PREVALENCE OF SINGLE UMBILICAL ARTERY AND ASSOCIATED CONGENITAL ANOMALIES - A FOETAL STUDY

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ABSTRACT

BACKGROUND

Congenital anomalies form one of the leading causes of foetal loss and infant mortality. The survival of the foetus during the gestational period depends upon the state of the umbilical cord and the vascularity that it provides. Compromise of the foetal blood flow through the blood vessels can have serious effects on the health of the foetus and the new born. Various congenital anomalies are present in relation to the single umbilical artery. Since umbilical cord anomalies can be diagnosed prenatally, the potential to improve foetal survival is more.

The aim of the present study was to find out the pattern of congenital anomalies and its association with single umbilical artery.

MATERIALS AND METHODS

A total of 110 foetal autopsy cases were considered for this study. Descriptive analytical methods were used to assess the patterns of intra-group findings in both foetus and umbilical cord.

RESULTS

The overall prevalence of congenital malformation obtained in this study was 48.18% and of these 47.17% were with multiple congenital anomalies and 52.83% with single anomaly. There were 6 single umbilical artery cases, which constituted a prevalence of 5.45%. Of the 6 single umbilical artery cases, 4 were associated with congenital anomalies (66.67%). Vertebral anomalies were the most common congenital anomalies followed by meningomyelocele and webbed neck.

CONCLUSION

Since umbilical cord lesions can be diagnosed prenatally, awareness and detection of the conditions in the antenatal period will improve foetal survival and reduce infant mortality.

KEYWORDS

Umbilical Cord, Single Umbilical Artery, Congenital Anomalies, Infant Mortality.

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BACKGROUND

Umbilical cord is the 'Life-Line' between the foetus and the placenta. It is formed by the 5th week of intrauterine development and it functions throughout pregnancy to protect the vessels that travel between the foetus and the placenta. Compromise of the foetal blood flow through the umbilical cord vessels can have serious deleterious effects on the health of the foetus and newborn.¹ Cross-section of normal umbilical cord contains two arteries and one vein which are embedded within a spongy, proteoglycan rich matrix known as Wharton's jelly.

Congenital anomalies are the leading cause of infant mortality rate accounting for approximately 21% of infant deaths.² They are also the fifth leading cause of years of loss of potential life prior to age 65 and a major contributor to disabilities. They may be single or multiple and of minor or

major clinical significance. Single minor anomalies present in 14% of newborn, alert the clinician to the possible presence of an associated major anomaly. The cause of most congenital anomalies (40% - 60%) is unknown. Most common cause is multifactorial, i.e. result from a complex interaction between genetic and environmental factors (20%).²

Many obstetrically important umbilical cord lesions can be diagnosed prenatally and foetal survival can be improved with better prenatal surveillance and timely intervention. Detailed examination of the umbilical cord after birth is an absolute necessity, because of the strong association between umbilical cord anomalies and adverse perinatal outcomes.³

Objectives

The present study is a combined work of examining the umbilical cord vasculature and gross anatomy of dead foetuses and to find out the following gross and morphologic parameters: morphological changes in the umbilical cord vasculature, commonly observed congenital malformations seen, prevalence of Single Umbilical Artery/SUA and the pattern of congenital anomalies seen associated with SUA.

MATERIALS AND METHODS

A total of 110 foetuses from the Department of Pathology, Medical College, Thiruvananthapuram for autopsy were considered for this study. Each autopsy was done only after getting the wilful signature of the informed consent by the

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mother of the dead foetus, after explaining the benefits and risks of this study. Foetuses showing evidence of life-like breathing, heartbeat, pulsation of umbilical cord at the time of delivery were not considered for this study. Foetuses of mothers with chronic hypertension, diabetes mellitus, chronic nephritis, TORCH infections and taking teratogenic drugs like anti-cancer drugs, warfarin, phenytoin, phenobarbitone and isotretinoin also were excluded from this study.

For statistical purposes, foetal deaths were classified into 3 categories according to the gestational age. Early foetal death that occurred at less than 20 weeks of gestation, intermediate foetal death at 20 - 27 weeks of gestation and late foetal death at greater than 28 weeks of gestation. Study incorporated procedures conducted during and after the foetal autopsy. The foetuses were numbered for identification and all the findings were entered in a master chart, which also included the age and sex of the foetus. The findings were assessed under the following headings.

Gross and Morphologic Parameters

During the foetal autopsy, different parameters were measured. These included crown-rump length, bi-parietal diameter, abdominal circumference, femur length, head circumference, crown-heel length and foot length. The age of the foetus (in weeks) was assessed using the calculation; Age of foetus (in weeks) = Crown-heel length in inches x 2. Sex of the foetus was also noted.

The foetus and the placenta were weighed separately. These were weighed three times and the average of these three independent observations was recorded.

Congenital Anomalies

During the autopsy, the gross structural anomalies in the musculoskeletal system, urogenital system, cardiovascular system, gastrointestinal system, central nervous system and other anomalies were recorded.

Single Umbilical Artery

Umbilical cord tissue was collected from each case and immediately transferred to 10% formalin for fixation. The fixed tissue bits were then subjected to routine histological processing.⁴ The blocks thus obtained were sectioned at 0.5 micron. The slides were numbered and the key to these numbers contained the age and sex of the foetus from whom the specimens were taken. Sections are carefully transferred to the surface of water bath using paint brush. Then collect the sections on a clean glass slide. Haematoxylin and Eosin staining method is used to study the tissue. The slides thus prepared were examined under light microscopy and the number of vessels noted.

Single Umbilical Artery and Associated Congenital Anomalies

The section of the umbilical cords were studied in detail and the SUA when confirmed were entered in the master chart and its associated anomaly noted.

RESULTS

The present study evaluated the gross morphologic parameters, congenital anomalies, SUA and SUA associated congenital anomalies. The study was based on the data collected from 110 foetal autopsies.

Gross Morphologic Parameters

The findings with respect to the various parameters of the 110 foetuses were entered and the mean and the standard error of mean calculated. The descriptive statistics of different parameters is given in Table 1.

Parameter	N (No. of Cases)	Mean $\pm$ SEM
Age of Foetus (Weeks)	110	23.52 $\pm$ 0.70
Weight of Foetus (Grams)	110	671.79 $\pm$ 65.13
Weight of Placenta (Grams)	110	385.79 $\pm$ 45.08
Crown Rump Length (cm)	110	19.47 $\pm$ 0.65
Head Circumference (cm)	110	21.06 $\pm$ 0.66
Crown Heel Length (cm)	110	29.46 $\pm$ 0.90
Foot Length (cm)	110	4.10 $\pm$ 0.15

Table I. Descriptive Statistics

The mean age of the foetuses studied was 23.52 weeks (SD of 7.29). The minimum age was 10 weeks and the maximum age found was 40 weeks. These data were analysed to check whether there is any significant difference in the above-mentioned parameters between the foetuses with SUA and others.

Table II shows the distribution and significance of these parameters with reference to the umbilical artery status.

Parameter	Mean $\pm$ SEM		P value
	Single Umbilical Artery Cases (N=6)	Normal Umbilical Artery Cases (N=104)	
Age (Weeks)	19.50 $\pm$ 1.20	23.75 $\pm$ 0.73	0.014
Weight of Foetus (Grams)	279.73 $\pm$ 76.0	694.41 $\pm$ 68.1	0.001
Weight of Placenta (Grams)	301.17 $\pm$ 99.73	390.67 $\pm$ 47.36	NS
Crown Rump Length (cm)	17.27 $\pm$ 1.44	19.60 $\pm$ 0.68	NS
Head Circumference (cm)	19.70 $\pm$ 1.22	21.14 $\pm$ 0.69	NS
Crown Heel Length (cm)	24.22 $\pm$ 1.27	29.76 $\pm$ 0.95	0.004
Foot Length (cm)	3.33 $\pm$ 0.39	4.14 $\pm$ 0.16	NS
NS: Not significant			

Table II. Distribution of Parameters Based on Umbilical Artery Status

Compared to foetuses with single umbilical artery status, the age, weight and crown heel length were more, for foetuses with normal umbilical artery status. With regards to age, foetal weight and crown heel length ($p < 0.05$), there is a statistically significant difference between the foetuses with normal umbilical cord status and single umbilical artery. This states that foetuses with normal number of vessels in the umbilical cord survive and grow better than those with single umbilical artery.

Congenital Anomalies

The occurrence of congenital malformations was noted during the foetal autopsy. There were 48.18% (N = 53) congenital anomalies. Of these 47.17% (N = 25) were with multiple congenital anomalies and 52.83% (N = 28) with single anomaly. A detailed description is given in Table III.

System	No. (N)	Percentage (%)
Musculoskeletal System		
Club Foot	10	9.09
Vertebral Anomalies	5	4.55
Cleft Lip	4	3.64
Cleft Palate	3	2.73
Syndactyly	3	2.73
Sirenomelia	1	0.91
Cardiovascular System		
ASD	2	1.82
VSD	1	0.91
Gastrointestinal System		
Omphalocele	8	7.27
Oesophageal Stenosis	1	0.91
Imperforate Anus	1	0.91
Central Nervous System		
Anencephaly	6	5.45
Meningomyelocele	4	3.64
Hydrocephalus	4	3.64
Holoprosencephaly	1	0.91
Microcephaly	1	0.91
Others		
Cystic Hygroma	9	8.18
Single Umbilical Artery	6	5.45
Pulmonary Hypoplasia	5	4.55
Webbed Neck	4	3.64
Hydrops Foetalis	4	3.64
Diaphragmatic Hernia	2	1.82
Pulmonary Aplasia	1	0.91

Table III. Distribution of Congenital Anomalies in the Study Group (N = 110)

The most commonly found anomaly is club foot, 9.09% (N = 10). This was followed by cystic hygroma in 8.18% cases (N = 9) and omphalocele in 7.27% (N = 8).

Musculoskeletal System

There were 10 club foot cases (9.09%). Bilateral club foot was observed in a 27-week-old male foetus (Figure IA).

There were five vertebral anomaly cases (4.55%). In vertebral anomalies, spina bifida associated with meningocoele was observed (Figure IB).

Figure IA. Bilateral Club Foot

Figure IB. Meningocoele

Four cleft lip (3.64%) in Fig. IIA and 3 cleft palate cases (2.73%) were also noted. There were 3 syndactyly cases (2.73%) Fig. IIB shows syndactyly between third and fourth fingers.

Figure IIA. Upper Right Lateral Cleft Lip

Figure IIB. Syndactyly

There was one sirenomelia case (0.91%). This was noted in a 20-week-old male foetus (Fig. IIIA). Upper limbs were normal and the lower limbs were fused. Only one toe was present in the right foot and no toes were present in the left

foot. Anal opening was absent. Urinary system was not formed. The umbilical cord was examined and it was associated with single umbilical artery (Fig. IIIB).

Figure IIIA. Sirenomelia

Figure IIIB. Single Umbilical Artery

Urogenital System Anomalies

There were 6 malformed external genitalia cases (5.45%) and 4 cases of hydronephrosis (3.64%). There were 3 cases of renal agenesis and mullerian duct agenesis (2.73%). There was one case each of renal hypoplasia and horseshoe kidneys (0.91%).

Cardiovascular System

There were 2 cases (1.82%) of ASD and one case (0.91%) of VSD.

Gastrointestinal System

There were 8 cases (7.27%) of omphalocele and one case each of oesophageal stenosis and imperforate anus (0.91%). Fig. IV shows omphalocele in a 34 weeks foetus.

Figure IV. Omphalocele in a 34 Weeks Old Foetus

Central Nervous System

There were 6 cases of anencephaly (5.45%). An anencephalic foetus of 16 weeks gestation is shown in Figure V. There were 4 cases each of meningocele and hydrocephalus (3.64%). One case each of holoprosencephaly and microcephaly (0.91%) was also present.

Figure V. Anencephaly

Others

9 cases of cystic hygroma (8.18%) are noted. A 19-week-old male foetus with cystic hygroma is shown in Figure Vi; 13.5 cases of pulmonary hypoplasia were noted (4.55%); 4 cases each of webbed neck and hydrops foetalis (3.64%) were noted; 2 cases of diaphragmatic hernia (1.82%) and one case of pulmonary aplasia (0.91%) are noted.

Figure VI. Cystic Hygroma

Single Umbilical Artery and associated Congenital Anomalies

There were 6 cases of single umbilical artery (5.45%). Cross-section of an umbilical cord showing SUA is shown in the Figure VIIA and its histological picture in Figure VIIIB.

Figure VIIA. Cross-Section of UC showing SUA

Figure VII B. Section of Umbilical Cord, Hx and E Stain showing Single Artery (A) and One Vein (V)

In cases with single umbilical artery, the distribution of congenital anomalies was analysed. Of the six single umbilical arteries four are associated with congenital anomalies (66.67%). The detailed description of the types of congenital anomalies is seen in fetuses with SUA as given below in Table IV.

System	No. (N)	Percentage (%)
Musculoskeletal System		
Vertebral anomalies	3	50.00
Club foot	1	16.67
Sirenomelia	1	16.67
Gastrointestinal System		
Omphalocele	1	16.67
Central Nervous System		
Meningomyelocele	2	33.33
Others		
Webbed neck	2	33.33

Table IV. Distribution of Congenital Anomalies in Fetuses with SUA (N = 6)

Of the six SUA cases, there were ten associated different congenital anomalies. Vertebral anomalies were the most common followed by meningomyelocele and webbed neck. This was followed by meningomyelocele and webbed neck.

DISCUSSION

The present study on the fetuses was based on the following aspects: Gross morphologic parameters and their association with SUA, various congenital anomalies observed, prevalence of SUA and the relation between congenital anomalies with SUA.

Gross Morphologic Parameters

Compared to fetuses with single umbilical artery status the age, weight and crown heel length were more, for fetuses with normal umbilical artery status. So fetuses with normal number of vessels in the umbilical cord survive and grow better than those with single umbilical artery. Meiling Hua⁵ found out an increased risk of IUGR associated with presence of SUA. They also reported an increased antepartum stillbirth in fetuses with SUA, which means a reduced age compared with normal vessels.

Congenital Anomalies Observed

A variety of congenital malformations of various systems were noted. They included anomalies of musculoskeletal system, urogenital system, cardiovascular system, gastrointestinal system, central nervous system and others. Toshio Fujikura⁶ observed 71% of malformed infants had multiple congenital malformations.

Musculoskeletal System

In this study musculoskeletal anomalies are having a higher incidence (50%) in accordance with the study of Luz A. Froehlich⁷ and Mohamed⁸ has stated a higher incidence of musculoskeletal system than CNS.

Urogenital System

In this, malformed external genitalia was the most common anomaly followed by hydronephrosis. Luz A. Froehlich⁷ found that in Genitourinary system, polycystic kidney and renal aplasia are the most common anomalies seen.

Cardiovascular System

Atrial septal defect and ventricular septal defect were the common anomalies observed in this study in accordance with the study of Rizk Francine.⁹

Central Nervous System

The most common anomaly was anencephaly followed by meningomyelocele. Luz A. Froehlich⁷ had reported that in central nervous system anomalies anencephaly microcephaly and hydrocephaly are seen. But in the present study, anencephaly showed a high prevalence and microcephaly showed a decreased prevalence. Kanan Shah¹⁰ also found out CNS anomalies were the highest followed by musculoskeletal system. Swain¹¹ also stated a higher incidence of CNS anomalies.

Gastrointestinal System

Omphalocele was the most common anomaly followed by oesophageal stenosis and imperforate anus. Luz. A. Froehlich⁷ found that in gastrointestinal system, omphalocele pyloric stenosis and diaphragmatic hernia are seen.

Others

There were cases of cystic hygroma followed by single umbilical artery pulmonary hypoplasia, webbed neck, hydrops foetalis, diaphragmatic hernia and pulmonary aplasia in this study. Luz A. Froehlich⁷ found that in the respiratory system, hypoplasia of lung and diaphragmatic hernia were also seen. Smith¹² reported sirenomelia was frequently associated with SUA.

Prevalence of SUA

There were six SUA cases, which constituted a prevalence of 5.45% of the total 110 cases. The studies of Lorena Mesquita¹³ described a 2%, Meiling Hua⁵ a 0.61%, Fatemeh Ghatresaman¹⁴ a 1.1% and Cristina Martinez-Payo¹⁵ an incidence of 0.7% by prenatal ultrasound diagnosis. Kristofferson¹⁶ stated that the incidence of SUA based on autopsies varies between 2.7 - 12%. The present study on autopsied fetuses showed an incidence within this range.

Relation between Congenital Anomalies and SUA

Of the six single umbilical arteries, four were associated with congenital anomalies (66.67%) and these anomalies were present in the musculoskeletal system, gastrointestinal system, central nervous system and in others. Toshio Fujikura⁶ observed that frequency of congenital malformations associated with SUA was 18.4%. Gastrointestinal and skeletal malformations were more frequent than lesions of the CNS; 71% of malformed infants had multiple congenital malformations. Kristofferson¹⁶ reported 15% - 48% and even greater, 49.1 - 93%, in autopsied material. According to Heifetz,¹⁷ a variety of malformations have been associated with SUA including CVS malformations, CNS defects, GIT defects, musculoskeletal and urogenital defects. Benirschke and Brown¹⁸ found out an incidence of 1% SUA with 46% malformed infants and Fred A. Lyon¹⁹ observed the foetal anomalies associated with SUA like hydrocephalus, Arnold-Chiari malformation, spina bifida with myelomeningocele, hypoplastic lungs, polycystic horseshoe kidneys, CTEV and anencephaly. According to Heifetz,¹⁷ a variety of malformations have been associated with SUA including CVS malformations, CNS defects, GIT defects, musculoskeletal and urogenital defects. Benirschke and Brown¹⁸ reported that 76% of malformed infants had multiple congenital malformations.

CONCLUSION

The present work combined both gross anatomical and associated congenital anomalies with particular reference to the SUA. The overall congenital malformation prevalence obtained in the study was 48.18% and of these 47.17% were with multiple congenital anomalies and 52.83% with single anomaly. Musculoskeletal system anomalies were the most common followed by gastrointestinal and central nervous system anomalies. There were six SUA cases, which constituted a prevalence of 5.45%. Of the six single umbilical arteries, four were associated with congenital anomalies (66.67%).

Since many obstetrically important congenital anomalies can be diagnosed prenatally, awareness and detection of these conditions antenatally have the potential to improve foetal survival. So the present study will be helpful in gaining some knowledge regarding prevalence of SUA and its association with various congenital anomalies.

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