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Normal Doppler flow velocity waveforms in the fetal ductus arteriosus in the first half of pregnancy

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ABSTRACT

Ductus arteriosus flow velocity patterns were studied in 298 women between 9 and 25 weeks of gestation using transvaginal or transabdominal Doppler ultrasound. Technically acceptable recordings were first obtained at 11 weeks resulting in 231 women for further analysis. Ductal waveforms show a significant change in shape from early pregnancy to mid-pregnancy, in that end-diastolic velocities are absent until 13 weeks, are present in 50% at 15 weeks and are present in all cases from 17 weeks. Regression analysis demonstrated a statistically significant linear increase with advancing gestational age for all flow velocity parameters except for the pulsatility index which remained stable during the entire study period.

INTRODUCTION

With the advent of high-resolution real-time ultrasound and in particular color Doppler imaging, a number of reports have appeared on fetal ductal flow velocity waveforms during late second- and third-trimester pregnancies[1,2]. It has been demonstrated that under physiological conditions fetal ductal flow velocities are behavioral state-dependent[3,4]. Ductal constriction will occur as a result of maternal indomethacin administration in premature labor[5–7].

The introduction of transvaginal Doppler ultrasound has opened the possibility of studying the fetal circulation as early as 10–11 weeks of pregnancy[8,9]. Between 10 and 16 weeks, cardiac and extracardiac flow velocity waveforms suggest a change from a high to a low fetoplacental vascular resistance associated with increased ventricular compliance[10]. These changes may also be reflected in ductal flow velocities. Information on these velocities would therefore be of interest.

The objective of the present study was to establish the fetal ductal flow velocity waveform pattern in normal late first- and second-trimester pregnancies.

MATERIAL AND METHODS

A total of 298 women with a clinically uneventful singleton pregnancy consented to participate in the study. Preliminary duration, which was confirmed by ultrasonic measurements of the crown–rump length and/or biparietal diameter, varied between 9 and 25 weeks of gestation (mean 15 weeks).

Fetal ductal flow velocity waveform recording was carried out using either a Hitachi 450 (Tokyo, Japan) or a Toshiba 270 (Tokyo, Japan), both equipped with a combined sector scanner and pulsed wave Doppler system with vaginal and abdominal probes. For the Hitachi, the carrier frequency of the vaginal probe was 6.5 MHz and of the abdominal probe 3.5 MHz. For the Toshiba, the carrier frequency of the vaginal probe was 5 MHz and of the abdominal probe 3.75 MHz. In a previous study, intermachine variation was calculated between these two ultrasound systems. The Toshiba 270 depicts slightly lower values than the Hitachi, but these differences never exceed 10% of the standard deviation per parameter[11]. Vaginal and abdominal probes operated at power outputs of less than 100 mW/cm^2 spatial peak/temporal average in both imaging and Doppler modes by manufacturer's specifications. Until 13 weeks of gestation, a transvaginal approach was adopted, whereas afterwards waveforms were collected using transabdominal ultrasound. In order to limit the exposure of the fetus to transvaginally applied energy levels[12], a maximum recording time of 15 min was introduced.

Two-dimensional imaging was used to ensure the correct position of the Doppler interrogation beam both before and after each Doppler tracing was obtained. Maximum flow velocity waveforms from the ductus arteriosus were collected from the conventional short-axis view. The Doppler beam was positioned closely to the junction of the ductus arteriosus and descending aorta[13]. Doppler tracings were accepted when the angle between the Doppler beam and the assumed direction of flow was 20° or less.

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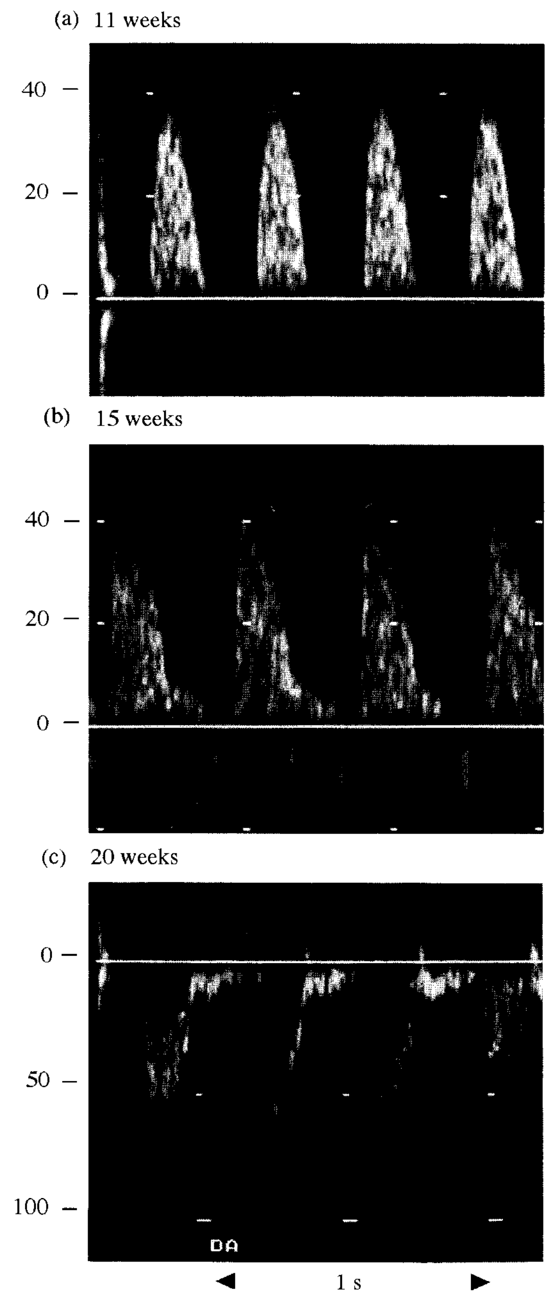

Figure 1 Ductus arteriosus flow velocity waveforms change in appearance from (a) week 11 through (b) week 15 to (c) week 20. End-diastolic velocities appear between week 14 and 17

All blood velocity waveforms were obtained during fetal apnea, since later in pregnancy ductal waveforms are modulated by breathing movements[3].

All blood velocity waveforms were stored on videotape. Analysis was performed using a computerized off-line system described previously[14], using hardcopies printed on a Sony A4 printing device. Four consecutive waveforms of similar appearance were analyzed in each case using a conventional microcomputer linked to a graphics tablet. Resolution of the analyzing program was 0.325 mm for the x-axis and 0.5 mm for the y-axis of one hardcopy. Flow velocity waveform analysis consisted of tracing the outer border of the densest part of the Doppler spectrum envelope of each waveform with a

Table 1 Regression analysis, linear model $y = a+bx$ where a = intercept, b = slope and p-value of analysis of variance

Parameter	*Intercept (SE)*	*Slope (SE)*	*p-value*
Peak systolic velocity (cm/s)	−12.09 (2.86)	4.10 (0.16)	< 0.0001
Time-averaged velocity (cm/s)	−3.93 (1.39)	1.24 (0.07)	< 0.0001
Pulsatility index	2.76 (0.12)	−0.014 (0.0068)	< 0.12
Acceleration time (ms)	26.42 (5.03)	1.39 (0.28)	< 0.0001
Flow velocity integral (cm)	−2.69 (0.53)	0.65 (0.03)	< 0.0001

SE : standard error

cursor and defining the onset, the maximum and the end-point of each waveform.

The following parameters were determined: peak systolic velocity, acceleration time, time-averaged velocity, end-diastolic velocity, flow velocity integral, pulsatility index and period time.

Peak velocities were measured from the zero line to the highest point of the Doppler velocity tracing. The acceleration time was defined as the time interval between the onset of ejection and peak systolic velocity. The time-average velocity was calculated by dividing the sum of velocities over one period time by the number of data points. The end-diastolic velocities were obtained by measuring from the zero line to the lowest point at the end of the diastole. The flow velocity integral was determined by multiplying time-averaged velocity with period time.

The collected data were entered into a DBASE IV (Ashton Tate, Torrance, CA, USA) database and exported to the STATGRAPHICS (Rockville, Md, USA) statistical program.

The relationship between each waveform parameter and gestational age was first analyzed using a simple linear regression analysis. For each parameter the best fitting line was determined from:

$$y = ax + b$$

where y = the flow velocity parameter, x = gestational age, a = the intercept of the regression line and b = slope of the regression line. A two-sided prediction band was calculated. As this provided a skewed distribution at gestational ages beyond 20 weeks for end-diastolic velocity and period time, a quadratic equation was chosen for these two parameters and a two-sided 95% prediction band was calculated.

RESULTS

No ductal flow velocity recordings were obtained at 9–10 weeks of gestation. The percentage of technically acceptable recordings rose from 50% at 11–13 weeks to 90% at 16 weeks, resulting in a cross-sectional study population of 231 women between 11 and 25 weeks of gestation for further analysis.

Ductal waveforms showed a significant change in shape from early pregnancy to mid-pregnancy (Figure 1), because the end-diastolic velocities are absent until 13

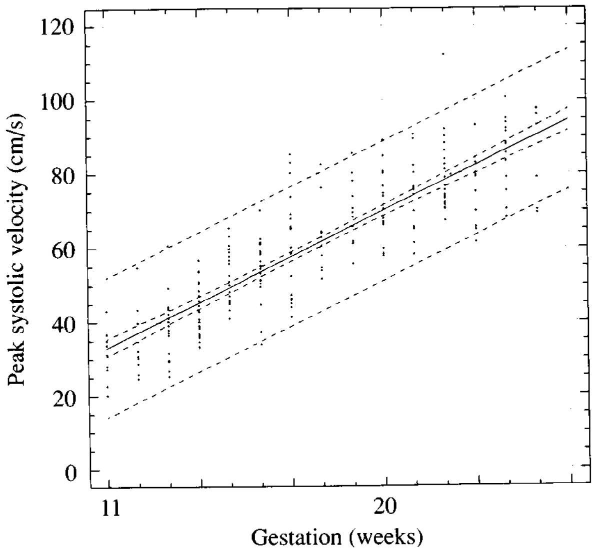

Figure 2 Ductus arteriosus peak velocities from weeks 11 to 25 with two-sided 95%-prediction band

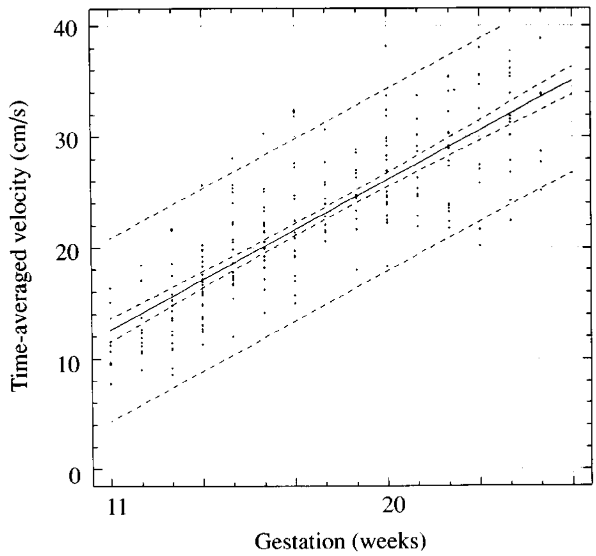

Figure 3 Ductus arteriosus time-averaged velocity

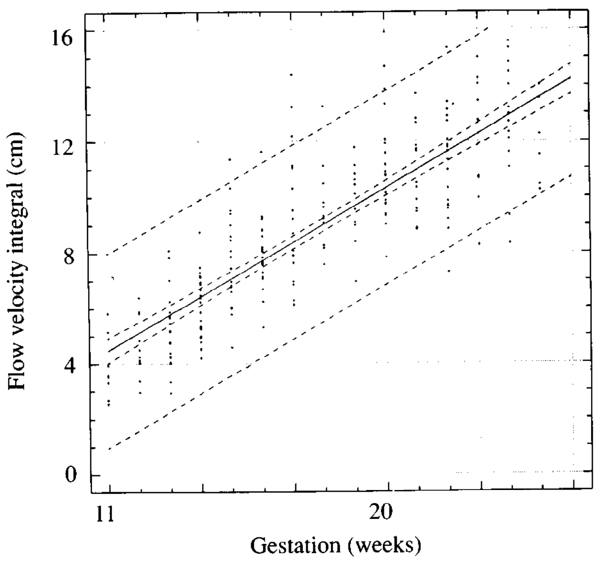

Figure 4 Ductus arteriosus flow velocity integral

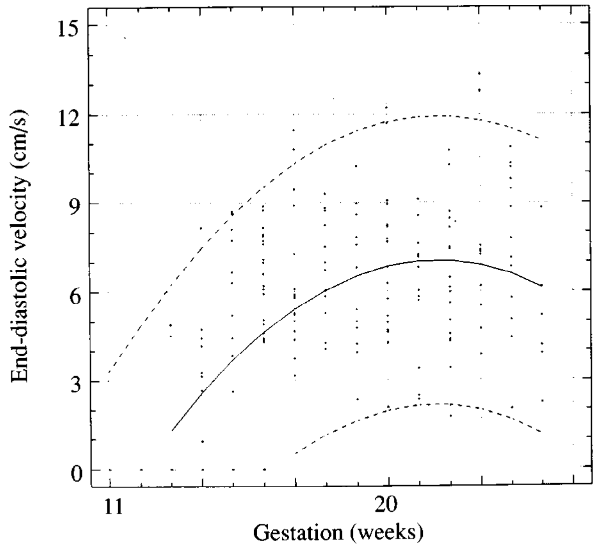

Figure 5 Ductus arteriosus end-diastolic velocity starts to appear between week 13 and 17

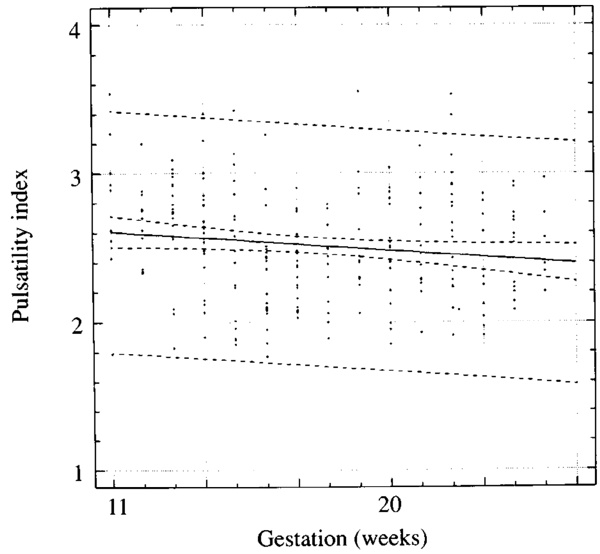

Figure 6 Pulsatility index of ductus arteriosus flow remains virtually unchanged between gestational weeks 11–26

weeks, are present in 50% of the patients at 15 weeks and are present in all cases from 17 weeks.

The values for a and b for each flow velocity parameter as well as the p-values are shown in Table 1. A statistically significant linear increase with advancing gestational age was observed for peak systolic, time-averaged velocity as well as flow-velocity integral ($p < 0.001$; Figures 2–4) and acceleration time ($p < 0.001$). Using the quadratic relationship, a statistically significant linear increase was established for end-diastolic velocity (Figure 5) and period time ($p < 0.001$; Table 2). No significant change with advancing gestational age was seen for the pulsatility index (Figure 6).

DISCUSSION

To our knowledge, this is a first report using human fetal ductal flow velocity waveform recordings as early as the late first trimester of pregnancy. The earliest recordings

Table 2 Regression analysis, quadratic model. The *p*-value is < 0.001 for both parameters

Parameter	*Intercept (SE)*	*Linear term (SE)*	*Quadratic term (SE)*
End-diastolic velocity (cm/s)	−29.28 (3.58)	3.36 (0.41)	−0.078 (0.01)
Period time (ms)	112.51 (32.22)	28.09 (3.71)	−0.68 (0.10)

were collected at 11 weeks; from this point onwards it gradually became possible to visualize the important landmarks such as the pulmonary artery and the aortic arch. Recording failure was highest (50%) before 14 weeks, which is partly due to the small size of the relevant structures and partly due to the extreme mobility of the fetus this early in gestation. End-diastolic flow velocities first appear at 13–14 gestational weeks which coincides with the appearance of end-diastolic velocities in the descending aorta and umbilical artery. This could therefore be the result of reduced umbilical–placental vascular resistance.

The ductus arteriosus acts as a right-to-left shunt in the fetal heart, preventing blood from passing through both cardiac chambers. An increase with advancing gestational age was found for all flow velocity parameters concerned. The gestational age-related rise in ductal peak systolic and time-averaged velocities is in agreement with previous observations on ductal flow velocities between 18 weeks and term[2] and may be determined by both an increase in ventricular stroke volume and a decrease in the right ventricular afterload. The right ventricular afterload is largely determined by the placental vascular resistance which has been shown to decrease with advancing gestational age[15].

The flow velocity integral, calculated from time-averaged velocity and the period time, could be used to determine the volume flow if information on the ductal diameter were available. This is not possible with present techniques. However, assuming that the ductus is maximally dilated[16], the age-related rise in flow velocity integral suggests a steady increase in right ventricular stroke volume and output during the observation period.

The pulsatility index varies between 2 and 3 and does not change significantly with gestational age. A pulsatility index below 1.9 is seen as reflecting ductal constriction as a result of maternal indomethacin administration[17]. The pulsatility index has been widely used as an indicator of placental and fetal peripheral vascular resistance[18]. A gradual decline in umbilical pulsatility index has been demonstrated as from 12–13 weeks' gestation, suggesting a decrease in placental vascular resistance. The reduction in ductal pulsatility index will only be observed as a result of vessel constriction during maternal indomethacin administration[19]. Therefore a change in ductal pulsatility index will represent a pathophysiological phenomenon which is completely different from that seen in the umbilical artery because ductal waveforms do not directly reflect vascular resistance. As acceleration time is a fraction of period time, the increase in the acceleration time over the period observed is not unusual. However, a large scatter of data on acceleration time was observed. This is in agreement with an earlier report from our own group[14] in which it was demonstrated that the acceleration time determined from fetal ductal flow velocity waveforms during the second and third trimester of pregnancy displayed a relatively poor reproducibility compared with the other waveform parameters.

CONCLUSION

It can be concluded that ductal flow velocities may be recorded as early as 11 weeks of gestation. End-diastolic flow velocities first appear at 13 weeks of gestation, probably as a result of a decreasing afterload. Both an increase in the right ventricular stroke volume and a decrease in the afterload may be responsible for the rise in ductal peak systolic and time-averaged velocities.

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