INTRODUCTION
Currently, the attention of many researchers is directed at determining the patterns of the chronological sequence of development and formation of topographic and anatomical relationships between organs and structures of different systems during the prenatal period of human ontogenesis, which is important for the elucidation of the morphological preconditions for the emergence of anatomical variants and congenital malformations [1]. The obtained and systematized embryotopographic data should play one of the decisive roles in the prevention of perinatal pathology [2, 3].
The rapid development of perinatal gynecology requires from the anatomists comprehensive studies of the patterns of prenatal morphogenesis and the development of toponographic and anatomical relationships of female reproductive organs in the human fetuses of different age groups [4].

Adequate conducting of sonographic research, performing surgical operations on the fetal organs in the womb, interpreting the results of computer and magnetic resonance imaging and fetal dissections are based on objective anatomical data [3, 5]. However, there is now a paradoxical situation in which many diagnostic and therapeutic manipulations are carried out on the fetuses, but still there is a lack of systematic and generalized fetal anatomy manuals [6].

R.H. John [7] indicates that the proliferation of cells in the dorsal wall of the urogenital sinus (UGS) leads to the formation of epithelial expulsion of the entire vagina, replacing the epithelium of the uterovaginal canal up to the cervix. This conclusion is based on histological studies performed on prefersuses and female fetuses [8].

Clinical observations of full uterine and vaginal duplication, starting from vaginal vestibule, contradict the current opinion about the development of the vagina from various embryonic sources: the proximal part of the vagina – from the paramesonephral ducts (PMD), and the distal one – from the odd UGS. L.V. Adamyan, Z.N. Makyan [9] in none of their observations (in norm and with different anomalies) noted the anatomical and histological differences between the proximal and distal parts of the vagina, which would confirm their development from various embryonic sources. At the same time, the authors concluded that the uterine tubes, uterus and vagina develop from mesonephral ducts (MD). However, according to this concept, the development of vaginal vestibule occurs independently of MD and PMD. This assumption is based on the observation of the normal development of vaginal vestibule in all patients with Rokitansky-K?ster syndrome (with uterine and vaginal aplasia), with atresia of the hymen membrane and aplasia of the distal part of the vagina [10, 11]. Researchers believe that the vaginal vestibule develops from UGS, which also contradicts the development of endometrioid cysts of large vestibular glands [12, 13]. According to M. Sanchez-Ferrer, P. Acien, Sanchez Del Campo et al. hypothesis [14] the vagina develops from MD and M?ller's tube. PMD are brought closer until fused into a common duct and are finally connected in the region of UGS (M?ller's tube). The latter is the distal part of the MD. This is evidenced by the localization of markers (GZ1 and GZ2), specific for MD cell membranes, in immunohistochemical staining. Muller's tube is observed between these elements. A number of authors [11, 15] argue that the derivatives of MD are the source of vaginal development. Hence, the problem of normal morphogenesis of the vagina during the prenatal period of human ontogenesis remains unclear until now.

**THE AIM**

To study the development and formation of the vaginal topography in the prenatal period of human ontogenesis.

**MATERIALS AND METHODS**

The study has been conducted based on 23 series of histological and topographic-anatomical sections of human prefersuses aged 9-12 weeks with 31.0-80.0 mm of crown-rump length (CRL) and 83 specimens of female human fetuses aged 4-9 months with 81.0-345.0 mm of CRL by means of a complex of adequate morphological methods of investigation, which includes: macroscopy, manufacturing and microscopy of series of sequential histological and topographic-anatomical sections of human prefersuses, ordinary and fine preparation under the control of binocular magnifying glass, injection of vessels, three-dimensional computer reconstruction and morphometry.

The age of the objects of study was determined by B.M. Patten (1959), B.P. Khvatov, Yu.N. Shapovalov (1969) tables on the basis of CRL measurements. The study also involved the series of histological and topographic-anatomical sections of human prefersuses with 31.0-80.0 mm of CRL, as well as specimens of female urogenital organs of fetuses of various ages from the Museum of the Department of Human Anatomy named after M.H. Turkевич of Bukovinian State Medical University. Specimens of fetuses weighing over 500.0 g were studied directly in Chernivtsi Regional Children's Pathology and Anatomy Bureau. The Commission on Biomedical Ethics of Bukovinian State Medical University revealed no moral and legal violations during medical scientific research.

**RESULTS**

In the result of conducted study it was determined that vaginal formation occurs during the 9th week of embryogenesis (prefersuses of 31.0-41.0 mm of CRL) due to the fusion of two different embryonic structures: mesodermal PMD and endodermal UGS. In this case, the caudal regions of the PMD are transformed into the uterus and the superior two thirds of the vagina. The inferior third of the vagina develops from the UGS, in particular, from the area where M?ller's tubercle develops.

Common uterovaginal canal, around which there is a pronounced concentration of mesenchymal cells, is formed in the female prefersuses of 38.0-43.0 mm of CRL due to the fusion of the caudal regions of the PMD in the area of the posterior wall of the UGS. Mesenchymal septum divides uterovaginal canal into right and left cavities, which have the appearance of fissures. The thickness of the septum of the uterovaginal canal in the superior and inferior regions ranges from 38 to 44 µm, and in the middle region it equals to 26-29 µm. After the formation of the Y-shaped uterovaginal canal, its caudal end enters the dorsal wall of the UGS, resulting in the development of the protuberance – M?ller's tubercle. From the latter in its distal region there is the beginning of the formation of the vestibular bulb. Vestibular bulbs are paired endodermal protrusions, which, in the form of taenia, arise from the UGS to the caudal regions of the uterovaginal canal, and participate in the vaginal structures formation. The structures of the vaginal wall, along with the vestibular bulbs, separate the UGS to the
level of the perineum. Such a transformation leads to the corresponding anatomical position of the female urethra.

Dissolving of the mesenchymal septum of the uterovaginal canal begins in the female fetuses of 44.0-53.0 mm of CRL, at the same time the thinning of its middle part occurs, and at subsequent stages (fetuses of 55.0-58.0 mm of CRL) complete dissolving of the septum is observed (Fig. 1).

The superior vertical sections of the urogenital taenia in female fetuses of 62.0-66.0 mm of CRL due to the reduction of MD, involve predominantly PMD, which are divided by a loose mesenchymal layer. Fallopian tubes develop from these PMD sections. Oblique (middle) PMD sections are transformed into the intrauterine portions of the fallopian tubes. The inferior PMD sections are transformed into the uterus and the upper two thirds of the vagina. Uterovaginal canal is lined with a pseudo-multinucleated epithelium, outside of which there is a considerable layer of densely located mesenchymal cells (Fig. 2). There also appears a significant accumulation of mesenchymal cells between the bladder and the rectum.

In 4-month-old female fetuses the posterior surface of the bladder adjoins the body and cervix of the uterus. The latter in relation to the vagina is tilted to the front at an obtuse angle. The vagina is tube-shaped, filled with a white mushy mass. The supravaginal portion of the cervix is covered by a peritoneum and is separated from the inferior portion of the posterior wall of the bladder by a minor layer of loose cellular tissue. The peritoneum from the superior-posterior surface of the bladder passes to the anterior surface of the uterus, forming a cystic-uterine excavation. The latter has a fissure-like appearance 5.0-7.5 mm deep at the sagittal section. Longitudinal plicae of the mucous membrane of the uterus are absent. The uterine fundus in 4-month-old fetuses is not developed and is located below the level, where fallopian tubes arise. In most fetuses, the superior minor portion of the vagina adjoins the inferior part of the posterior wall of the bladder and is separated from it by a thin layer of loose cellular tissue. The peritoneum from the superior-posterior surface of the bladder passes to the anterior surface of the uterus, forming a cystic-uterine excavation. The latter has a fissure-like appearance 5.0-7.5 mm deep at the sagittal section. Longitudinal plicae of the mucous membrane of the uterus are absent. The uterine fundus in 4-month-old fetuses is not developed and is located below the level, where fallopian tubes arise. In most fetuses, the superior minor portion of the vagina adjoins the inferior part of the posterior wall of the bladder and is separated from it by a thin layer of loose cellular tissue. The latter in the pelvic section forms a flexure with convexity towards the posterior surface, and at the transition to the peritoneal section – with a backward convexity. In the frontal plane, the rectum forms two lateral flexures, which, in their convexity, are directed to the right and to the left. The rectum is more or less filled with meconium. The muscle-constrictor of the vagina, 2.8-4.5 mm in length, is represented by single fibers, which in the form of a band envelop the vaginal vestibule and cover the vestibular bulbs. The muscle-levator of the anus is usually quadrangular in shape. The internal (medial) bundles of the pubococcygeal muscle, as a part of the muscle-levator of the anus, are closely adjacent to the lateral walls of the urethra and the vagina and are attached to the anterior and lateral walls of the rectum. In 4 out of 6 examined 4-month-old female fetuses, the medial bundles of the pubococcygeal muscle inosculate with the posterior part of the lateral walls of the vagina (Fig. 3, 4).

In 5-month-old fetuses vagina is located in the lower part of the minor pelvis, in front of it there is the fundus of the bladder, and the urethra is below it. Female urethra is a short, slightly curved tube, which begins with the internal ostium of the urethra and opens on the front of the vaginal opening (Fig. 5). The length of the urethra in the 5-month-old fetuses is 10.09±0.1 mm. The peritoneum, covering the superior part of the posterior wall of the vagina, passes to the rectum. Large pudendal lips represent the skin folds, located in the sagittal plane. Small pudendal lips near the upper ends of which there is a clitoris are located medially to the large pudendal lips. In the clitoris, at this stage of development, the head, body and crura are determined. The latter are attached to the lower branches of the pubic bones. The clitoris is divided into two halves – cavernous bodies and is surrounded by a thin fascia that passes over to the pubic symphysis. Blood supply of the vagina is provided by the branches of the uterine, lower bladder, medial rectal and internal pudendal arteries. External female genital organs are supplied with blood by the branches of internal and external pudendal arteries.

At this stage of development, longitudinal folds of the mucous membrane of the uterine cavity are observed. The cervix of the uterus related to vagina is bent towards the front at an obtuse angle of 110°-160°. The supravaginal part of the cervix is covered by a peritoneum and separated from the lower part of the posterior wall of the bladder with a small layer of loose cellular tissue. The distance from the fundus of the cystic-uterine excavation to the anterior vault ranges from 3.2 to 4.8 mm. The cystic-uterine excavation in the sagittal section has a fissure-like appearance. The rectum is adjacent to the posterior surface of the uterus, and is separated from it by the peritoneum, passing to the vagina. It should be noted that the peritoneum covers only the upper 1/3 of the posterior wall of the vagina. The depth of the rectal-uterine excavation is 6.0-8.8 mm. The upper part of the uterus is placed at 2.0-4.5 mm above the entrance cavity into a true pelvis, and the cervix is 4.5-7.0 mm below the entrance cavity into a true pelvis. The vaginal cavity is fissure-shaped. The anterior wall of the vagina is tightly fused to the urethra’s posterior wall. The female urethra has the form of a short tube, from 7.5 to 8.3 mm in length.

The rectum is adjacent to the posterior wall of the vagina. One, at least two, longitudinal and transverse folds of the mucous membrane are detected on the anterior and posterior walls of the vagina for the first time. The inferior part of the posterior wall of the vagina and the inferior part of the rectum are tightly fused to the perineum tendon center. The latter in the form of a wedge passes between them. Minor layer of loose cellular tissue adjoins the vagina on both sides. The anterior and posterior vaginal vaults of the same depth are formed at this stage of development.

By the end of the 5th month of intrauterine development (fetuses of 170.0-185.0 mm of CRL), vaginal canalization in the caudo-cranial direction is observed, at the same time there is no clear boundary between the uterovaginal canal and the UGS. The epithelium of the vagina in the upper third is derived from the uterovaginal canal, and in the lower two thirds of the vagina – from the UGS. The
PECULIARITIES OF PRENATAL VAGINA MORPHOGENESIS

**Fig. 1.** Frontal section of the prefetus of 58.0 mm of CRL. Van Gieson’s stain. Micro specimen. Lens 8, eyepiece 7:
1 – urethral lumen;
2 – paramesonephral ducts;
3 – mesonephral ducts;
4 – ovaries;
5 – rectum.

**Fig. 2.** Frontal section of pelvic organs of female prefetuses of 76.0 mm of CRL. Hematoxylin and eosin staining. Micro specimen. Lens 8, eyepiece 7:
1 – uterovaginal canal;
2 – paramesonephral ducts;
3 – reduced mesonephral ducts;
4 – ureters.

**Fig. 3.** Sagittal section of pelvic organs of female fetus of 110.0 mm of CRL. Micro specimen. Lens 8, eyepiece 10:
1 – bladder; 2 – urethra; 3 – uterus;
4 – uterine tube; 5 – vagina;
6 – vaginal vestibule; 7 – rectum;
8 – anus; 9 – pubic bone.

**Fig. 4.** External female genital organs of the fetus of 85.0 mm of CRL. Macro specimen. Magnification 3,6x:
1 – clitoris; 2 – vagina;
3 – large pudendal lips;
4 – anus; 5 – umbilical cord.
The fibrous-muscular wall of the vagina is developed from the surrounding mesenchyma.

In 6-month-old female fetuses in the front part of the bladder, the pubic symphysis is determined, and in the back part there is the body and cervix of the uterus, ovaries and rectum. The peritoneum extends between the urinary bladder and the uterus, forming a cystic-uterine excavation. Between the urinary bladder and the cervix the sagittal section demonstrates the bladder-cervical fissure, bounded from above by the peritoneum of the cystic-uterine excavation, in the front – by the fascia of the urinary bladder, behind – by the fascia of the cervix and from the bottom by the fusion of the cystic fascia with the cervix. The cystic-vaginal cavity, in accordance with the position of the vagina, is directed downwards and to the front. Upwards cystic-vaginal fissure reaches the fusion of the bladder fascia with the cervix. It should be noted that at the level of the urethra, the cystic-vaginal fissure is not determined, since the urethra is tightly connected with the vaginal fascia. The cystic-cervical and cystic-vaginal fissures are limited by connective tissue taenia, forming cystic-uterine ligaments.

Rectal-vaginal fissure is narrow, placed frontal and filled with loose cellular tissue. The rectal-vaginal fissure is limited by the peritoneum of the uterine-rectal excavation from above, by the fascia of the vagina in the front, and by the fascia of the rectum from the back side. On the sides, the rectal-vaginal fissure is transformed into the rectal taeniae containing vessels of the rectum, and lymph vessels of the uterus. The distance from the fundus of the cystic-uterine...
excavation to the anterior vault of the vagina is 4.0-6.5 mm. Transverse folds of the mucous membrane of the uterine cavity are observed for the first time at this stage of development. The cervix of the uterus is placed 5.0-7.3 mm lower than the entrance cavity into a true pelvis. It should be noted that the cervix in relation to the vagina is inclined at an obtuse angle of 110-165°. Only the superior minor part of the vagina adjoins the inferior part of the posterior wall of the urinary bladder. The variability of the shape of the vaginal cavity in the 6-month-old fetuses has been revealed. Thus, in the superior and middle third of the vagina, the following types of shape occur: oval (5 cases), elongated-oval (2 observations), stellate (1 case); in the lower third, the H-shaped form was predominantly found (6 fetuses). Transverse folds are found throughout the mucous membrane of the vagina. They are better pronounced in the region of the upper third of the vagina. In two cases (fetuses of 195.0 and 220.0 mm of CRL) of 8 examined fetuses aged 6 months the vaginal vaults were not determined at the sagittal section. The anterior wall of the vagina is tightly connected to the urethra’s posterior wall. Venous outflow in female fetuses occurs into the vaginal venous plexus.

The hymen membrane is formed as a result of the expansion of the caudal vaginal regions, followed by the invagination of the posterior wall of the UGS and till the end of the fetal period of ontogenesis it serves to separate the lumen of the vagina and the UGS cavity. Hymenorrhexis occurs in the perinatal period, and its remains represent a thin duplication of the mucous membrane. In the sources of literature, there are the data that the hymen membrane is a part of the urogenital membrane. The proliferation of the hymen membrane occurs at the end of the 6th – at the beginning of the 7th month of prenatal development (fetuses of 220.0-245.0 mm of CRL). It should be noted that the absence of timely proliferation in the hymen membrane can lead to its atresia, and premature proliferation of the hymen membrane leads to the appearance of transverse vaginal septa.

The longitudinal and transverse folds of the mucous membrane of the uterine cavity are clearly determined in
the 7-month-old fetuses. The cervix of the uterus relatively to vagina is inclined to the front at an angle of 115-160°. The anterior uterine wall is adjacent to the lower half of the posterior wall of the bladder (Fig. 6). An insignificant layer of loose cellular tissue separates the supravaginal part of the cervix from the lower part of the posterior wall of the bladder. The peritoneum covers the upper 1/3 or 1/4 part of the posterior wall of the vagina which the rectum adjoins. The anterior wall of the vagina is adjacent to the posterior wall of the urethra. It should be noted that if in the early fetuses the vagina looked like a narrow tube, then in the 8-month-old fetuses the vagina becomes considerably wider compared to the urethra (Fig. 7).

In the fetuses of 315.0-330.0 mm of CRL the anterior wall of the vagina tightly adjoins the bladder and urethra (Fig. 8). The anterior wall of the vagina is shorter than the posterior one. 6.0-7.5 mm of the superior part of the posterior wall of the vagina is covered by the peritoneum, and its inferior part is tightly adjacent to the rectum, separating from it by the plate of the pelvic fascia. Small and large vestibular glands open between the vaginal and the external urethral ostium.

CONCLUSIONS

1. The formation of the vagina occurs during the 9th week of embryogenesis (fetuses of 31.0-41.0 mm of CRL) due to the fusion of two different embryonic structures: mesodermal paramesonephral ducts and endodermal urogenital sinus. In this case, the caudal regions of the paramesonephral ducts are transformed into the uterus and the upper two thirds of the vagina, and the lower third of the vagina develops from the urogenital sinus.

2. In the female fetuses of 38.0-43.0 mm of CRL due to the fusion of the caudal regions of the paramesonephral ducts in the area of the posterior wall of the urogenital sinus common uterovaginal canal develops, mesenchymal septum divides it into the right and left cavities. Complete dissolving of the septum of the uterovaginal canal occurs in fetuses of 55.0-58.0 mm of CRL.

3. The anterior and posterior vaginal vaults of the same depth are formed in 5-month-old fetuses. Canalization of vagina in the caudo-cranial direction is observed in the fetuses of 170.0-185.0 mm of CRL, with no clear boundary between the uterovaginal canal and the urogenital sinus. The vaginal epithelium in the upper third part originates from the uterovaginal canal, and in the lower two thirds of the vagina – from the urogenital sinus.

4. In the 6-month-old fetuses there was detected the variability of the shape of the superior and middle third of the vagina, namely: oval (5 cases), elongated-oval (2 cases), stellate (1 case); in the lower third, the H-shaped form was predominantly found (6 fetuses).

5. The proliferation of the hymen membrane occurs in fetuses of 220.0-245.0 mm of CRL. The absence of timely proliferation of the hymen membrane can lead to its atresia, and its premature proliferation causes the appearance of transverse vaginal septa.

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