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Original Article

Developing growth reference charts for the head circumference of Pakistani children aged 6 to 18 years

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ABSTRACT

Background. Head circumference (HC) measurement is a significant measure of brain volume. It is also considered a powerful predictor in the evaluation of developmental and neurological disorders in children. This study aims to develop smoothed reference curves for HC of the Pakistani children of age 6 to 18 years.

Methods. A cross-sectional dataset, consisting of 9194 school-going children of age 6-18 years, were obtained using a multi-ethnic anthropometric survey. For the measurement of HC (cm), the standard procedure was adopted. For both sexes, the smoothed centile curves of HC were developed by using the lambda-mu-sigma (LMS) statistical approach. Moreover, we compared our 50th percentile curves to those produced for few other countries.

Results. The centiles curves of both sexes indicated that the HC increased with age. Until the age of 10 years, the boys had larger HC percentiles than those of the girls. From the age of 11 years, upper percentiles (90th, 95th and 97th) of the girls were higher than those of the boys. The comparison of our 50th percentile data for the HC with the data from the United States (US) and Turkish children revealed that the Pakistani children of both genders had smaller head sizes in all ages when compared to those reported for the latter stated countries.

Conclusions. Our results show the larger disparity of HC percentiles in different countries. This comprehensive study suggests that the references from the US Centers for Disease Control and Prevention data and other populations are not suitable for Pakistani children. Therefore, each country is required to create its own HC reference curves, separately.

Key words: head circumference, lambda-mu-sigma method, Pakistani children, growth reference curves.

Measuring the head circumference (HC) is one of the most crucial tasks during a pediatric physical examination. The HC of infants and children correlates with cognitive functions, intracranial volume, and brain volume.[1-3] Therefore, pediatricians and neurologists frequently use the HC standard charts as a valuable tool to trace the brain development in children and diagnose neurological diseases, if any.

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In 2000, the HC growth charts for US children were produced by the Centers for Disease Control and Prevention (CDC).[4] In this research, only children aged birth to 36 months were studied. In 2002, the US epidemiological researchers found that the HC was shown to be an "important magnitude to predict the brain volume in children aged 7 to 16 years (r = 0.67)" as well as a "excellent predictor of brain volume in children aged 1.7 to 6 years (r = 0.93).[1] Similar correlation was also reported for adults aged 17 to 42 years (r = 0.69).[1] After that, various studies in different countries have reported the HC charts for the justification of monitoring head growth beyond 36 months. For example, Rollins et al.[5] included the US pediatric population

aged birth to 21 years for presenting the HC growth reference charts and Neyzi et al.[6] in 2015, produced HC growth reference curves for the sample of Turkish children, aged birth to 18 years. Another study[7] established the HC reference charts for 5 to 18 years old Turkish children. Zaki et al.[8] presented the HC data by using a sample of 27,826 healthy Egyptian children and adolescents.

The reference data on head size for children of different developing countries is very limited. To the best of our knowledge, one study[9] from Iran presented the HC standards for school-going children aged 6.5-11.5 years using a sample of 2237 children during the years, 2002-3 and a more recent study[10] during 2016 from Pakistan, presented the HC charts for children of 2 to 5 years. However, the HC reference data for children aged 6 to 18 years are still not that much available. There is also a significant disparity in head sizes among the children of different countries as well as among different ethnicities of the same country[6-9], suggesting that growth references for each country should be established separately. Therefore, we present a study with the developed HC growth reference curves for 6 to 18 years Pakistani children. This data would be helpful not only for the child neurologists in Pakistan but also for neurologists of the region.

Material and Methods

Study population and design

Our study enrolled 9194 school-going children who participated in a multi-ethnic anthropometric survey (MEAS) conducted in 2016. The MEAS was conducted in three densely populated cities of the Punjab province (i.e., Lahore, located in central Punjab; Rawalpindi, located in North of Punjab and Multan, located in south Punjab) and the capital city, Islamabad. The main reasons for choosing these cities were their growing educational & health facilities and sufficient job opportunities in the public and private sectors. For these reasons, families have more commonly migrated to these cities from the other regions of the country. Furthermore, the Pakistan National Human Development Report (PNHDR-2017) also placed these cities in the medium to high human development category.[11] The mixed- ethnic population of these cities can be expected to be a representative of Pakistan's pediatric population. In previous studies[12,13], further information on the children's selection in this multi-ethnic survey may be found. Briefly, the studied children aged 6 to 18 years were sampled from different schools. On demand of an investigator, Punjab, and the Federal Department of Education (Schools) provided a grade-by-grade complete list of schools (i.e., elementary, secondary, and higher secondary schools) in the designated cities, and schools were picked using simple random sampling from the lists. Each school's classes were chosen at random, and all the children present on the day of data collection were invited to take part in the study. In order to obtain the HC measurement, a written informed consent was taken from both the school's heads and children's parents. The authors claim that all procedures used in this study adhere to the Helsinki Declaration and the ethical norms of relevant national and institutional committees on human experimentation (2013). The Departmental Ethics Committee of Bahauddin Zakariya University, Multan. Pakistan approved this study (Approval Date: 13 March 2017, IRB #: Stat-271/2017).

Although in the MEAS, different measurements were collected by the data collection team members, but the measurement of HC is of concern here. The HC was measured using a non-stretch tape after following the standard techniques.[14] During measurement, the children was instructed to look straight, and tape was placed over the child's head in the distance from above the eyebrows and ears and around the back of the head to get the maximum circumference. The HC measures were collected by the same experts to avoid possible bias (for further details about the data collection, see Aslam et al.[10] and Asif et al.[12]).

For this study, inclusion criteria were: (a) agreeing to participate in the study, (b) age between 6 and 18 years, (c) absence of congenital disorders that may affect the HC (confirmed based on information from the parents). Whereas exclusion criteria were (a) having a chronic, disease such as renal failure, cystic fibrosis, Celiac disease, and non-idiopathic epilepsy etc. (b) history of premature delivery.

Statistical analysis

The descriptive analyses for quantitative variables, age (years) and HC (cm) are described as mean with standard deviation (SD). The LMS statistical method, proposed by Cole[15,16], was used to estimate the age and gender specific smoothed set of centiles "3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97th" of HC. This technique represents the evolving HC distribution in terms of three curves: the Box-Cox power (L) to remove skewness from the data by age, the median (M), and the coefficient of variation (CV) (S). The smooth spline function in R was used to smooth these three curves. The needed centile (C) value for a given age was calculated as C= M (1+LSZ) 1/L, where L, M, and S are the fitted curve values, and Z is the normalized distribution's Z-score. Z was substituted as -1.88, -1.645, 0.00, 1.645, and 1.88, respectively, for predicting the 3rd, 5th, 50th, and 95th and 97th percentile values.[15] The software "Statistical Package for Social Sciences (SPSS) version 21.0" and R version 3.2.0 were used to analyze the data.

Results

Mean, standard deviation (SD), the frequency distribution of subjects by age and age-and-sex-specific smoothed percentile values of HC are listed in Table I. Fig. 1(a) and Fig. 1(b) displayed the HC percentile curves for both boys and girls, respectively. The centiles curves of both sexes indicated that HC increase with age. Sex-wise notable differences in data of the HC were also seen. The lower percentiles (3rd, 5th, 10th and 25th) of boys were higher than girls except between the ages of 11 and 12 years. It was noted that the girls' HC during 11- and 12-years of age was larger than those of boys. The upper percentiles (90th, 95th and 97th) of girls were also higher than of boys after 13 years of age. The LMS-derived median (50th) percentile curves were compared with those for the data from the US[5] and Turkish children[6] through Fig. 2 (a + b). The HC values for the Pakistani children of both genders were lower than the reference values from the latter stated studies.

Discussion

Growth monitoring during infancy and childhood age is very crucial for pediatric care and growth charts of length /height, weight and HC are commonly used for this purpose. The gathering of reference data for the study of growth in HC among children of similar ethnic backgrounds is a fundamental goal of auxologic investigations.[17] The HC growth charts of children are considered as powerful anthropometric tools for monitoring brain growth and diagnosing neurological disorders, because the size of HC is tightly connected to cognitive function, intracranial volume, and brain volume.[1,3,17,18] Furthermore, microcephaly and macrocephaly may be linked to a variety of medical issues, including different syndromes.[17] According to Winter and Baraitser[19], there are 114 syndromes that are linked to macrocephaly. Among these, macrocephaly perseveres into adulthood and the most common of which is Fragile X syndrome.[20] Some intrauterine infections may also be related to both microcephaly and macrocephaly.[17] All of these emphasize the need for some valid HC reference charts for higher ages also.

Up to 3 years of age, head size reaches approximately 90% of the adult size and clinicians usually do not recommend the routine follow-up of the HC growth after this age for normal developing children. However, some neurological disorders and genetic syndromes may appear after 3 years of age among abnormally developing children and any significant reduction in the HC found

Table I. Age-and- gender-specific Mean, SD and smoothed HC (cm) percentiles (3rd to 97th) for the Pakistani boys and girls, aged 6-18 years.

Age (years)	Smoothed Percentiles										Mean (SD)
	N	3rd	5th	10th	25th	50th	75th	90th	95th	97th	
Boys (n=4972)											
6	292	46.79	47.14	47.69	48.64	49.74	50.88	51.95	52.61	53.05	49.77 (1.66)
7	279	47.09	47.45	48.02	48.98	50.09	51.23	52.30	52.95	53.38	50.17 (1.73)
8	273	47.20	47.59	48.19	49.21	50.33	51.46	52.49	53.31	53.66	50.31 (1.58)
9	247	47.43	47.86	48.57	49.48	50.57	51.76	52.92	53.37	54.05	50.71 (1.71)
10	420	47.56	48.05	48.74	49.68	50.79	51.97	53.10	53.61	54.02	50.84 (1.74)
11	439	47.69	48.14	48.82	49.92	51.09	52.22	53.19	53.76	54.12	51.06 (1.67)
12	675	48.18	48.59	49.22	50.27	51.42	52.56	53.58	54.18	54.57	51.43 (1.79)
13	593	48.80	49.16	49.74	50.72	51.84	53.00	54.08	54.74	55.17	51.80 (1.63)
14	563	49.16	49.60	50.27	51.35	52.51	53.62	54.59	55.15	55.51	52.50 (1.75)
15	546	49.72	50.16	50.83	51.90	53.04	54.13	55.07	55.62	55.97	53.01 (1.68)
16	381	50.26	50.65	51.24	52.23	53.31	54.39	55.34	55.91	56.28	53.32 (1.59)
17	169	50.69	51.02	51.54	52.43	53.44	54.50	55.49	56.10	56.50	53.44 (1.53)
18	95	51.10	51.41	51.88	52.71	53.68	54.71	55.68	56.29	56.70	53.76 (1.46)
Girls (n=4222)											
6	405	46.00	46.36	46.94	47.93	49.09	50.31	51.48	52.20	52.68	49.17 (1.80)
7	381	46.39	46.77	47.38	48.41	49.58	50.80	51.94	52.63	53.09	49.61 (1.66)
8	376	47.00	47.40	48.02	49.08	50.28	51.50	52.63	53.10	53.56	50.30 (1.90)
9	336	47.28	47.68	48.30	49.37	50.57	51.79	52.92	53.60	53.76	50.60 (1.77)
10	459	47.47	47.88	48.51	49.57	50.78	52.00	53.12	53.80	54.24	50.82 (1.71)
11	325	48.12	48.54	49.18	50.27	51.49	52.72	53.84	54.52	54.96	51.45 (1.85)
12	436	48.39	48.80	49.45	50.54	51.75	52.99	54.11	54.78	55.22	51.80 (1.90)
13	460	48.68	49.11	49.78	50.89	52.12	53.34	54.44	55.10	55.52	52.17 (1.86)
14	341	48.98	49.45	50.17	51.34	52.59	53.80	54.86	55.48	55.87	52.50 (1.84)
15	257	49.23	49.71	50.44	51.62	52.87	54.08	55.12	55.73	56.12	52.83 (1.81)
16	191	49.56	50.00	50.67	51.78	53.01	54.22	55.31	55.95	56.37	52.92 (2.04)
17	129	49.95	50.31	50.87	51.86	53.03	54.29	55.50	56.27	56.78	53.13 (1.67)
18	126	50.26	50.56	51.03	51.90	53.01	54.32	55.73	56.73	57.45	53.22 (1.77)

HC: head circumference, SD: standard deviation

in malnourished children may have serious implications for their future performance and achievement.[18] A colossal literature have also demonstrated that serial HC measurements taken in infancy or prepubertal period are a reliable predictor of brain volume and may be used to map the course of brain growth, hence predicting cognitive performance later in life.[1,3,21,22] A Helsinki Birth Cohort Study (HBCS) has demonstrated that infancy, childhood, and adolescent periods are critical for the development of intellectual abilities and slow HC growth during infancy may continue to appear in childhood and adolescents that extend widespread consequences on mental health throughout the lifespan.[23] In a prospective study of children aged 9 to 10 years old from Southern India, HC was found to be positively linked with learning and visio-spatial abilities.[22,24] Thus, population-specific HC references are needed for clinical evaluations and early detection of HC overgrowth and undergrowth.

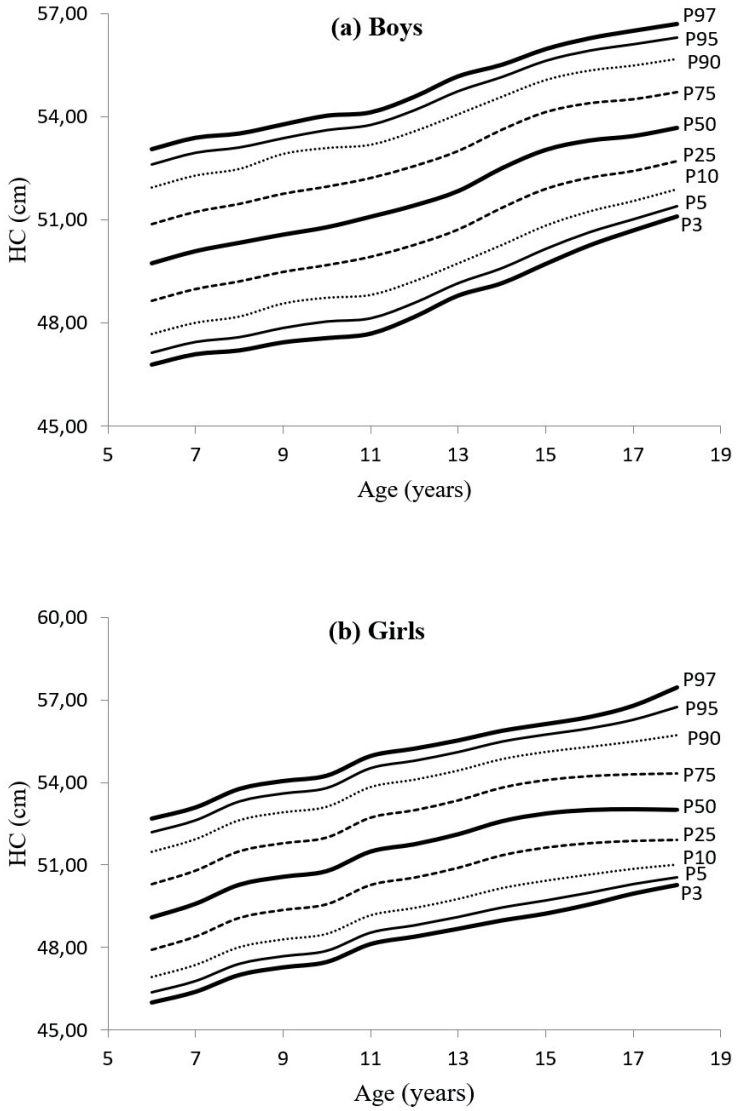

Fig. 1. (a) and (b): Smoothed head circumference growth curves for the Pakistani boys and girls using the LMS method.

To the authors' best knowledge, after an Iranian research[9], this is the first comprehensive study in the developing nations that presented the reference values of HC for 6 to 18 years aged children using a standardized measurement technique. As a result, we attempted to compare our findings to those of Iranian[9] and other international investigations.[5-7] Our findings revealed that, except for the ages 11 to 13 years, boys have higher mean HC values than. A study with Iranian children[9] found parallel findings for the mean values of HC and the mean HC of girls was higher around 11 years age. In our study, the mean differences in HC between boys and girls decreases before puberty, become negative around pubertal age, and increases after puberty. These findings were also consistent with the Iranian study.[9] The most recent study by Kara et al.[7] also accounted for the lower differences in pubertal age (around 0.54 to 0.59cm) and after puberty, the difference gradually increases. This lower difference in pubertal age may be due to the fact that pubertal growth spurt occurs earlier in girls than boys.

Similar to the previous studies[5-7,9], the percentile values (3rd to 97th) of HC increased in both sexes with age. Sex-related differences in HC percentiles indicated that all percentile values among boys were larger than girls till the age of 10 years. From 11 years of age, upper percentiles (90th, 95th and 97th) of girls were higher than boys that were consistent with a study of Iranian children.[9] Another study with the Turkish children[25] aged between 6 and 12 years also report a higher percentile (98th) value for girls at the age of 12 years.

Several studies[26,27] confirmed the disparity in the head sizes of children belongs to different countries as well as in the children of different ethnic groups of the same country. Recent data from Turkish children collected by Kara et al.[7] greatly differed from the US children and Iranian data by Ayatollahi and Shayan[9] also highly differed from the Japanese, Turkish, Irish and US children. We also compared our 50th percentile values for HC with the data from the US[5] and Turkish studies.[6] Our HC reference values were moving parallel to those of other countries. However, they were considerably smaller than the corresponding international data (see Fig 2. (a) and (b). It is important to discuss here some visible factors that may associate with the low HC percentile values in children. Children grow differently over the globe[28], and we know that the growth and body shape of children is assessed by different anthropometric parameters in the form of height for age, weight for age, and body mass index (BMI) for age etc. The studies[29,30] with the Pakistani children already showed that Pakistani boys and girls had lower height, weight and BMI as compared to the WHO and US CDC references population. A study by Bushby et al.[31] emphasized that the HC was closely related to the height of the individual. Another study by Nguyen et al.[32] with Canadian male adults also found a significant positive correlation between HC and height and weight. This could explain the results of our study in which we indicated that HC 50th percentile of Pakistani children and adolescents was significantly smaller than the US population. Moreover, multiple environmental factors also have a great influence on the head size of children including maternal education and diet, maternal intelligent quotient, maternal BMI, socio-economic profile, child birth weight, exclusive breast feeding, maternal smoking and maternal reproductive history etc.[33] These factors are very common among Pakistani women and may have caused the disparity in HC references values in different populations and emphasize the need for every population to develop their own HC standards.

In Pakistan, WHO HC growth standards[34] (birth to 5 years) are used by child neurologists to see the growth in the brain of children. But there are no HC standards over 5 years of age children. The major strength of our study is that we developed HC reference data by using a sample of healthy Pakistani children aged 6 to 18 years that are free from any neurological disorders. Our developed reference data are satisfactory for local use than for use in other countries. This information can be used to identify neurological abnormalities in children whose head size are beyond the normal ranges and these abnormal population of children can be referred to neurologists for further neurological diagnoses and monitoring as mentioned in an earlier study.[9] Using the LMS method, we presented HC-for-age growth reference curves based on a comprehensive sample of Pakistani children from 6 to 18 years of age which is the first for the Pakistani pediatric population of a wide age range. It was reported that boys had a larger average head size than girls except for pubertal age. The results showed a significant disparity between our centiles and centiles of the other populations. Based on these findings and to avoid wrong interpretation, it is recommended that each country should produce its own HC growth charts. Since the current and earlier local published study[10] did not include the HC data of newborn children or children up to 2 years of age and the results of this study suggest that this gap might be filled because a sufficient increase in head size is shown during this age.

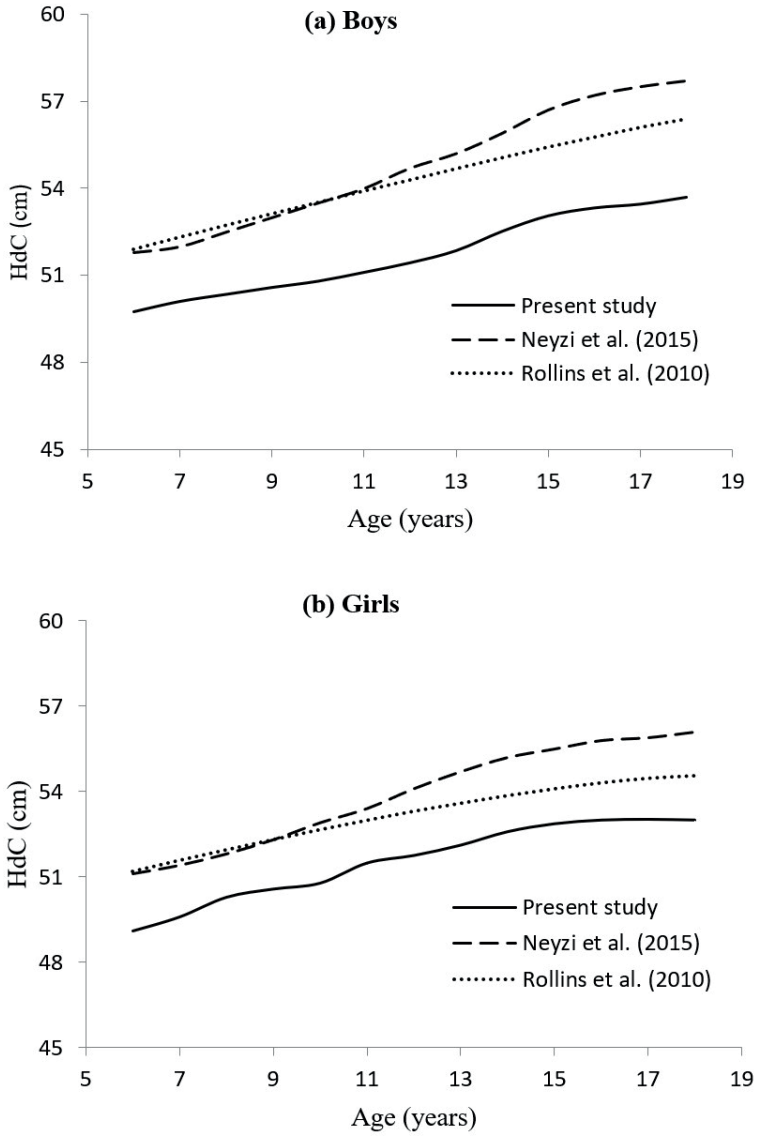

Fig. 2. (a) and (b): Comparison of median (50th) head circumference (cm) percentiles for the Pakistani boys and girls with the US (Rollins et al., 2010) and Turkish children (Neyzi et al., 2015).

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Author contribution

The authors confirm contribution to the paper as follows: study conception and design: MA and TI and MA; data collection: MA, AR, NS; analysis and interpretation of results: MA, MA, NS; drafting of manuscript: MA, TI, NA,

AR; critical review of manuscript: MA, AR, and TI. All authors reviewed the results and approved the final revision of the manuscript as submitted.

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Conflict of interest

The authors declare that there is no conflict of interest.

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