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Histogenesis of the Camel(*Camelus dromedarius*) Foetal Ovary with Special Emphasis to the Follicular Development and its Histometric Characteristics

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

The aims of the present study are to investigate the histology of the different components of the foetal camel ovary, with special emphasis to the ovarian follicles and to determinate some histometric characteristics of the ovary during prenatal life. The present study was conducted in 79 foeti at different ages of development. The specimens were classified into first trimester (19 foeti), second trimester (26 foeti) and third trimester (34 foeti) according to the equation .The curved crown vertebral rump length (CVRL) equation Y= 0.366X-23.99 which was described by ELWishy ***et al.,*** (1981) was used for the determination of the foetal age (X) in days from the known (Y) curved crown rump length in centimeters. Then the standard histological techniques were used to prepare the histological slides. The primordial germ cells migrated through the mesentery and were found between the cells of the surface epithelium. The first primordial follicles appeared at (25 cm CVRL) about (134 days old foetus) while at (28 cm CVRL) about (142 days old foetus) the first primary follicle was observed and at (65 cm CVRL) about (243 days old foetus) the first growing follicle was formed. The antral follicles were found only during the third trimester.

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1. INTRODUCTION

The only two existing species of camels are the dromedary or one humped camels or Arabian camels (*Camelus dromedarius*) and the Bactrian camel or two humped camels (*Camelus bactrianus*) in the world.

Taxonomy included the existing members of camels in the infraorder tylopoda and order artiodactyla [1-4].

The camelidae are among the most neglected and ignored mammals [2] although they play vital socioeconomic roles and support millions of people in the dry and arid zones of Asia and Africa [5-7].

Camels have been used traditionally for transport, draft animals for agriculture, as an animal of burden, to supply hides, meat, wool and milk and some are used as racing camels [3,8]. Camels have proven to be the unique domestic animals during severe drought periods, not only surviving such drought, but also producing and reproducing [9,6].

They are seasonal breeders with a relatively short breeding period during which ovarian activity is increased and induced ovulatores [10,11,4,12,13].

Reproduction in domestic animals, as a major source of food and other products for human, has a great importance and study of related subjects gonadogenesis (ovarian development) during foetal life can solve many questions on the normal development and various disorders of urogenital system [14]. The pivotal processes in ovarian development include primordial follicle assembly which occurs prenatally .These events are essential for determining fertility in adult live [15].

Also the development and regression of follicles are associated with major structural and functional changes; important to classify follicles accurately as healthy or atretic at all stages of development [16]. Therefore this study was conducted to investigate the development of the camel ovary during prenatal development.

2. REVIEW OF LITERATURE

Black and Erickson [17] and El-Ghannam and El-Nagger [16] are suggested that, there are four ovarian cell types in the foetal ovary, distinguished according to their morphological properties, which are classified into primordial germ cells, granulosa cells, thecal cells and stromal cells. In four months of human foetus, two important changes are taking place: (1) the ovary enlarges rapidlydue to the deposition of a definitive cortex upon the original plastimal mass. This secondary cortex arises by the division of primordial germ cells and other cells of the superficial plastima and also through a renewal of proliferation by the germinal epithelium. (2) In growth of connective tissue from the region of the rete ovarii produces supporting structures similar to the septa of the testes; these structures isolate the cortical substance into cord-like mass or ovigerous cords [18].

At the 4^{th} month of gestation, in buffalo foetus, the germinal epithelium invades the gonad to form the epithelial cords and the rete ovarii, while the germinal cells are still at the oogonia stage [16]. Moreover, at the 7th and 8^{th} months of gestation in buffalo foetus, the tunica albuginea reaches its maximum thickness, at which cells of germinal epithelium become flattened and few oogonia and most of germ cells become oocytes.

It has been mentioned that, the surface epithelium of the human foetal ovary undergoes diffuse proliferation during the 4^{th} and 5^{th} months of gestation, after which it reverts to a single layer separated from the developing cortex by a tunica albuginea. The epithelial changes occur during the same period that interstitial cells appear in the ovarian stroma [19].

In the foetal horse ovary, the developing germinal epithelium shows a great loss of oocytes during the meiotic phase (15 - 73 days of pregnancy). However, the first groups of oocytes to enter this phase undergo massive degeneration and eventually disappear and few oocytes develop to primordial follicles. Peripheral oogonia divided by mitosis giving rise to more oocytes which pass throw the same changes and also reduced by degeneration (Deanesly, 1975. Furthermore, Deanesly (1977), suggested that, during the 340 days pregnancy of horse, the germ cells in the foetal ovary show a meiotic prophase which begin in days (60-70) and may be prolongated after day 200. However, there are four successive oogonial meiotic proliferations passed into meiotic prophase but the great

majority of oocytes degenerate. Zamboni, Benzard and Mauleon [20] suggested that in sheep, the mesonephros plays a fundamental role in the morphogenesis of the foetal ovary as the source of the folliclular cells and as one of the organizers of specific ovarian structures.

The germinal component of the human ovary originates from primordial germ cells after migration (third to fourth week post-fertilization) and starts to colonize the gonad during the fifth week post fertilization; they are still sexually undifferentiated at this time [21]. The precursors of the somatic cell components, on the other hand, are found at the site of the developing gonad (coelomic epithelial and mesenchymal cells) and in the neighbouring tissues (mesonephros). In Monkey (*Macaca fasculacicularies*) the cortex and medulla are not formed in the ovary until 55-60 days of gestation and the remainder of the mesonephric mesenchymal blastima of the gonad supplies the rete system while the mesonephric tubules fuse secondarily with that system which is connected to the sex cords. Then its invades the medulla and penetrates the ovigerous cords of the cortex [22].

It has been stated that, human connective tissue cords of the cortical stroma begin to appear in 6th week-old embryos, while connective tissue elements of ovarian tunica albuginea appears on the 27^{th} week and by the 40^{th}week, the ovarian tunica albuginea is distinctly developed [23].

The ovarian surface and its associated germ cells in human foetus, from 12 weeks of age until term, have been studied by Motta and Makabe [21]. They mentioned that, the surface epithelium and related cords proliferate extensively, especially at midterm. The cords in the ovarian cortex appear to be linked with ingrowths from the surface epithelium and both structures have a common basal lamina. However, germ cells are always interspersed among the somatic cells of the surface epithelium and associated cords, and both the proliferating cords and surface epithelium may contribute to the formation of early follicles.

It was reported that, a large proportion of somatic cells of the developing ovary of mouse, human and rabbits stems from the mesonephric tissue. In the immature mouse ovary and in the 19 day old foetal rabbit ovary, the first steroid producing cells appear among the mesonephric derived cells within the ovary. However, in human, the first steroid producing cells arise in the inner part of the cortex and differentiate concomitantly with the formation of the small follicles [24]. Byscov [25] added that, the mesonephric cells are probably the precursors of the steroid producing cells.

In female foetuses of domestic animals, Noden and de Lahunta [26] mentioned that, the epithelial gonadal cord breaks up into many small clusters called follicles; each one has one or more germ cells in the center. Most of germ cell clusters are situated peripherally close to the hypertrophied epithelium which will form the mesothelial surface of the gonad;however there is no tunica albuginea in the ovary. According to Noden and de Lahunta [26] the ovaries of the mare have exceptional development that, the cell clusters are distributed throughout the ovary, not only in the cortical region.

In mouse, Satoh [27] reported that the gonads are mainly formed of clear cell cords originated from mesonephric tubules into which germ cells have entered.

The human foetal ovary at 12 weeks of gestation consists of two components: the cortex, which is a hyper cellular layer containing germ cells, and the medulla, which is centrally located and consists of fibrovascular tissue. The cortex is packed with germ cells having large, round nuclei and pale cytoplasm, intermingled with pregranulosa cells which are spindle-shaped cells with small nuclei and dark cytoplasm. Since the germ cells and the pregranulosa cells are closely apposed, almost without any intervening connective tissue, the cortex is clearly demarcated from the medulla [28].

In bovine foetus, the formation of the cords of connective tissue cortical stroma and medulla rudiment appear at 1.5 month old embryo and the cords were developed in dorso-ventral direction towards the covering epithelium of the gonad in the 6 months old foetus [29].

In mice ovaries, germ cell cords are still not observed at a stage immediately following the gonadal sex differentiation in the male. at about 15 days postcoitum, connective tissue including many capillaries penetrates into the ovaries, resulting in obvious formation of germ cell cord-like arrangements. At the same time, the coelomic epithelium-derived cells as well as the mesonephros-derived cells appeared (Kanai, Kurohmaru, Hayashi Nishida,1989).

Moreover, at the tenth week, the gonad of human embryo takes shape and is separated from the mesonephros at the twelfth week. Hoang-Ngoc *et al.* [30] added that, the gonad is formed of two zones; an outer zone formed by epithelial clusters arranged in rossets around the oocytes and an inner mesenchymal zone which becomes the medulla.

It was suggested that, the gonad develops on the surface of the mesonephros and formed of three principal cells types: ceolomic epithelium, cells of mesonephros and germ cells [31] In ewe foetus, McNatty *et al.* [32] mentioned that, mesonephros and genital ridge can be identified at day 20 and 23 of gestation respectively. Furthermore, oogonia can be observed at the genital ridge from as early as day 23. And around day 55 of gestation some germ cells enter meioses coincided with the arrival of mesonephric – derived somatic cells. From days 75, 100, 120 and 135 of gestation, primordial (one layer of flattened granulosa cells), primary early preantral (one complete layer of cuboidal granulosa cells), secondary (preantral) and tertiary (antral) follicles are develops within the innermost regions of ovarian cortex respectively.

In the ovaries of human foetus and at 18-20 weeks post conceptional age, the cortex is composed of sex cords and clusters made up of somatic and germ cells, oogonia and oocytes at different stages of development, whereas Primordial follicles are presented adjacent to the medulla [33].

Lun *et al.* [34] suggested that, the female and male gonads in sheep foetus are steroidogenically active after sexual differentiation, that the steroidogenic enzymes develop before sexual differentiation and the mesonephros is a site of steroid synthesis.

In ewe foetus ovary, Laurel, Quirke, Juengel, Tisdall, Heath and. McNatty [35] reported that, the steroidogenic cells are initially located at the boundary between the cortex and medulla but become increasingly restricted to the mesonephric-derived cell streams.

The primitive cortex and medulla of the developing ovary contains three types of cells that could be identified by light microscope; germ cells or oogonia, pregranulosa cells or follicular cells and mesenchymal cells or stromal cells. The germ cells are spherical in shape, larger than any other cell types and appear more numerous toward the peripheral primitive cortex than the medulla. Pregranulosa cells are smaller in size and are in close contact with oogonia while mesenchymal cells are fusiform or stellate in shape and characterized by thin cytoplasmic processes [33].

Silva, Van Den Hurk, Matos, Santos, Pessoa, Moraes and Figueiredo [36], Janis and Rudolf [37] and Burno *et al.* [38] reported that, the developmental stages of prenatal ovary of domestic animals consist of primordial (one layer of flattened granulosa cells around the oocytes), growing (intermediate, one layer of flattened to cuboidal granulosa cells), primary (one layer of cuboidal cells) and secondary follicles (two or more layers of cuboidal granulosa cells around the oocytes).

It has been mentioned that when primordial germ cells arrive in the gonad of a genetic female (XX), they are differentiated into an oogonia which undergo a number of mitotic divisions, and by the end of the third month, they are arranged in clusters surrounded by a layer of flat epithelial cells. All oogonia in one cluster are probably derived from a single cell, whereas the flat epithelial cells known as follicular cells are originate from the surface epithelium covering the ovary [39].

Ding, Wang, Zahou, Zang, Hung, Shi and Taya [40] stated that, in sow (female pig) foetus less than 70 days post coitum, the ovary has a distinct cortex and medulla. In the cortex, the vast majority of germ cells are oogonia enclosed in ovigerous cords which located within the cortex. In 90 days post coitum, the primordial follicles comprised the majority of the ovarian germ cells, although primary follicles are also observed. In the foetus more than 90 days post coitum, primordial and primary follicles are present in the cortex in multiple layers, whereas secondary follicles are located at the interface of cortex and medulla.

It was reported that, mouse oocytes developed in clusters of interconnected cells called germ line cyst and shortly after birth the majority of cysts break apart and primordial follicles are formed and consist of one oocyte surrounded by one layer of granulosa cells [41].

In birds, primordial germ cells are generally believed to migrate from the early endoderm of the upper yolk sac. When they first appear toward the end of third day of incubation, the left

and right gonad contain nearly the same number of primordial germ cells. During the fourth day, many germ cells are transferred from the right gonad to the left one [42].

George and Fahmy [43] reported that, the covering epithelium of the ovary of the camel foetus at the early stage of development (8-12 weeks) is formed of cuboidal cells and gradually change to columnar cells as the development proceeds. From 32-36 weeks, the covering epithelium consists mainly of columnar cells. Furthermore, at (8-12 weeks) of gestation, the germinal epithelium forms continuous layer around the ovary. It consists mainly of a single layer of cuboidal epithelial cells and scattered between them large vesicular elements with vesicular nuclei and clear cytoplasm; those are the primitive germ cells.

Mohammed [44] stated that, the follicles are found in the form of follicular nests in the foetal camel ovary.

The enfolding of the camel foetus ovary increases in depth with foetal development until the foetus reaches 32 weeks in which it become much deeper and extends to the medulla, then with the advancement of foetal life, the enfolding appears to be much shallower than the previous stages [43,45].

Abd El-Razik [46] and Abdel Hafez [45] mentioned that, the gonads of the camel embryo at early stage of development are covered by elongated wedge-shaped coelomic epithelium (cells with a narrow proximal end implanted to the underlying gonadal stroma and thick distal end adapted to the neighboring cells and houses a spherical or oval lightly stained nuclei). These cells become columnar and cuboidal at the 5^{th} month and columnar with distally situated nuclei at 6^{th} and 7^{th} month and by the 9^{th}, 10^{th} and early 11 month the epithelial covering of the foetal ovary becomes low columnar, cuboidal and flattened cells respectively.

2.1 Ovary of the Adult

Archbald, Schultz, Fahninig, Kurtz and Zemjanis [81] stated that, the cells of the rete ovarii in heifers (young cow) are located in the ovarian medulla and are composed of oval-shaped nuclei with prominent chromatin and small amounts of light staining cytoplasm. These cells are arranged both as a single layer and a pseudo stratified layer. Tube-like and circular arrangements of the rete ovarii were observed. The circular arrangement is reminiscent of the structure of primordial ovarian follicles.

Byscov and Moore [47] described the rete ovarii in mouse as a structure composed of association of cell cords and tubules which extend from the ovary into preovarian tissue hilus region and they are present into three distinctive regions: intraovarian, outer ovarian and connection between the above two.

It was proposed that, in all animals, the extra ovarian rete cells are actively secreting. According to Byscov [48] in the cat, mink and ferret, the rete system interacts with the cortex to initiate the start of meiosis, and that the rete cells as well as cells of the surface epithelium contribute to granulosa cell layer. Moreover, there are open connections between the intra ovarian rete cords and the groups of germ cells as well as between the surface epithelium and the germ cells. The germ cells which are found in the inner part of the cortex, in contact with the rete cells, are the first group to enter the meiotic prophase [48].

Cahill and Maule′on [49] classified the small follicle population in ewe in relation to either the follicle, oocyte size or morphological feature into dormant, transitory and growth phases of the follicles.

The ovary has a thick peripheral zone or cortex, which surrounds the medulla; follicles are embedded in the connective tissue of the cortex and contain female sex cells (oocytes). Furthermore, the follicles are present in a wide range of sizes representing various stages of their development [50].

Leeson, Leeson and Paparo [51] described the interstitial cells as large spherical epithiloid cells which contain small lipid droplets and may be derived from the theca interna of follicles which undergo atresia in rodent ovarian stroma.

In many mammals, the ovarian stroma contains conspicuous clusters and cords of large epitheloid interstitial cells which have been shown to secrete estrogen in some species. The interstitial glands are less well develop in human ovary and the interstitial cells are found in greatest number during the first year of live when atretic follicles are most numerous and they are believed to arrive from the hypertrophied theca interna of regressing follicles [50].

Evidence from several species indicates that, the initial stages of follicular growth proceed very slowly. In contrast, the stages after antrum formation are much more rapid; however, atresia seems to be most prevalent as follicles approach the size at which they could be recruited for potential ovulation [52].

The ovary of brown bear consists of cortex and medulla and covered by simple cuboidal epithelium, bounded by tunica albuginea which is rich in collagen fibers and reticular fibers and poor in elastic fibers. Connective tissue cells, interstitial cells and all types of follicles and corpora lutetia are present in the cortex [53].

Preantral follicles, which include primordial, primary and secondary follicles, have no vascular supply on their own and depend on vessels in the surrounding stroma. However, during antrum development, the thecal layer acquired a vascular sheath consisting of two networks of capillaries located in the theca interna and externa [54]. These newly formed ovarian blood vessels provide an increased supply of gonadotropins.

Follicle wave is an organized development of cohort gonadotrophin-dependent follicles all of which initially increase in size, but most of them subsequently regress and die by atresia [55].

Each follicle within the cortex of each ovary consists of a primary oocyte and surrounded by supportive cells, the follicular cells, which in turn become surrounded by specialized stromal cells. Each follicle has the potential to undergo a progressive series of changes that result in four specific stages of development, comprising the formation of primordial follicles, primary follicles, secondary follicles and tertiary follicles [50,56].

The cortex of the ovary contains a somewhat loosely arranged framework of connective tissue that forms the stroma and surrounds follicles at various stages of development [50,55] Cells within the stroma include clusters of fibroblasts that can vary in their morphology and interstitial gland cells which are endocrine and form cords in bitches, rodents and queens and thecal cells associated with follicular development [56].

In the ovaries of bitch, queens and rodents, interstitial endocrine cells are prominent. They arrive chiefly from the epithiloid theca interna cells of atretic antral follicles or from hypertrophied atretic granulosa cells [37]. The interstitial cells are polyhydral, epithiloid and contain lipid droplets.

It has been stated that, the mammalian ovary contains numerous immature preantral follicles that are not dependent on the endocrine supports, unlike the more mature dependent antral follicles [57].

Hunt and Hassold [58] suggested that, the critical events of oogenesis in human occurred during three distinct developmental stages: meiotic initiation in the foetal ovary, follicle formation in the prenatal period, and oocyte growth and maturation in the adult.

Ropinson, Wood, Hummond, Larid, Hunter and Mann [59] revealed that, both primordial and primary follicles receive sufficient nutrient and oxygen by passive diffusion from stromal blood vessels. However, the formation of an individual capillary network around each follicle is required for follicles to grow beyond this stage.

Healthy and atretic primordial, pre-vitellogenic and vitellogenic follicles in the ovaries of the sexually immature ostrich were studied by Madekurozwa and Kimaro [60]. They mentioned that, atresia occurred during all stages of follicular development. Furthermore, atretic primordial and pre-vitellogenic follicles are characterized by the presence of a shrunken oocyte surrounded by a multilayered granulosa cells. Moreover, there are two forms of atresia (types 1 and 2) identified in vitellogenic follicles, at the advanced stages of type 1 atresia, are dominated by a hyalinized mass. In contrast, in type 2 atresia, the granulosa and theca interna are differentiated into interstitial gland cells.

The surface epithelium of camel ovary is covered by a single layer of cuboidal cells except at the hilus region, and there is a narrow zone of tunica albuginea which is made up of dense irregular connective tissue [61].

The histological appearance of the atretic follicle in camels varies enormously depending on the stage of development and the progression of atresia [62,60]. However, in Graafian follicle or preovulatory follicle, the secondary oocytes are detached from the granulosa cell layers.

Mohammed, [45] suggested that, the interstitial gland cells are never encountered in the camel ovary, while Salman [8] and Osman [12] detected the interstitial cells in cortical stroma of the adult

camel ovary and also observed leukocytes cells in the ovary of the pregnant camel. Mohammed [45] and Salman [8] stated that, the stroma of the adult camel ovary consists of a network of reticular fibers.

Shehata [63,83] described the presence of intercommunicating tubular structures within the medulla of the ovary of the she- camel. These structures resemble glandular acini which are lined by cuboidal to columnar cells and they are not simple vestiges from embryonic life, but they may perform an active endocrine function.

The connective tissue in the cortex and medulla of the ovary takes a reticular form in which the stroma is rich in argirophilic fibers with a few collagenus fibers but no elastic fibers. Elastic fibers were observed only in the wall of blood vessels which are muscular arteries [12].

3. MATERIALS AND METHODS

The material used in the present study consisted of (79) female foetuses of one –humped camels (*Camelus dromedarius*) which were collected from Nyala, Elpugaa (Omdurman) and Tampol slaughter houses.

The foetus was taken out of the carcass soon after evisceration of the she camel which slaughtered by accidence for meat consumption purpose. The collected specimens were ranged from 3 cm curved crown rump length CVRL about 73.7 days old foetus to 119 cm curved crown rump length CVRL about 390.6 days old foetus. The collected foeti were divided into three groups according to the method described and adopted by Eisa [7] as follows:

i. Early age group (first trimester) 1 – 4.4 months of gestation and include 19 foeti.
ii. Middle age group (second trimester) 4.5 – 8.4 months of gestation and include 26 foeti.
iii. Late age group (third trimester) 8.5 – 13 months of gestation and include 34 foeti.

The curved crown rump length (CVRL) equation Y= 0.366X-23.99 which was described by ELWishy, Himeida, Omer, Mobarak, and El Sayed (1981) was used for the determination of the foetal age (X) in days from the known (Y) curved crown rump length in centimeters. The measurement of the (CVRL) started from the point of the forehead (crown) up to the base of the tail along the dorsum of the foetus using a tape meter. A number of samples were also measured by using the chest circumference (CC) equation Y= 0.214X-16.24 which was described by El Wishy et al. [11]. Y=chest circumference in cm and X= age in day. The procedure was done to check the accuracy of the first equation and it was found that the difference between the two equations was about 1-2 days.

The details of the age of the foeti used in this study were shown in Table (1). The abdomen and pelvic regions of the female foeti were incised immediately after obtaining the foeti and the ovaries were collected from them. The female foeti were identified by the shape of their external genitalia as described by Abdel Hafez [45]. Some specimens at the indifferent stage were also used.

3.1 Histology Fixation

Samples (ovaries) were collected within 1\2 from slaughtering and fixed in different fixatives like 10% formalin, formal saline, Bouins solution, and buffered formalin. Gender fluid and cold acetone were used to fix the samples which were used for investigating glycogen and phosphatase enzymes respectively.

3.2 Processing

After proper fixation, the processing of tissue was carried out either manually or by the aid of automatic processing machine. The processing included dehydration through increasing concentrations of alcohol (70%, 80 %, 90% and absolute ethanol), clearing either in chloroform or Xyline, impregnation in paraffin wax and then blocking (embedding) in paraffin waxs.

3.3 Sectioning

Sagittal and transverse sections were obtained at 4-5 µm in thickness using rotatory microtome.

3.4 Staining

The prepared sections were stained using the following methods: - Haematoxylin and Eosin (H and E) was used for general histological examination [64,65].

For examination of special components of the ovary, the followed staining methods were used:

1. Van-Gieson stain for determination of collagen fibers [64].

2. Massons trichrome stain for identification of smooth muscle fibers
3. (Culling, [64]; Durary and Wallington [66,79].
4. Aldehyde fuchsin and Verhoeffs for illustration of elastic fibers [66].
5. Gordon and Sweet for staining of reticular fibers (collagen type III) [66,65].

3.5 Histometry

Histometrical measurements were carried out in the developing ovary of camel foetuses of different ages. The follicular diameter, the thickness of both granulosa layer and theca layer and the diameter of germ cells were measured. Erma Inc-Japan microscope was utilized in this work, using ocular micrometer lens. The objective lenses X4, X10 and X40 were used for determining the measurements after calibrating the ocular scale of the microscope [67,83]. Three measurements were recorded for each structure and the mean average was calculated. These measurements were carried out in selected histological sections stained with Haematoxylin and Eosin.

Table 1. Showing the CVRL and age in days of the foetus during the three trimesters

A N	CVRL	Age in day	Gestation period
1	3	73.7	First trimester
2	3.2	74.3	first trimester
3	3.5	75	first trimester
4	4	76	first trimester
5	4.5	77.8	first trimester
6	4.8	78.6	first trimester
7	5	79	first trimester
8	6	81.9	first trimester
9	7	84.6	first trimester
10	8	87.4	first trimester
11	8.4	88.4	first trimester
12	10	92.9	first trimester
13	13	101	first trimester
14	15	106.5	first trimester
15	15.3	107.3	first trimester
16	16	109.2	First trimester
17	16.5	110.6	first trimester
18	22	125.6	first trimester
19	24	131	first trimester
20	25	133.9	Second trimester
21	25	133.9	second trimester
22	28	142	second trimester
23	29	144.7	second trimester
24	29.3	145.6	second trimester
25	30	147.5	second trimester
26	31	150	second trimester
27	33.3	156.5	second trimester
28	35	161	second trimester
29	36	164	second trimester
30	39	172	second trimester
31	39.3	172.9	second trimester
32	40	174.8	second trimester
33	41.5	178.9	second trimester
34	43.3	183.9	second trimester
35	47	194	second trimester
36	48	196.7	second trimester
37	48	196.7	second trimester
38	49	199.4	second trimester
39	49	199.4	second trimester

40	51	204.9	second trimester
41	54.3	214	second trimester
42	56	218.6	second trimester
43	57	221.2	second trimester
44	59	226.7	second trimester
45	64	240.4	second trimester
46	64	240.4	second trimester
47	65	243	second trimester
48	67.5	249.9	Third trimester
49	69	254	third trimester
50	70	256.8	third trimester
51	71	259.5	third trimester
52	72	262	third trimester
53	75.5	271.8	third trimester
54	75.5	271.8	third trimester
55	76	273	third trimester
56	78	278.7	third trimester
57	83	292.3	third trimester
58	85	297.8	third trimester
59	85	297.8	third trimester
60	88	305 .9	third trimester
61	89	308.7	third trimester
62	90	311	third trimester
63	90	311	third trimester
64	90.3	312	third trimester
65	91	314	third trimester
66	93	319.6	third trimester
67	98	333	third trimester
68	98	333	third trimester
69	99	336	third trimester
70	99.3	336.9	third trimester
71	100	338.8	third trimester
72	101	341.5	third trimester
73	103	347	third trimester
74	103.5	348	third trimester
74	104	349.7	third trimester
75	104	349.7	third trimester
76	110	366	third trimester
78	114	377	third trimester
79	119	390.6	third trimester

AN= foetal Number; CVRL= Curved Crown Rump Length

4. RESULTS

4.1 Histology

4.1.1 First trimester

4.1.1.1 Early stage of the first trimester

During the early stage of development, large spherical or slightly irregular shaped primordial germ cells were found within the mesothelium of the mesonephros and the mesonephric tissue (Fig.1).

In 6 cm CVRL (82 days old) foetus, the ovary was connected to the mesonephros by dense irregular connective tissue (mesovarium) rich in fibroblasts and mesenchymal cells. The ovary was covered by elongated wedge shaped cells and these cells did not rest on clear basement membrane and the tunica albugenia was absent (Fig.2). Groups of primordial germ cells were found scattered between the germinal epithelial cells (Fig.3).The cortex of the ovary consisted of many types of cells. Mesenchymal cells or stromal cells had fusiform shape, oval nuclei and cytoplasmic processes (Fig. 3). The oogonia were large and spherical in shape with centrally located circular nuclei and occupied the outermost region of the cortex nearest to the germinal epithelium. The follicular cells were

small in size with oval nuclei and surrounded the oogonia in addition; cortical stroma at this stage was rich in fibroblasts (Fig. 4). The medulla could be considered as the extension of the connecting region between the mesonephros and the ovary. This region contained small capillaries and some cells with dark nuclei; these cells may be the precursor of the rete ovarii. White blood cells like monocyte and neutrophils were also seen. Also the mesonephroic Bowman capsules were lined by simple cuboidal epithelium while in the metanephros the epithelium was simple squamous.

4.1.1.2 Middle age of the first trimester

In 15 cm CVRL (106.5 days old) foetus, the ovary was connected to the mesonephros by dense irregular connective tissue (mesovarium) rich in fibroblasts and mesenchymal cells (Fig. 5). The surface of the ovary was covered by simple cuboidal epithelium, and few primordial germ cells were randomly scattered between cells of the germinal epithelium. The cortical zone was wider than the medulla and the boundary between the cortex and the medulla appeared (Fig.6). The oogonia increased in number in compression to the early stages of development and were distributed in clusters or in cord-like arrangement. The cortical stroma was rich in fibroblasts and mesenchymal cells. Blood and lymph vessels were noticed (Fig.6).

4.1.1.3 Late stage of the first trimester

In 22 cm CVRL (126 days old) foetus, the cortex of the ovary was covered by simple cuboidal epithelium and the oogonia were distributed in clusters separated by septa originated from the cortical stroma which contained blood vessels

Reticular fibers during the early stages of first trimester (6 cm CVRL, 82 days old foetus), were very thin and distributed randomly in the ovarian stroma, while at 22 cm CVRL (126 days old) foetus, reticular fibers were found in the septa which separated the ovigerous cords.

Collagen fibers were fewer than reticular fibers and they were randomly scattered within reticular fibers during early stages of first trimester (Fig.7). Then with advancing age, they were found in the stromal septa which separated ovigerous cords.

4.1.2 Second trimester

4.1.2.1 Early stage of the second trimester

In 25 cm CVRL (134 days old) foetus, the ovary was covered by simple cuboidal epithelium the tunica albuginea was poorly developed. The ovigerous cords were more developed than in the earlier stages. The first primordial follicles were found in the deep cortical region, near the boundary between the cortex and medulla.

In 28 cm CVRL (142 days old) foetus, the ovary was covered by simple cuboidal epithelium and the tunica albuginea was poorly developed and ovigerous cords zone occupied the greater part of the cortex (Fig. 8). The inner most zone of the ovigerous cords showed signs of degeneration earlier than the outermost region. Most of the follicles were primordial with a few number of primary follicles situated deep in the cortex. The medulla consisted of loose connective tissue rich in mesenchymal cells and fibroblasts and contained lymph and blood vessels.

In 33.3 cm CVRL (156.5 days old) foetus, the ovary had a kidney shape and covered by short simple cuboidal epithelium followed by a thin layer of tunica albuginea. The ovigerous cords were arranged in different directions (longitudinal, transverse and oblique) and separated by narrow septa of the cortical stroma (Fig.8,9).

All follicles which were embedded in cortical stroma were primordial (primary oocytes surrounded by one layer of squamous cells) and primary follicles (primary oocytes surrounded by one layer of simple cuboidal cells). Some of these follicles showed atretic signs (absence of primary oocytes or degenerated of follicular cells).

4.1.2.2 Middle stage of the second trimester

In 43.3 cm CVRL (183.9 days old) foetus, the ovary still had a kidney shape, and covered by simple cuboidal epithelium followed by a thin layer of tunica albuginea. The ovigerous cords which were separated by septa contained oogonia and follicular cells and occupied the major part of the cortical stroma. Next to the ovigerous cords zone, primordial follicles (primary oocytes surrounded by one layer of squamous cells) were observed and some of them had. binucleated Primary follicles were also seen and some of them showed atretic sings (Figs. 8,9).

The stroma of the medulla consisted of loose connective tissue and contained many fibroblasts, smooth muscle fibers, mesenchyal cells, lymph vessels with valves and blood vessels.

In (48- 49) cm CVRL (196.7-199 days old) foetus, the ovary had a kidney shape and covered by crowded cuboidal epithelium followed by a medium sized layer of tunica albuginea. Ovigerous cords were arranged in different directions and contained oogonia and follicular cells and filled most of cortex). Most of the follicles were primordial with a few number of primary follicles embedded in the deep region of the cortex. A few numbers of atretic follicles were also present.

4.1.2.3 Late stage of the second trimester

In 51 cm CVRL (204.9 days old) foetus, the ovigerous cords zone was wider than the follicular zone and most of the follicles showed signs of degeneration. A few numbers of primary follicles were seen. Some primordial follicles were observed in the right ovary (Figs. 8,9).

In 65 cm CVRL (243 days old) foetus, the ovary was covered by simple cuboidal epithelium with shallow fissures followed by a narrow layer of tunica albuginea. The innermost region of the ovigerous cords showed degenerated sings earlier than the outermost region of the ovigerous cords. In the follicular zone, the small follicles were at primary stage and some of them showed atretic signs. A number of growing follicles (the follicular cells proliferated and formed several layers around the ovum) were found in the deep cortical stroma (Fig.10). Reticular fibers were found in the boundary tissue between the cortex and medulla and extended toward the surface epithelium of the ovary to surround the ovigerous cords, primordial and primary follicles and also in the tunica albuginea which separated the surface epithelium from the ovigerous cords (Fig.11). During this stage the collagen fibers were found within the reticular fibers and they were distributed in a similar manner to the reticular fibers.Elastic fibers were not observed except in the tunica intema of the ovarian artery and its branches.

4.1.3 Third trimester

4.1.3.1 First stage of the third trimester

In 67.5 cm CVRL (249.9 days old) foetus, the ovary was covered by simple cuboidal epithelium with deep fissures followed by a narrow layer of tunica albuginea. The ovigerous cords which occupied the innermost region of the cortex showed degenerative sings earlier than those which were found in the outermost region of the cortex. Both primordial and primary follicles were present and the medulla contained islets of interstitial cells in the vicinity of the blood vessels (Fig.12).

In 70 cm CVRL (256.8 days old) foetus, the ovary was covered by short simple cuboidal epithelium followed by a narrow layer of tunica albuginea. The ovigerous cords were separated by septa from the cortical stroma and contained primordial, primary and secondary follicles. Groups of interstitial cells were present in the deep cortical stroma.

In 75.5 cm CVRL (271.8 days old) foetus, the surface of the ovary was covered by simple cuboidal epithelium and showed many fissures on its free surface. The ovigerous cords zone was slightly narrower than the follicular zone. Atretic primordial follicles were located next to the zone of ovigerous cords. A number of secondary and growing follicles were present and some of them were atretic and atretic antral follicles were observed. The medulla contained blood vessels and rete ovarii which extended towards the hilus (Fig. 12).

In 85 cm CVRL (297.8 days old) foetus, the ovary was flat and covered by simple cuboidal epithelium with fissures extended deep in the cortical zone. A layer of tunica albuginea was seen. The ovigerous cord zone is narrower than the follicular zone and most of the small follicles were atretic while the normal small follicles were either primordial or primary follicles. Secondary follicles were seen and some of them were enlarged. The growing follicles began to be surrounded by blood capillaries and the antral follicles started to appear (Fig. 12). Groups of interstitial (endocrine) cells were found in many parts of the deep cortical stroma adjacent to blood vessels.

4.1.3.2 Middle stage of the third trimester

In 88 cm CVRL (306 days old) foetus, the ovary was covered by simple columnar epithelium with deep fissures. A few numbers of primordial germ cells were found between the surface epithelial cells. Primordial and primary follicles were present in the outer cortical zone; the majority of follicles were growing and antral follicles (Fig.13).

The follicles were situated deep in the cortex, Atretic preovulatory follicles were present both in the left and right ovaries. The medulla consisted of loose connective tissue and contained blood

and lymph vessels and rete ovarii which were lined by a layer of simple cuboidal epithelium.

In 90 -90,3 cm CVRL (311-312 days old) foetus, the ovary had irregular shape due to the presence of many fissures and covered by simple cuboidal epithelium. The ovigerous cords disappeared completely. Primordial, primary and secondary follicles were present and some of them showed atretic signs .The small follicles were found in a nests forms (Fig.14). The medulla contained blood and lymph vessels.

4.1.3.3 Late stage of the third trimester

In 98 cm CVRL (333 days old) foetus, the ovary was covered by simple cuboidal epithelium with fissures and the ovigerous cord zone was absent and many capillaries were developed in this area. Both primordial and primary follicles were present but most of primordial follicles were atretic and both primordial and primary follicles had elongated shape due to the presence of secondary and preovulatory follicles which were located deep in the cortical stroma together with small islets of interstitial (endocrine) cells in the vicinity of blood vessels.

In 100 cm CVRL (338.8 days old) foetus, the surface of the ovary was covered by simple cuboidal epithelium with fissures but no ovigerous cord zone. There were many large atretic preovulatory follicles. All small follicles were primary and some of them were atretic. Most of the preovulatory follicles were situated deep in the cortical region and were extended towards the surface epithelium. The vesicular follicles had no corona radiata around the ovum|(Fig.15). The internal wall of the follicles consisted of granulosa cells (stratum granulosum) and the external wall contained two layers of theca; the internal layer (theca interna) consisted of cells and the external layer (theca externa) consisted of fibers (Fig. 15).

In 101 cm CVRL (341.5 days old) foetus, the ovary has irregular shape and covered by short simple cuboidal epithelium with shallow fissures. A few primordial follicles were seen and the primary follicles were large and located in the deep cortical region in addition to secondary follicles. Large antral and atretic preovulatory follicles were found in the greater part of the cortical region (Fig.16).

In 103 cm CVRL (346.9 days old) foetus, the ovary was covered by simple cuboidal epithelium with fissures. The majority of small follicles were primary with a few numbers of primordial follicles and some of them showed atretic sings. Secondary follicles were present in the deep cortical region and some of them began to be surrounded with capillaries. The medullary region contained blood vessels and rete ovarii. In a foetus (103 and 103.5) cm CVRL (346.9 and 348 days old), the reticular fibers isolated the primary follicles and formed thick bundles between the large follicles in the deep portion of the cortex and the atretic follicles. The reticular fibers were also found in the medulla and surrounded the rete ovarii, lymph and blood vessels (Fig.17).

In 110 cm CVRL (366 days old) foetus, the ovary was covered by simple cuboidal epithelium followed by tunica albuginea. The follicles occupied most of the cortical zone. All small follicles were primary; no primordial follicles. The vesicular follicles were large and surrounded by blood vessels. Collagen fibers were found within the reticular fibers and they were distributed in a similar manner to the reticular fibers (Fig.18).

Smooth muscle fibers were scattered randomly in the stroma of the ovary, in the tunica albuginea, the septa between the ovigerous cords and around the follicles in the cortex, while in the medulla the smooth muscles fibers were found around the rete ovarii and the blood vessels and in the medullary stroma.

4.2 Histometry

4.2.1 First trimester

The diameter of the intraovarian primordial germ cells, ranged between 7.8 and 11.7 µm with an average of 9.2 µm. The diameter of the primordial germ cells which were observed in the mesonephric tubules and the mesothelium ranged between 7.8 and 10.4 µm with an average of 8.9 µm. The diameter of the oogonia ranged between 13 and 16.9µm with an average of 15.7 µm. The thickness of the cortex ranged between 192.60 and 246.10 µm with an average of 219.35 µm, while the thickness of the medulla ranged between119.84 and157.7 µm with an average of 195.74 µm.

4.2.2 Second trimester

The diameter of the primordial follicles ranged between 22.4 and 36.7 µm with an average of 30.1 µm. The thickness of the tunica albuginea ranged between 32.4 µm and 51.5 µm with an

average of 43.4 µm. The thickness of the cortex ranged between 302.17 and 573.52 µm with an average of 383.01 µm, while the thickness of the medulla ranged between 267.50 and 710.48µm with an average of 344.34µm.

4.2.3 Third trimester

The diameter of the primordial follicles ranged between 24.3 µm and 44.3 µm with an average of 33.6 µm.The diameters of primary follicles ranged between 27.8 and 67.5 µm with an average of 48.03 µm while the diameter of primary oocytes ranged between 9.8 µm and 13 µm with an average of 10.9 µm. The diameter of growing follicles ranged between 145.75 and 343 µm with an average of 205.8 µm.

The diameter of the antral (preovulatory follicles) ranged between 596.25 and 1192.5 µm with an average of 887.55 µm, while the diameter of the cavity of the antral follicles ranged between 452.05 and 667.3 µm with an average of 549.55 µm. The thickness of the stratum granulosum ranged between 41.2 and 247.2 µm with an average of 113 µm and the thickness of the theca layer ranged between 103 and 287 µm with an average of 180 µm. The thickness of the tunica albuginea ranged between 72.1 and 82.4 µm with an average of 77.25 µm. The thickness of the cortex ranged between 278.20 and 633.44 µm with an average of 450.95 µm, while the thickness of the medulla ranged between 700.78 and 1443.79 µm with an average of 905.89 µm.

Table 2. Showing the diameter of different types of germ cells during first trimester

		Diameter	
Germ cells	**Minimum**	**Maximum**	**Average**
Extra ovarian Primordial germ cells	7.8 µm	10.4 µm	8.9 µm
Intra ovarian Primordial germ cells	7.8 µm	11.7 µm	9.2 µm
Oogonia	13 µm	16.9 µm	15.7 µm

Table 3. Showing the diameter of primordial follicles and the thickness of the tunica albuginea during second trimester

Diameter	**Minimum**	**Maximum**	**Average**
Primordial follicles	22.4 µm	36.7 µm	30.1 µm
Tunica Albuginea	32.4 µm	51.5 µm	43.4 µm

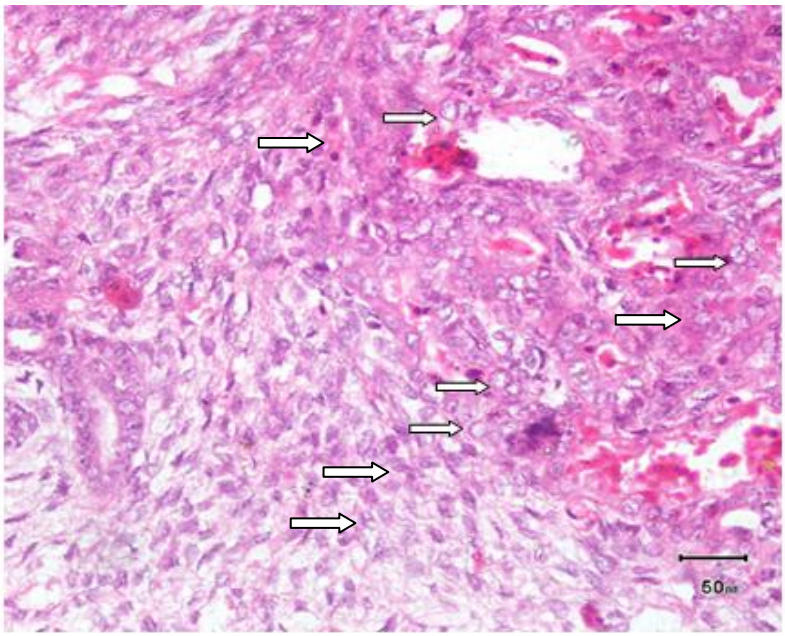

Fig. 1. Photomicrograph of the connective tissue between the ovary and mesonephros during the early stage of first trimester (8 cm CVRL, 87days old foetus);
Note the presence of a few primordial germ cells during their migration towards the ovary (arrows). H &E stain, X 400

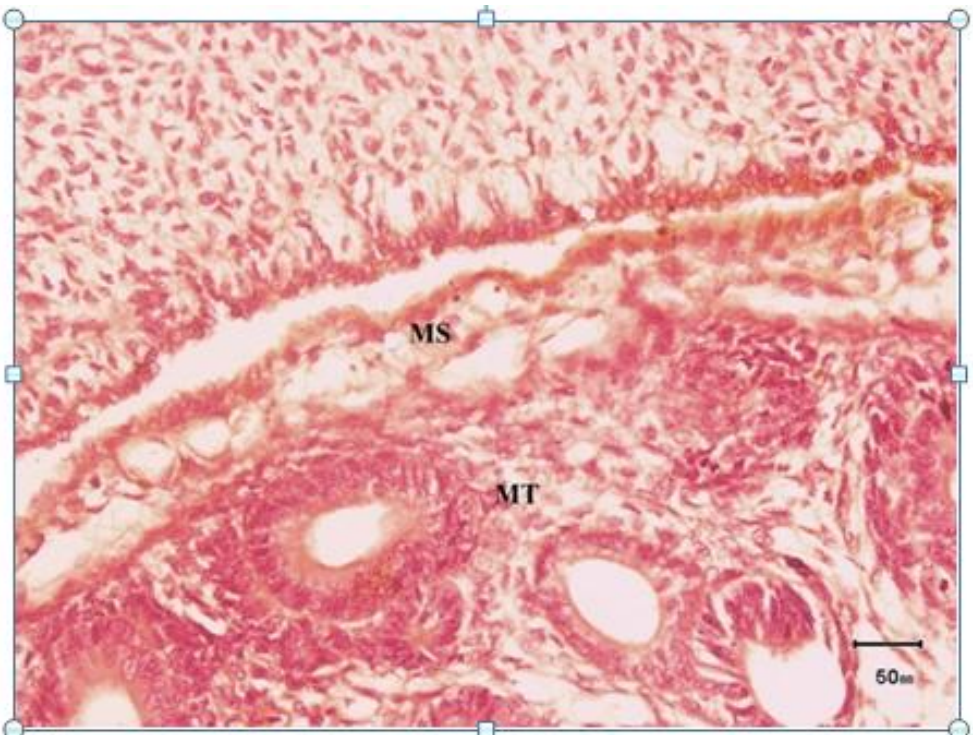

Fig. 2. Photomicrograph in the outer zone of the developing ovary during the early stage of the first trimester (6 cm CVRL, 82 days old foetus); The surface epithelium consists of elongated wedge-shaped cells and the basement membrane and tunica albuginea were absent (MS): mesothelium and the (MT): Metanephros. H &E stain, X 100

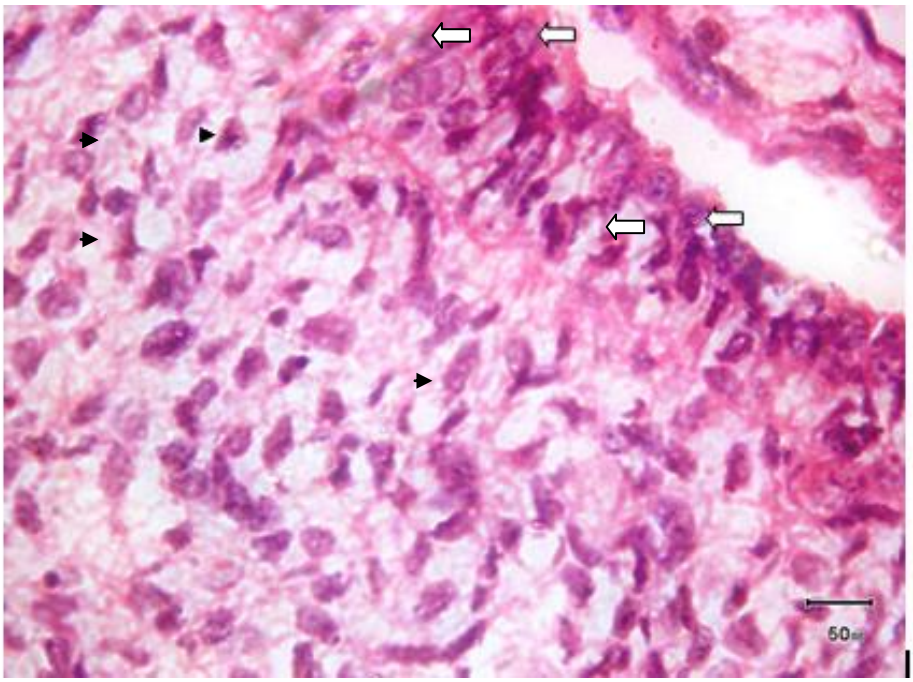

Fig. 3. Photomicrograph during the early stage of the first trimester (6 cm CVRL, 82 days old foetus); The primordial germ cells were seen within the cells of the surface epithelium (white arrows);

Note the mesenchymal cells with cytoplasmic processes are present (arrow black). H &E stain, X 1000

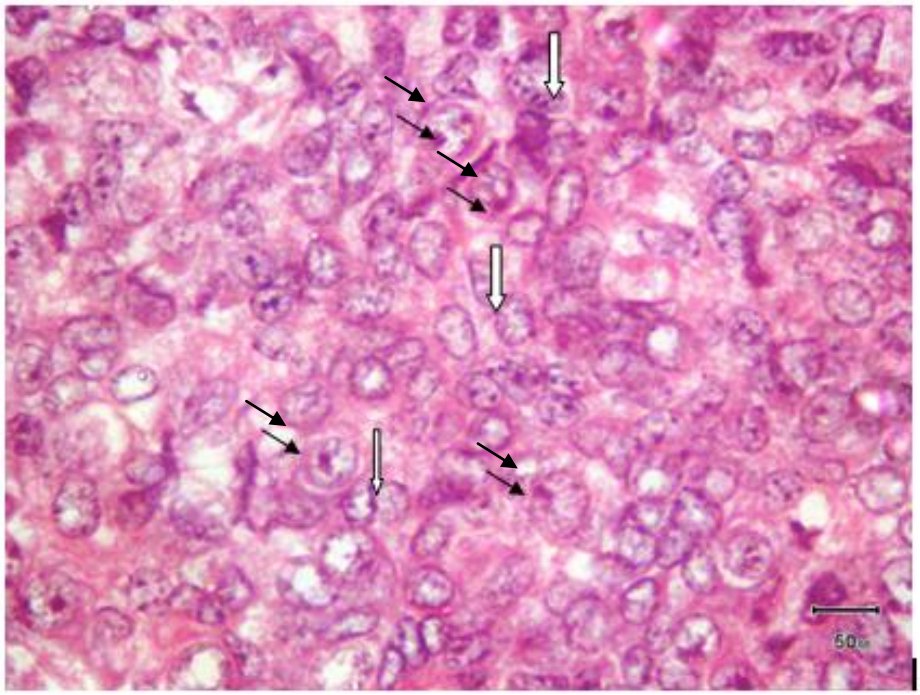

Fig. 4. Photomicrograph showing the cortical zone of the ovary during the early stage of the first trimester (6cm CVRL, 82 days old foetus);

Note the ovigerous cords formation (Somatic cell- germ cell complex). Follicular cells, small and oval shaped, (arrows) found adjacent to the large oogonia (arrows heads). H &E stain, X 1000

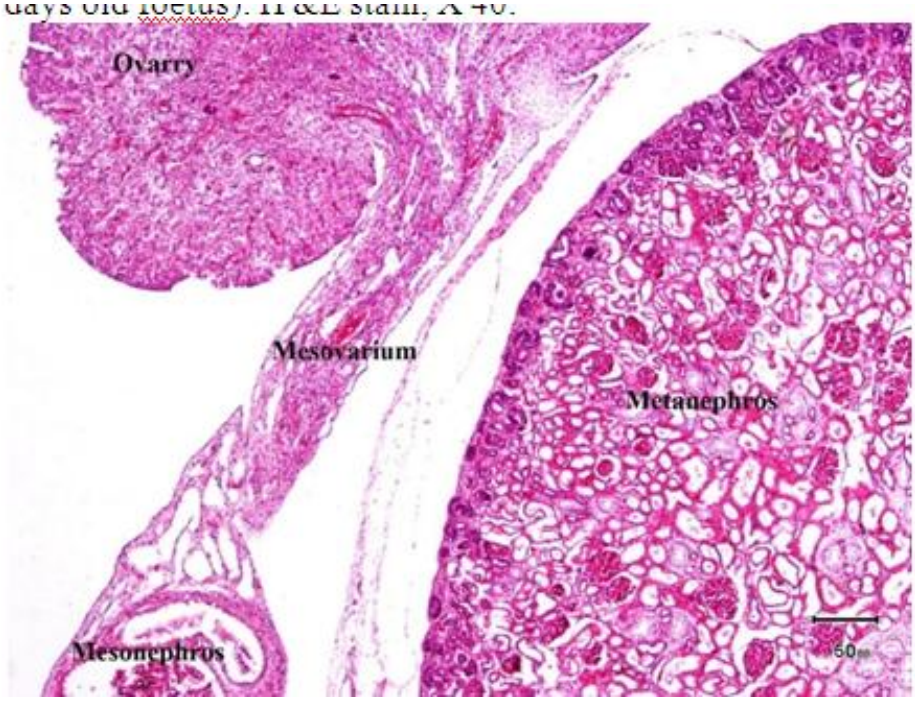

Fig. 5. photomicrograph showing the topography of the ovary in relation to the mesonephros, metanephros and the mesovarium during the first trimester, (15 cm CVRL, 106.5 days old foetus)

H &E stain, X 40

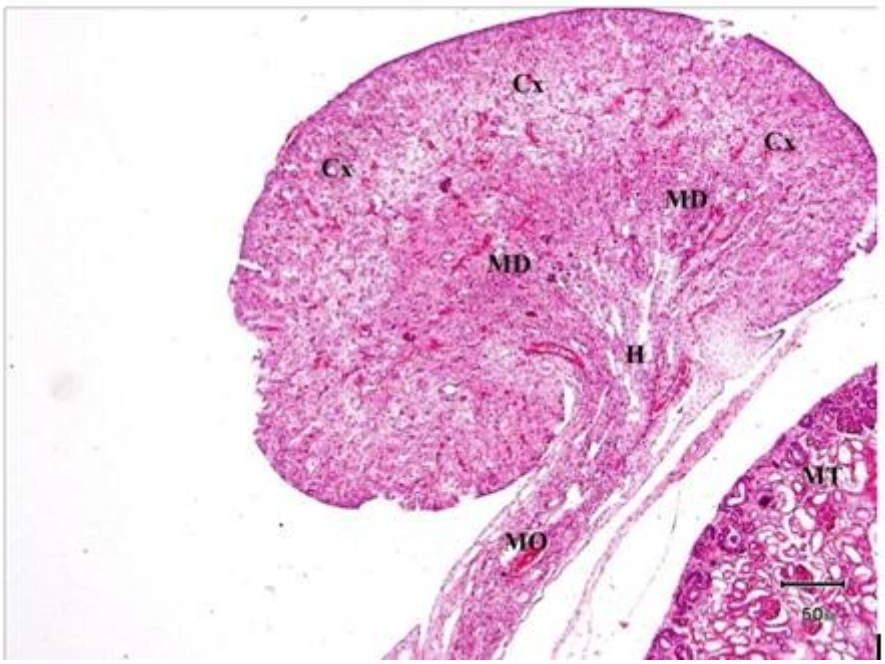

Fig. 6. Photomicrograph of the ovary during the first trimester, (15 cm CVRL, 106.5 day old foetus). Showing the cortex (Cx), the medulla (MD), the hilus (H), mesovarium (MO) and the metanephros (MT)

H &E stain, X 40

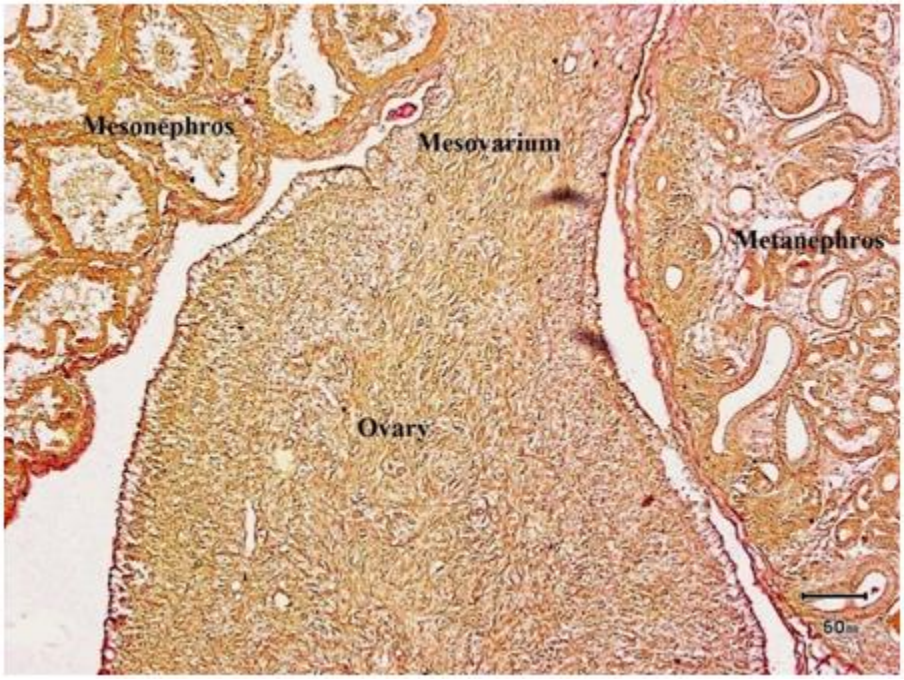

Fig. 7. Photomicrograph illustrating the ovary during the early stage of the first trimester (6 cm CVRL, 82 days old foetus) and the relation between the ovary, mesonephros, mesovarium and metanephros

VanGieson stain, X100

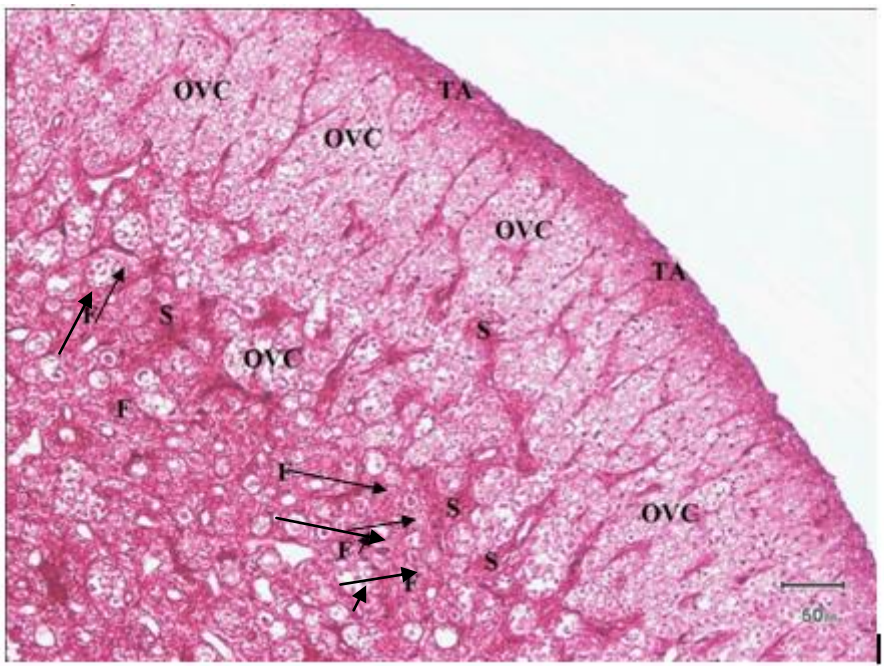

Fig. 8. Photomicrograph of the cortex of the ovary during the second trimester (49 cm CVRL, 199.4 days old foetus) demonstrating the surface epithelium (arrows), the tunica albuginea (TA), the ovigerous cords (OVC), the septum between the ovigerous cords (S) and small follicles (F)

H &E stain, X 100

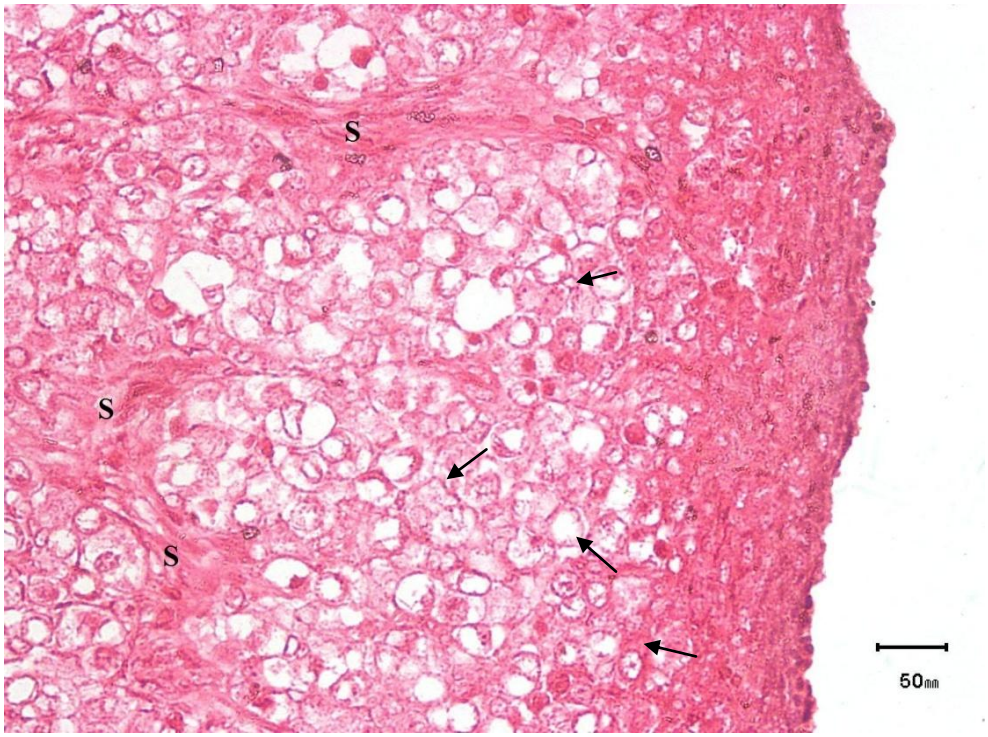

Fig. 9. Photomicrograph of higher magnification from (figure, 25) showing the ovigerous cords separated by septa (S) and contained oogonia (arrows) and follicular cells (arrows heads)

H &E stain, X 400

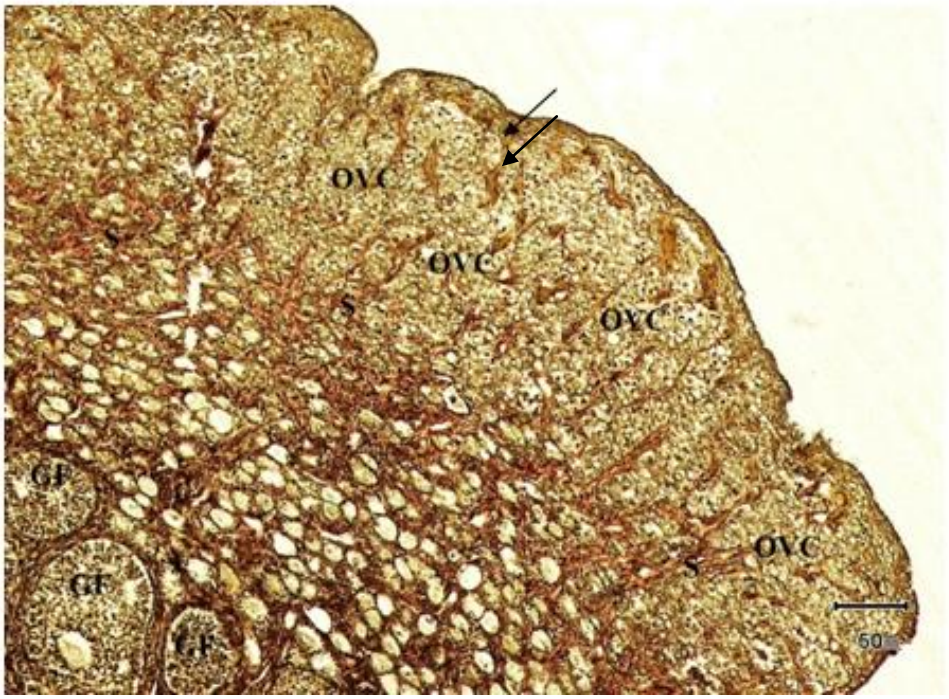

Fig. 10. Photomicrograph of the cortex of the ovary during the second trimester (65 cm CVRL, 243 days old foetus). Note the surface epithelium (arrows), the septum (S), the ovigerous cords (OVC) and growing follicle (GF)
Verhoeffs stain X 100

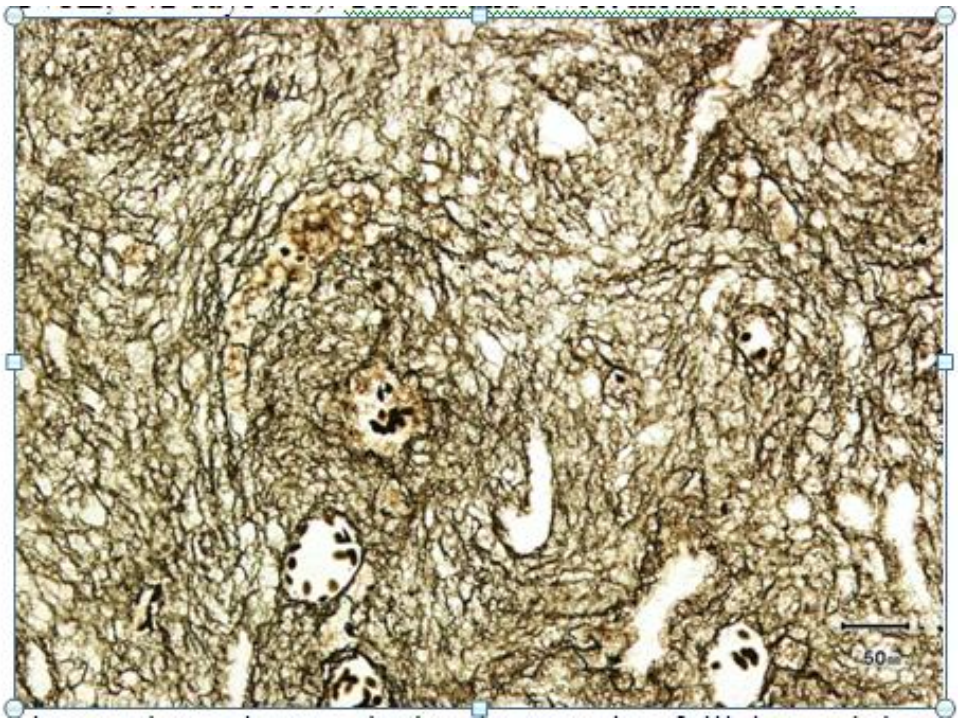

Fig. 11. Photomicrograph demonstrating the reticular fibers in the medulla of the ovary during second trimester (28 cm CVRL, 142 days old)
Gordon and Sweet method, X 100

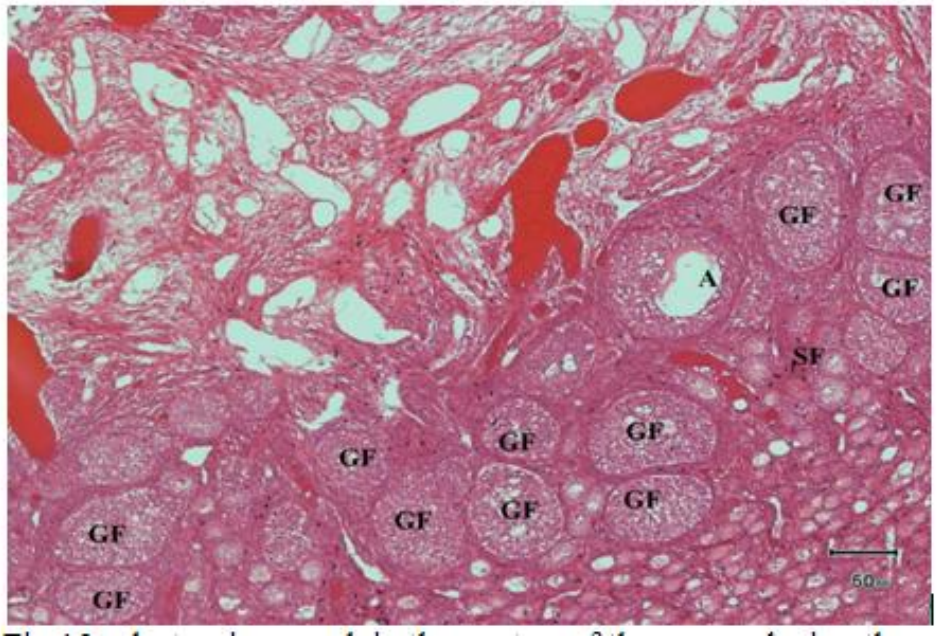

Fig. 12. photomicrograph showing growing follicles and the beginning of antral formation during the third trimester (75.5 cm CVRL, 271.8 days old foetus). Note the growing follicles (GF), the secondary follicles (SF), and the antrum (A)
H &E stain, X 100

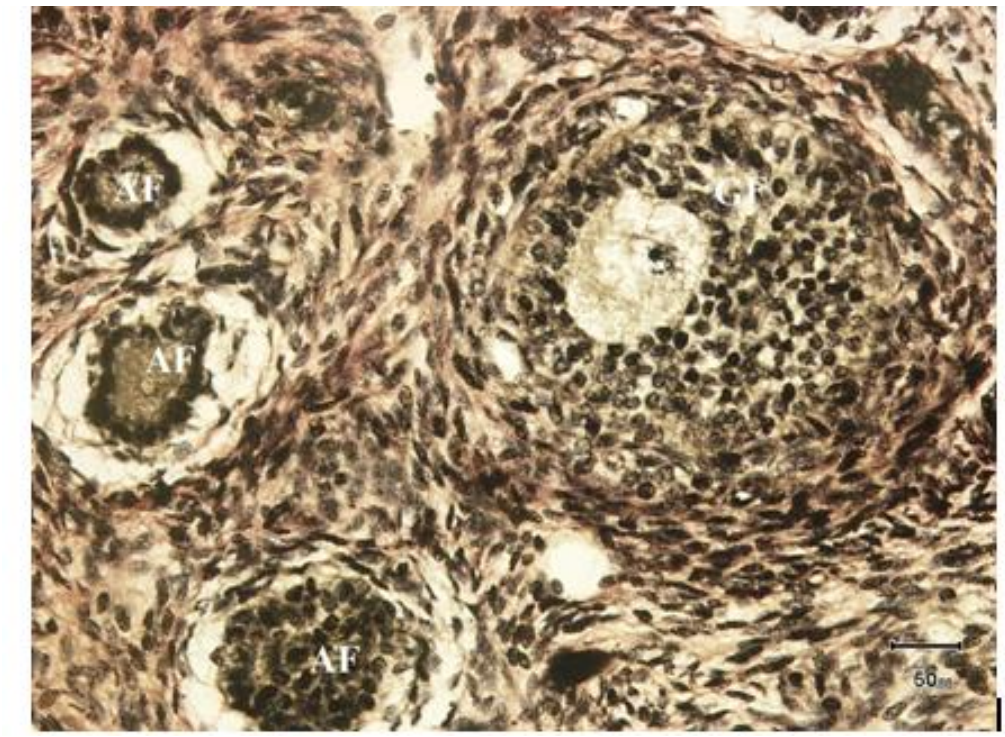

Fig. 13. Photomicrograph in the cortex of the ovary during the third trimester (85 cm CVRL, 297.8 days old foetus) showing a growing follicle (large and the atretic follicle (AF)
Verhoeffs stain X400

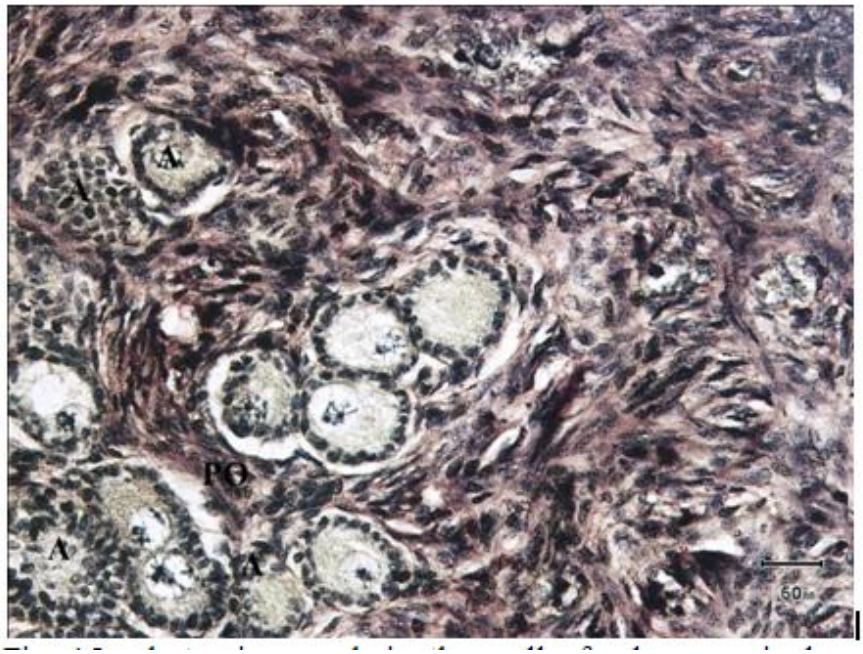

Fig. 14. Photomicrograph in the cortex during third trimester (90 cm CVRL, 311 days old foetus) showing primary follicle in a nest form, the atretic follicles (A) and the primary oocytes (PO)

Verhoeffs stain X400

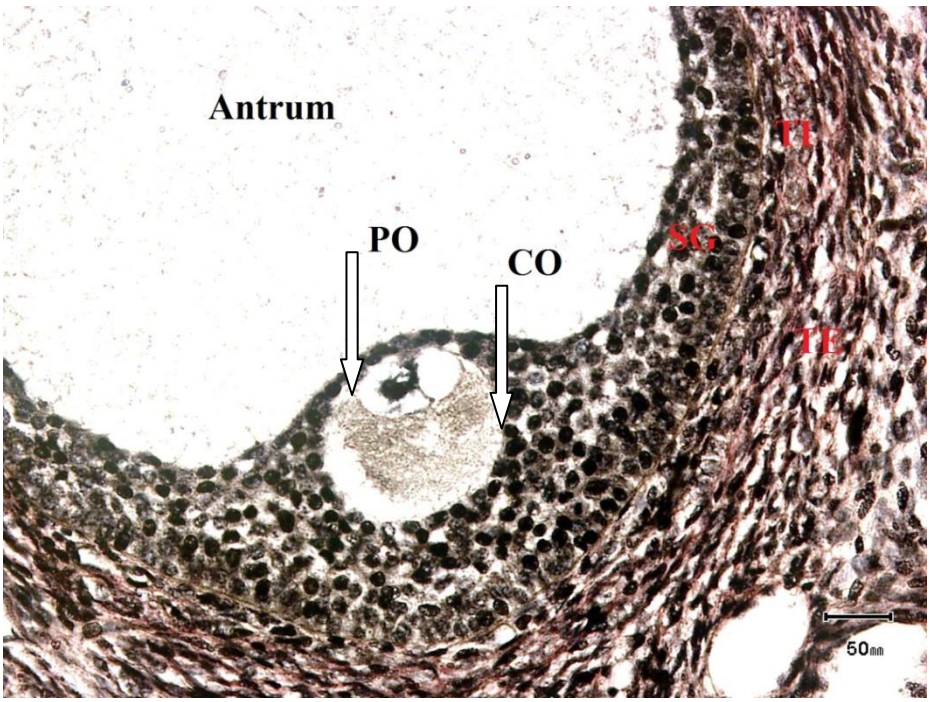

Fig. 15. Photomicrograph in the wall of a large vesicular follicle during the third trimester (100 cm CVRL, 338.8 days old foetus). The stratum granulosum (SG), the theca interna (TI), the theca externa (TE), the cumulus oophorus (CO), the primary oocyte (PO), and the antrum (Antrum) were seen

Verhoeffs stain X400

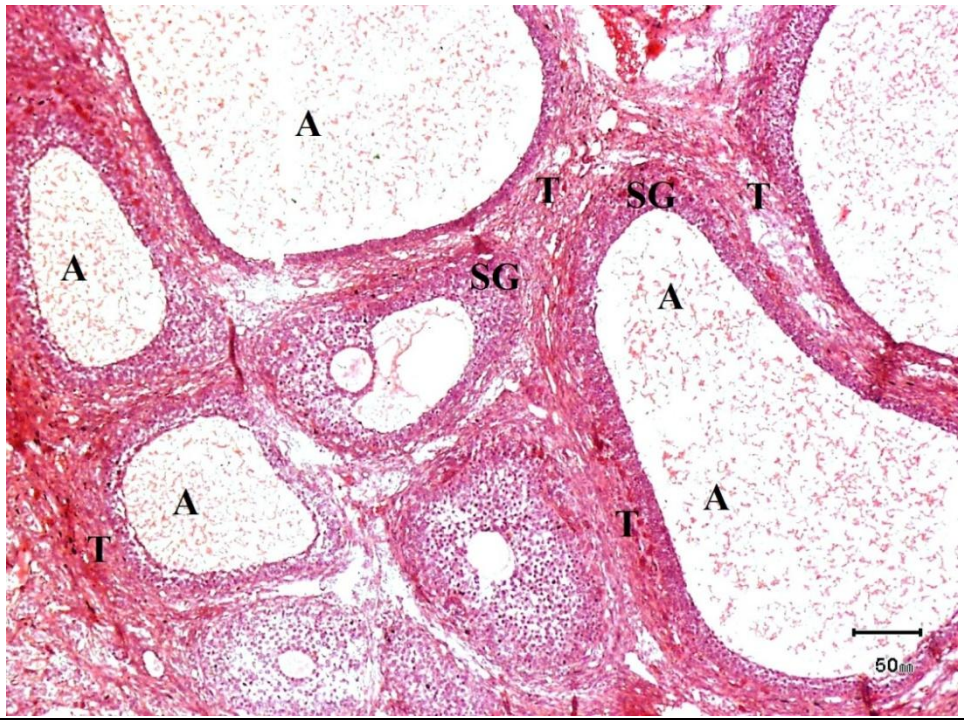

Fig. 16. Photomicrograph of a large atretic growing and antral follicles during the late stage of the third trimester (101 cm CVRL, 341.5 days old foetus). Note the stratum granulosum (SG), antrum (A) and theca layer (T)

H &E stain, X 100

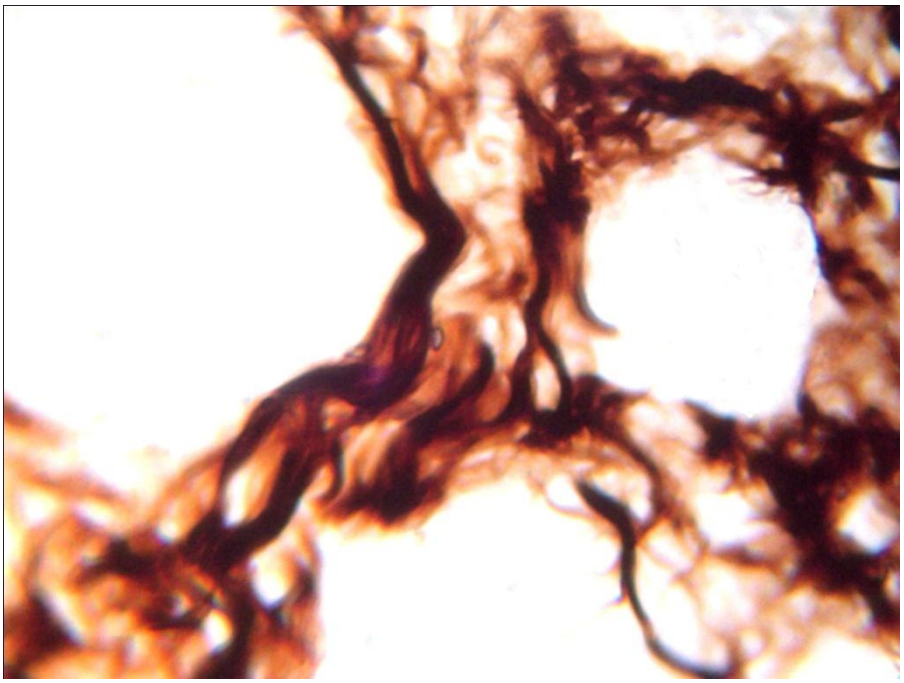

Fig. 17. Photomicrograph illustrating bundles of reticular fibers (dark black colors) between the ovarian follicles during the third trimester (103 cm CVRL, 347 days old)
Gordon and Sweet method, X 1000

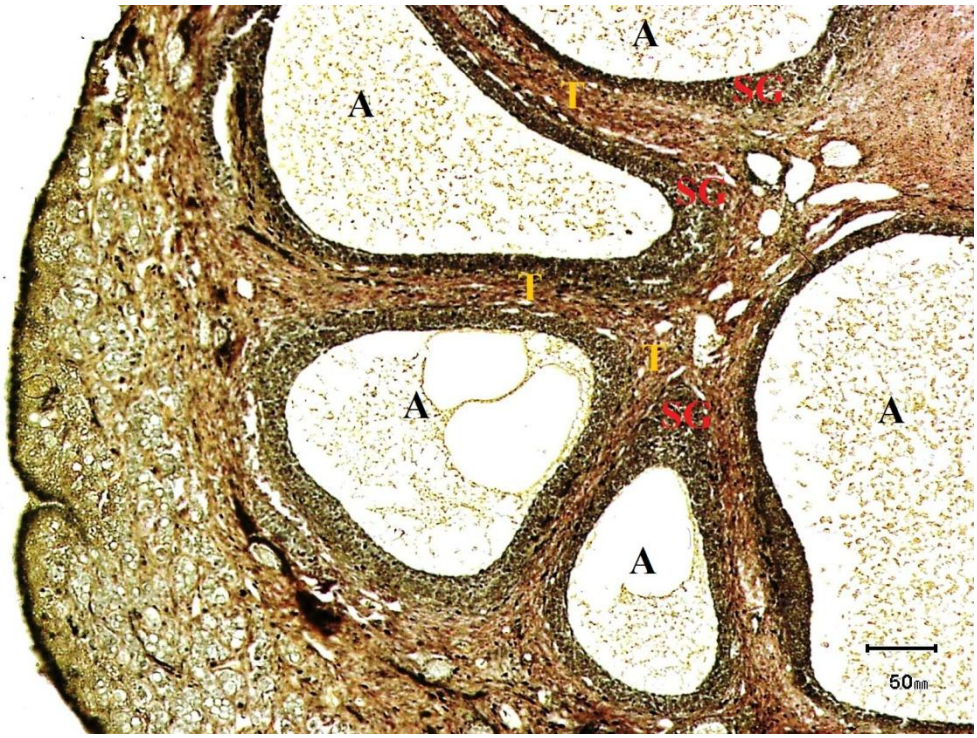

Fig. 18. Photomicrograph of a large atretic vesicular follicles during the late stage of the third trimester 104 cm CVRL (349.7 days old foetus).Showing stratum granulosum (SG), theca layer (T) and antrum (A)
Verhoeffs stain X40

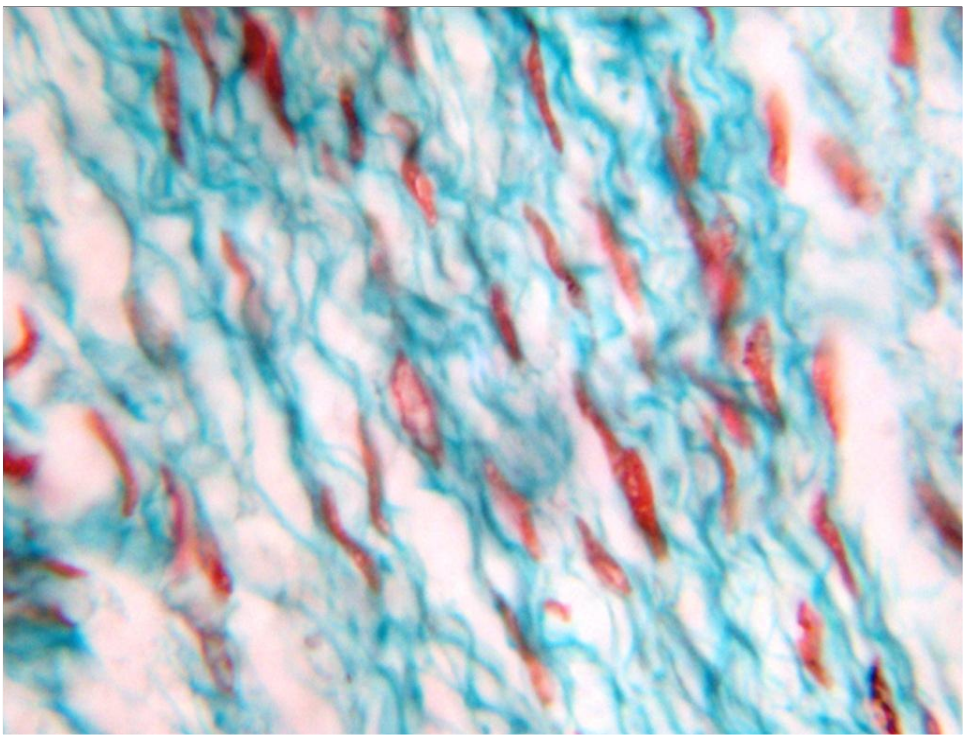

Fig. 19. Photomicrograph at higher magnification showing the smooth muscle fibers (red) and the collagen fibers (green) Massons Trichrome stain X 1000

Table 4. Showing the diameter of primary oocytes and different types of ovarian follicles and the thickness of some structures during third trimester

Follicles\cells	Minimum	Maximum	Average
Primordial follicles	24.3 µm	44.3 µm	33.6 µm
Primary follicles	27.8 µm	67.5 µm	48.03 µm
Primary oocytes	9.8 µm	13 µm	10.9 µm
Growing follicles	145.75 µm	343 µm	205.8 µm
Antral follicles cavity	452.05 µm	667.3 µm	549.55 µm
Diameters of antral follicle	596.25 µm	1192.5 µm	887.55 µm
Thickness of stratum granulosum	41.2 µm	247.2 µm	113 µm
Thickness of theca layer	103 µm	287 µm	180 µm
Tunica Albugenia	72.1 µm	82.4 µm	77.25 µm

Table 5. Showing the thickness of the cortex and medulla per µm

AN	CVRL	AID	Cortex	Medulla
1	6	82	192.6	119.84
2	15	106.5	246.1	195.74
3	25	134	302.17	267.5
4	30	147.5	338.12	276.5
5	33.3	156.5	342.4	214.00
6	43.3	183.9	450.83	338.12
7	48	196.7	291.04	259.45
8	64	240	573.52	710.48
9	75.5	271.8	633.44	700.78
10	78	278.7	430.85	462.24
11	85	297.8	278.2	481.5
12	89	308.7	542.13	10.80.13
13	104	349.7	404.46	1266.88
14	114	377	416.56	1443.79

Table 6. Showing the thickness of the cortex and medulla during first, second and third trimester

gestation		cortex			medulla	
period	**minimum**	**maximum**	**average**	**minimum**	**maximum**	**average**
first	192.60	246.10	219.35	119.84	157.7	195.74
second	302.17	573.52	383.01	267.50	710.48	344.34
third	278.20	633.44	450.95	700.78	1443.79	905.89

AN= foetal number, CVRL = curved crown rump length, AID= age in day

5. DISCUSSION

In the present investigations, there are three ovarian cell types during the early stage of development, distinguished by their morphological properties as germ cells or oogonia, pregranulosa cells or follicular cells, and stromal or mesenchymal cells. This finding is in accordance with Black and Erickson [17] in pig, El-Ghannam and El-Naggar [16] in buffalo foetus, Sawyer *et al.* [68] in sheep and Abdel Hafez [45] in camels. Sawyer *et al.* [68] stated that, in 5th weeks ovine foetus, there are five distinct cells types: 1- mesothelial cells that comprise the surface epithelium, 2- endothelial cells that lined the blood vessels, 3- mesenchymal cells or stromal cells, 4- follicular cells and 5- germ cells or oogonia. Black and Erickson [17] Sawyer *et al.* [68] Abdel Hafez [45,80] and Sadler [39] described Oogonia as spherical shaped cells and appeared to be more numerous toward the peripheray than the central region of the developing ovary. Mesenchymal cells are characterized by fusiform shape and cytoplasmic processes, while the follicular cells are smaller in shape and have oval dark nuclei and are found adjacent to the germ cells. These findings confirmed the finding in the present study. In the present study, the primordial germ cells were observed within in the mesothelium

and mesonephric tissue and were characterized by the large spherical or slightly irregular in shape (Amoeboid shape). Abdel Hafez [45] observed similar cells in the mesentery of the camel foetal gut during the early stages of development. The present findings and that of Abdel Hafez [45] indicated that in camel the primordial germ cells reached the gonads through the mesentery by amoeboid movement.

Both Sawyer *et al.* [68] and Abdel Hafez [45,83] detected somatic cell-germ cell complex in the cortex of the early developing ovary in sheep and camel respectively. Sawyer *et al.* [68,78] suggested that, once a pregranulosa cell has made a contact with an oogonium, it appears that these somatic cell-germ cell complexes progressively fuse to give rise to tube like structures, the ovigerous cords which contain the oogonia. Juengel, Sawyer, Smith, Quirke, Heath, Lun, Wakefield and McNatty [69] and Abdel Hafez [45] stated that, the establishment of the pregranulosa cell-oogonial cell complexe marks the initial contact between the somatic cell and germ cells and is the first recognizable step in the process of ovigerous cords formation. These results are in accordance with the observation in the present study in 4.8 cm CVRL and 6 cm CVRL foeti that, the pregranulosa cells are laid adjacent to the oogonia. Abdel Hafez [45] suggested that, in camel foetus ranged between (8-12) cm CVRL (87.4-98 days old foetus); the ovigerous cords become more densely packed and more elongated. The ovigerous cords development progresses with advancing age and become more extensive and more convoluted and occupy the whole thickness of the ovary in 19 cm CVRL (117.5 days old foetus).Similar finding were demonstrated in the present study.

The apoptosis of germ cells is a type of physiological cell death which occurs in proliferating tissues In the present study, the death of germ cells was detected by intensely stained and irregularly shaped cells. This observation is in agreement with De Pol ***et al.*** [33,82,83] in human foetal ovary. Degeneration of germ cells is characterized by eosinophilia of the cytoplasm and intensely staining and clumped nuclear material as reported by Deanesly [70] in ferret and Challoner [71,78] in golden hamster ovary.

In the present study, during the early stages of development, the foetal ovary is covered by a single layer of different shapes of epithelial cells which are loosely arranged and do not rest on clear basement membrane. These results are in accordance with those of Abd El-Razik [46] and Abdel Hafez [45] in camel. In the above mentioned investigations, the tunica albuginea and the basal membrane of the germinal epithelium, during early stages of development, were absent. Its suggested that, the absence of those structures may allow the primordial germ cells to invade the developing ovary [46,45].

The present study and that of George and Fahmy [43] revealed that, the primitive germ cells are demonstrated among the ovarian germinal epithelial cells in camel foetus during development. Similar finding is detected by Arey [18] and Motta and Makabe [21] in human foetus, Abd El-Razik [46] and Abdel Hafez [45] in camel foetus. Those authors stated that, germ cells are always interspersed among the cells of the surface epithelium. Furthermore, Motta and Makabe [21] and sawyer *et al.* [68] indicated that, both the proliferating cords and the surface epithelium may contribute to formation of the early follicles.

Abdel Hafez [45] stated that, the formation of ovigerous cords and rete ovarii begins during the early stage of development in about 4 cm CVRL (76 days old foetus).

In the present observation, the precursor cells of the rete ovarii were detected at 6 cm CVRL (about 82 days old foetus) by the appearance of oval cells with dark chromatin and flat nuclei arranged in different ways in the prospective medullary region, and the ovigerous cord zone did not appear clearly until the age of 15 cm CVRL (106.5days old foetus) and at this age the septa between the ovigerous cord zones were poorly developed. The present finding is in agreement with that of Abdel Hafez [45].

The present investigation indicates that, the surface epithelium of the foetal ovary is simple cuboidal cells at first, changes to groups of small cells in (6.1- 6.6) month and then changes to a single layer of simple cuboidal cells or flat cells. These observations are in agreement with Gondos [19] in human foetal ovary in which the surface epithelium undergoes diffused proliferation during the fourth and fifth months of gestation after which is reversed to a single layer separated from the developing cortex by a tunica albugine and Makabe [21] stated that, they originate from the surface epithelium and related cords. Byscov [25] and Satoh [31] are of the

opinion that, these cells originate from the mesonephric precursor cells while Janis and Rudolf [37] supported the idea that they originate from the epithiloid cells of the theca interna and Osman [12] from atretic follicles. Our observation confirms both Byscov [25] and Satoh [31] because similar cells were observed in the mesonephric tissue and disagreed with the other authors.

Byscov ***et al.*** [24] suggested that the early steroid-producing cells of the rabbit ovary differentiate among the medullary mesonephric-derived cells long before follicles formation. In the immature mouse ovary and in the foetal human ovary, the initial steroid-producing cells differentiate only at the time when the follicles begin to grow.

Fawcett [50] mentioned that the stroma of the ovary contains conspicuous clusters and cords of large epithiloid interstitial cells in some species; they have been shown to secrete estrogen. Sardul and Gilbert [72] reported that interstitial cells in the hamster ovary occur as patches in different sizes and originate from theca hypertrophy. The finding in the present study is in agreement with Sakai [73] who claimed that, the interstitial cells are scattered randomly in a single manner during the first stage of development and with further development they are found in groups (small islets) in the vicinity of the blood vessels in the horse. Deanesly [74] observed that the interstitial cells are found in all parts of ovarian stroma including the hilus region in the guinea pig.

Both Salman [8] and Osman [12] observed leukocytes in the ovary of pregnant camels. Similar observation is detected in the present study in the first trimester foetal ovary; the leukocytes seen include neutrophils and monocytes which may act as protective cells (defensive cells).

The observations in the present study revealed that, the connective tissue in the cortex and medulla of the ovary takes a reticular form, in which the stroma is rich in argirophilic fibers with a few collagen fibers but no elastic fibers. Sakai [73] in horse sow and cow foetus and Mohammed [44] and Salman [8] in adult camels stated that, the stroma of the ovary of these animals consists of a network of reticular fibers. In the present investigation, elastic fibers were observed only in the walls of blood vessels and this observation is in agreement with that of Osman [12] in adult camel ovary. In the present study, the smooth muscle fibers were scattered randomly in the stroma of the ovary, in the tunica albuginea, in the septa between the ovigerous cords and around the follicles in the cortex, while in the medulla the smooth muscle fibers were found around the rete ovarii and the blood vessels and in the medullary stroma.

Byscov [48] stated that the first follicular formation occurs at the innermost parts of the ovary. McNatty *et al.* [32] reported that, the formation of the primordial follicle in the ewe foetal ovary occurs in the late stage of the first trimester (75 day of gestation) and Sawyer ***et al.*** [67] is of the opinion that the formation of the first follicles in ewe foetus occurs at the boundary between the cortex and the medulla. Abdel Hafez [45] stated that folliculogenesis started earlier in embryonic period and the first follicle was observed at 24 cm CVRL(131 days old foetus) camel foetus.

In the present study, the folliculogenesis starts during the early stages of the second trimester. This finding is in accordance with McNatty *et al.* [32] and Abdel Hafez [45] who stated that the first follicle formation is detected in the early stages of second trimester in (24) cm CVRL (131 days old) foetal ovary in the cortical zone adjacent to the boundary between the cortex and medulla.

The present study revealed that, the folliculogenesis starts during the early stage of the second trimester about 25 cm CVRL (134 days about days old foetus) and the first primordial follicle was observed in the interface between the cortex and medulla. In 28 cm CVRL (about 142 days old foetus) the first primary follicle was detected. During the last stages of the second trimester (65 CVRL about 243 days old foetus) the first growing follicle was observed and the antral follicles were observed during the early stages of the third trimester, while the large vesicular preovulatory follicles were found during the middle and late stages of the third trimester. Abdel Hafez [45] suggested that, folliculogenesis started earlier in 24 cm CVRL about (131 days old) foetus and both primary and growing follicles were demonstrated during (62-77) cm CVRL (235-276 days old foetus) while the antral follicles appeared in full term foetus. McNatty *et al.* [32] mentioned that, from day 75, 100, 120 and 135 days of gestation, primordial (one layer of flattened granulosa cells), primary (one complete layer of cuboidal granulosa cells; early

preantral), secondary (preantral) and tertiary (antral) follicles respectively developed within inner most regions of sheep foetal ovarian cortex. Lundy, Smith, O`Connel Hudson and McNatty [75] stated that, according to the configuration of the granulosa cells, the primordial follicle are classified into type (I) which consists of one layer of flattened granulosa cells and type (II) transitory follicle which consists of one layer of mixture of flattened and cuboidal cells.

The presence of nests of small follicles in the foetal ovary was detected in the present study during the second and third trimester. This observation was in accordance with the finding of Mohammed [44] who also observed follicular nests in the foetal camel ovary. The foetal ovary lacks a corona radiata in the antral follicles in the present study and this is also true in the adult camel ovary as reported by Mohammed [44] and Osman [12].

Follicular atresia is a phenomenon observed in most histological specimens in the present study as well as in adult camel as observed by Nawar, Abul Fadle and Mahmoud [76] Sakai [73]. stated that the follicle atresia in the foetal ovary was observed in cattle but not in the sow and horse.

El-Ghannam and EL-Naggar [16] claimed that, during the late stages of pregnancy in buffalo foetus, hormonal activity is indicated by the presence of vesicular follicles which then become atretic.

Isofolliculia is a phenomenon characterized by the presence of large antral follicles almost equal in size and coincided with a sudden increase in weight and dimensions of both left and right ovaries and an increase in the plasma level of follicle stimulation hormone and luteinizing hormone [77]. These authors also mentioned that, the whole cortical parts of the ovary is occupied by large antral follicles with equal size and have well expressed theca interna but no interstitial cells were observed during early postnatal development of the lamb. Many researchers (Sakai, [73] Erickson 1966; and El-Ghannam and El-Naggar [16] have found, in prenatal ovaries in different animals, an increase in antral follicles growth during the late stage of pregnancy but did not identified this as Isofolliculia. Sakai [73] suggested that, the mature follicles were observed in the last period in prenatal bovine ovary while Erickson (1966) and El-Ghannam and El-Naggar [16] suggested that, the sudden increase in weight of the bovine and buffalo foetus ovaries during the late stage of gestation is coincided with the development of atretic vesicular follicles and with the increase in the maternal plasma follicle stimulation hormone level at that time. Sardul and Gilbert [72] reported that, the atresia of vesicular follicles is due to the lack of sufficient endogenous gonadotrophin which prevents these follicles from maturation. In camels, Abd El-Razik [46] observed that the ovaries of camel foetus during 12 month of gestation have many antral follicles of variable size. Antral follicles were observed in the foetal sheep ovary around day 135, which is about 12 days before parturition [69]. Abdel Hafez [45] demonstrated antral follicles in the late stage of prenatal development (108 cm CVRL, 360.6 days old foetus) in the camel foetus. In the present study, the large atretic vesicular follicles were found in the late stage of third trimester (85-119) cm CVRL (297.8-390.6 days old foetus) and were found in both left and right ovaries and they increased in number with the increase of the foetal age to reached 27 follicles in full term foetus (119 cm CVRL, 390.6 days old foetus) and their presence was associated with the absence of the interstitial cells. The increase of vesicular follicle is associated with an increase of both weight and dimensions of the ovary. This phenomenon suggested an interaction between the maternal and foetal hormones through the placental barrier and the beginning of hormonal secretion by the foetus. The present finding supports the suggestion of Saki (1955) and Erickson (1966) in bovine and Abd E-Razik [46] in the camel prenatally and that of Mahdi and Khalili [77] in sheep postnatally.

The histological appearance of the atretic follicle in adult camels varied enormously depending on the stage of development and the progression of atresia [62,60]. These authors also mentioned that, in the Graafian follicle or preovulatory follicle, the secondary oocytes was detached from the granulosa cell layers. Similar observation has been detected in the present study but the oocytes were detached during the primary stages of follicular development.

The present investigation shows that, during the early stages of the first trimester, the precursors of the rete ovarii cells were scattered in a random manner in the inner most region of the ovary and contained oval dark nuclei. With the advancement of development, these cells assembled in simple tubules which were lined with dark and light cells. Then these cells

proliferated and the tubules became more branched and contained a secretory material in their Lumina.

It was suggested that the secretion of these tubules is associated with the division of ovarian germ cells. Sakai [73] stated that, the medullary cords in the foetal ovary of the swine and cattle precede the ovigerous cords in development and they occupy the medullary region at the beginning but they show a rapid degeneration coincided with the degeneration of the ovigerous cords. It was suggested that the medullary cords arise from the mesenchymal tissue rather than the remainder of the mesonephros [73]. Byscov [48] suggested that the rete ovarii have a role in meiosis and follicular formation and in all animals the extra ovarian rete cells were actively secreting. Moreover, the rete system interacts with the cortex and initiates the starts of meiosis, and the cells of the rete system as well as the cells of the surface epithelium contribute to the granulosa cells.

Archbald *et al.* (1971) reported that the cells of the rete ovarii were located in the ovarian medulla and were composed of cells with oval-shaped nuclei with prominent chromatin and small amount of lightly stained cytoplasm. These cells were either arranged in a single layer or in a pseudostratified layer. Tube-like and circular arrangements of the rete ovarii were observed. The circular arrangement was reminiscent of the structure of primordial ovarian follicles. Byscov and Moore [47] and McGeady *et al.* [78] described the rete ovarii as structure composed of association of cell cords and tubules which extended from the ovary into pre ovarian tissue hilus region as well as intraovarian, extra ovarian and connection between intraovarian and extra ovarian portions.

Shehata [63] documented the presence of intercommunicating tubular structures within the medullary region of the ovary of the she-camel. These structures resemble glandular acini which are lined by cuboidal to columnar cells and they are not simple vestiges from embryonic life, but they may perform an active endocrine function. Similar observation was recorded in the present study.

A secretary activity in the rete ovarii was observed in the mouse [47] cat, mink and ferret [48] heifer (Archbald *et al.*, 1971) and camel [63]. Abdel Hafez [45] observed acidophilic secretion in the lumen of the rete ovarii. In the present study, a weak acidophilic secretion was observed. Arey [18] described the primitive rete ovarii in human foetus as a compact cellular mass bulged from the medulla into the mesovarium. These observations were similar to the present study.

The presence of fissures in the outer surface of the camel ovary was observed by George and Fahmy [43] during 12-16 weeks of gestation. The germinal epithelium forms a number of enfolding of varying degrees; some of them involve the whole thickness of the cortex. These fissures become much deeper with advancing development until the foetus reached (20-24 weeks) after which they gradually become shallow until they completely disappear. Similar finding was stated by Abdel Hafez [45]. The finding in the present study is in agreement with both George and Fahmy [43] and Abdel Hafez [45]. In the present investigation, the irregularity in the surface epithelium, during the third trimester foetal ovary may be due to the active division and proliferation of the cortical cells and the presence of the large follicles.

The present study showed that, in 22 cm CVRL (126 days old foetus) camel foetus, the whole cortical region was filled with ovigerous cords and the follicular zone was completely absent. In 28 cm CVRL(142 days old foetus), two distinct zones in the cortex were distinguished; the ovigerous cords zone which is a large zone and occupied the major part of the cortex and the follicular zone which is a narrow zone and situated in a narrow space in the cortex. With advancing age, the ovigerous cord zone regressed and the follicular zone increased in size until the ovigerous cords zone disappeared completely during the late stages of the third trimester. These findings are in agreement with Sawyer et al. [67] in sheep and Abdel Hafez [45] in camel.

5.1 Histometry

The present study revealed that, the average diameter of the germ cells gradually increases from 9.2 µm in the primordial germ cells to reach 15.7 µm in the oogonia, while the primary oocyte showed decrease in the average diameter 10.9 µm. The average diameter of the primordial follicles increases from 30.1 µm in the second trimester to reach 33.6 µm in the third trimester, while the average diameters of the primary follicles, growing follicles and vesicular preovulatory follicles are 41.5 µm, 205.8 µm and 887.5µm respectively.

Abdel Hafez [45] revealed that, the diameter of the prenatal germ cells in female camel is about 7.3 µm in the primordial germ cells and 10.4 µm in the oogonia, while the diameter of primary oocyte in different stages of the first miotic division are 11.01 µm, 9.9 µm, 10.1 µm and 11.5 µm in leptotene, zygoten, pachytene and deploten respectively. The figures in the present study are different from those of Abdel Hafez [45]. This may be due to difference of breeds of camels or type of fixation and processing in the two investigations.

6. CONCLUSIONS

- The development of the camel foetal ovary is in general similar to the development of the other domestic mammals ovary but with special features of its own.
- There are indications that the primordial germ cells reached the gonad through the mesentery like other domestic mammals.
- The first primordial follicle appeared at 25 cm CVRL, about 134day old foetus, the first primary follicle was observed at 28 cm CVRL, about 142 days old foetus. During the last stage of the second trimester 65 cm CVRL, about 243 days old foetus the first growing follicle was observed. The antral follicles and the large vesicular follicles were observed during early and last stages of the third trimester respectively.
- The ovigerous cords disappeared at 90 cm CVRL, about 311 day old foetus.
- The surface epithelium consisted of different shapes of cells which did not rest on a clear basement membrane or tunica albuginea. The primordial germ cells were scattered among these cells.
- Oogonia with large round vesicular elements were found in the outer cortex and surrounded by the follicular cells.
- The ovigerous cords, which contained the oogonia in different stages of division and follicular cells, became more convoluted and filled the major part of the cortex in 22 cm CVRL 126 day old foetus and then began to degenerate during the formation of the first follicle.
- Future work is needed to study the ultrastructure of the cellular elements and the immunohistochemistry of the developing ovary of the camel during the prenatal life.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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Competing interests

Authors have declared that no competing interests exist.

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