INTRODUCTION

Umbilical cord is comprised of two umbilical arteries, one umbilical vein and Wharton’s jelly surrounding them and by fragments of the allantoids. It is responsible for feto-maternal blood flow. Assessment of morphometric alterations of umbilical cord by prenatal sonography at different gestational ages permits the identification of adverse perinatal outcomes. Alteration of these reference ranges validates antenatal and perinatal complications including preeclampsia, growth restriction, pregnancy induced hypertension, fetal heart rate disturbances, fetal aneuploidy, macrosomy, and intrauterine demise.

The purpose of the present study was to determine the reference range measurements, via ultrasonography, for the cross-sectional areas of umbilical arteries, umbilical vein and Wharton jelly at different gestational ages.
METHODS

The present cross-sectional study was done on 300 pregnant women having no complications, with gestational age between 28-39 weeks at the Department of Radiodiagnosis, Sri Siddhartha Medical College, Tumakuru, Karnataka, India during the period from January 2015-June 2018. Informed consents were collected from all the patients.

Selection criteria

Normal singlet pregnant women between the age group of 20-35 years and gestational age 28-39 weeks based on last menstrual period (LMP) were included in the study. Exclusion criteria were pregnancies related with co-morbid conditions like gestational diabetes, preeclampsia, PIH, IUGR, oligohydramnios, polyhydramnios and Intrauterine Death (IUD). All foetuses with the congenital anomalies were excluded.

After getting approval from Institutional ethics committee, all the patients underwent a routine antenatal sonogram performed by a single operator on a commercially available ultrasound machine GE voluson pro730 with a 3-3.5-MHz curvilinear (Convex) abdominal probe. A single measurement of each parameter was recorded. The sonographic cross-sectional areas of the umbilical cord, umbilical arteries and umbilical vein were measured in a plane close to the cord insertion at the fetal abdomen. The cord and its vessels were manually circled, and their cross-sectional areas were automatically calculated by the ultrasonography (Figure 1). The cross-sectional area of the Wharton jelly was obtained by subtracting the total vessel area from the total cross-sectional area of the umbilical cord.

Statistical analysis

The data obtained were statistically analysed using SPSS software version 18.0. The mean and standard deviation of the cross-section area (CSA) of the umbilical arteries, vein and Wharton’s jelly were calculated in accordance with gestational age. The 5th, 10th, 50th, 90th and 95th percentile for gestational age for the measurements were also calculated. Polynomial regression analysis was performed to identify the regression curves that best fitted the data point. Student test was done for calculating the mean and standard deviation of the CSA and circumference of the umbilical cord, vein and arteries in each group (before and after 34 weeks of gestational age). Statistical significance was considered when p value was >0.05.

RESULTS

Table 1 presents the patients characteristics. The mean age of the patients was 25.1 years with an average gestational age of 34.3 weeks. Average birth weight of the neonates was 2855 gm. Majority of them were nulliparous (51%).

Table 1: Patient characteristics (n=300).

| Characteristics          | Mean±S.D |
|--------------------------|----------|
| Maternal age (years)     | 25.10 ± 3.61 |
| Gestational age at delivery (weeks) | 34.36 ± 2.69 |
| Birth weight (g)         | 2855 ± 418.6 |
| Parity                   | n (%)    |
| Nullipara                | 153 (51%) |
| >1                       | 147 (49%) |

The regression equation for the mean umbilical artery (y) according to gestational age (x) was $y = -0.226-0.005 GA+0.01GA^2$.

Figure 2: Scatter diagram of umbilical artery with gestational age.

Table 2 presents the mean cross-sectional areas of the umbilical arteries, umbilical veins and Wharton’s jelly for each gestational age respectively. The mean cross-sectional area of umbilical artery and Wharton’s jelly was...
increased from 28th gestational week to 36th week, followed by decrease from 37th week as shown in Figure 2 and 3.

The regression equation for the mean Umbilical vein (y) according to gestational age (x) was $y = -0.119 + 0.008GA + 0.001GA^2$.

Figure 3: Scatter diagram of umbilical vein with gestational age.

The regression equation for the mean Wharton’s Jelly (y) according to gestational age (x) was $y = -2.335 + 0.021GA + 0.008GA^2$.

Figure 4: Scatter diagram of Wharton’s jelly with gestational age.

Table 2: Descriptive mean cross-sectional areas of umbilical artery, umbilical vein and Wharton’s Jelly according to gestational age.

| Gestational age (Weeks) | Number (n=300) | Umbilical artery cross sectional area Mean±S.D (cm²) | Umbilical vein cross sectional area Mean±S.D (cm²) | Wharton’s jelly cross sectional area Mean±S.D (cm²) |
|------------------------|----------------|-----------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| 28 (1-6)               | 17             | 0.126±0.044                                         | 0.490±0.112                                     | 0.789±0.195                                     |
| 29 (1-6)               | 09             | 0.127±0.025                                         | 0.560±0.106                                     | 0.811±0.258                                     |
| 30 (1-6)               | 07             | 0.140±0.020                                         | 0.563±0.070                                     | 0.834±0.074                                     |
| 31 (1-6)               | 15             | 0.143±0.074                                         | 0.573±0.104                                     | 0.891±0.416                                     |
| 32 (1-6)               | 15             | 0.159±0.417                                         | 0.534±0.045                                     | 0.948±0.245                                     |
| 33 (1-6)               | 20             | 0.142±0.073                                         | 0.536±0.132                                     | 0.984±0.296                                     |
| 34 (1-6)               | 41             | 0.145±0.053                                         | 0.530±0.126                                     | 0.996±0.394                                     |
| 35 (1-6)               | 66             | 0.162±0.060                                         | 0.568±0.127                                     | 0.913±0.307                                     |
| 36 (1-6)               | 49             | 0.171±0.064                                         | 0.585±0.182                                     | 0.966±0.323                                     |
| 37 (1-6)               | 40             | 0.149±0.055                                         | 0.595±0.122                                     | 0.819±0.305                                     |
| 38 (1-6)               | 12             | 0.167±0.063                                         | 0.581±0.222                                     | 0.895±0.399                                     |
| 39 (1-6)               | 09             | 0.123±0.30                                          | 0.433±0.144                                     | 0.579±0.282                                     |

The correlation of mean cross-sectional areas of umbilical artery, umbilical vein and Wharton’s Jelly before and after 34 weeks of gestational age.

Table 3: Correlation of mean cross-sectional areas of umbilical artery, umbilical vein and Wharton’s Jelly before and after 34 weeks of gestational age.

| Gestational age (weeks) | N   | Mean | SD  | Min. | Max. | t value | P value |
|------------------------|-----|------|-----|------|------|---------|---------|
| Umbilical artery       |     |      |     |      |      |         |         |
| <34                    | 79  | 0.129| 0.087| 0.05 | 0.70 | 7.861   | 0.005   |
| >34                    | 221 | 0.153| 0.058| 0.06 | 0.36 |         |         |
| Total                  | 300 | 0.147| 0.067| 0.05 | 0.70 |         |         |
| Umbilical vein         |     |      |     |      |      |         |         |
| <34                    | 79  | 0.506| 0.148| 0.20 | 1.05 | 7.711   | 0.006   |
| >34                    | 221 | 0.560| 0.151| 0.17 | 1.16 |         |         |
| Total                  | 300 | 0.546| 0.152| 0.17 | 1.16 |         |         |
| Wharton’s jelly        |     |      |     |      |      |         |         |
| <34                    | 79  | 0.983| 0.396| 0.21 | 1.88 | 2.922   | 0.088   |
| >34                    | 221 | 0.903| 0.346| 0.18 | 2.42 |         |         |
| Total                  | 300 | 0.924| 0.361| 0.18 | 2.42 |         |         |
Statistically significant correlation was observed between cross sectional areas of umbilical artery and vein when compared with gestational age of pregnant women before and after 34 weeks (p=0.005 and 0.006 respectively) but no significant correlation was noticed with the cross-sectional area of Wharton’s jelly (p=0.088) (Table 3). Table 4-6 shows the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles for the measurements of the cross-sectional area of the components of umbilical cord for each gestational age considered.

**Table 4: Percentile distribution of umbilical artery cross sectional area.**

| Gestational age (weeks) | Percentiles |
|------------------------|-------------|
|                        | 5  | 10  | 25 | 50  | 75  | 90  | 95  |
| 28 (1-5)               | 0.06 | 0.068 | 0.095 | 0.12 | 0.155 | 0.2 | - |
| 29 (1-6)               | 0.1 | 0.11 | 0.16 | 0.12 | 0.145 | - | - |
| 30 (1-6)               | 0.12 | 0.12 | 0.14 | 0.15 | - | - | - |
| 31 (1-6)               | 0.08 | 0.08 | 0.09 | 0.09 | 0.23 | 0.266 | - |
| 32 (1-6)               | 0.07 | 0.088 | 0.14 | 0.2 | 0.204 | - |
| 33 (1-6)               | 0.061 | 0.08 | 0.08 | 0.105 | 0.193 | 0.269 | 0.28 |
| 34 (1-6)               | 0.08 | 0.08 | 0.1 | 0.13 | 0.18 | 0.21 | 0.276 |
| 35 (1-6)               | 0.08 | 0.09 | 0.11 | 0.16 | 0.2 | 0.263 | 0.287 |
| 36 (1-6)               | 0.085 | 0.1 | 0.12 | 0.16 | 0.2 | 0.28 | 0.32 |
| 37 (1-6)               | 0.09 | 0.09 | 0.103 | 0.135 | 0.198 | 0.22 | 0.259 |
| 38 (1-6)               | 0.1 | 0.103 | 0.123 | 0.15 | 0.17 | 0.302 | - |
| 39 (1-6)               | 0.1 | 0.1 | 0.11 | 0.12 | 0.12 | - | - |

**Table 5: Percentile distribution of umbilical vein cross sectional area.**

| Gestational age (weeks) | Percentiles |
|------------------------|-------------|
|                        | 5  | 10  | 25 | 50  | 75  | 90  | 95  |
| 28 (1-6)               | 0.24 | 0.352 | 0.42 | 0.46 | 0.575 | 0.65 | - |
| 29 (1-6)               | 0.42 | 0.42 | 0.46 | 0.58 | 0.68 | - | - |
| 30 (1-6)               | 0.48 | 0.48 | 0.5 | 0.54 | 0.62 | - | - |
| 31 (1-6)               | 0.37 | 0.418 | 0.5 | 0.56 | 0.66 | 0.722 | - |
| 32 (1-6)               | 0.49 | 0.49 | 0.5 | 0.52 | 0.58 | 0.608 | - |
| 33 (1-6)               | 0.209 | 0.381 | 0.433 | 0.57 | 0.64 | 0.69 | 0.737 |
| 34 (1-6)               | 0.36 | 0.36 | 0.445 | 0.5 | 0.62 | 0.758 | 0.789 |
| 35 (1-6)               | 0.367 | 0.427 | 0.48 | 0.57 | 0.63 | 0.7 | 0.834 |
| 36 (1-6)               | 0.32 | 0.35 | 0.44 | 0.61 | 0.705 | 0.8 | 0.85 |
| 37 (1-6)               | 0.352 | 0.44 | 0.52 | 0.62 | 0.645 | 0.816 | 0.83 |
| 38 (1-6)               | 0.31 | 0.319 | 0.368 | 0.59 | 0.758 | 0.961 | - |
| 39 (1-6)               | 0.34 | 0.34 | 0.35 | 0.39 | 0.44 | - | - |

**Table 6: Percentile distribution of Wharton’s jelly cross sectional area.**

| Gestational age (weeks) | Percentiles |
|------------------------|-------------|
|                        | 5  | 10  | 25 | 50  | 75  | 90  | 95  |
| 28 (1-6)               | 0.37 | 0.458 | 0.675 | 0.79 | 0.955 | 1.028 | - |
| 29 (1-6)               | 0.49 | 0.49 | 0.6 | 0.74 | 1.09 | - | - |
| 30 (1-6)               | 0.71 | 0.71 | 0.77 | 0.85 | 0.9 | - | - |
| 31 (1-6)               | 0.21 | 0.21 | 0.68 | 0.91 | 1.11 | 1.574 | - |
| 32 (1-6)               | 0.72 | 0.72 | 0.72 | 0.85 | 1.05 | 1.398 | - |
| 33 (1-6)               | 0.533 | 0.595 | 0.83 | 0.92 | 1.11 | 1.458 | 1.803 |
| 34 (1-6)               | 0.334 | 0.508 | 0.715 | 1.01 | 1.315 | 1.562 | 1.723 |
| 35 (1-6)               | 0.498 | 0.589 | 0.74 | 0.885 | 1.03 | 1.226 | 1.43 |
| 36 (1-6)               | 0.415 | 0.5 | 0.765 | 0.97 | 1.125 | 1.44 | 1.485 |
| 37 (1-6)               | 0.275 | 0.374 | 0.545 | 0.86 | 1.095 | 1.159 | 1.38 |
| 38 (1-6)               | 0.29 | 0.329 | 0.462 | 0.97 | 1.15 | 1.46 | - |
| 39 (1-6)               | 0.42 | 0.42 | 0.42 | 0.46 | 0.745 | - | - |
**DISCUSSION**

Umbilical cord is a unique organ consisting of two umbilical arteries, one umbilical vein and Wharton’s jelly, which are sophisticated structures and performs vital functions to supply the necessary requirements to the foetus from the mother during the period of pregnancy. The umbilical cord begins to appear from the 4th-8th weeks of gestation from the amnion tissue from the body stalk, the omphalomesenteric duct and the umbilical coelom and establishment of blood flow within the cord starts by the end of the 5th week of gestation.

The left and right umbilical arteries are developed from the internal iliac arteries and supplies deoxygenated blood from foetus to the placenta. Umbilical veins arise from the convergence of venules that drain the extra-embryonic allantois. The right umbilical vein will disappear at the end of 6th week of gestation and left umbilical vein persists till the birth of the baby. It carries oxygenated blood from the placenta to the foetus.

Wharton’s jelly is a mucous connective tissue that surrounds the umbilical cord vessels. It originates from extra embryonic mesoderm and composed of proteoglycans and myofibroblasts. Hyaluronic acid is the important proteoglycan of Wharton’s jelly and helps in resisting external pressure and acts as a physical buffer in the regulation of fetoplacental circulation.

During foetal development, a number of abnormalities affect the umbilical cord that results in intrauterine growth restriction to fetal demise. They are related to morphology, cord insertion, cord length, cord diameter, number of vessels and blood flow. The most important among them was single umbilical artery. About 1% of singleton and about 5% of multiple pregnancies have only one umbilical artery. This leads to increase the risk of birth defects such as chromosomal abnormalities and defects in cardiovascular, urinary tract and central nervous systems.

Umbilical cord cysts (true or false) are found in about 3% of pregnancies. Both types of cysts are associated with chromosomal abnormalities, abdominal and kidney defects in the foetus. About 1% of the babies are born with umbilical cord knots. Tight knots result in miscarriage or stillbirth in 5% of cases. Nuchal cord abnormality was seen in about 25% of babies. Most of them are usually healthy but some shows heart rate abnormalities during labor and after delivery. Vasa previa is another abnormal condition that arises when umbilical cord vessels are unprotected by Wharton’s jelly that leads to tearing of blood vessels and can result in life-threatening bleeding in the baby.

Most of these abnormalities are diagnosed by non-invasive procedures before delivery but some are observed during or after delivery. Ultrasound and Doppler flow techniques helps in visualizing the morphology and foetal blood flow through umbilical cord vessels. By assessing the amount of blood flow through the umbilical artery during both fetal systole and diastole, an overall measure of fetal health can be obtained. But some clinical conditions such as fetal anaemia, high risk for several congenital and genetic defects like Down’s syndrome necessitate invasive approach. In such conditions foetus blood samples are to be collected by cordocentesis.

The two umbilical arteries and umbilical vein forms a cylindrical helix structure measuring one coil per 5 cm in length. It develops around 40 spirals with some straight portions reversal of spiral in between in most of the cases. Clinically hypocoiled umbilical cords have been associated with incidence of interventional deliveries, higher cord pH and heart rate disturbances and hypercoiling of umbilical cords were associated with preterm labour, preterm birth and growth restriction.

Hence it is very important to measure the cross-sectional areas of umbilical cord components at different stages of fetal development. The changes in these components are responsible for variations in umbilical cord dimensions. During gestational period, the umbilical cord has an average length of 50-60 cm. The cord length less than 30 cm is termed as short and associated with intrauterine growth restriction, congenital abnormalities, delayed foetal descent, premature placental separation. The cord length more than 100 cm termed as long cord and was related with prolapse, looping of the cord around the foetal neck, entanglement, distress and intrauterine demise.

Very few studies have been conducted for assessing the relationship between cross sectional areas of umbilical cord components and gestational age. The present study is the first among Indian population to assess the reference interval of umbilical cord components and gestational age. The first study to evaluate the cross-sectional areas of umbilical cord and its portions by sonography were done by Weissman and colleagues. They determined reference measures for the diameters of umbilical arteries, umbilical vein and Wharton’s jelly and their findings suggested that diameter of the cord increases with the increase in gestational age. Raio and his co-workers established reference measures for the cross-sectional areas of umbilical cord and found an increase in the cross-sectional area of umbilical cord upto 32 weeks followed by its fall.

The present study revealed the reference measures for the cross-sectional areas of umbilical artery, umbilical vein and Wharton’s jelly.

Umbilical arteries carry deoxygenated and nutrient depleted blood from foetus to placenta. Any abnormality in the health of foetus can be identified by measuring the amount of forward blood flow in umbilical arteries during systole and diastole. It is sufficient to measure diameter of one umbilical artery as both the arteries have similar
lumen diameters. However, there will be a difference in about 0.7-1.4% cases, one of the arteries will be smaller than the other with a difference of around 1-3 mm.\(^3\)\(^4\) In the present study, an increase in the cross-sectional area of umbilical artery was noticed from 28th gestational week to 36\(^{th}\) week, followed by decrease from 37th week. These observations were in accordance with the observations of Togni et al.\(^4\) In another study by Skulstad et al, an increase in umbilical artery diameter was noticed according to gestational age up to the 31st week and remaining stable to the end of the gestation.\(^5\)\(^6\)

The average diameter of umbilical vein ranges from 2 mm at 14-15 weeks of gestation to 7-8 mm to term.\(^7\) In the present study, the mean cross-sectional area of umbilical vein was increased up to 37th week and declined on 38th and 39th gestational week. These results were almost similar to the observations noticed by Togni et al.\(^4\) In his study, the cross-sectional area of the umbilical vein increased up to the 34\(^{th}\) week, stabilized in the 38\(^{th}\) week, and declined from the 39\(^{th}\) week onwards.

Cross sectional areas of Wharton’s jelly increase with gestational period. Changes in the cross-sectional areas of Wharton’s jelly describe the abnormal conditions during gestation. Absence of Wharton’s jelly around the umbilical cord vessels found in cases of perinatal mortality whereas larger cross sectional area of Wharton’s jelly defined in conditions of diabetes mellitus.\(^5\)\(^7\) The mean cross sectional areas of Wharton’s jelly was 0.79 cm\(^2\) during 36\(^{th}\) week to 40\(^{th}\) week of gestation.\(^8\) In the present study, the cross sectional area of Wharton’s jelly increased from 28\(^{th}\) gestational week to 36\(^{th}\) week, followed by decrease from 37\(^{th}\) week. Similar observations were also made by Togni et al.\(^4\)

In present study, statistically significant correlation was established between cross sectional areas umbilical arteries (p<0.005) and veins (p<0.006). These results were consistent with the findings of Rostamzadeh et al.\(^3\)\(^4\) However, no significant association was observed between cross sectional areas of Wharton’s jelly and gestational age. This was in agreement with the observations of Barbieri et al.\(^9\) This week correlation between Wharton’s jelly and gestational age was also supported by Ghezzi et al.\(^9\) This might be due to the result of the overlap of two altered conditions as a function of gestational age; i.e., a strong correlation for earlier gestational ages and a weak correlation for later gestational ages.

**CONCLUSION**

The findings of the study concluded that the cross-sectional area of umbilical cord components are to be considered as an important evaluating factors at different gestational ages for assessing the fetal growth. The ranges obtained in this study can be taken as references for further studies to correlate with the anthropometric parameters to estimate the fetal growth disorders and pregnancy disorders such as PIH and gestational diabetes.

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