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K21 the development of the extremities of Turkish fetuses during the fetal period

Işık Tuncer
Assıst. Prof., Department of Anatomy, Meram Faculty of Medıcıne, Necmettin Erbakan Unıversıty, Konya, Turkey

Abstract
Objective: The aim of this study was to investigate the morphologic structure of the extremities of Turkish fetuses during the fetal period and to measure the morphometric values.
Materials and Methods: 81human fetuses (36 male, 45 female) that had no anomaly and aged between 7 and 37 gestational weeks were used. This study was performed the Anatomy Department of Meram Medical Faculty, at Necmettin Erbakan University between 2006 and 2007. Shoulder width (SW), arm circumference (AC), forearm circumference (FC) and hand length (HL) were measured in the upper extremity. Iliac crest width (ICW), thigh circumference (TC), crus circumference (CC) and foot length (FL) were measured in the lower extremity. The measurements were obtained through tape measure and electronic compass and the results were evaluated according to gestational age and sex.
Results: It was shown that all measurements of extremities are significantly different across groups (all $p<0.001$). However, there were no significant differences between the genders for all extremity measurements ($p>0.05$). In all measurements, the mean values of extremities were in males greater than females.
Conclusion: The measurements of the extremities during fetal period are reliable parameters for use in the assessments of gestational age. Despite a significant biological variability of the morphometric values, availability of reference ranges could be of help in the early diagnosis of fetal skeletal anomalies.

Keywords: upper extremity, lower extremity, fetus, morphometry

Introduction

The extremity buds first appear as small elevations on the ventrolateral body wall during the fourth week. The upper extremity buds are visible by day 26 or 27, and the lower extremity buds are usually recognizable by day 28 [1]. The extremity buds elongate by the proliferation of mesenchyme within them. The upper extremity buds appear disproportionately low on the embryo's trunk because of the initial dominance of the development of the head and neck regions of the embryo [1].

The interest in the anatomy of extremity development has increased recently. Morphometric data of the extremity structure anatomy have become important thanks to the newly developed techniques for the diagnosis of both congenital malformations during the prenatal period and natal extremity problems. Moreover, it has been suggested that such data can be used in discriminative diagnosis of fetal development anatomy of extremities [2]. Between the 3rd and 8th week of the development, each of the germ leaves form their own tissue and organ systems displaying advanced changes. This period is known as embryonic period [2].

Intrauterine period which begins at the beginning of the third month (12 weeks) and lasts till the birth, and during which body develops very fast, and the period which is characterized by the maturation of tissues and organs is called fetal period [2]. While there are detailed studies on the development of extremities in animals, there are few studies about the development of upper and lower extremities in human fetuses. Particularly, as a result of auxiliary imaging techniques, morphometric data of the upper and lower extremities are becoming important for the early diagnosis and treatment [2]. In this study, it was aimed to go over the development stages of upper and lower extremities morphometrically during the fetal life.

Materials and Methods

This study was carried out using spontaneous abortus fetuses obtained from the Department of Anatomy, Meram Medical Faculty, Necmettin Erbakan University between 2006 and 2007. This study was approved by the ethical committee of Meram Medical Faculty (2008/170). We used 81 fetuses (36 male, 45 female) without any morphological malformation and whose development ages were determined according to their Crown Rump Length (CRL). The fetuses were divided into three groups as 1st, 2nd and 3rd trimester according to their CRL (15 fetuses in the1st trimester, 51 in the 2nd and 15 in the 3rd trimester) The measurements of the fetuses established using immersion method with 10% formalin was conducted via a tape measure and a digital compass sensitive to 0.01mm [3-9].

Parameters used for evaluating (Fig A, B, C, D)

Shoulder width (SW): Biacromial distance between acromions.
Arm circumference (AC): It was determined measuring in the mid of the arm with a tape measure while it was hanging down freely.
Forearm circumference (FC): It is measured in the mid

point of the forearm in the anatomic position.

Hand length (HL): The distance between the styloid process and the most distal fingertip.

Thigh circumference (TC): The thigh circumference in the middle of thigh length.

Crus circumference (CC): It is measured in the middle of crus in anatomic position.

Foot length (FL): The distance between the back of the heel and the ends of the toes.

Iliac crest width (ICW): The transverse distance between the most lateral end points of the iliac crest.

The measurements of each fetus were performed by the same person

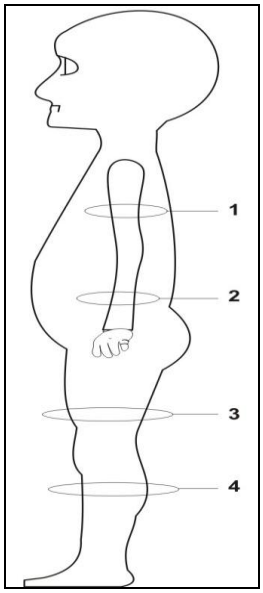

Fig A: The schematic figures of measurement used for the evalation of upper end lower extremity

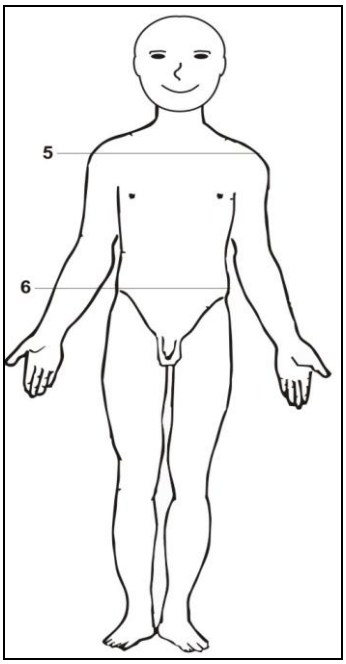

Fig B: The schematic figures of body measurement

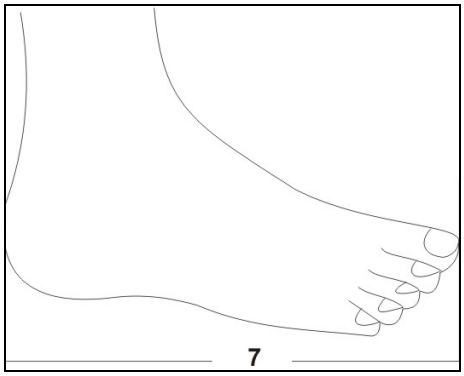

Fig C: The schematic figure of foot measurement

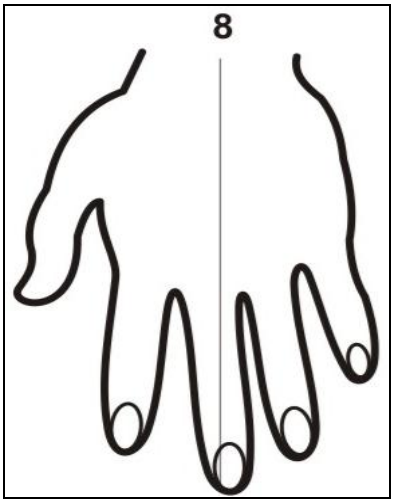

Fig D: The schematic figure of hand measurement

Fıgure Legends

1. Arm circumference
2. Forearm circumference
3. Thigh circumference
4. Crus circumference
5. Shoulder width
6. Iliac crest width
7. Foot length
8. Hand length

Statistical Evaluation

The measurements belonging to upper and lower extremities of fetuses were assigned to MS Excel program and data were checked twice. All analyses were performed by SPSS 19.0 (IBM Incorp., Chicago, IL) software. The variables were presented as frequencies and percentages for categorical variables, mean±SD for numerical variables. Continious variables were detected for normality by Kolmogorov-Smirnov test. Many of the variables were not distributed normally. Therefore non-parametric methods were used for comparing groups. Mann-Whitney U test was used for two independent groups and Kruskal-Wallis test was used for several groups with post-hoc tests. Spearman's Rho correlation analysis was used to see the relation between gestational age and extremity measurements. $p<0.05$ value was considered statistically significant taking type-I error as 5%.

Results

We measured total of eight distances, half of them is about upper extremity and other half belongs to lower extremity on totally 81 human fetuses (36 male, 45 female). All fetuses have CRL range between 60 and 390 mm. Greater than half of the fetuses were female (55.6%) and male ratio was 44.4%. the gender information of only one fetus couldn't be determined. The number of fetuses of first and third trimester groups were equal (18.3%). Second trimester group has the highest ratio (63.4%). The gestational ages of fetuses had several weeks changing from seven to 37 weeks. In 17 gestational age, there were nine fetuses (11%). The descriptive statistics of fetuses can be seen in Table 1. The minimum value of foot and hand lengths were equal (0.70 mm). The minimum value of thigh circumference was 1.30 mm and was the highest value among other measurements. The minimum value of shoulder width, arm and forearm circumference, crus circumference and interiliac width were equal at the beginning (1.0 mm). But shoulder width reached to 40 mm whereas other measurements reached up to 14 or 16 mm.

Table 1: Descriptive statistics of upper and lower extremity of fetuses.

Parameters		Minimum	Maximum	Mean	SD
SW	*mm*	1.00	40.00	12.57	8.43
AC	*mm*	1.00	16.00	5.50	2.79
FC	*mm*	1.00	9.50	3.69	1.65
HL	*mm*	0.70	9.00	3.20	1.69
TC	*mm*	1.30	14.00	3.85	2.49
CC	*mm*	1.00	14.50	4.68	2.85
FL	*mm*	0.70	11.00	3.91	2.07
ICW	*mm*	1.00	10.00	3.88	1.88

All measurements of upper and lower extremities were compared according to trimester groups. The descriptive statistics can be seen in Table 2 with *p* values. It was shown that all measurements of extremities are significantly different across groups (all $p<0.001$). Moreover, the pairwise comparisons were significant across all trimester groups. All extremity measurements were compared according to gender of fetuses. However, there were no significant differences between the genders for all extremity measurements ($p>0.05$). The descriptive statistics for gender groups can be seen in Table 3. In all measurements, the mean values of extremities were in males greater than females.

The descriptive statistics were calculated according to gestational age and presented in Table 4. As seen in the table, the values for 24 ages were extraordinary since there was only one fetus for 24th week. There was a significant positive correlation between the gestational age and the mesurements of both upper and lower extremities ($p<0.001$). The lowest correlation coefficient belonged to thigh circumference (R=69.5%; $p<0.001$), and foot length measure had the highest correlation value (R=0.948; $p<0.001$). All correlation coefficients can be seen in Table 5.

Table 2: Descriptive statistics of upper and lower extremity of fetuses according to trimester groups.

Parameters		1st Trimester (n=15)	2nd Trimester (n=51)	3rd Trimester (n=15)	*p*
SW	*mm*	3.67±2.57	13.11±6.62	19.63±10.27	*<0.001**
AC	*mm*	2.30±1.10	5.56±1.98	8.53±2.92	*<0.001**
FC	*mm*	1.67±0.59	3.58±0.87	6.15±1.33	*<0.001**
HL	*mm*	1.19±0.56	3.12±0.98	5.53±1.60	*<0.001**
TC	*mm*	2.18±0.74	3.36±1.41	7.28±3.41	*<0.001**
CC	*mm*	1.97±0.94	4.24±1.82	8.93±2.48	*<0.001**
FL	*mm*	1.33±0.77	3.78±1.15	6.93±1.57	*<0.001**
ICW	*mm*	1.6±0.86	3.74±1.03	6.69±1.40	*<0.001**

Table 3: Descriptive statistics of upper and lower extremity of fetuses according to gender.

Parameters		Male (n=36)	Female (n=45)	*p*
SW	*mm*	12.93±7.96	12.16±8.91	*0.430*
AC	*mm*	5.82±2.85	5.21±2.77	*0.360*
FC	*mm*	3.86±1.66	3.54±1.66	*0427*
HL	*mm*	3.44±1.76	3.00±1.64	*0.336*
TC	*mm*	4.38±3.12	3.46±1.82	*0.332*
CC	*mm*	5.21±3.11	4.30±2.62	*0.175*
FL	*mm*	4.26±2.22	3.61±1.95	*0.319*
ICW	*mm*	4.19±2.04	3.63±1.77	*0.286*

Table 4: Descriptive statistics of upper and lower extremity of fetuses according to gestational age.

Gestational Age (week)	SW	AC	FC	HL	TC	CC	FL	ICW
7 (n=2)	2.25±0.35	1.5±0.0	1±0.0	0.8±0.0	1.75±0.35	1.0±0.0	0.8±0.0	1.0±0.0
8 (n=1)	1.0±…	1.5±…	1.5±…	1.0±…	1.5±…	1.3±…	0.7±…	1.0±…
9 (n=2)	1.75±0.35	1.25±0.35	1±0.0	0.7±0.0	1.5±0.0	1.4±0.14	0.75±0.07	1.15±0.21
10 (n=2)	2.75±1.06	1.5±0.0	1.5±0.0	0.9±0.14	2±0.0	1.5±0.0	1±0.0	1.35±0.21
11 (n=2)	6±4.95	3.25±1.77	1.75±0.35	1.4±0.85	2.2±0.42	2.25±1.06	1.5±0.71	1.7±0.28
12 (n=6)	4.75±2.38	3±0.84	2.17±0.52	1.55±0.6	2.72±0.88	2.67±0.98	1.87±0.92	2.1±1.19
13 (n=7)	9.5±3.79	4.69±1.36	2.79±0.47	2.16±0.65	2.39±0.83	2.81±1.08	2.64±0.51	2.67±0.59
14 (n=6)	10.67±8.22	3.92±0.86	2.75±0.27	2.2±0.57	2.7±1.08	3.03±0.7	2.53±0.33	2.53±0.61
15 (n=2)	8.0±4.36	4.55±1.48	3.0±0.0	2.5±0.5	4.37±2.03	3.5±1.32	2.83±0.29	3.4±0.66
16 (n=4)	12±4.55	5.3±1.36	3.05±0.33	2.58±0.43	3.08±1.64	3.85±1.11	3.2±0.24	3.28±0.54
17 (n=9)	11.56±4.84	4.89±1.47	3.44±0.39	3.08±0.55	3.03±1.3	3.79±1.26	3.54±0.58	3.69±0.78
18 (n=4)	9.38±5.85	4.5±1.35	3.38±0.48	2.93±0.79	3.33±1.46	4.13±0.63	3.68±0.83	4.13±0.48
19 (n=6)	14.03±6.07	5.75±1.86	3.77±0.72	3.3±0.55	3.92±1.44	4.48±1.03	4.33±0.53	4.17±0.69
20 (n=3)	20.33±1.26	7.83±0.58	4.5±0.5	4.37±0.71	3.6±0.46	6.67±0.76	5.07±0.51	4.83±0.76
21 (n=2)	13.25±7.42	6±2.12	4.5±0.71	3.75±0.35	5±2.83	4.25±1.77	5±0.0	5.25±1.06
22 (n=3)	24.17±1.44	8.9±0.96	5±0.0	4.57±0.4	3.3±0.75	6.03±2.98	5.5±0.87	4.63±0.59
23 (n=3)	21.3±4	8.67±2.08	5±0.5	4.53±0.55	3.67±0.85	6.67±3.54	5.67±0.58	4.87±0.85
24 (n=1)	7.0±…	4.5±…	4.0±…	4.0±…	7.0±…	4.5±…	5.0±…	4±…
25 (n=2)	9.0±0.0	5.5±0.71	4.5±0.0	4±0.71	7.25±1.77	5.5±0.71	5±0.0	6.75±1.06
26 (n=2)	10±1.41	5.5±0.71	4.75±0.35	3.5±0.71	7.5±0.71	6.25±0.35	5.25±1.06	5.75±1.06
28 (n=5)	27.9±1.95	10±0.67	6.34±0.59	6.4±0.65	4.24±0.37	9.7±1.1	7.4±0.65	5.88±0.39
30 (n=1)	13.0±…	7.0±…	6.0±…	4.5±…	11.0±…	8.0±…	6.5±…	6.5±…
31 (n=1)	12.0±…	7.0±…	6.0±…	5.5±…	12.5±…	9.5±…	7.5±…	10.0±…
32 (n=2)	19.5±12.02	9.5±2.12	7.25±0.35	5.75±1.77	7.5±4.95	10±2.12	7.25±0.35	7.4±2.26
33 (n=2)	17.75±6.72	7.5±0.71	5.65±0.49	5.25±0.35	8.7±7.5	9±1.41	6.25±1.06	5.8±0.99
37 (n=1)	40.0±…	16.0±…	9.5±…	9.0±…	6.0±…	14.5±…	11.0±…	8.2±…

Table 5: Spearman's Rho correlation values between gestational age and extremities.

Gestational Age (week)	SW	AC	FC	HL	TC	CC	FL	ICW
Rho	0.702	0.795	0.939	0.917	0.695	0.843	0.948	0.911
p	*<0.001**	*<0.001**	*<0.001**	*<0.001**	*<0.001**	*<0.001**	*<0.001**	*<0.001**

Discussion

This study was conducted on total 81 fetus cadavers (36 male, 45 female) aged between 7 and 37 weeks. The lengths and circumferences of the structures were taken. Statistical studies, which were considered to give an idea about the development anatomy, were performed on 81 subjects that were regarded as normal after their measurements were taken.

Recent studies on the development of the extremity during the fetal period have often emphasized on the investigation of upper and lower extremity that has clinical importance congenitally. Though the reliability of the data to be obtained from these studies is controversial, it has been emphasized that they should be taken into consideration as an essential criteria to help early diagnosis. Therefore, morphometric analyze values of upper and lower extremities in the fetal life are important for diagnosis of congenital upper and lower extremity diseases [10].

Comparing the values to each other has proved difficult due to both different materials and methods followed in the studies; however, it is possible to compare with the limited data in the literature. Although there are no compared results between the genders in the literature, we have not established statistically significant morphometric differences between the genders in this study.

Lower values of these parameters were determined in female fetuses. While considerable differences occurred in the measurements between the trimesters ($p<0.001$), there was a significant positive correlation between the gestational age and the mesurements of both upper and lower extremities ($p<0.001$).

It has been stated that foot length is essential for determining gestational age and it also can be used for neonatal anthropometry. Platt's study [11] demonstrates the marked accuracy of real-time ultrasound in the measurement of fetal foot length. If the recommended values for gestational age assessment used by Hern [12] are compared with the predicted values in this study, there is almost uniform agreement between the intrauterine and extrauterine measurements. In no case in this study was the fetal foot measurement unobtainable. At times, Because of fetal position, it was more difficult to evaluate, but perseverance and careful attention to detail overcame these difficulties. That the fetal foot can now be measured easily, and has been proved in postmortem examinations to be reliable, encourages its use as an alternative method of assessing the gestational age of the fetus [7, 25].

It has been established that thigh circumference is a parameter reflecting soft tissue, and it decreases in the fetuses with intrauterine growth retardation and increases in macrosomia.

Formulas incorporating thigh circumference may be proven most useful in predicting fetal weight when growth abnormalities are present. Fetal growth aberrations

(intrauterine growth retardation or macrosomia) are associated with changes in soft tissue mass, which is decreased in growth retardation and is macrosomic fetuses. Pediatric experience has shown that thigh circumference is a parameter that reflects soft tissue mass. Vintzileos group's [24] has also shown that the ultrasonically determined thigh circumference is decreased in fetuses with intrauterine growth retardation and increased in fetuses with macrosomia.

As a result of this study, general morphologic features and morphometric assessments of the structures of upper and lower extremities and elements involved in formation in human fetuses have been obtained. Since the materials used in this study were provided from the abortus fetus collection, the morphologic structures of these materials were considered as normal. However, both the factors affecting intrauterine growth process and possible relations which have negative effects causing abortus should not be ignored.

It is believed from the results of this study that the establishing the normal growth width and length values of upper and lower extremities of human fetuses, and determining the rates with one another can help to identify pathological changes in the upper and lower extremities that are likely to occur at different gestational ages and thus, they can be used to diagnose congenital upper and lower extremity diseases.

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