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"CONGENITAL ANOMALIES OF THE UTERUS" EMBRYOLOGICAL BASIS AND ITS CLINICAL IMPORTANCE

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ABSTRACT

Mullerian abnormalities are made of a group of different congenital anomalies of the female genital system. The aim of this article is to juxtapose the normal development of the uterus with the abnormal development so a clear understanding of the cause of congenital anomalies of the uterus can be generated and correlated with the clinical significance.

Introduction

The uterus also known as the womb is a major female hormone-responsive reproductive sex organ of mammals. The uterus is a muscular organ that is responsible for nourishment and care of the fetus until birth. The development of the fetus during gestation usually happens within the uterus. The uterus has a body and cervix. It is made up of three layers which are the endometrium, myometrium, and perimetrium.

The uterus receives ovum (either fertilized which implants in the endometrium or unfertilized which sheds out as menstruation). The fertilized ovum receives nourishment from blood vessels. The fertilized ovum develops into an embryo and attaches to the wall of the uterus and later and the placenta develops (now responsible for the nourishment, waste elimination, immunity and gaseous exchange of the fetus until childbirth).

Normally at week six, in the intrauterine life, there is two genital ducts named paramesonephric (Mullerian) duct and mesonephric (Wolffian) duct for the female and male embryos respectively. The paramesonephric duct arises from the invagination of epithelium. This duct can be divided into three parts as they move laterally to the mesonephric duct, anterior and medial where both Mullerian ducts get close to each other and finally run downward where they meet and join at the definitive urogenital sinus (DUGS) to form the Mullerian tubercle also called the paramesonephric tubercle. The two ducts are separated by uterovaginal (UV) septum but later fuse (due to the resorption of the UV septum) to form the uterine (uterovaginal) canal. The caudal tip of the joined ducts projects into the posterior wall of the urogenital sinus where there is a small swelling called the paramesonephric (Mullerian) tubercle. Failure of the UV septum to be reabsorbed, failure of one or more of the paramesonephric ducts to develop, failure of normal fusion of the ducts and failure of the ducts to canalize might lead to cervical atresia, septate, arcuate, didelphys, Unicornuate, uteri.

Based on previous works, the American Fertility Society (AFS) classified the Mullerian anomalies according to the extent of the failure of normal development into groups with similar clinical manifestations. There six major uterine classifications namely Type I-hypoplasia/agenesis, Type II-Unicornuate uterus. The Type-II includes, A. With a communicating and undeveloped horn. B. With a non-communicating undeveloped horn. C. With an undeveloped horn without a cavity. D. Without an undeveloped horn. The Type III- didelphys uterus, Type IV-bicornuate uterus (A. Complete. B. Partial.), type V-septate uterus (A. Complete. B. Partial) and the Type VI-arcuate uterus.

Septate, arcuate and partial bicornuate uteri can be corrected by using hysteroscopic techniques. The correction of complete bicornuate uterus requires a more complicated surgery. Didelphys and Unicornuate uteri cannot be corrected [32, 36, 37].

Incidence

Uterine abnormalities are made of a group of different congenital anomalies of the female genital system. The true incidence of these abnormalities in the general population is not known because of the diagnosing methods used. The mean incidences of the different malformations are arcuate uterus 15%, septate uterus 22% (complete 9%, partial 13%), bicornuate uterus 46% (complete 9%, partial 37%) and didelphys uterus 4.5%. The mean prevalence in the general population and in the population of fertile women is about 4.3%, in infertile patients is about 3.5% and in patients with recurrent pregnancy, losses are about 13%. Septate uterus is the most common uterine anomaly with the mean incidence of about 35% followed by bicornuate uterus (partial bicornuate uterus) about 26%, Unicornuate uterus about 10%, didelphys uterus about 8% and the arcuate uterus is about 20%.

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Patients with untreated uterine malformations are about 50% with Unicornuate and didelphys uterus having delivery rates of 45%, bicornuate and septate uterus having delivery rates of 40% and arcuate uterus having 65% delivery rate [32].

Ontogenesis of the normal fate of Mullerian duct

At week six of intrauterine life, both male and female embryos have two sets of paired genital ducts named the Mullerian (paramesonephric) ducts and the Wolffian (mesonephric) ducts. Their genital systems are structurally identical at this indifferent stage, though cellular differences are present. In female embryos, the Wolffian ducts and tubules degenerate due to the absence of testosterone but there are two remnants, Epoophoron, and Paroohoron. These remnants are nonfunctional and are located in the mesentery of the ovary. During this time, the Mullerian ducts develop in two opposite directions along the lateral aspects of the gonads, the regressing remnants of the Wolffian ducts provide a template for the developing Mullerian ducts.

The paramesonephric duct originates from the longitudinal invagination of coelomic epithelium on the anterolateral surface of the urogenital ridge. The paramesonephric ducts elongate at week 9, with three recognizable regions namely the cranial vertical, horizontal, and caudal vertical. Each region has a different function in the formation of the female reproductive tract. Cranially, the ducts open into the abdominal cavity with a hollow cone-like structure. Caudally, the duct runs lateral to the mesonephric duct, and then crosses anteriorly to grow caudomedially.

The unfused cranial parts of the paramesonephric ducts develop into the fallopian tubes, oviducts or uterine tubes and the funnel-shaped cranial openings of the paramesonephric ducts become the infundibulum of the fallopian tubes (Fig 1A). The caudal vertical parts of the paramesonephric ducts fuse by the uterovaginal septum at the midline to form the uterovaginal canal or uterine canal which develops into the uterus, cervix of the uterus and form upper one-fifth of the vagina (Fig 1C). Internally, the uterovaginal septum separates the caudal vertical part of the paramesonephric ducts (which absorbs later to form the uterine cavity) (Fig 1B) and externally, it looks fused. The uterus and cervix of the uterus are surrounded by a layer of mesenchyme that forms the muscular covering of the uterus which is the myometrium, and its peritoneal covering which is the perimetrium. After the fusion, a broad transverse pelvic fold is shown which extends from the lateral sides of the fused paramesonephric ducts towards the wall of the pelvis is the broad ligament of the uterus. The uterine tube lies in the upper border of the broad ligament of the uterus and the ovary lies on its posterior surface. The uterus and broad ligaments divide the pelvic cavity into the uterorectal pouch and the uterovesical pouch [33, 36, 37, 38].

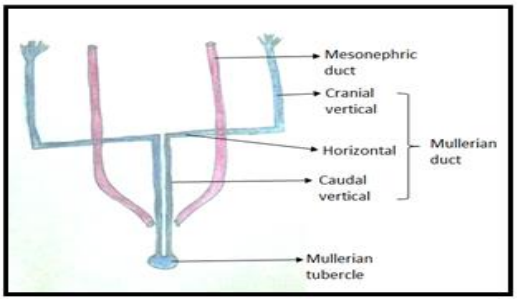

Fig 1A. Pairs of genital duct present during the indifferent stage of the embryo.

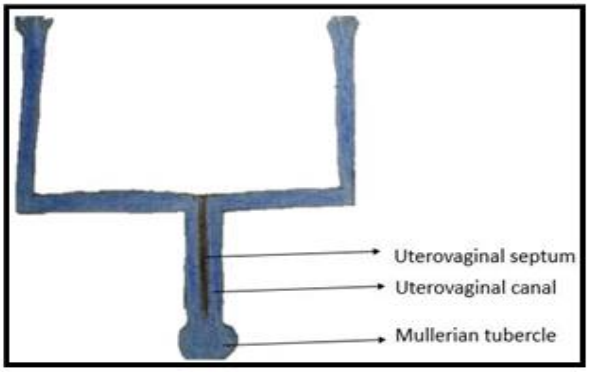

Fig 1B. The paramesonephric duct showing the uterovaginal septum which separates the caudal vertical part of the paramesonephric ducts.

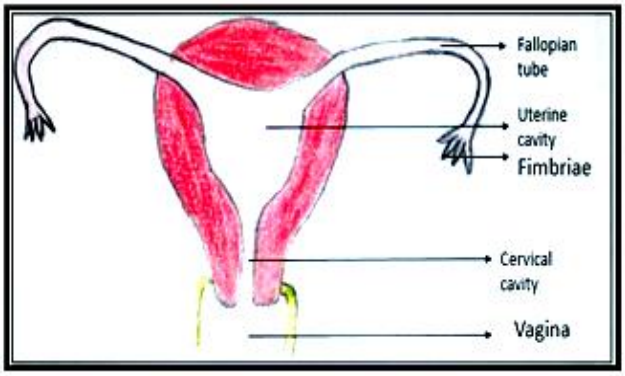

Fig 1C. The derivatives of the paramesonephric ducts (the uterus, cervix, fallopian tubes, fundus of the uterus and upper one-fifth of the vagina).

Ontogenesis of the abnormal fate of Mullerian duct

Normally at the eight week, the paramesonephric duct fuses and the uterovaginal septum absorbs. This forms the fundus and cervix of the uterus and upper one-fifth of the vaginalis there is any interruption in the development of the paramesonephric duct (such as incomplete development and fusion of paramesonephric ducts, failure of one or both paramesonephric ducts development, failure of the paramesonephric ducts to canalize,) would lead to various anomalies of the uterus. The American Fertility Society (AFS) in 1988 classified the female reproductive tract anomalies according to the degree of failure of normal development into groups with similar clinical manifestations, treatments and possible prognoses for the reproductive performance. These classes of congenital uterine anomalies include;

Type I-Hypoplasia/agenesis (Fig-2):

This happens when one or both Mullerian ducts fail to develop. It is concerning the paramesonephric ducts which can result in lower vaginal agenesis, cervix agenesis, uterus and cervix hypoplasia, and uterine tube agenesis [32, 34, 36].

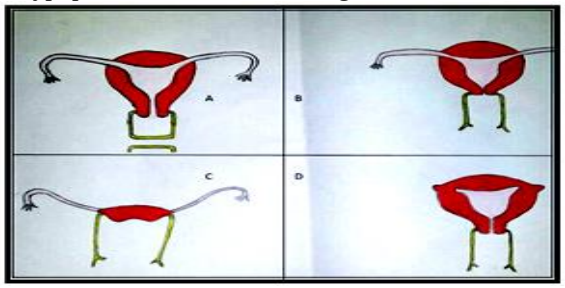

Fig 2. Class-I Mullerian hypoplasia and agenesis anomalies. A. Lower vaginal agenesis. B. Cervix agenesis. C. Uterus and cervix hypoplasia. D. Uterine tube agenesis.

Type II- Unicornuate uterus (Fig-3):

This is can be divided into communicating and non-communicating which is the subdivided depending on if the uterine cavity is present. They include Unicornuate uterus with a communicating undeveloped horn, Unicornuate uterus with a non-communicating undeveloped horn, Unicornuate uterus with an undeveloped horn without a cavity and Unicornuate uterus without an undeveloped horn. When one or both Mullerian ducts fails to develop can cause Unicornuate uterus without an undeveloped horn. Also, when the Mullerian ducts fail to canalize can cause Unicornuate uterus with undeveloped horn without proper cavities. This can result in ipsilateral (the same side) renal and ureter agenesis [32, 34].

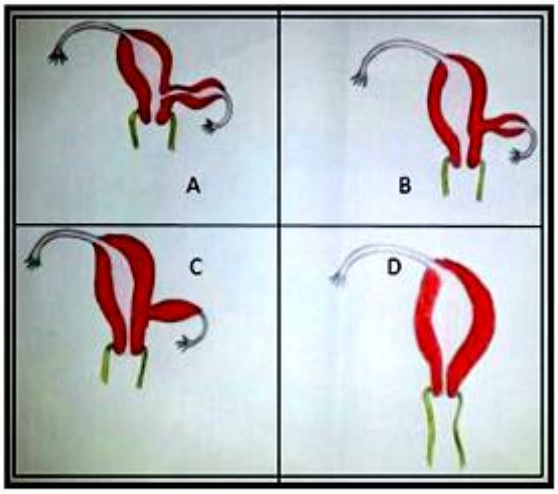

Fig-3: Class-II Unicornuate anomalies. A. Unicornuate uterus with a communicating rudimentary horn. B. Unicornuate uterus with a non-communicating rudimentary horn. C. Unicornuate uterus with a rudimentary horn containing no uterine cavity. D. Unicornuate uterus.

Type III- didelphys uterus (Fig-4)

This happens when the paramesonephric duct fails to fuse or fuses abnormally. This results in the complete or partial duplication of the vagina, cervix, and uterus [32, 34].

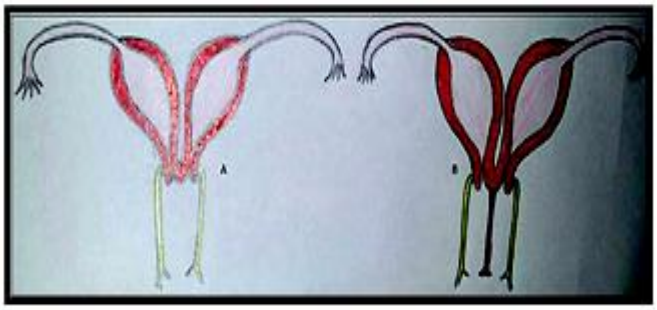

Fig 4. Class-III didelphys (double uterus) anomalies. A. Didelphys with the normal vagina. A hysterosalpingography shows a double uterus with a single normal vagina. B. Didelphys with the complete vaginal septum.

Type IV-bicornuate uterus (Fig-5):

This is subdivided into complete and partial bicornuate uteri. It happens (bicornuate uterus) when the paramesonephric duct fails to fuse or fuses abnormally. The complete bicornuate uterus is characterized by a uterine septum that extends from the fundus to the cervical os. The partial bicornuate uterus demonstrates a septum, which is located at the fundus. In both variants, the vagina and cervix have a single chamber each [32, 34].

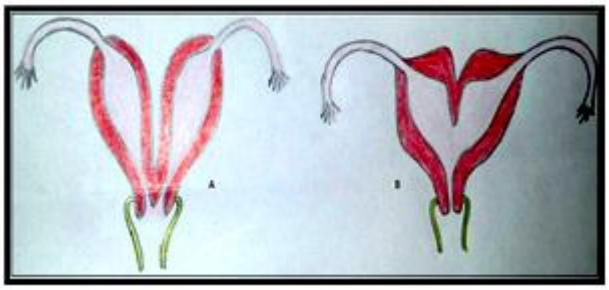

Fig 5. Class-IV bicornuate anomalies. A. Bicornuate uterus with complete division down to the internal os. B. Bicornuate uterus with the partial division.

Type V-septate uterus (Fig-6):

This is subdivided into complete and partial septate uteri. This occurs when the uterovaginal septum between the caudal vertical parts of the paramesonephric duct fails to resorb completely or partially. A complete or partial midline septum is present within a single uterus [32, 34].

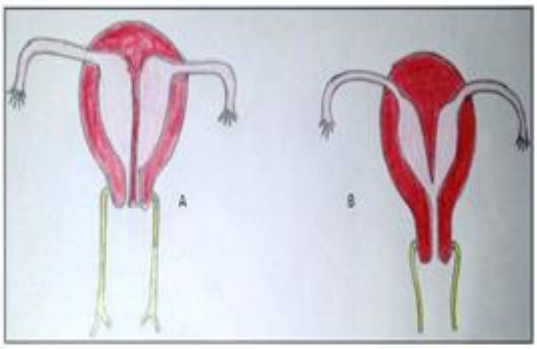

Fig 6. Class-V septate uterus anomalies. A. Septate uterus with complete septum down to the external os. B. Septate uterus with the partial septum.

Type VI-arcuate uterus

In this defect, there is a small septate indentation (Fig-7) is present at the fundus.

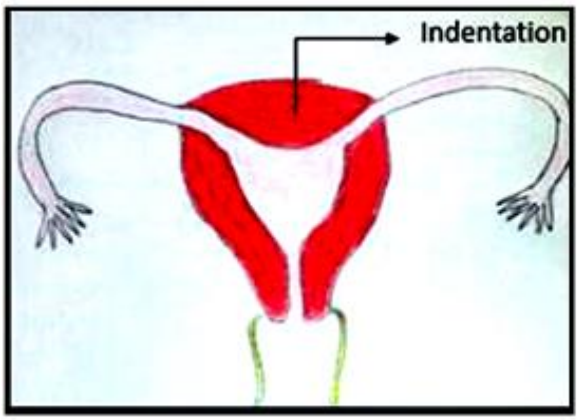

Fig 7. Class-VI arcuate uterus anomalies indentation [37].

Discussion

The cause of infertility in most women can be characterized by congenital anomalies of the uterus or acquired uterine abnormalities (those abnormalities that occur after birth). This can lead to repeated pregnancy loss and can make it difficult to carry a pregnancy to term. Uterine anomalies are not symptomatic (that is showing no signs and symptoms) until the age of puberty when the females with these anomalies do not menstruate. Doctors who are experts can diagnose and

treat uterine anomalies with the use of developed imaging techniques such as hysterosalpingograms (HSG) and transvaginal ultrasounds in reproductive-aged women. In Type-I, Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome can be seen.

In Type-II, malpresentation, intrauterine growth retardation, and preterm birth are common complications. However, three separate reports describing the existence of a Unicornuate uterus with ipsilateral (the same side) ovarian agenesis has led some authorities to consider that in some cases. When a related horn is present, this class is subdivided into communicating (the main uterine cavity is evident) and non-communicating (the main uterine cavity is not obvious). The non-communicating type is further subdivided on the basis of whether an endometrial (uterine) cavity is present in the undeveloped horn. These malformations are classified under asymmetric lateral fusion defects. The most clinically significant and common Unicornuate subtype is the non-communicating accessory horns that have a uterine cavity. This subtype is related with increased sickness (morbidity) and death (mortality). When the accessory horn becomes obstructed, complications such as hematometra (retention of blood in the uterus) can develop. There is also an increased risk of the development of endometriosis which usually resolves after the removal of the horn (if diagnosed early). Although there is normal occurrence of pregnancies, childbirth outcomes are generally poor in this group. Most obstetric complications occur in the first twenty weeks and can result in abortion, uterine rupture, or maternal death. In Type-III, renal agenesis mostly occurs in association with this defect than with any other type of Mullerian anomaly. In this setting, there is the rare although well-established congenital Herlyn-Werner-Wunderlich syndrome. It is characterized by anomalies of both the Mullerian and Wolffian ducts, consisting of the triad: uterus didelphys obstructed hemivagina and ipsilateral renal agenesis. Single studies of didelphys uterus occur in association with other anomalies such as bladder exstrophy with or without vaginal hypoplasia, congenital vesicovaginal fistula with hypoplastic kidney and cervical agenesis. In many cases, the capability of didelphys uterus is that sexual intercourse is possible in both vaginas. Simultaneous pregnancies can occur in each uterus although it rarely happens. Some experts consider each pregnancy to be separate pregnancies and the twins are always dizygotic. This theory is supported by reports in which the second twin was delivered after a long interval, ranging from 3 hours to 5 days to 8 weeks, after delivery of the first twin. Lactation starts to occur after the birth of the second twin. These anomalies can be diagnosed during puberty age and in the pre-pubertal period; normal external genitalia and age-appropriate developmental indicators often cover abnormalities of the internal reproductive organs. After the beginning of puberty, young women often present to the gynecologist with menstrual disorders. Infertility and obstetric complications are late presentations.

Type-IV which is bicornuate uterus is considered as a supplementary finding. The uterine bicornuate has been recognized as a rare component of a mild non-lethal, alternate of the urorectal septum malformation. Women with this defect usually have reproductive related problems. The condition usually remains undiagnosed until when cesarean delivery or other procedures reveal its presence. Mullerian anomalies suffer from the same pathologic conditions affecting the normal uterus such as cancer. A rate of endometrial carcinoma developed in one horn of the bicornuate uterus after the patient receiving tamoxifen therapy for breast cancer is high.

Type-V septate uterus is the most common structural abnormality of all Mullerian defects. A rare different septate uterus is Robert uterus. This is characterized by a complete septum and non-communicating hemiuteri with a blind horn. Patients usually present with unilateral (one lateral side) hematometra and dysmenorrhea. Fertility does not appear to be considerably compromised in patients with this defect. Type VI has been said to be problematic. In the classification system of Buttram and Gibbons, it was considered a mild form of the bicornuate uterus. In the AFS classification, a separate class was created for this anomaly on the basis of its external fusion, which differentiates it from the septate uterus. Both classification systems risk whether the arcuate uterus is a normal alternate. Compared with other Mullerian defects, an arcuate uterus is clinically benign despite an uncommon association with contrary obstetric outcomes and may not affect reproductive outcomes.

Conclusion

A good patient history and clinical examination is key to the management of congenital anomalies of the uterus because the management is usually specific to the manifestation of the uterine congenital anomaly in the patient. Factors such as pregnancy loss in a patient's history and a bicornuate uterus could be indicated for surgery and a unification; while if the bicornuate uterus is discovered incidentally on routine examination, no surgical intervention is needed but close monitoring of the patient is advised during pre-natal care. Generally, physicians should strive to be up to date with the latest research and best practice for management of congenital anomalies of the uterus so they can give the right clinical intervention that will be beneficial to the patient [30, 31, 32, 35, 36].

References

[1] Ganesh Elumalai, Sushma Chodisetty. Anomalous "Mutilated Common Trunk" Aortic Arch Embryological Basis and its Clinical Significance. Texila International Journal of Basic Medical Science. 2016; 1(1): 1-9.

[2] Ganesh Elumalai, Emad Abdulrahim Ezzeddin. "The sudden soul reaper" - hypertrophic cardiomyopathy – its embryological basis. Elixir Embryology. 2016; 99: 43284-43288.

[3] Ganesh Elumalai, Muziwandile Bayede Mdletshe. "Arteria lusoria"- aberrant right subclavian artery embryological basis and its clinical significance. Elixir Embryology. 2016; 99: 43289-43292.

[4] Ganesh Elumalai, Sushma Chodisetty, Pavan Kumar D.2016. Ganesh Elumalai et al Classification of Type - I and Type - II "Branching Patterns of the Left Arch Aorta". Imperial Journal of Interdisciplinary Research. 2(9): 161-181.

[5] Ganesh E, Sushma C. The deer horn aortic arches" embryological basis and surgical implications. Anatomy Journal of Africa.2016; 5(2): 746 – 759.

[6] Ganesh Elumalai, Sushma Chodisetty. Teratological Effects of High Dose Progesterone on Neural Tube Development in Chick Embryos. Elixir Gynaecology. 2016; 97: 42085-42089.

[7] Ganesh Elumalai, Sushma Chodisetty. "The True Silent Killers" - Bovine and Truncus Bicaroticus Aortic Arches its Embryological Basis and Surgical Implications. Elixir Physio. & Anatomy. 2016; 97: 42246-42252.

[8] Ganesh Elumalai, Sushma Chodisetty, Bridget Omo Usen and Rozminabanu Daud Patel. "Patent Ductus Caroticus" - Embryological Basis and its Clinical significance. Elixir Physio. & Anatomy. 2016; 98: 42439-42442.
[9] Ganesh Elumalai, Sushma Chodisetty, Eliza Arineta Oudith and Rozminabanu Daud Patel. Common anomalies origin of left vertebral artery and its embryological basis. Elixir Embryology. 2016; 99: 43225-43229.
[10] Ganesh Elumalai, Sushma Chodisetty, Sanjoy Sanyal. Common Nasal Anomalies and Its Implications on Intubation in Head and Neck Surgeries. Journal of Surgery. 2016; 4 (4): 81-84.
[11] Ganesh Elumalai, Malarvani Thangamani, Sanjoy Sanyal, Palani Kanagarajan. Deficient sacral hiatus cause mechanical low back pain: a radiological study. Int J Anat Res. 2016; 4(1):1758-64.
[12] Ganesh Elumalai, Amal Satheesh Sujitha. "Anomalies origin of left coronary artery" its embryological basis and clinical significance. Elixir Embryology. 2016; 100: 43446-43449.
[13] Ganesh Elumalai, Anto Sicily Norbert. "APVC - Anomalies Pulmonary Venous Connections" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43450-43453.
[14] Ganesh Elumalai, Nnolika Millington. "Coarctation of Aorta" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43425-43428.
[15] Ganesh Elumalai, Logeshwaran Anbazhagan. "Laryngomalacia" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43420-43424.
[16] Ganesh Elumalai, Amodini Dharmalingam. "Left superior vena cava" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43429-43432.
[17] Ganesh Elumalai, Thelma U. Ebami. "Patent Ductus Arteriosus" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43433-43438.
[18] Ganesh Elumalai, Mouna Arumugam. "Persistent Left superior vena cava" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43454-43457.
[19] Ganesh Elumalai, Moganelwa Sharline Mampa. "Pulmonary Agenesis" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43439-43441.
[20] Ganesh Elumalai, Shubham Jain. "Subglottic stenosis" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43458-43461.
[21] Ganesh Elumalai, Hariharan Arjet. "Tracheoesophageal fistula" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43414-43419.
[22] Ganesh Elumalai, Jenefa Princess. "Transposition of Great Vessels" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43442-43444.
[23] Ganesh Elumalai, Manoj P Rajarajan. "Type-I vascular rings" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43700-43705.
[24] Ganesh Elumalai, Ebenezer Asare Sakyi. "Right sided aortic arch" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43706-43709.
[25] Ganesh Elumalai, Enian Senguttuvan. "Double aortic arch" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43710-43713.
[26] Ganesh Elumalai, Danesha Sanicharan. "Abnormal origin of the right subclavian artery from the right pulmonary artery" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43714-43718.
[27] Ganesh Elumalai, Siva Brinda Jeyapaul. "Choanal Atresia" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43719-43722.
[28] Ganesh Elumalai, Kelly Deosaran. "Congenital diaphragmatic hernia" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43723-43728.
[29] Ganesh Elumalai, Basim Arif. "Subclavian Steal Syndrome" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 4372943733.
[30] Columbia university department of obstetrics and gynecol ogy. Uterine anomaly. www.columbiaobgyn.org/condition_tre atments/ uterine- anomaly
[31] Congenital uterine anomalies. Medfem. www. medfem. co.za/ congenital – Uterine - anomalies
[32] Grimbizis F. Grigoris. Clinical implications of uterine mal formations and hysteroscopic treatment results. PubMed. 2001 ; vol. 7(1): pg. 161-173.
[33] Keith L. Moore, Atthur F. Dalley, Anne M.R. Agur. Moore clinically oriented anatomy. Lippincott Williams & Wilkins. 2014; 7th ed.: 324
[34] Lawrence S. Amesse. Mullerian duct anomalies. WebMD. 2016. emedicine.medscape.com/article/273534-overview
[35] Marıa Luisa Martınez Frıas. Congenital anomalies in the offspring of mothers with a bicornuate uterus. Aappublication. 1998; vol. 101(4): pg. 1-3.
[36] Ronald W. Dudek. BRS Embryology. Lippincott Williams & Wilkins.2016; 6th ed: 171, 175.
[37] Sadler, T. &Langman, J. Langman's Medical Embryology. Lippincott Williams & Wilkins. 2012; 12th ed: 248-250.
[38] Schoenwolf Gary C. Larsen's Human Embryology. Churchill Livingstone Elsevier. 2008; 4thed: 518-520.