Reference values for ductus venosus Doppler indices of normal gestation at 22-37 weeks: A Vietnamese cohort study

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Abstract

Prenatal doppler ultrasound of the ductus venosus plays an important role in the evaluation of fetal circulation and fetal heart function. We aimed to establish the percentile of Resistivity Index (RI) and Pulsatility Index (PI) of the Ductus Venosus (DV) among normal Vietnamese fetuses with a gestation from 22 to 37 weeks in a cohort study. Normal Vietnamese fetuses with a gestation ranging from 22 to 37 weeks were examined in a cohort study. The PI and RI were recorded from the DV. We analyzed 640 participants who all fulfilled the inclusion and exclusion criteria of our study. Results: There was a significant correlation between RI, PI and gestational age as shown with the equations y = 0.077x – 0.003x^2 + 3.493e^-5x^3 (r=0.97) and y = 0.106x – 0.004x^2 + 4.5e^-5x^3 (r=0.94), respectively. A centile module was constructed for the DV RI and PI indices among normal Vietnamese fetuses with gestation from 22 to 37 weeks.

Materials and Methods

Patient population

In this study a total of 640 women with normal singleton pregnancy were examined between the 22nd and 37th weeks of gestation. Fetal age is calculated from the last menstrual period and confirmed by the crown-rump length ultrasonographic measurement. The following people were omitted from our study: women with gestational diabetes, preterm labor, antepartum congenital abnormalities, and maternal systemic diseases, women on a regimen of tocolytic and antihypertensive agents, and women for whom it is impossible to determine the exact gestational stage. The research was authorized by the Institutional Review Board at National Hospital of Obstetrics and Gynecology, Hanoi, Vietnam, and a written informed consent document was issued for each individual involved in the research.

Ultrasonography

A Voluson 730 Pr 4D colour Doppler ultrasound system (GE Healthcare, Milwaukee, WI, USA) was used to conduct all the ultrasonography procedures. Using an ultrasonic 3.5 MHz frequency probe with color coded doppler and pulse doppler, the DV is a target of evaluation.

We initially trace the horizontal segment along the fetal spine and then we see the aorta that descends. The anterior thorax is the right fetal heart ventricle in front of the aorta that leads to the inferior vena cava. The most prominent landmark is the umbilical vein that flows into the fetal liver. We may find a branch from the umbilical vein into the lower vena cava, which is the DV (Figure 1), by the umbilical vein.

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Key words: Ductus venosus, Doppler ultrasound, Resistivity index, Pulsatility index.

Contributions: NTH and NMD contributed equally to this article as co-first authors. NTH and NMD gave a substantial contribution in acquisition, analysis, and data interpretation. NMD and HQH prepared, drafted, and revised manuscript critically for important intellectual content. Each author gave the final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of interest: The authors declare no conflict of interest.

Ethical approval and informed consent: Institutional Review Board at National Hospital of Obstetrics and Gynecology (Hanoi, Vietnam) approved this prospective study. Written informed consent of patients was obtained.

Received for publication: 10 March 2020. Accepted for publication: 13 May 2020.

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Pediatric Reports 2020; 12:8535 doi:10.4081/pr.2020.8535

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when the ruler is set to the highest point of the S, D, a waves; conduct a second revision of the measurements, taking the mean of the two measurements as the data to be obtained in the test. The DV doppler indices are used in the study (Figure 2): Pulsatility index (PI): PI = S-a/TAMX, Resistivity index (RI): RI = S-a/S.

Statistical analysis
Data were analyzed using the software SPSS for Windows, version 15.0 (SPSS Inc., Chicago, IL, USA). Analyze the developmental rules of the mean values of the DV doppler indices by the method of calculating the correlation between two quantities for each function y = f (x) where y is the doppler index, x is gestational age, with correlation when r>0.5 and correlated closely when r>0.7. Based on the correlation coefficient, the data table established, the upper and lower limits of each doppler index were determined using 5%, 10%, 50%, 95%, and 97% centile curves for each doppler index by gestational age.

Results
A total of 640 qualified participants meeting the inclusion and exclusion requirements were evaluated during the period June 2014 to January 2017 at the National Obstetrics and Gynecology Hospital. The crude PI mean was relatively stable and marginally decreased with gestation of 22 to 37 weeks. In order to prove and find out the PI development rules from the week of 22-37, we determined the correlation between y (PI) and x (gestational age) for each of the first, second, and third order functions, to decide the function with the highest correlation coefficient representing proper development rules. Solution of the third-order function chosen after replacing x with gestational age will obtain the mean PI values per gestational age shown in Table 1.

We implemented Table 2 on the basis of the formula for calculating the values corresponding to the centile lines and draw the following diagram for clinical use (Figure 3).

Similar to the calculation of the PI, the functions selected for calculating the centile lines for the RI from 22 to 37 weeks are the third order function y = 0.077x - 0.003x^2 + 3.493e - 5x^3.

The chosen variable rule calculates the mean values and the corresponding values for the centile lines from the third order function: 3, 5, 10, 50, 95, 97 as shown in Table 3. We drew the DVPI centile curve for gestational age from 22-37 weeks from the table above (Figure 4).

Table 1. The y (PI) to x (gestational age) association.

| Function   | Equation                | r  |
|------------|-------------------------|----|
| First order| y = 0.025x              | 0.79|
| Second order| y = 0.067x – 0.001x^2 | 0.88|
| Third order| y = 0.106x – 0.004x^3 +4.5e - 5x^3 | 0.90|

Table 2. The y (RI) to x (gestational age) association.

| Function   | Equation                | r  |
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The DV has an operation like a sphincter. It is a small vessel transmitting a high-velocity jet later to re-change the foramen ovale. The high peak velocity in the DV, comparable with arterial velocities, probably gives enough momentum to the blood to replenish the foramen ovale without extensive mixing with the deoxygenated blood.\textsuperscript{10,11} DV velocimetry brings new diagnostic possibilities for preload or heart function assessment. The typical doppler flow waveform of the ductus venosus shows the continuous flow of the triphasic forward throughout the cardiac cycle with a peak during the systole, another one during the diastolic filling, and an atrial nadir during the contrast.\textsuperscript{12,13} Many research investigated the diagnostic importance of ductus venosus blood flow in the diagnosis of fetuses with congenital heart disease, hypoxic or congestive fetal myocardial diseases from both a clinical and a scientific viewpoint. There is now a well-documented link between irregular DV flow, chromosomal anomalies, and adverse fetal outcomes.\textsuperscript{14-16} Consequently, the purpose of this study was to create longitudinal references for RI, PI, and suitable diameter for use with serial measurements for fetal surveillance, and we have also provided the necessary terms for individual conditional reference intervals suitable for individual serial measurements. The fetal movement was often examined with the DVPI. According to our results, the DVPI was closely correlated with gestational age according to a third-order feature in typical pregnancies from 22 to 37 weeks. Some authors developed a PI reduction chart based

### Table 2. PI values corresponding to centile lines 3, 5, 10, 50, 90, 95, 97 for 22-37 weeks of gestational age.

| Gestational age | N  | SD  | 3% | 5% | 10% | 50% | 90% | 95% | 97% |
|-----------------|----|-----|----|----|-----|-----|-----|-----|-----|
| 22              | 54 | 0.13| 0.63| 0.66| 0.71| 0.88| 1.04| 1.09| 1.12|
| 23              | 49 | 0.14| 0.61| 0.64| 0.69| 0.87| 1.05| 1.10| 1.13|
| 24              | 41 | 0.14| 0.59| 0.63| 0.68| 0.86| 1.05| 1.10| 1.13|
| 25              | 38 | 0.15| 0.57| 0.61| 0.66| 0.85| 1.05| 1.10| 1.14|
| 26              | 40 | 0.16| 0.55| 0.59| 0.64| 0.84| 1.04| 1.10| 1.14|
| 27              | 45 | 0.16| 0.53| 0.57| 0.62| 0.83| 1.04| 1.10| 1.14|
| 28              | 42 | 0.17| 0.50| 0.54| 0.60| 0.82| 1.03| 1.10| 1.14|
| 29              | 40 | 0.17| 0.48| 0.52| 0.58| 0.81| 1.03| 1.09| 1.13|
| 30              | 39 | 0.18| 0.46| 0.50| 0.56| 0.80| 1.03| 1.09| 1.13|
| 31              | 42 | 0.19| 0.43| 0.48| 0.54| 0.78| 1.02| 1.09| 1.13|
| 32              | 50 | 0.19| 0.41| 0.45| 0.52| 0.77| 1.02| 1.09| 1.13|
| 33              | 35 | 0.20| 0.39| 0.43| 0.51| 0.76| 1.01| 1.08| 1.13|
| 34              | 32 | 0.20| 0.37| 0.41| 0.49| 0.75| 1.01| 1.08| 1.13|
| 35              | 32 | 0.21| 0.34| 0.39| 0.47| 0.74| 1.01| 1.08| 1.13|
| 36              | 31 | 0.22| 0.33| 0.38| 0.46| 0.73| 1.01| 1.09| 1.14|
| 37              | 30 | 0.22| 0.31| 0.36| 0.44| 0.73| 1.01| 1.09| 1.14|
on the first, second-order functions such as Tongprasert et al.,17 Bahlmann et al.,18 Axt-Fliedner et al.,19 The authors had a common remark that the DVPI was associated with gestational age and given various correlation functions based on race of population. The authors set a table of reference values for the DV doppler index for different countries from the correlation equation. There are several explanations for this difference: gestational age, methods of analysis, methods of processing data and ethnicity of the population. From the literature review, the authors found that the DVPI in typical pregnancies decreased with gestational age that properly reflected placental circulation physiology.20,21 As the placental papilla grew, the capillary system was broad, the blood vessels were wide, the cell culture layers at the end of pregnancy were gradually thin to facilitate the metabolism between mother and fetus, and help the baby grow well. The fetal DVPI had however the features of different racial groups.22,23 Hence it is necessary to develop the physiological constants of the DVPI in different countries for each population group. In our research the RI was closely correlated with gestational age in average pregnant women at 22-37 weeks of gestation. Compared with other authors in the world, the correlation coefficient between RI and gestational age showed that the majority of authors selected a first-order function like Tongprasert et al.,17 Bahlmann et al.,18 Comparison of the correlation function between the RI and the gestational age of the authors worldwide revealed that the authors developed an RI histogram for gestational age with the functions of the first and second order.24-26 We chose the third-order function in this analysis because we noticed that the third-order function had a higher correlation coefficient and suggested that RI’s variable law decreased more reliably with an increase in gestational age. Differences in correlation functions may be due to different authors’ gestational age at the start of the study, method of study, method of data analysis. Our study results were likewise compatible with some other writers in the world.27,28 DVRI value decreased steadily as gestational age increased, indicating the RI of decreased placental circulation, suggesting easy maternal and fetal metabolism was facilitated by circulation in the placental papilla. It facilitated the fetus’ development without the risk of retiring the uterus’ fetal production. Therefore, the risk to the fetus was very small, when the DVRI was normal. Studies have shown that the DVRI is different and has features across different racial groups. Therefore it is important for each population race to establish physiological constants of DVPI.

### Conclusions

Ductus venosus doppler indices may constantly decrease with an increase in the age of gesture. The need to set normal range is therefore of great importance. A centile module was constructed for the ductus venosus RI and PI indices among normal Vietnamese fetuses with gestation from 22 to 37 weeks. Further studies should perform and validate our findings.

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