# THE DEVELOPMENT OF THE AORTA IN PRENATAL HUMAN LIFE

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# ABSTRACT

**Introduction.** The anatomy and role of the aorta in prenatal life differ from those in postnatal life.

**Aim.** We aimed at investigating the development of the aorta during a period between the 4<sup>th</sup> and 8<sup>th</sup> months of fetal life. We also analyzed the influence of sex on the values of the parameters examined.

**Materials and methods.** We examined the diameters of aortas in 223 human fetuses, including 108 males and 115 females, aged between 4 and 8 months of prenatal life. The entire material was obtained from the Department of Histology and Embryology at the Collegium Medicum, Nicolaus Copernicus University in Bydgoszcz, Poland. All fetal specimens had been conserved in a 9% formaldehyde solution for a period of more than 3 months. Only spontaneously aborted fetuses of a normal morphology and a normal karyotype were used in this research. We measured the diameter of the proximal and distal ascending aorta, of the aortic arch, and of the proximal thoracic aorta. The measurements were taken in the following locations: the diameter of the distal ascending aorta was taken at the level of the brachiocephalic trunk; the diameter of the aortic arch was taken between the ostium of the left common carotid artery and the left subclavian artery; the diameter of the proximal thoracic aorta was measured just beneath the arterial duct.

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**Results, Discussion and Conclusions.** All analyzed diameters grew linearly in time. We found no significant differences in the anatomy of the aorta with respect to sex. The ascending aorta is broader than the descending, thoracic aorta.

Key words: aorta, human fetus, prenatal life

#### INTRODUCTION

The circulation of blood differs between the fetal and postnatal life. These differences involve the changing pressure load of the proximal aorta. In prenatal life, the ascending aorta and the aortic arch carry half of the blood volume that flows through the distal, i.e., thoracic aorta. The initial segment of the aorta also carries less blood in the prenatal period than in the postpartum period. Blood from the ascending aorta and the aortic arch is directed to the upper part of the body, primarily to the head and the central nervous system. This is possible due to vascular structures specific for prenatal life, i.e., the arterial duct and the aortic isthmus. The unique anatomy and functioning of prenatal circulation call for a meticulous monitoring of the growth of particular segments of the aorta as a means of evaluating the development of the entire circulatory system [3, 18, 19, 23, 25, 31, 34].

## AIM

We aimed at investigating the development of the aorta during that period between the 4<sup>th</sup> and 8<sup>th</sup> months of fetal life. We analyzed the proximal and distal part of the ascending aorta, the aortic arch, and the initial segment of the thoracic aorta. We assessed how the anatomy of this vessel varies depending on sex. We also analyzed the relationship between the diameters of the ascending and descending aortas.

## MATERIALS AND METHODS

Research material consisted of 223 human fetuses, including 108 males and 115 females, aged between 4–8 months of prenatal life. The entire material for this project was obtained from the Department of Histology and Embryology of the Collegium Medicum, Nicolaus Copernicus University in Bydgoszcz, Poland. This study was approved by the Research Bioethics Committee of the Nicolaus Copernicus University (resolution KB/433/2004). All fetuses had been conserved in a 9% formaldehyde solution for a period of at least 3 months. Only spontaneously aborted fetuses with a normal morphology and a normal karyotype were included in this study. None of the analyzed specimens demonstrated any visible malformations, or developmental abnormalities upon close inspection. The morphological age of each fetus was estimated according to the crown-rump length (vertex-tuberale). To this end we used a regression function initially proposed by Iffy et al. [17] in a paper evaluating a population of white U.S. fetuses. All specimens were categorized into monthly subgroups according to the determined morphological age. Different numbers of fetuses were allocated to particular age groups.

The vessel beds were filled with latex LBS 3060, without distorting the dimensions of the vessels, at an amount of approximately 15–30 mL, through a catheter, which was inserted by dorsal access into the thoracic aorta. All measurements of the parameters related to the aorta were taken by two independent investigators. With the aid of binocular magnifying glasses (MBS-9, Russia, magnification  $0.6-7 \times 14$ ), they used digital calipers (INCO, Poland, resolution 0.01 mm) to collect all measurements, with an accuracy range of 0.01 mm. All measurements were taken twice by each investigator for consistency and verification purposes. The mean value of the two obtained values was considered for further quantitative analysis.

The diameters of the proximal and the distal ascending aorta, the aortic arch, and the proximal thoracic aorta were measured. The measurements were taken in the following locations: the diameter of the proximal ascending aorta was taken at the level of the aortic valve (1); the diameter of the distal ascending aorta (2) was taken at the ostium of the brachiocephalic trunk (BCT); the diameter of the aortic arch (3) was taken between the ostium of the left common carotid artery (LCCA) and the left subclavian artery (LSA); the diameter of the proximal thoracic aorta was taken just beneath the arterial duct (AD) (4) (Fig. 1).



**Fig. 1.** Ascending aorta, aortic arch, thoracic aorta and branches of aorta in a 24-weeks old female fetus. Comments: BCT – brachiocephalic trunk, LCCA – left common carotid artery, LSA – left subclavian artery, AD – arterial duct. Points of measurements: 1 – the diameter of the proximal ascending aorta, 2 – the distal ascending aorta, 3 – the aortic arch, 4 – the proximal thoracic aorta

Statistica 8.0 software (StatSoft Polska) was used for statistical analysis of the obtained data. We calculated mean values and standard deviations for each age group with respect to sex. In order to compare the means from particular groups, we applied univariate (age) and bivariate (age and sex) analyses of variances (ANOVA) for independent variables and Tukey's HSD post hoc test for non-equal populations. Statistical significance was defined as  $p \le 0.05$ .

## RESULTS

All analyzed diameters: of the proximal and the distal ascending aorta, the aortic arch, and the proximal thoracic aorta, increased with age according to a linear regression curve. All diameters had a high regression coefficient (r) with respect to age – above 0.92, which was statistically significant – p < 0.001 (Fig. 2–5).



Fig. 2. Regression curve for the diameter of the proximal ascending aorta versus fetal age (x)



Fig. 3. Regression curve for the diameter of the distal ascending aorta versus fetal age (x)



Fig. 4. Regression curve for the diameter of the aortic arch versus fetal age (x)



Fig. 5. Regression curve for the diameter of the thoracic aorta versus fetal age (x)

The diameter of the proximal ascending aorta in the 4<sup>th</sup> month was 1.25±0.27 mm, and it reached 3.89±0.24 mm in the 8<sup>th</sup> month. The mean diameter was 2.46±0.71 mm and it did not differ significantly between sexes (p=0.2598). It was 2.52±0.73 mm in males and 2.41±0.69 mm in females. This difference did not reach the level of significance for any month of fetal life (p>0.05) (Tab. 1). The diameter of the distal ascending aorta in the entire group was  $2.19\pm0.63$  mm, and it was similar in both sexes (p=0.2645). Also, in particular age subgroups there were no differences between the sexes (p > 0.05) (Tab. 2). The diameter of the aortic arch was  $2.08 \pm 0.58$  mm in females and 2.00±0.53 mm in males. Within the entire group, the average aortic arch diameter was  $2.04\pm0.55$  mm. Both in the entire group (p=0.3304) and in monthly subgroups there were no sex related differences (p>0.05) (Tab. 3). The last analyzed parameter was the diameter of the proximal segment of the thoracic aorta. The mean value of this parameter was 2.03±0.55 mm for the entire group and it did not statistically differ in males  $(2.06\pm0.57 \text{ mm})$  and females  $(1.99\pm0.52 \text{ mm})$  (p=0.3937). The diameter of the thoracic aorta was not different with regard to sex in any of the monthly age subgroups (p>0.05). In the 4<sup>th</sup> month the diameter of the thoracic aorta was  $1.01\pm0.22$  mm and in the 8<sup>th</sup> month it was 3.16±0.19 mm (Tab. 4). The increase of all analyzed diameters of the aorta for the entire group in consecutive months (i.e., the 5<sup>th</sup> and the 4<sup>th</sup>, the 6<sup>th</sup> and the 5<sup>th</sup>, the 7<sup>th</sup> and the 6<sup>th</sup>, the 8<sup>th</sup> and the 7<sup>th</sup> months) was statistically significant (p < 0.05). This also holds true for both sexes analyzed separately.

Age	Ν			X <u>+</u> SD [mm]			Draha
[month]	total	male	female	total	male	female	P value
4	18	8	10	1.25 <u>+</u> 0.27	1.24 <u>+</u> 0.29	1.26 <u>+</u> 0.28	0.8439
5	70	32	38	1.87 <u>+</u> 0.18*	1.88 <u>+</u> 0.19*	1.87 <u>+</u> 0.17*	0.9304
6	105	50	55	2.75 <u>+</u> 0.27*	2.76 <u>+</u> 0.27*	2.74 <u>+</u> 0.28*	0.5467
7	18	12	6	3.33 <u>+</u> 0.33*	3.31 <u>+</u> 0.32*	3.33 <u>+</u> 0.38*	0.9855
8	12	6	6	3.89 <u>+</u> 0.24*	3.95 <u>+</u> 0.32*	3.85 <u>+</u> 0.12*	0.4659
Total	223	108	115	2.46 <u>+</u> 0.71	2.52 <u>+</u> 0.73	2.41 <u>+</u> 0.69	0.2598

**Tab. 1.** Mean diameter of the proximal ascending aorta in particular monthly age groups shown for the entire group and with regard to sex

Comments: \* – indicates statistically significant difference of the marked subgroup when compared to the immediately younger subgroup (p < 0.05), N – number, X – parameter value, SD – standard deviation, P value – the differences between mean values in the female and male fetuses in particular age groups (p < 0.05).

**Tab. 2.** Mean diameter of the distal ascending aorta in particular monthly age groups shown for the entire group and with regard to sex

Age	Ν			X±SD [mm]			Devilee
[month]	total	male	female	total	male	female	P value
4	18	8	10	1.11 <u>+</u> 0.24	1.10 <u>+</u> 0.26	1.12 <u>+</u> 0.25	0.8448
5	70	32	38	1.66 <u>+</u> 0.16*	1.67 <u>+</u> 0.17*	1.66 <u>+</u> 0.15*	0.8774
6	105	50	55	2.44 <u>+</u> 0.24*	2.46 <u>+</u> 0.24*	2.43 <u>+</u> 0.25*	0.6091
7	18	12	6	2.96 <u>+</u> 0.29*	2.96 <u>+</u> 0.29*	2.96 <u>+</u> 0.34*	0.9957
8	12	6	6	3.47 <u>+</u> 0.21*	3.51 <u>+</u> 0.29*	3.42 <u>+</u> 0.11*	0.4659
Total	223	108	115	2.19 <u>+</u> 0.63	2.24 <u>+</u> 0.64	2.14 <u>+</u> 0.61	0.2645

Comments: \* – indicates statistically significant difference of the marked subgroup when compared to the immediately younger subgroup (p < 0.05), N – number, X – parameter value, SD – standard deviation, P value – the differences between mean values in the female and male fetuses in particular age groups (p < 0.05).

**Tab. 3.** Mean diameter of the aortic arch in particular monthly age groups shown for the entire group and with regard to sex

Age	Ν			X±SD [mm]			D 1
[month]	total	male	female	total	male	female	P value
4	18	8	10	1.02 <u>+</u> 0.22	1.01 <u>+</u> 0.23	1.03 <u>+</u> 0.23	0.8392
5	70	32	38	1.63 <u>+</u> 0.16*	1.65 <u>+</u> 0.15*	1.61 <u>+</u> 0.16*	0.3782
6	105	50	55	2.24 <u>+</u> 0.22*	2.25 <u>+</u> 0.22*	2.23 <u>+</u> 0.23*	0.5551
7	18	12	6	2.72 <u>+</u> 0.27*	2.71 <u>+</u> 0.26*	2.72 <u>+</u> 0.31*	0.9928
8	12	6	6	3.19 <u>+</u> 0.19*	3.24 <u>+</u> 0.27*	3.16 <u>+</u> 0.09*	0.4659
Total	223	108	115	2.04 <u>+</u> 0.55	2.08 <u>+</u> 0.58	2.00 <u>+</u> 0.53	0.3304

Comments: \* – indicates statistically significant difference of the marked subgroup when compared to the immediately younger subgroup (p < 0.05), N – number, X – parameter value, SD – standard deviation, P value – the differences between mean values in the female and male fetuses in particular age groups (p < 0.05).

Age	N			X±SD [mm]			Devilee
[month]	total	male	female	total	male	female	P value
4	18	8	10	1.01 <u>+</u> 0.22	1.00 <u>+</u> 0.23	1.02 <u>+</u> 0.23	0.8523
5	70	32	38	1.63 <u>+</u> 0.16*	1.60 <u>+</u> 0.16*	1.66 <u>+</u> 0.15*	0.1169
6	105	50	55	2.22 <u>+</u> 0.22*	2.23 <u>+</u> 0.22*	2.21 <u>+</u> 0.23*	0.5767
7	18	12	6	2.69 <u>+</u> 0.27*	2.69 <u>+</u> 0.26*	2.69 <u>+</u> 0.31*	0.9902
8	12	6	6	3.16 <u>+</u> 0.19*	3.21 <u>+</u> 0.26*	3.12 <u>+</u> 0.31*	0.4796
Total	223	108	115	2.03 <u>+</u> 0.55	2.06 <u>+</u> 0.57	1.99 <u>+</u> 0.52	0.3937

**Tab. 4.** Mean diameter of the proximal thoracic aorta in particular monthly age groups shown for the entire group and with regard to sex

Comments: \* – indicates statistically significant difference of the marked subgroup when compared to the immediately younger subgroup (p < 0.05), N – number, X – parameter value, SD – standard deviation, P value – the differences between mean values in the female and male fetuses in particular age groups (p < 0.05).

Tab. 5. The ratio of the diameter of the proximal ascending aorta and the diameter of the thoracic aorta (x)

Age [month]	Ν	Х	P value
4	18	1.32	0.7659
5	70	1.15	0.6512
6	105	1.24	0.5690
7	18	1.24	0.4532
8	12	1.18	0.2591
Total	223	1.21	0.4892

Comments: SD – standard deviation. There is no difference between consecutive age groups (p > 0.05), P value – the differences between mean values in the female and male fetuses in particular age groups (p < 0.05).

The ratio of the diameters of the proximal ascending aorta to proximal thoracic aorta in the entire group and in particular age subgroups ranged between 1.15 (5<sup>th</sup> month) and 1.32 (4<sup>th</sup> month). For the entire group this ratio was 1.21 (Tab. 5). It was similar in both sexes.

#### DISCUSSION

Several published papers point to a greater diameter of the aorta in the male sex [21, 22, 24]. However, no differences were found when the size of the aorta was correlated with the total body area. Gielecki et al. [13, 14] and Szpinda [28, 29, 30] also found the aorta diameters to be similar in both male and female fetuses. Our results lead to a similar conclusion.

The linear growth of the aorta in time, as assessed by the analysis of diameter changes in selected vessel segments (the ascending aorta, aortic arch, and the thoracic aorta), that we discovered was also reported by other authors. Ursell et al. [32] in a group of 274 human fetuses, aged between 3 and 7 months of intrauterinal life,

demonstrated a linear growth pattern of the exterior diameters of the aorta (at the level of the aortic valve and of thoracic aorta). Also Hornberger et al. [15] in their study concerning 92 fetuses, aged between 5 and 10 months, proved that the diameters of 5 segments of the aorta grew linearly in time. Firpo et al. [11] who investigated the prenatal growth of the main arteries of the thorax, reached a similar conclusion. According to Hyett et al. [16], the diameter of the aorta between the 3<sup>rd</sup> and the 5<sup>th</sup> months increased linearly. Also Gembruch et al. [12] in a study group of 136 fetuses and Achiron et al. [1, 2] in a similar group, both demonstrated a linear growth pattern of the aorta with respect to fetus age. According to Zalel et al. [35], who investigated a very large group of 338 fetuses, aged between 4 and 7 months, the diameter of the initial segment of the aorta grew linearly in time. This observation was confirmed on the basis of the proximal segment of the ascending aorta by Chaoui et al. [9]. Szpinda [28, 29, 30] demonstrated that the linear model best described the mode of growth of the aorta. Also, Gielecki et al. [13, 14] found that in fetuses aged between 4 to 8 months, the diameter of the aortic arch grew linearly. Similar conclusions can be found in many other papers [4–8, 10, 20, 27].

Castillo et al. [8] in their study concerning the development of the aorta between 4 and 6 months of fetal life discovered that the diameter of the ascending aorta ranged between 2.1 mm and 4.2 mm. According to these authors [8], the external diameter of the aortic arch ranged between 1.92 mm and 3.8 mm as compared with 1.75-3.35 mm found in the proximal thoracic aorta. These results are very similar to the data obtained by Szpinda [29, 30]. According to Szpinda [29], the diameter of the proximal ascending aorta changed from 2.02±0.26 mm in the 5<sup>th</sup> month to 6.84±0.63 mm in the 9<sup>th</sup> month. At the same time, the diameter of the distal ascending aorta changed from 1.73±0.2 mm to 6.29±0.52 mm. According to this author [30], the diameter of the proximal thoracic aorta during the same time period changed from 1.25±0.28 mm to 5.65±0.48 mm. Our data confirm these findings. Similar results were reported by Gielecki et al. [13]. In their study the diameter of the aortic arch increased from 1.77 mm to 4.09 mm [13]. Also Ursell et al. [32] analyzed the dimensions of the proximal ascending and the proximal thoracic aorta. These were 0.9 mm and 0.7 mm respectively in the youngest group (the 3<sup>rd</sup> month of prenatal life) versus 3.1 mm and 2.3 mm respectively in the oldest group (the 7<sup>th</sup> month).

Most investigators found the diameter of the ascending aorta to be larger than that of the thoracic aorta [8, 32, 33]. Rosenberg et al. [25] found the ascending aorta to be broader than the thoracic aorta. They found the ratio of these diameters to be 1.13. Van Meurs-van Woezik and Krediet [20] determined this ratio to be 1.25. Hornberger et al. [15] and Angellini et al. [5] confirmed this ratio in their echocardiography studies. According to Szpinda [28], the diameters (proximal and distal) of the thoracic aorta were smaller than the diameters (proximal and distal) of the ascending aorta. Our data confirm this relation; the calculated mean value of the ratio in question is 1.2.

## CONCLUSIONS

- 1. In the period between the 4<sup>th</sup> and 8<sup>th</sup> months of fetal life, aorta growth is linear in all analyzed vessel segments.
- 2. There are no sex related differences with regard to dimensions of this vessel.
- 3. The proximal ascending aorta is broader than the proximal thoracic aorta.

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