International Journal of Anatomy and Research,
Int J Anat Res 2015, Vol 3(4):1669-74. ISSN 2321- 4287
DOI: http://dx.doi.org/10.16965/ijar.2015.311

Case Report

SIRENOMELIA: A DETAILED FETAL AUTOPSY STUDY

Parimala Sirikonda *[1], Nalluri Himabindu [2].

[*1] Assistant Professor, Department of Anatomy, Bhaskar Medical College, Yenkapally, Moinabad, Telangana, India.

[2] Associate Professor, Department of Anatomy, Bhaskar Medical College, Yenkapally, Moinabad, Telangana, India.

ABSTRACT

Sirenomelia also known as mermaid syndrome, characterized by fused lower limbs, is a lethal and rare congenital abnormality. This is an extreme example of caudal regression syndrome caused by vascular steal of single umbilical artery. Sirenomelia is found approximately one in 100,000 live births and is usually fatal because of complications associated with pulmonary hypoplasia, abnormal development of the kidneys and urinary bladder. Most of the cases are associated with maternal diabetes and single umbilical artery.

We report a case of sirenomelia terminated at 21weeks of gestation due to multiple congenital abnormalities. Antenatal scan of a25-year old primi revealed a single live fetus of 21 weeks gestation with severe olighydramnios, non-visualization of kidneys and bladder and lower part of the spine. This pregnancy was terminated and the specimen sent to the department of anatomy for fetal autopsy. On external examination,a tail like rudimentary single midline lower limb without foot was noted. There were no external genitalia and anal orifice. Internal examination revealed hypoplastic lungs, atrial septal and ventricular septal defects, aberrant right subclavian artery, hypoplastic abdominal aorta distal to the single umbilical artery, complete agenesis of urinary system, rectal agenesis and rudimentary indeterminate gonads.

We would like to discuss the clinical features, etio- pathogenesis and review of literature of sirenomelia. Early diagnosis and termination of this lethal congenital anomaly results in minimizing the trauma related to the termination of pregnancy at advanced gestation.

KEY WORDS: Sirenomelia, Caudal regression syndrome, Vascular steal, Maternal diabetes, Single umbilical artery.

Address for Correspondence: Dr. Parimala Sirikonda, Assistant Professor, Department of Anatomy, Bhaskar Medical College, Yenkapally, Moinabad, Telangana, India. **E-Mail:** pari.siri@gmail.com

Access this Article online

Quick Response code

DOI: 10.16965/ijar.2015.311

Web site: International Journal of Anatomy and Research
ISSN 2321-4287
www.ijmhr.org/ijar.htm

Received: 06 Nov 2015 Accepted: 05 Dec 2015
Peer Review: 06 Nov 2015 Published (O): 31 Dec 2015
Revised: None Published (P): 31 Dec 2015

INTRODUCTION

Sirenomelia or Mermaid syndrome is characterized by fusion of lower limbs also associated with flexion and inversion in external rotation of the lower limbs, anomalies of lumbar and sacral spine, imperforate anus, agenesis of kidneys and urinary tract & agenesis of internal genital organs [1]. As reported by Johnson,1966; Martinez Frias et al.1992; Murphy et al.,1992, incidence varies between 1.1 to 4.2 per 100,000 births [2,3,4]. Most of the cases are sporadic and have very less chance of recurring in a next pregnancy. Our aim is to present the features of a Sirenomelia foetus, with detailed autopsy findings, and discussion of etio-pathogenesis and a brief review of literature.

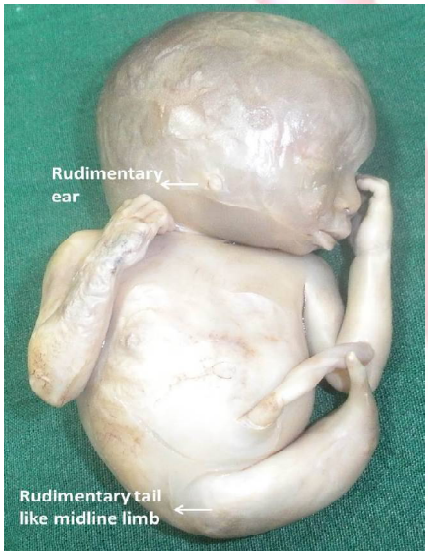
CASE REPORT

A 25-year old primigravida at 21 weeks of gestation was admitted for termination of

pregnancy due to ultrasound diagnosis of multiple congenital anomalies in the fetus. Routine anomaly scan performed during this pregnancy at 21 weeks revealed a single live foetus corresponding to 20 weeks of gestation with severe oligohydramnios,non-visualization of kidneys and urinary bladder, &agenesis of caudal spine. Both lower limbs could not be clearly assessed due to severe oligohydramnios. In view of these findings, a repeat ultrasound scan was done which confirmed the same. There was no history of consanguinity, drugs or radiation exposure or any other illness during pregnancy. There were no medical or obstetric risk factors. There was no personal or family history for diabetes mellitus or congenital abnormality. As these anomalies indicate guarded prognosis, the couple opted for termination of pregnancy. The fetus obtained was sent for detailed autopsy.

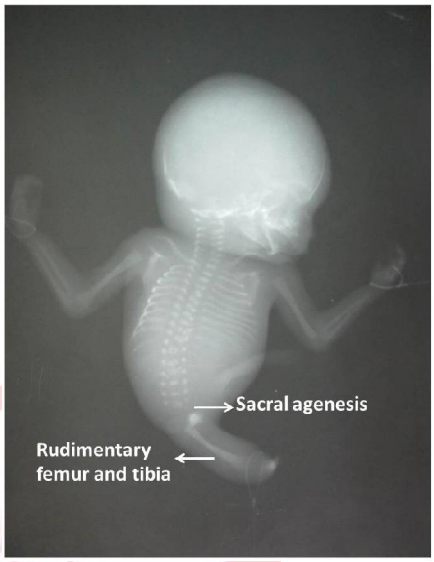
External examination of the fetus revealed: Potters' facies, hypertelorism, low set ears (right ear was rudimentary with no external acoustic meatus (EAM) and left ear was normal), flattened nasal bridge and tip of the nose, and micrognathia. The upper torso of the body was normal. There were no external genitalia, no urethral and anal openings. Lower limb ended in a single tapering midline structure (Fig. 1).

Fig. 1: Foetus with Sirenomelia.



Post mortem radiograph (Baby gram) showed pelvic aplasia, single midline rudimentary femur & rudimentary tibia. Fibula, tarsals, metatarsals, phalanges were not seen.Vertebral column was normal till lumbar region,then agenesis of sacrum and coccyx.Upper limb bones on both sides were normally present and developed as per gestational age (Fig.2).

Fig. 2: X-ray of the foetus showing with rudimentary femur and tibia.



Internal examination of the fetus showed: single umbilical artery which was arising from the abdominal aorta, which was hypoplastic distal to that origin (Fig. 3). The liver, stomach, small intestine, spleen and pancreas were unremarkable. There was no gallbladder. The large intestine ended as a blind pouch at sigmoid colon. There was complete agenesis of rectum and anal canal. There was bilateral renal agenesis & agenesis of ureters and urinary bladder. The adrenals were flat and discoid lying on posterior abdominal wall. There were no uterus and vagina. There was an indeterminate gonad-like structure, bilaterally present. Histology showed rudimentary primitive indeterminate gonad (Fig. 4).

Fig. 3: Hypoplastic Aorta and SIngle umbilical artery.

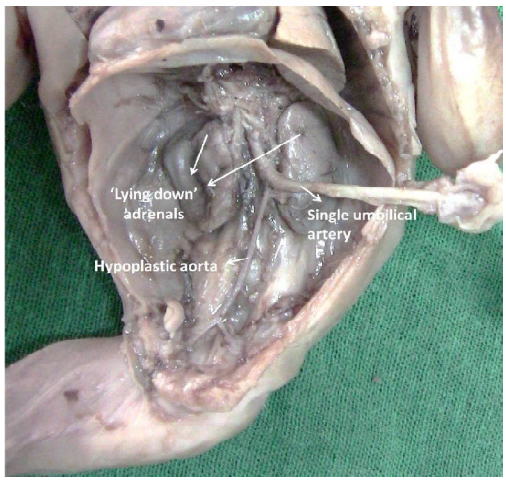
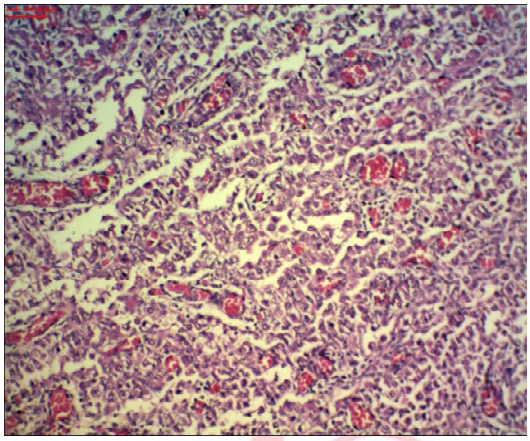
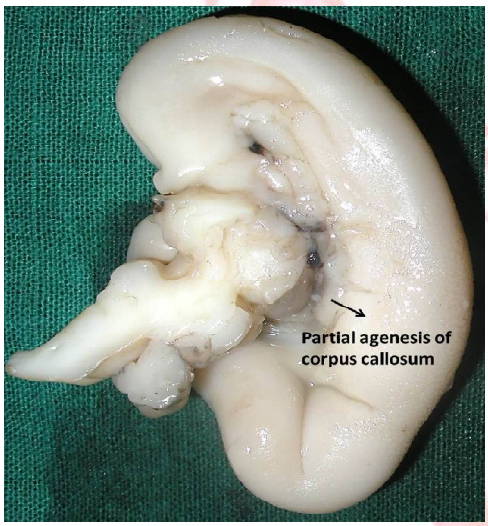


Fig. 4: Microscopic picture of primitive gonad.



Cardiovascular examination delineated atrial septal defect and ventricular septal defects. There was aberrant right subclavian artery arising as fourth branch of arch of aorta and it coursed from left to right behind esophagus and trachea. There was pulmonary hypoplasia. Brain was appropriate for the gestational age but there was partial agenesis of corpus callosum: splenium was not formed (Fig. 5). Spinal cord below the lumbar segments was deficient.

Fig. 5: Partial agenesis of corpus callosum.



Spine was normal till the lumbar region, C1-L5 vertebrae were normal. The sacral and coccygeal vertebrae were absent. There was a rudimentary midline femur which had a rounded mass fused to a rudimentary pelvic bone and rudimentary tibia with condyles.

DISCUSSION

Sirenomelia is a lethal congenital anomaly with abnormal development of the caudal region of the body involving varying degrees of fusion of the lowerlimbs with or without bony defects. In addition to the leg fusion phenotypes, Sirenomelia presents with abnormal pelvic or uro-genital organ development affecting the kidney, ureter, bladder, rectum and external genitalia. Owing to the visceral abnormalities, sirenomelia is incompatible with life.

Hind limb fusion types: Stocker and Heifetez (1987) classified Sirenomelia into 7 types - Type I to Type VII mainly according to the presence of skeletal elements in the thigh and leg. In type I, the mildest form, all bones in the two fused limbs are present and the fusion only affects superficial tissues. In type VII, the most severe form, only a single bone is present, with no indication of legs or feet [5]. Our case falls in Type VII.

Visceral malformations: Kallen et al., 1992 stated that all the human cases of Sirenomelia analysed showed a variable degree of renal and urethral dysplasia, with total renal agenesis being very frequently reported [6]. Goodlow et al., 1998, Kallen et al., 1992 stated that malformation of the urinary tract is consistently associated with genital malformations. These affect mainly the external genitalia, which were either absent or represented by an indistinct tag of tissue, where as the gonads were usually unaffected [7,6].

In our case there were no external genitalia and even the gonads were indistinct. On microscopic examination of the gonads, a picture of primitive indeterminate gonad was observed.

Kallen et al., 1992 reported the presence of gastrointestinal anomalies in Sirenomelia as a common feature, the most frequent being a blind ending colon, rectal atresia and imperforate anus [6].

Our case had a blind ending sigmoid colon, with agenesis of rectum and anal canal.

Vascular malformations: Heifetezet al.1984 & Stevenson et al.1986, reported that the vascular abnormalities in Sirenomelia deserve special mention owing to their possible relevance to pathogenesis. The human umbilical cord normally contains two umbilical arteries (returning deoxygenated blood from the fetus to the placenta) and a single umbilical vein (supplying oxygenated blood to the fetus).

However, fetuses with Sirenomelia almost invariably exhibit a single umbilical artery (SUA) [8,9]. Martinez – Frias et al.2008, reported that

this SUA has an abnormal origin, branching off the abdominal aorta quite high in the abdomen. Below the origin of SUA, the aorta becomes abnormally narrow and lacks a considerable number of branches that normally supply the kidneys, large intestine and genitalia. This results in abnormal blood supply to the caudal parts of the fetus because the SUA carries blood to the placenta. The vessel steals the blood from the structures below its origin – Vascular steal hypothesis. The SUA has also been referred to as the persistent vitelline artery to indicate its possible derivation from the vitelline plexus, and to distinguish it from other cases of SUA that are found in about 1% of newborn but that have normal origin and are not related to other malformations [10].Heifetez et al.1984 &Stevenson et al.1986, considered the presence of SUA of vitelline origin as characteristic or even pathognomonic of sirenomelia and proposed it to be used for the differential diagnosis of other malformations of the lower body such as caudal dysgenesis [8,9]. However there are occasional cases of Sirenomelia with two symmetrical umbilical arteries, although they are of abnormal origin according to Opitzet al.2002 &Thottungal et al.2010; [11,12] whereas others have only one umbilical artery but that is of normal origin according to Jaiyesimi et al.1998 [13]. Reciprocally, aberrant umbilical arteries have also been described in individuals with caudal dysgenesis by Duesterhoeft et al. 2007 [14].

Other malformations associated with Sirenomelia: Among other abnormalities that are commonly observed in Sirenomelia, are lumbosacral and pelvic malformations including sacral agenesis, malformed vertebrae and hemi-vertebra, and also corresponding anomalies of central nervous system according to Stocker and Heifetez.1987 & Kjaer et al. 2003 [5,15].

Our case showed sacral and coccygeal agenesis. Spinal cord was hypoplastic with deficiency of lumbosacral segments.There was partial agenesis of corpus callosum. Sirenomelia sometimes is also associated with malformations of upper body including cleft palate, upper thoracic and cervical vertebral abnormalities, pulmonary hypoplasia and cardiac defects according toKallen and Winberg 1974, Rodriguez etal.1991, Kallen et al.1992, Rodriguez and Palacios1992, &DrossouAgakidou et al. 2004 [16-19].

Our case showed pulmonary hypoplasia and cardiac defects viz. Atrial Septal Defect (ASD) and Ventricular Septal Defect VSD) and aberrant right subclavian artery.

According to the defective blastogenesis hypothesis, sirenomelia is a primary defect of blastogenesis that occurs during the final stages of gastrulation at the tailbud stage, corresponding to the third gestational week in humans as reported by Opitz et al. 2002,Duesterhoeft et al. 2007,&Davidson 1993 [11,14,20].

Although the vascular steal hypothesis and the deficient blastogenesis hypothesis do not exclude one other, it is reasonable to assume that deficient blastogenesis would concomitantly affect organ and vessel development.

Genetic aspects of Sirenomelia in animal models: A Sirenomelia-like phenotype has been observed in several genetically modified mouse strains with either gain of function of Retinoic acid (RA) signaling or loss of function of bone morphogenic protein (BMP) signalling [21].

RA, maternal diabetes and heavy metals, have been described as important environmental risk factors for caudal malformations. The involvement of RA signalling in the genesis of sirenomelia is well established in experimental models and represents a potentially interesting connection to the environment, because RA levels can be modified by genetic, nutritional and iatrogenic causes. However, to date, sirenomelia has not been reported among the malformations of RA-exposed human fetuses. Maternal diabetes is considered as a causative environmental factor for Caudal Dysgenesis (CD) because 10–15% of affected children have diabetic mothers according to Passarge and Lenz, 1966,Kalter 1993,Twickler et al. 1993, Lynch and Wright 1997,Assimakopoulos et al. 2004 & Castori et al. 2010 [22-27]. However, this association remains controversial for sirenmelia because only 0.5%–3.7% of reported cases have diabetic mothers according to Stocker and Heifetz 1987, Duncan and Shapiro 1993, Lynch

and Wright 1997,&Duesterhoeft et al. 2007 [5,28,25,14]. Finally, exposure to heavy metals is associated with CD and sirenomelia in both experimental models according to Ferm and Carpenter 1968, Hilbelink and Kaplan 1986; and in humans as reported by Castilla et al. 2008, &Orioli et al. 2009 [29-32]

Association of Sirenomelia with new reproductive technologies, namely Intra Cytoplasmic Sperm Injection (ICSI) was also described [33].

Karyotyping of the specimens was normal as reported by other researchers. This was not done in our case.

CONCLUSION

Sirenomelia is a rare and fatal congenital anomaly. Early prenatal diagnosis by first trimester scan should be the aim to minimize the trauma related to the termination of pregnancy at advanced gestation. Colour Doppler imaging can be helpful in identifying the single large vitelline artery and the absence of renal arteries. 3D sonography and MRI may complement the 2D-sonographic findings.

Post-mortem pathologic examinations and experimental animal studies will remain necessary to determine the exact patho-genetic mechanisms involved in the congenital malformations. Unless one searches carefully and systematically for these anomalies, they may remain unnoticed. Often, they play an important part in the gravity of the total disorder, because functional disturbances resulting from these associated malformations may in themselves lead to death. Although in our case the mother did not have evidence of the risk factors, the couple should be counselled about early screening in the subsequent pregnancy.

We hope the detailed report of our case may help in the wider understanding of the many possible features & perhaps also the patho-genetic mechanisms of sirenomelia; which would indirectly contribute toward better medicare in the world.

ABBREVIATIONS

SUA - Single Umbilical Artery
RA - Retinoic Acid
CD - Caudal Dysgenesis

Conflicts of Interests: None

REFERENCES

[1]. Bernard Duhamel et al, From the mermaid to Anal Imperforation: The syndrome of caudal Regression. 1960
[2]. Johnson B. L. Sirenomelia (Mermaid Fetus). Br. J. Clin. Pract. 1966;20:198–201.
[3]. Martinez-Frias M. L.,Cucalon F., Urioste M. New case of limb body-wall complex associated with sirenomelia sequence. Am. J. Med. Genet. 1992;44:583–585.
[4]. Murphy J. J., Fraser G. C., Blair G. K. Sirenomelia: case of the surviving mermaid. J. Pediatr. Surg. 1992;27:1265–1268.
[5]. Stocker J. T., Heifetz S. A. Sirenomelia.A morphological study of 33 cases and review of the literature. Perspect.Pediatr.Pathol. 1987;10:7–50.
[6]. Kallen B., Castilla E. E., Lancaster P. A., Mutchinick O., Knudsen L. B., Martinez-Frias M. L., Mastroiacovo P., Robert E. The cyclops and the mermaid: an epidemiological study of two types of rare malformation. J. Med. Genet. 1992;29:30–35.
[7]. Goodlow O. G., Sibley R. I., Allen B. G., Kamanda W. S., Gullattee A. C., Rayfield W. C. Sirenomelia: mermaid syndrome. J. Natl. Med. Assoc. 1988;80:343–346.
[8]. Heifetz S. A. Single umbilical artery. A statistical analysis of 237 autopsy cases and review of the literature. Perspect.Pediatr.Pathol. 1984;8:345–378.
[9]. Stevenson R. E., Jones K. L., Phelan M. C., Jones M. C., Barr M., Jr, ClericuzioC., Harley R. A., Benirschke K. Vascular steal: the pathogenetic mechanism producing sirenomelia and associated defects of the viscera and soft tissues. Pediatrics 1986;78:451–457.
[10]. Martinez-Frias M. L., Bermejo E., Rodriguez-Pinilla E., Prieto D. Does single umbilical artery (SUA) predict any type of congenital defect? Clinical-epidemiological analysis of a large consecutive series of malformed infants. Am. J. Med. Genet. 2008;146A:15–25.
[11]. Opitz J. M., Zanni G., Reynolds J. F., Jr, Gilbert-Barness E. (2002). Defects of blastogenesis.Am. J. Med. Genet. 2002;115:269–286.
[12]. Thottungal A. D., Charles A. K., Dickinson J. E., Bower C. Caudal dysgenesis and sirenomelia-single centre experience suggests common pathogenic basis. Am. J. Med. Genet. 2010;152A:2578–2587.
[13]. Jaiyesimi F., Gomathinayagam T., Dixit A., Amer M. Sirenomelia without vitelline artery steal. Ann. Saudi Med. 1998;18:542–544.
[14]. Duesterhoeft S. M., Ernst L. M., Siebert J. R., Kapur R. P. Five cases of caudal regression with an aberrant abdominal umbilical artery: further support for a caudal regression-sirenomelia spectrum. Am. J. Med. Genet. 2007;143A:3175–3184.

[15]. Kjaer K. W., Keeling J. W., Opitz J. M., Gilbert-Barness E., Hartling U., Hansen B. F., Kjaer I. Sirenomelia sequence according to the distance between the first sacral vertebra and the ilia. Am. J. Med. Genet. 2003;120A:503–508.

[16] Kallen B., Winberg J. Caudal mesoderm pattern of anomalies: from renal agenesis to sirenomelia. Teratology 1974;9:99–111.

[17]. Rodriguez J. I., Palacios J., Razquin S. Sirenomelia and anencephaly. Am. J. Med. Genet. 1991;39:25–27.

[18]. Rodriguez J. I., Palacios J. Craniorachischisistotalis and sirenomelia. Am. J. Med. Genet. 1992;43:732–736.

[19]. Drossou-Agakidou V., Xatzisevastou-Loukidou C., Soubasi V., Kostopoulou E., Laporda A., Pantzaki A., Agelidou S., Kremenopoulos G. Rare manifestations of sirenomelia syndrome: a report of five cases. Am. J. Perinatol. 2004;21:395–401.

[20]. Davidson E. H. Later embryogenesis: regulatory circuitry in morphogenetic fields. Development 1993;118:665–690.

[21]. Carlos Gamido – Allepuz et al. A Clinical and experimental overview of Sirenomelia: insight into the mechanism of congential limb malformations. Disease models & Mechanisms 2011;4:289-299.

[22]. Passarge E., Lenz W. Syndrome of caudal regression in infants of diabetic mothers: observations of further cases. Pediatrics 1966;37:672–675.

[23]. Kalter H. Case reports of malformations associated with maternal diabetes: history and critique. Clin.Genet. 1993;43:174–179.

[24]. Twickler D., Budorick N., Pretorius D., Grafe M., Currarino G. Caudal regression versus sirenomelia: sonographic clues. J. Ultrasound Med. 1993;12:323–330.

[25]. Lynch S. A., Wright C. Sirenomelia, limb reduction defects, cardiovascular malformation, renal agenesis in an infant born to a diabetic mother. Clin.Dysmorphol. 1997;6:75–80.

[26]. Assimakopoulos E., Athanasiadis A., Zafrakas M., Dragoumis K., Bontis J. Caudal regression syndrome and sirenomelia in only one twin in two diabetic pregnancies. Clin. Exp. Obstet. Gynecol. 2004;31:151–153.

[27]. Castori M., Silvestri E., Cappellacci S., Binni F., Sforzolini G. S., Grammatico P.Sirenomelia and VACTERL association in the offspring of a woman with diabetes. Am. J. Med. Genet. 2010;152A:1803–1807.

[28]. Duncan P. A., Shapiro L. R. Interrelationships of the hemifacialmicrosomia-VATER, VATER, and sirenomelia phenotypes. Am. J. Med. Genet. 1993;47:75–84.

[29]. Ferm V. H., Carpenter S. J. The relationship of cadmium and zinc in experimental mammalian teratogenesis. Lab. Invest. 1986;18:429–432.

[30]. Hilbelink D. R., Kaplan S. Sirenomelia: analysis in the cadmium- and lead-treated golden hamster. Teratog.Carcinog.Mutagen. 1986;6:431–440.

[31]. Castilla E. E., Mastroiacovo P., Lopez-Camelo J. S., Saldarriaga W., Isaza C., Orioli I.M. Sirenomelia and cyclopia cluster in Cali, Colombia. Am. J. Med. Genet. 2008;146A:2626–2636.

[32]. Orioli I. M., Mastroiacovo P., Lopez-Camelo J. S., Saldarriaga W., Isaza C., Aiello H., Zarante I., Castilla E. E. Clusters of sirenomelia in South America. Birth Defects Res. A Clin. Mol. Teratol. 2009;85:112–118.

[33]. Nievelstein et al. MR of the caudal Regression syndrome: Embryologic Implications. AJNR 1994;15:1021-1029.

How to cite this article:

Parimala Sirikonda, Nalluri Himabindu. SIRENOMELIA: A DETAILED FETAL AUTOPSY STUDY. Int J Anat Res 2015;3(4):1669-1674. **DOI:** 10.16965/ijar.2015.311