is advancing (H&E; ×20).

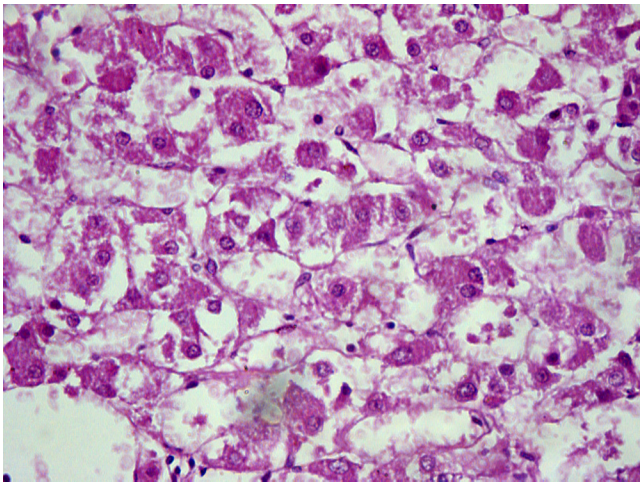

Fig. 6. Cells in fetal zone were polyhedral (P) with eosinophilic cytoplasm and also large (L) oval shaped cells, whose nuclear chromatin basophilic and single acidophilic cytoplasmic inclusion bodies darkly stained nucleus at 15 weeks (H&E; ×20).

normal suprarenal gland. The difference was statistically significant <0.05 (Table 3).

IHC was done using S-100 antibody, few immunostained cells were found in the region of adrenal cortex known as sustentacular cells, these cells they were round, chromatin rich nucleus sparse cytoplasm, cytoplasmic extensions were seen (Fig. 8a).

Medulla comprised of ganglionic cells which were oval in shape, pale staining spherical nucleus intensely staining nucleolus, had big cytoplasmic processes, with presence of coarse granules. Ganglionic cells were observed 3–4/field in both the glands.

In anencephalic fetuses the medullary tissue was observed to be more (range 27.5–74.4 μm) as compared to the normal fetuses(-range 13.6–54 μm), the difference was statistically significant.

3.2. Group B (>15–20 weeks)

Capsule: In normal suprarenal gland the collagen fibers was uniform, in the form of thick bundles throughout the periphery measuring average 59 ± 4.6 μm (24–62 μm), there was presence sympathogonia cells (S) along with blood vessels in the capsule.

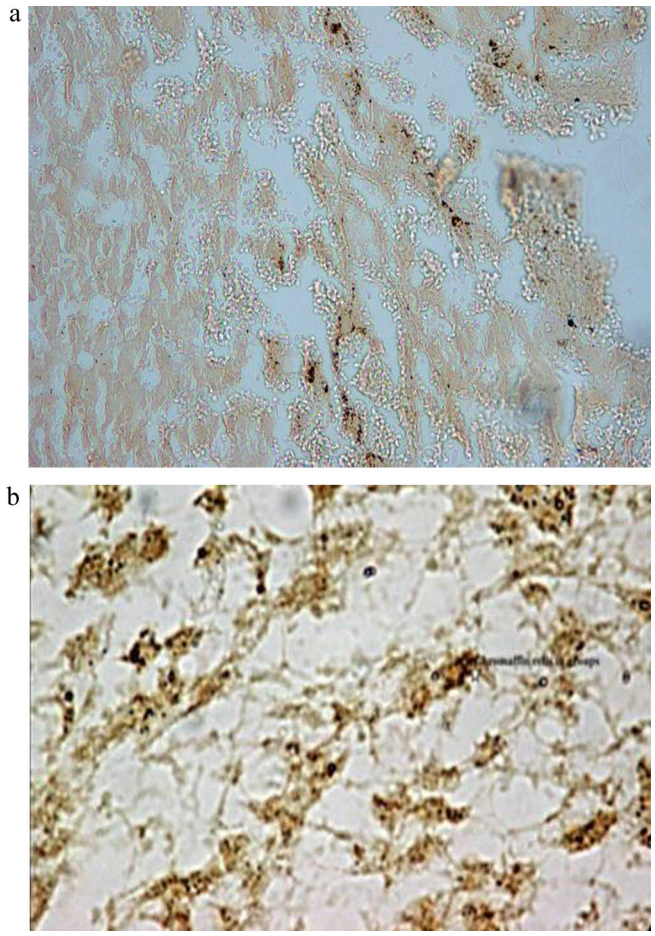

Fig. 7. Chromaffin cells in clusters and cords (a) and presence of granules in chromaffin cells (b) stained intensely with Singh's modification of argentaffin technique ×40, ×60.

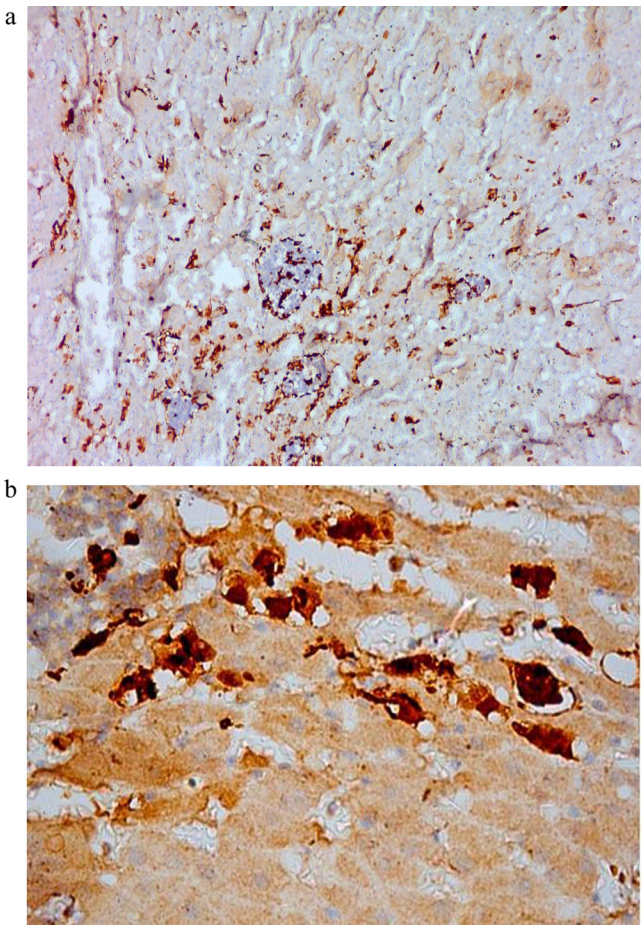

Fig. 8. IHC done using S-100 antibody, immunostained cells in the region of adrenal medulla known as sustentacular cells (a), sustentacular cells scattered inside the cell accumulation, mingling with sympathogonia cells (b) (×40, IHC).

In anencephalic fetuses the capsule was present as thick band of collagen fibers bundle again there was loosely arranged, measured 64 ± 5.4 μm (32–70 μm) in the periphery (Fig. 1b).

3.2.1. Permanent cortex

In both the glands the cells in *permanent cortex* was reorganized in the form of semilunar arc/groups. The average thickness of permanent cortex in normal fetuses was 29.48 ± 4.98 μm (range 18.5–35.0 μm) which was less than in anencephalic fetuses 48.06 ± 3.56 μm (range 19–50 μm). The difference statistically significant (<0.05) (Fig. 5b).

3.2.2. Fetal cortex

Deep to this zone fetal cortex was 194.8 ± 4.8 μm (range 163.5–195 μm) in normal fetuses, 7.78 ± 2.0 μm (range 4–8.5 μm) thick in anencephalic fetuses (Fig. 10). At this gestation fetal cortex is less appreciated. Cells of fetal cortex toward medulla were arranged in loose network. Fasciculoreticular zone was 5–6 layered thick in normal fetuses whereas in anencephalic fetuses the fasciculoreticular zone was 1–2 cell layered thick. Sinusoidal spaces were better seen at this gestational age in both the groups. Bulk of the fetal cortex in anencephalic fetuses was formed by adipose cells (Fig. 9) interspersed with observed large oval shaped cells, whose nuclear chromatin was basophilic and single or multiple acidophilic cytoplasmic inclusion bodies darkly stained nucleus which was centrally placed, few cells were binucleated. In the cytoplasm rim of small vacuoles was seen giving foamy appearance to the cell.

Medulla: Degenerative change in medulla was noticed by the presence of a fibrous zone consisting of collagen fibers with fibroblasts (Fig. 10). Maximum number of sympathogonias (S) were observed at this gestational age group in cortex and medullary region in normal fetuses 7–8/field, maximum average size of nodule was 224 μm × 215 μm, minimum 20 μm × 30 μm. In anencephalic fetuses the sympathogonia cells were present in

Table 3
The drastic reduction of fetal cortex in anencephalic fetuses beyond >20 weeks.

Groups	Fetal cortex (μm)		*T* test
	Normal Mean ± SD, range (mm)	Anencephalic Mean ± SD, range (mm)	
A	164.4 ± 5.6 (100–165)	26 ± 2.6 (11–26)	<0.05 (significant)
B	194.8 ± 4.8 (163.5–195)	7.78 ± 2.0 (4–8.5)	<0.05 (significant)
C	220 ± 5.6 (110–230)	–	–
D	100 ± 3.5 (72–100)	–	–

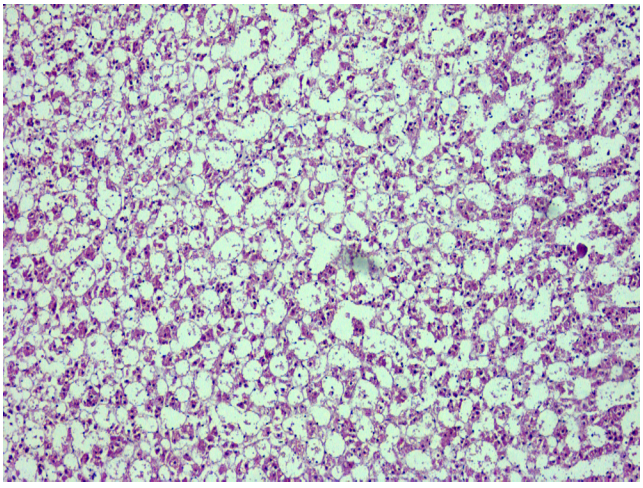

Fig. 9. Adipose cells in fetal cortex in anencephalic fetuses (H&E; ×60).

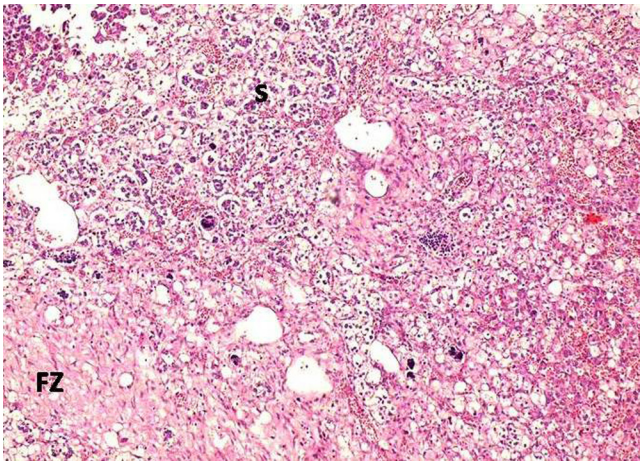

Fig. 10. Fibrous zone and clusters of sympathogonia cells in medullary region in anencephalic fetuses in 20 week (H&E; ×20).

small clusters 10–15/field max average size 30 μm × 20 μm, minimum 10–15 μm. Cystic changes were observed in sympathogonia cells. The chromaffin cells were arranged in trabeculae cords, they contained granules that stained intensely with Singh's modification of argentaffin technique in both the glands. Ganglionic cells were 2–3/field. Sustentacular cells were observed which encircled accumulation of sympathogonia cells, few cells were also scattered inside the cell accumulation, mingling with sympathogonia cells (S) (Fig. 8b). In anencephalic fetuses the medullary cells were more in number which were empty looking because of increased cytoplasm and large vesicular nuclei some cells were also binucleated. In anencephalic fetuses the medullary tissue was observed to be more 101.7 ± 3.8 μm as compared to the normal fetuses 47 ± 3.39 μm.

3.3. Group C (>20–25 weeks)

Capsule was uniformly arranged in both the fetuses measuring 72 ± 2.8 μm (range 47–74 μm) in normal fetuses and 64 ± 2.0 (range 44–65 μm) in anencephalic fetuses. At this gestational age in normal fetuses there was glomerular arrangement of cells observed in permanent cortex. The fetal cortex was 220 ± 5.6 μm (110–230 μm) thick as compared to the permanent cortex 47.57 ± 5.7 μm (24–50 μm).

But in anencephalic fetuses the permanent cortex did not show this kind of arrangement and permanent cortex was more developed at this gestation 60.27 ± 4.09 (47–62) and the fetal zone was not appreciated (Fig. 5c).

Fasciculoreticular zone is 2–4 cell layered thick in normal fetuses whereas in anencephalic fetuses the fasciculoreticular zone was not seen at this gestation.

3.3.1. Medulla

Sympathogonia cells (S) had cystic changes and were observed more in anencephalics as compared to normal, these nodules were present more in medullary region, they were 2/3 per field maximum average size was 214 μm × 271 μm minimum 20–30 μm. In anencephalic fetuses the clusters of sympathogonia was present throughout the cortex and medulla, they were 7–8/field maximum size 230 μm × 250 μm, minimum 10–15 μm (Fig. 11). Adipose cells were disposed throughout the gland parenchyma and sustentacular cells were observed in medulla in anencephalic fetuses. The chromaffin cells were arranged in cords, they contained granules that stained intensely with Singh's modification of argentaffin technique in both the glands (Fig. 7b).

In anencephalic fetuses the medulla was forming the bulk of the gland (178 μm) and degenerative changes in medulla were also seen.

3.4. Group D (>25 weeks)

In normal suprarenal gland cells in permanent cortex (60.48 ± 2.8 μm) were arranged in clusters and in the capsule the collagen fibers was densely present and trabecula was extending from it. Fasciculoreticular zone was 1–2 cell layered thick. Cells of permanent cortex were well defined arranged in rows forming zona glomerulosa and adult zona fasciculata. Fetal cortex was forming bulk of the gland measuring 100 ± 3.5 μm (72–110 μm). The cells had reticular arrangement giving rise to zona reticularis.

In anencephalic the capsule was uniformly arranged present as thin rim around the gland, the permanent cortex measured 74.47 μm. Fetal cortex was not appreciated so, there was formation of zona glomerulosa and fasciculata but zona reticularis was not appreciated (Fig. 5d).

Medulla was recognized by presence of blood vessels at the center with ganglionic cells (Fig. 12). In anencephalic fetuses medulla was forming 4/5th of the cortex at this gestational age, sympathogonia cells (S) and adipose cells were still observed but

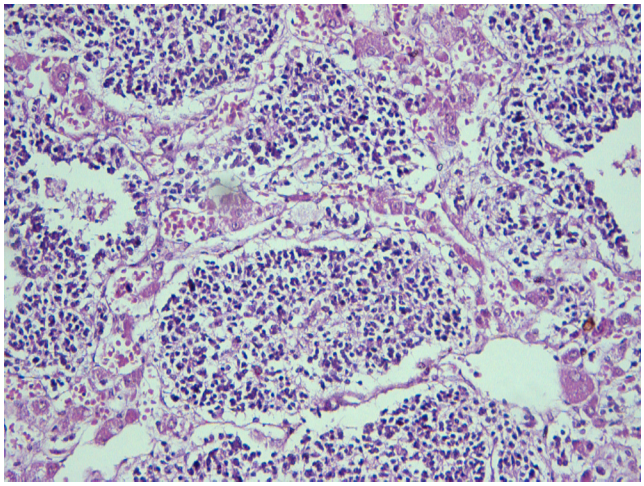

Fig. 11. Sympathogonia cells present throughout the gland in anencephalic fetuses at 24 weeks and cystic changes observed in sympathogonia (H&E; ×60).

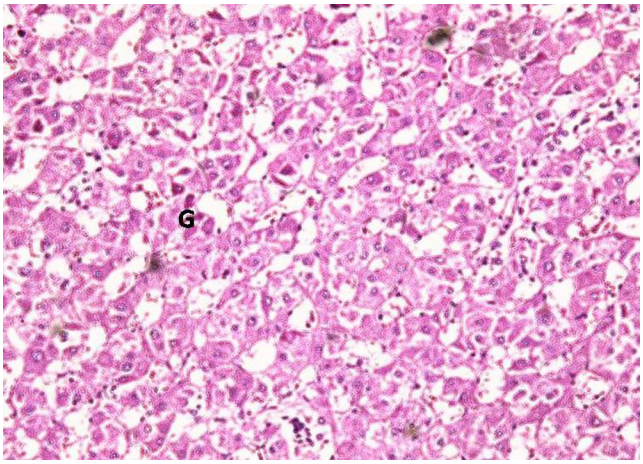

Fig. 12. Ganglionic cells in medullary region in normal fetuses (H&E; ×20).

these cells were not observed in the normal fetuses. Sinusoidal vessels were numerous as compared to previous gestational age groups in both the glands. Sustentacular cells, chromaffin cells, were observed in both the fetuses.

4. Discussion

The histogenesis of suprarenal gland has been subject of, interest by large number of researchers. The gland parenchyma has two parts, cortex and medulla. Both these parts differ in their development. The fetal suprarenal cortex is mesodermal structure. It develops at 10 mm CRL stage (37 days) from columnar mesothelial cells situated on posterior abdominal wall in the angle between the root of mesentery and the developing gonad. The cells proliferate and form invasive cords which soon separate from coelomic epithelium and condense in the mesenchyme of the dorsal abdominal wall to form a large eosinophilic cell mass on each side of the dorsal aorta, where they differentiate into large acidophilic cells. To its initial proliferation is added, at about the 12 mm CRL stage (40 days) a second wave of smaller cells which are derived from the same general somatopleuric area and migrate to develop the first cluster forming the outer subcapsular layer. The smaller cells will become those of the definitive cortex while the initial proliferation becomes the fetal or primitive cortex which retrogresses after birth except the outermost layer which becomes zona reticularis.[7]

Adrenal cortical atrophy was well known to occur in anencephalic fetuses and may be due to involution of the fetal zone of the fetal cortex as a result of the absence of normal hypothalamic-pituitary function. The major secretory product of the definitive zone is cortisol, and the major product of the fetal zone is dehydroepiandrosterone sulfate (DHAS), which is transformed by the placenta to form several estrogens. Both these are produced from cholesterol and low-density lipoprotein in the fetal circulation. Both norepinephrine and epinephrine are produced by chromaffin cells and can be detected by gestation weeks 10–15.

Few authors studied development of fetal and fasciculata zones of adrenal cortex of anencephalic fetuses is affected because of lack of fetal ACTH secretion. ACTH is major regulator of fetal suprarenal gland during 2nd half of pregnancy. Zona glomerulosa in anencephalics is similar to that observed in normal suprarenal gland. So growth of zona glomerulosa is autonomous it does not depend on presence of fetal ACTH and is not affected.[9]

Few authors have studied suprarenal glands (both right and left) of different age groups to see the cytoarchitecture using hematoxylin eosin stains. They observed that suprarenal has superficial narrow zone of darkly stained cells underneath the capsule which is the permanent cortex and a deeper lighter zone called the fetal cortex. As the age advanced, fetal cortex became bulkier and before term it constituted about 5/6th of entire cortex. Medulla was characterized as centrally placed space filled with large blood vessels and few large cells having abundant cytoplasm with vesicular nuclei.[10–13]

Keene et al.[14] observed that degeneration of fetal cortex started during last 10 weeks of intrauterine life and was completed by the end of first year.

The origin of the suprarenal medulla is from a different source. The medulla of the suprarenal gland is composed of sympathetic nerve cells which is derived from the neural crest. These cells reach the medio-dorsal aspect of the primitive cortex at the 16 mm stage (44 days) and soon begin to invade it. Later they form a cell growth on the medial aspect of the extensive cortex. They show histological evidence of the presence of catecholamines by the 10th week of fetal life.[15,16]

Few authors described growth of adrenal medulla is retarded in anencephalic fetuses. But few said that adrenal medullary maturation is thought to be mediated in part by cortisol and by induction of the enzyme phenylethanolamine-n-methyltransferase (PNMT), the enzyme that catalyzes the conversion of norepinephrine to epinephrine. With advancing gestational age, there is an increase in the proportion of epinephrine relative to norepinephrine as PNMT increases in response to higher concentrations of cortisol in the medulla. Cortisol arrives in the medullary region via diffusion and centripetal flow from the surrounding cortex. The accelerated maturation of the medullary tissue of anencephalics resembles the maturation of the extra-medullary chromaffin system, which includes the organ of Zuckerkandl, compared to the normal adrenal medulla This phenomenon has been attributed to the low concentration of PNMT in the tissue. The concept of low PNMT, an enzyme induced by cortisol, in the anencephalic adrenal is consistent with reports of low cortisol levels in the cord blood in anencephaly. At present, however, it is not possible to exclude other changes in the adrenal endocrine milieu, including alterations of DHAS or nerve growth factor levels, as being the cause of the accelerated adrenal medullary maturation of anencephaly.[17–22]

Iwanaga et al. observed a gradual, linear increase in the number of chromaffin cells of developing adrenal medulla. They observed medullary chromaffin cells as small islands of cells dispersed throughout the gland, were more numerous in the central part and adjacent to the medial border. They consisted of 5–14 cells with dark, pynotic nucleus and scarce cytoplasm. These cells were also scattered singly.[23]

In the present study some cells were amoeboid shape which suggested that invasion of coelomic epithelium from dorsomedial aspect of the gland via loose areolar tissue at the hilum seen at 11–15 weeks. In the present study, under light microscopy, the capsule was initially thin and as the gestational age advanced it became thicker with condensation of the collagen fibers and increase in number of blood vessels. In the present study two zones were observed like the previous authors. In normal fetuses the superficial strip of dark zone (permanent cortex) occupied 1/4th of the cortex at 11–15 weeks of gestation which increased to 4/5th of cortex at >25 weeks. The cells were present in U shaped arrangement/clusters/groups and glomerular arrangement of cells was also seen. Deep to the dark zone there was deeper lighter zone (fetal cortex) constituting 3/4th of the cortex at 11–15 weeks which decreased to 1/5th of the cortex at >25 weeks which suggested that the permanent zone was becoming bulkier.

In anencephalic fetuses there was decrease in fetal zone and at 20 weeks permanent cortex was very well defined which constituted 3/4th of the cortex and there was absence of fetal zone.

In normal fetuses fasciculoreticular zone was 6–7 layered thick at 11–15 weeks and as the gestation advanced it decreased to 1–2 cell layer thick, fasciculoreticular zone was 1–2 layered thick at 11–20 weeks and then diminished in anencephalic fetuses.

In the present study in both normal and anencephalic fetuses the medulla was recognized by the presence of blood vessels at the center with a few ganglionic cells which increased at >25 weeks. The cells were oval shaped with big cytoplasmic processes. These also showed presence of coarse granules in it. Nuclei with nucleolus were also seen. The ganglionic cells were 3–4/field initially which increased to 25–30/field. The medulla in anencephalic fetuses was bulkier as compared to normal fetuses. In anencephalic fetuses cytomegaly and focal nucleomegaly was also observed.

Nests of sympathogonia and clusters were observed more in anencephalic fetuses as compared to normal fetuses. As the gestation advanced in normal fetuses these clusters of sympathogonia cells disappeared but in anencephalic fetuses clusters of sympathogonia cells were observed more in medulla and were present throughout the gestation.

In anencephalic fetuses adipose cells were seen more in definitive cortex as well as medulla up to 25 weeks. In the present study chromaffin cells were studied, the cells seen migrating via different layers of gland. The cells were lying singly/groups or trabeculae. There were few cells seen at 12 weeks and increased with increase in gestation. Few cells had granules in their cytoplasm. Some cells did not have any granules suggesting presence or absence of epinephrine and nor epinephrine at this stage. Sinusoidal vessels increased with increase in gestational age.

5. Conclusion

The knowledge of normal histogenesis of suprarenal gland is important to know the developmental changes occurring in anencephalic fetuses. As histology is also important in cases of hirsutism, intrauterine growth retardation, premature birth and hypertension in association with suprarenal cortical and medullary tumors.

Conflicts of interest

The authors have none to declare.

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Further reading

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