RESEARCH LETTER

Auxological Dynamics of Cephalic Index in Indian Children with Down Syndrome: A Longitudinal Study

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ABSTRACT

A hospital-based longitudinal observation study was conducted to determine the auxological dynamics of Cephalic Index (CI) and corresponding head shape among 1125 children with Down syndrome. Majority (88% males, 82% females) displayed brachycephaly.

Keywords: *Brachycephaly, Child, Head, Shape, Trisomy 21*

Down syndrome (DS) is the most common chromosomal aneuploidy with an incidence ranging from 1 in 600 to 1 in 1000 live births [1]. More than 100 different characteristic signs for DS have been reported, of which majority are in the craniofacial region [2]. Brachycephaly, qualitatively characterized by marked flattening of the occiput and a relative shortening of the occipito frontal diameter, is one of the main traits of infants with DS. Brachycephaly can also alter the head's center of mass, generating an imbalance in the neck's flexor and extensor muscles, resulting in poor postural stability. None of the earlier studies have attempted to quantitatively examine the head shape of children with DS. These have relied on the investigators' qualitative observations, rather than on standard anthropometric norms. Cephalic Index (CI), which measures a skull's proportion of breadth to length, is an objective and helpful metric for determining the shape of the skull. Based on CI, human head shape is categorized into five sub-types as ultra brachycephalic, hyper brachycephalic, brachycephalic (broad head), mesocephalic (normal head), and dolichocephalic (long head) as per Martin Saller classification [3]. The primary objective of this longitudinal observational study was to determine the type of head shape based on the CI among children with DS.

The study was conducted at a tertiary level hospital over 24 years (August 1994 to November 2018), after obtaining approval from the Institutional Ethics Committee. The study included children with DS, (karyotypically proven as free trisomy 21), aged 1month to 10 years, and born to healthy parents who resided in Northwestern India. Children with mosaicism and translocations were excluded. Informed consent was taken from parents/guardians of enrolled participants.

Following a mixed-longitudinal growth research design, these children were followed-up in the Growth Clinic every three months (time tolerance limit±15 days) for first six months of life and then yearly (± 1 month).

At each visit, a Spreading caliper (GPM Swiss made, least count 1mm) was employed to measure head length (HL) and head width (HW). The maximum HW was measured from glabella (anterior extreme in mid-sagittal plane at lower margin of the frontal bone, above frontonasal suture, and between superciliary arches) to opisthocranion (posterior extreme in midsagittal plane on superior squamous of occipital bone; which may or may not coincide with external occipital protuberance). Maximum HL was measured from the point eurion to eurion

(lateral extreme of the skull on either parietal bone or upper temporal bone avoiding any lower temporal protrusion or bulge). CI was calculated as HW/HL × 100. Head shape was categorized based on CI: dolichocephalic (male 71.0-75.9; female 72.0-76.9), mesocephalic (male 76-80.9; female 77-81.9), brachycephalic (male 81-85.4; female 82-86.4), hyper brachycephalic (male 85.5-90.9; female 86.5-91.9) and ultra brachycephalic (male 91-x; female 92-x) [3].

Statistical analysis was done using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Translocated Kolmogorov–Smirnov test was employed to check normality of the data. As our data were normally distributed; mean and standard deviation (SD) were computed for HL, HW and CI at each age. Independent *t*-test was used to compute gender differences for HL, HW and CI. Chi-square test was used to compare differences between two groups for categorical variables, with $P < 0.05$ indicating statistical significance.

The demographic profile of the study participants has been previously described [4]. Median number of visits per participant was 5 (range 1–44). Over the course of the study, 2327 HL and HW observations were made on 1,125 (male 752, female 373) DS children. The mean HL and HW of the participants showed a gradual but consistent increase from birth to 10 years. In contrast, the CI showed a decrease in mean values during the first three years where after, it became stable (**Web Fig. 1**). The boys displayed larger cranial values (HL and HW) compared to girls (**Table I**). The majority (males: 88%, females: 82%) possessed broad heads based on CI. Hyperbrachycephaly, noticed in 37.6% (*n* = 608) of boys and 28.7% (*n* = 204) of girls with DS, was the predominant head shape, followed by ultrabrachycephaly (male: 27.5%, *n* = 445; female: 27.2%, *n* = 193) and brachycephaly (male: 22.9%, *n* = 371; female: 26.1%, *n* = 185). Interestingly, 10% (*n* = 162) & 14.5% (*n* = 103) of male and female DS children even depicted mesocephaly.

Only a few studies on quantitative assessment of head shape and cranial indices have been identified in children with DS. Yesmin et al [5], reported hyperbrachycephaly as the most prevalent head shape among 44 Malay, Indian, and Chinese children with DS. An increased CI (88) indicating brachycephaly was reported among 50 DS patients aged 1-18 years from Southern India [6]. Rodrigues et al [7] demonstrated brachycephaly in people with DS by using magnetic resonance imaging. Shukla et al [8] found that 90% Indian individuals with DS (age: 6-40 years, *n* = 63) had brachycephalic or hyperbrachycephalic head shapes which may have been due to subjective assessment of head shape. A study from Germany [9] observed brachyfacial cranial shape among 85% participants with DS; *n* = 20, mean (SD) age: 11.69 (3.94) years, based on cephalometric analysis. Another Indian study describing clinical features in 208 children with DS, observed brachycephaly in 10.57% [10]. All the aforementioned studies show that occipital bone flattening causes brachycephaly, and reduction in head size typical of DS. This may be attributed to the proportionally greater reduction in antero-posterior growth of the skull relative to medio-lateral growth.

The heterogeneity in prevalence (10% to 98%) of brachycephaly in DS patients globally may be multi factorial. Distinct racial/sub-racial population stocks; varying cytogenetic profile that comprised the eligibility criteria i.e. we included free trisomy 21, most studies have also included translocation, and mosaicism, smaller

sample and difference in method of measurement may have contributed to the differences. The study is based on children with DS from Northwestern India, which is a constraint that may affect the generalizability of the findings. Further research on different population groups is recommended to explore the genetic and environmental factors contributing to these findings. To conclude, determining the profile of head shapes in DS based on objective standardized indices may make inter-population comparison more accurate and reliable. The conversion of such data may be explored to generate corresponding graphs.

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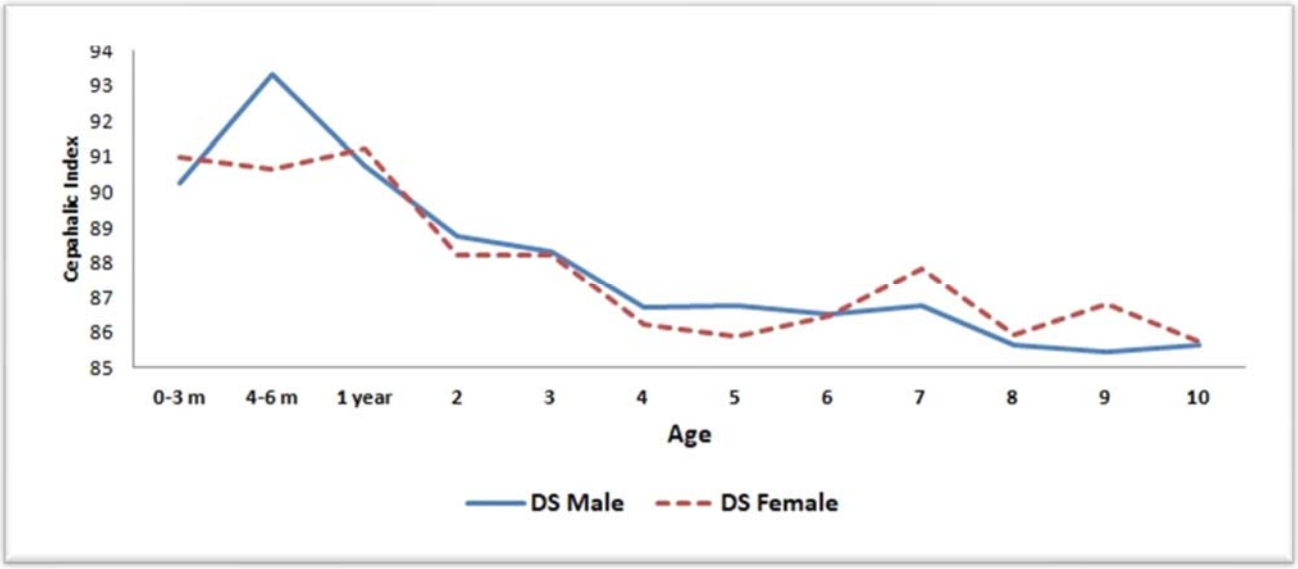
Table I Cranial Measurements in Children with Down Syndrome

Age	*Down Syndrome (Boys)*				*Down Syndrome (Girls)*				*Gender Differences (Independent 't' test) P value*		
	n	*Head length*[a]	*Head width*	*Cephalic Index*[a]	*n*	*Head length*[a]	*Head width*[a]	*Cephalic Index*[a]	*Head length*	*Head width*	*Cephalic Index*
0-3 m	64	11.84 (0.83) (11.65, 12.03)	10.68 (0.78) (10.51, 10.86)	90.27 (5.62) (89.07, 91.60)	37	11.54 (0.98) (11.17, 11.71)	10.48 (0.80) (10.18, 10.66)	91.01 (6.03) (89.43, 93.05)	0.071	0.162	0.409
4-6 m	75	12.86 (0.90) (12.67, 13.12)	11.94 (0.79) (11.72, 12.14)	93.34 (9.07) (90.66, 95.04)	41	12.47 (0.95) (12.10, 12.85)	11.26 (0.79) (10.95, 11.57)	90.65 (8.26) (87.45, 93.86)	0.074	< 0.001	0.188
1 year	255	13.70 (0.86) (13.60, 13.80)	12.39 (0.70) (12.31, 12.47)	90.73 (6.81) (89.96, 91.50)	131	13.49 (0.93) (13.40, 13.89)	12.27 (0.77) (11.96, 12.34)	91.23 (6.76) (89.28, 92.5)	0.016	0.084	0.484
2 years	236	14.62 (0.70) (14.53, 14.71)	12.95 (0.62) (12.87, 13.03)	88.76 (5.72) (88.04, 89.49)	107	14.30 (0.74) (14.16, 14.43)	12.58 (0.71) (12.46, 12.71)	88.22 (6.51) (87.03, 89.41)	< 0.001	< 0.001	0.419
3 years	216	14.95 (0.84) (14.83, 15.07)	13.16 (0.56) (13.08, 13.24)	88.32 (6.27) (87.43, 89.21)	110	14.60 (0.77) (14.44, 14.76)	12.83 (0.75) (12.68, 12.99)	88.22 (8.03) (86.57, 89.88)	0.001	< 0.001	0.910
4 years	198	15.34 (0.79) (15.23, 15.45)	13.27 (0.68) (13.18, 13.37)	86.70 (5.47) (85.92, 87.49)	73	15.03 (0.73) (14.86, 15.19)	12.93 (0.53) (12.81, 13.06)	86.25 (5.41) (85.02, 87.48)	0.004	< 0.001	0.539
5 years	185	15.43 (0.71) (15.31, 15.55)	13.36 (0.64) (13.26, 13.47)	86.77 (5.97) (85.81, 87.74)	68	15.15 (0.59) (14.98, 15.33)	12.99 (0.58) (12.83, 12.99)	85.91 (5.66) (84.27, 87.56)	0.015	0.001	0.384
6 years	92	15.51 (0.70) (15.37, 15.66)	13.40 (0.57) (13.29, 13.52)	86.54 (5.04) (85.51, 87.59)	44	15.19 (0.84) (14.94, 15.45)	13.09 (0.52) (12.93, 13.25)	86.45 (6.53) (84.49, 88.42)	0.021	0.002	0.927
7 years	73	15.62 (0.67) (15.47, 15.78)	13.53 (0.52) (13.42, 13.66)	86.78 (4.58) (85.74, 87.83)	29	15.22 (0.67) (14.97, 15.47)	13.34 (0.48) (13.16, 13.52)	87.85 (6.05) (85.59, 90.11)	0.007	0.077	0.328
8 years	65	15.68 (0.69) (15.52, 15.86)	13.55 (0.55) (13.28, 13.67)	85.63 (4.78) (84.47, 86.79)	19	15.51 (0.72) (15.17, 15.85)	13.38 (0.53) (13.03, 13.54)	85.93 (6.94) (82.68, 89.19)	0.317	0.366	0.825
9 years	52	15.94 (0.66) (15.76, 16.13)	13.61 (0.54) (13.45, 13.76)	85.43 (5.02) (84.04, 86.84)	19	15.54 (0.65) (15.19, 15.83)	13.43 (0.58) (13.15, 13.72)	86.83 (6.21) (83.84, 89.83)	0.016	0.230	0.335
10 years	107	16.09 (0.75) (15.96, 16.22)	13.75 (0.50) (13.66, 13.84)	85.65 (4.95) (84.79, 86.51)	31	15.66 (0.64) (15.46, 15.87)	13.48 (0.58) (13.21, 13.59)	85.72 (5.27) (84.04, 87.41)	0.002	< 0.001	0.937

[a]*Values expressed as mean (SD), (95% CI)*

CI Confidence interval, m Month, SD Standard deviation



Web Fig. 1 Longitudinal trajectory of cephalic index in children with Down syndrome