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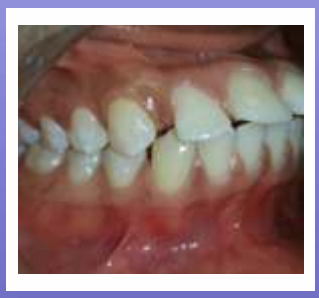
Cranial Base Dimensions in Down Syndrome: A Comparative Cephalometric Study



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"DENTISTRY'S FIRST SPECIALTY JOURNAL IN SUB SAHARAN AFRICAN"

Cranial Base Dimensions in Children with Down Syndrome: A Comparative Cephalometric Study

Aghimien OA[a], Ajayi EO[b], Ize-Iyamu IN[b]

Abstract

Background: To ascertain if there are differences between the anterior cranial base length (ACBL), posterior cranial base length (PCBL), total cranial base length (TCBL), and cranial base angle (CBA) in children with Down syndrome, compared to a control population of children without Down syndrome

Methods: This was a cohort study consisting of twenty (20) individuals with Down syndrome (DS) recruited from special needs schools and 20 control individuals recruited from pre-orthodontic patients who presented for orthodontic treatment at the University of Benin Teaching Hospital. The study population was made up of children between ages 10-15 years (mean 12.6 ± 2.1) consisting of 10 males and 10 females for both study groups. Comparative evaluation of findings from the linear measurements (ACBL, PCBL, TBL) and angular measurement (CBA) between individuals with Down syndrome and controls were made using the independent *t-test*. A significant level of $p<0.05$ was set for this study.

Results: Significant deviations in the parameters evaluated were observed among the Down syndrome individuals. Down syndrome individuals were observed to have a statistically significant reduction ($p<0.0001$) in their anterior cranial base length (ACBL), posterior cranial base length (PCBL), and total cranial base length (TCBL) when compared to the control individuals. However, the cranial base angle (CBA) among Down syndrome individuals was observed to be significantly larger ($p< 0.004$) than in the control group. This observation was the same for both genders.

Conclusion: This study shows that the cranial base dimensions of individuals with Down syndrome are significantly different from those of control individuals with the former having shorter linear dimensions and larger cranial base angles. Further flattening of the cranial base has been reported with the use of function/orthopaedic appliances in patients with Down syndrome. Orthodontists should therefore exercise caution when using this appliance for this group of patients.

Keywords: Down syndrome, cranial base dimension

ORIGINAL ARTICLE

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Introduction

Down syndrome (DS) was first described by John Langdon Down in 1866 when he published the physical characteristics of a group of individuals which he described as Mongolism. However, a French physician Dr. Jerome Lejeune, in 1959 discovered the chromosomal abnormality associated with this group of individuals.[1] It is the most common chromosomal disorder among humans.[2] The prevalence and incidence vary among different populations. In the United States, an estimated prevalence of 14.47 per 10,000 live births was reported[3], while the incidence of 1:800 and 0.125% prevalence have been reported among Brazillians.[4] Prevalence rates of 1.88%, 1.54% and 1.29% were reported among white, coloured, and black South Africans[5,6] respectively while an incidence of 1 in 865 has been reported among Nigerians.[7]

Three variants of this condition have been documented; trisomy 21, translocation and mosaic which account for 94%, 5% and 1% of cases respectively.[8] nondisjunction and translocation are possible causes of the extra 21st chromosome in Down syndrome.[9] The genes located on chromosome 21 are overexpressed in the cells and tissues of Down syndrome patients, and this contributes to the phenotypic abnormalities.[10]

The distinct facial characteristic features which include a flat face, abundant neck skin, small mouth and protruding tongue make it easy to recognize these individuals in childhood.[11] Hypoplasia of ectomesenchyme, endodermal, and mesodermal derived structures of the cranial and face of Down syndrome patients with resultant midface retrusion, smaller cranial base bones and increase cranial base angles have been reported.[12-16] The growth of the cranial base is said to contribute to the sagittal dimension of the midface.[16] Several authors[14,15,] have reported smaller cranial base and larger cranial base angle among Caucasian children with Down syndrome. Suri et al (2010)[15] reported smaller cranial base length and larger cranial base angles among Canadian Caucasian children with Down syndrome.

This present study was conducted among a group of Nigerian individuals with Down syndrome to determine if the observations made in a previous study[15] were obtainable among Nigerians. This study became necessary due to the dearth of information concerning the cranial base morphology of individuals with Down syndrome in Nigeria.

Materials and Methods

This cross-sectional comparative descriptive cohort study was conducted among 40 individuals comprising 20 patients with Down syndrome and 20 control individuals aged 10 -15 years of age (10 males and 10 females for both study groups). The mean age was 12.6 ± 2.1 years. It was conducted in the Orthodontic unit of the University Teaching Hospital.

Sample size determination

The sample size for this study.

$$N = \frac{Z^2Pq}{d^2}$$

Where: N = the desired sample size

Z = the standard normal deviate, set at 1.96 corresponding to a 95% confidence level,

P = the prevalence rate; q = 1.0-p; d = degree of accuracy desired (error margin) = 5% = 0.05.

An incidence of 1: 865 was used as documented in a previous study[7]

Prevalence was $\frac{1 \times 1000}{865} = 1.16$

The prevalence rate of 1.16% (P=0.0116) was used to calculate the sample size.

$$\frac{1.96 \times 1.96 \times 0.0116 \times \{1-0.0116\}}{0.05 \times 0.05} == 17.6$$

When an additional 10% of attrition (approximately 2) was added to the minimum calculated sample size of 17, a total of 19 study individuals were arrived at for each study group.

The total calculated minimum sample size was 38; with 19 Down syndrome individuals and 19 controls to allow for comparison. However, 20 participants were recruited for each study group which is higher than the calculated sample size.

Individuals were recruited using convenience sampling methods due to the rarity of the conditions.

Recruitment of study participants: Individuals with Down syndrome were recruited from schools for special needs students within the Benin City metropolis using the convenience sampling method, and their lateral cephalographs were taken at Shalom Dental Clinic. All the individuals with DS were objectively karyotyped and confirmed to be Trisomy 21 using cytogenetic analysis. The lateral cephalographs of the control individuals were recruited from the pool of pre-orthodontic patients at the Orthodontic clinic of the University of Benin Teaching Hospital.

Ethical consideration: Ethical approval (ADM/E 22/A/VOL VII/1236) for this research protocol was obtained from the hospital's Ethics and Research

Committee before data was collected. Written informed consents were obtained from the parents and guardians of the Down syndrome individuals before they were recruited for the study.

Selection criteria: The criteria for inclusion are; those within the study age group, individuals for whom informed consent had been given and those confirmed via karyotyping to be Down syndrome patients. Individuals with previous orthodontic treatment, those with difficult neck stability, and those with distorted radiographs were excluded. Individuals with an overall normal developmental pattern with no record of systemic abnormalities and of Nigerian descent were selected for the control group.

Data collection: The lateral cephalographs of the study individuals were manually traced on a matte acetate paper using a pointed HB pencil illuminated by a light box. A plastic meter rule was used to obtain linear measurements, while a protractor was used to obtain the angular measurement.

Intra-examiner reliability: Evaluations of the lateral cephalographs were at 2 different sessions of 2 weeks intervals for intra-assessor reliability assessment, which was 0.79.

Description of the anatomic landmarks:

Landmarks on the lateral cephalographs[17] used for the research were sella (S), basion (Ba) and nasion (N). The parameters analysed were anterior cranial base length (ACBL), posterior cranial base length (PCBL), total cranial base length (TCBL), and cranial base angle (CBA).

Sella (S) - The geometric centre of the pituitary fossa (sella turcica), determined by a constructed point in the mid-sagittal plane.

Nasion (N) - The intersection of the inter-nasal and fronto-nasal sutures, in the mid-sagittal plane

Basion (Ba) - The most anterior inferior point on the margin of the foramen magnum, in the mid-sagittal plane.

Anterior cranial base length (ACBL)- The reference plane connecting the S to N

Posterior cranial base length (PCBL)-The reference plane connecting the S to Ba.

Total cranial base length (TCBL)- The reference plane connecting the Ba to N

Cranial base angle (CBA)- The angle between the anterior and posterior cranial base, recorded as the inferior angle formed by the intersection of the lines BaS and SN. Also called the Boogard's base angle.

Data analysis: The data was analysed using the IBM SPSS version 20. The cephalometric measurements obtained from individuals with Down syndrome and the control were analysed using an independent t-test. A significant level of $p<0.05$ was set for this study.

Results

The cranial base parameters of 20 DS and 20 control individuals comprising 10 males and 10 females in each study group (DS and control) were evaluated.

Table 1 shows the comparison of the various mean within the two groups in relation to gender. Down syndrome male participants had larger measurements of all the linear parameters which include; anterior cranial base length, posterior cranial base length and total cranial base length than female Down syndrome participants. However, the differences were not statistically significant ($p>0.05$). On the contrary, the cranial base angle was larger among females with Down syndrome than males with Down syndrome ($p>0.05$). The means of the various parameters among the control showed that female participants only had a marginal longer anterior cranial base length than male control participants. The posterior cranial base length, total cranial base length, and cranial base angle were all larger among male-control than female-control participants. The difference observed in the posterior cranial base length between the male and female control participants was statistically significant ($p=0.011$), while the result

between male and female participants with Down syndrome was not statistically significant (p=0.628), as shown in table 1.

Table 2 shows that male Down syndrome (DS) participants had statistically significant (p<0.0001) shorter anterior cranial base length, compared with the control participants (DS, 51.7 ± 3.18; CON, 57.1 ± 1.54). A similar trend was observed with posterior cranial base and the total cranial base length (Table 2). However, the cranial base angle of male Down syndrome participants was statistically (p<0.004) higher than the male control participants. The linear parameters of female participants also showed that female Down syndrome participants had a statistically significant (p<0.001) shorter anterior cranial base length, posterior cranial base length, and total cranial base length. Table 3 also shows that the cranial base angle of female Down syndrome participants was more obtuse than the female control (CON) participants (DS, $140.6^0 \pm 4.52^0$; CON, $131.9^0 \pm 4.73^0$), p<0.001.

Table 1: Mean values of the cranial base dimensions among Down syndrome (DS) and control (CON) individuals in relation to gender.

Variables	Group	GENDR (n)	Mean (mm)	Mean difference	*p* value	95% CI of the difference	
						Lower	Upper
ACBL (mm)	DS	M (10) F (10)	51.7 ± 3.18 50.1 ± 1.78	1.641	0.298	-1.223	3.764
	CON	M (10) F (10)	57.1 ± 1.54 57.2 ± 3.53	-0.135	0.274	-1.117	3.874
PCBL (mm)	DS	M (10) F (10)	33.3 ± 3.06 32.8 ± 2.54	0.6525	0.628	-2.045	3.295
	CON	M (10) F (10)	39.1 ± 2.35 37.1 ± 2.89	2.647	***0.011**	0.842	5.370
TCBL (mm)	DS	M (10) F (10)	79.5 ± 2.74 78.8 ± 3.00	0.700	0.746	–2.788	3.688
	CON	M (10) F (10)	87.8 ± 1.09 86.0 ± 4.90	1.847	0.211	0.533	6.355
CBA (Degree)	DS	M (10) F (10)	$139.8^0 \pm 4.86^0$ $140.6^0 \pm 4.52^0$	-0.895	0.590	-6.235	3.652
	CON	M (10) F (10)	$132.1^0 \pm 5.37^0$ $131.9^0 \pm 4.73^0$	0.267	0.396	-5.532	3.293

KEY: ACBL, Anterior cranial base length; PCBL, Posterior cranial base length; TCBL, Total cranial base length; CBA, Cranial base angle. *p<0.05*

Table 2: Comparative evaluation of cranial base lengths and cranial base angle between Down syndrome males and control males' individuals

Variables	Group	No	Mean (mm)	Mean difference	*p* value	95% CI of the difference	
						Lower	Upper
ACBL (mm)	Down Syndrome	10	51.7±3.18	-5.450	*0.0001	-7.798	-3.102
	Control	10	57.1± 1.54				
PCBL (mm)	Down Syndrome	10	33.3±3.06	-5.800	*0.0001	-8.362	-3.237
	Control	10	39.1±2.3				
TCBL (mm)	Down Syndrome	10	79.5± 2.74	-8.250	*0.0001	–10.839	-5.662
	Control	10	87.8±1.09				
CBA (Degree)	Down Syndrome	10	139.80 ± 4.86^0	7.3650	*0.004	2.839	12.462
	Control	10	132.10 ± 5.37^0				

KEY: ACBL, Anterior cranial base length; PCBL, Posterior cranial base length; TCBL, Total cranial base length; CBA, Cranial base angle. $p<0.05$

Table 3: Comparative evaluation of cranial base lengths and cranial base angle between Down syndrome females and control females' individuals

Variables	Group	No	Mean (mm)	Mean difference	*p* value	95% CI of the difference	
						Lower	Upper
ACBL (mm)	Down Syndrome	10	50.1±1.78	-7.167	***0.001**	-9.957	-4.376
	Control	10	57.2± 3.53				
PCBL (mm)	Down Syndrome	10	32.8±2.54	-4.278	***0.004**	-7.001	-1.555
	Control	10	37.1±2.89				
TCBL (mm)	Down Syndrome	10	78.8± 3.00	-7.222	***0.002**	–11.278	-3.166
	Control	10	1086.0±4.90				
CBA (Degree)	Down Syndrome	10	$140.6^0\pm4.52^0$	8.666	***0.001**	4.042	13.291
	Control	10	$131.9^0\pm4.73$				

KEY: ACBL, Anterior cranial base length; PCBL, Posterior cranial base length; TCBL, Total cranial base length; CBA, Cranial base angle. $p<0.05$.

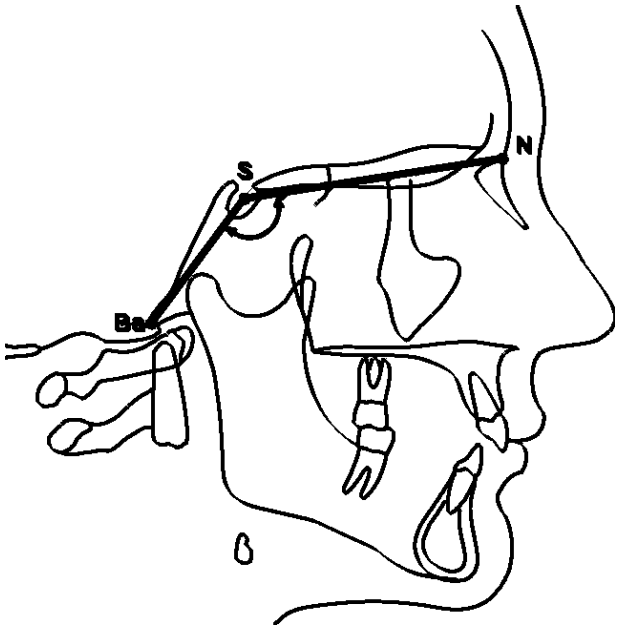

Figure 1: Landmarks used during the study. Showing the Ba, S and N points. The arrow is showing the cranial base angle.

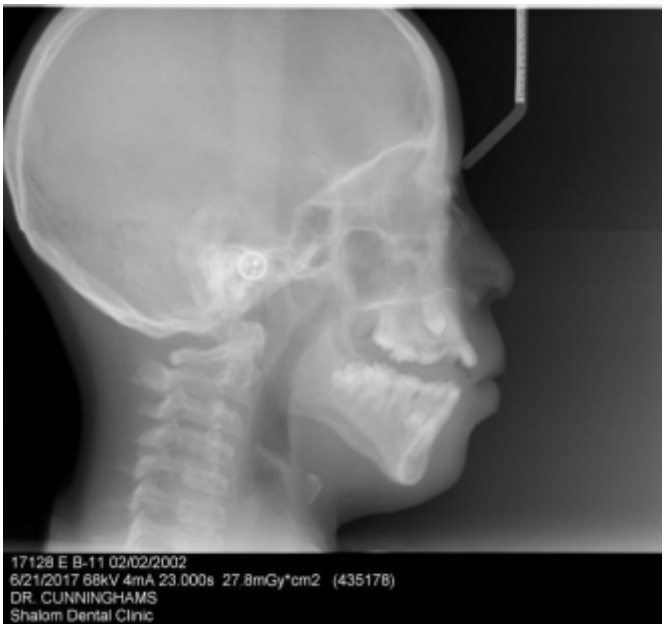

Figure 2: Lateral cephalograph of an individual with Down syndrome recruited for the study.

Discussion

As shown in our results, the flatter cranial base angle and the decrease in the linear dimensions of the anterior, posterior and total cranial base lengths in comparison with the control participants suggests that the chromosomal abnormality in Down syndrome has an effect on the central structures of the skull. These present findings are in agreement with previous observations made by earlier reseacrhers.[15,18,19,20-22]

According to Suri et al[15] greater reduction was noticed in the anterior cranial base length than the posterior, an observation which is only corroborated by results among the female Down syndrome study groups in comparison with female control in this present study. Even with the deficiency of the cranial base dimension, the growth rate among Down syndrome individuals is reported not to be different from normal individuals. [13,21] It therefore stands to reason that an abnormality in growth of the endo-cranial base structure among mongoloids may have been established at an earlier age, as reported by Fischer-Brandies[19]. Alio and coworkers hypothesized that the abnormality in the growth of the cranial base among Down syndrome individuals may have been established before the age of 8 years,[21] while another researcher reported a deficiency in growth as early as 4 years of age.[13] Hypoplasia of the central structures of the skull, delayed ossification of synchondroses, cerebral growth reduction, and inadequate elevation of the sella turcica could have contributed to the defective flattened cranial base angle in Down syndrome.[23] The spheno-ethmoidal and spheno-occipital synchondroses contribute to postnatal growth of the mid-face and the premature fusion (craniosynostosis) resulting from the chromosomal abnormality could impact negatively on the growth of the cranial base.[16,24]. This may account for the early establishment of structural differences, causing shorter anterior and posterior cranial base lengths[21] as observed in this present study. The significant difference in cranial base angle as observed in this study corroborates the observations made by Suri et al[15] but is at variance with the results of Burwood.[20] The author[20] revealed a limitation to the study as a result of a smaller number of abnormal dry skulls recruited for the study. Lack of pneumatization of the frontal sinus and underdeveloped nasal bone among individuals with Down syndrome may be the reason for the reduced anterior cranial base length.[12,25] Differences in the cranial base dimension seen in Down syndrome in relation to gender were made in this study, corroborating previous researches.[21] The

higher cranial base angle found among females with Down syndrome compared to their male counterparts, agrees with the findings of Alio and co-workers.[21]

Orthodontic treatment planning for individuals with Down syndrome should involve evaluation of the cranial base as a possible contributing aetiological factor to the development of malocclusion. Apart from a retruded midface that is prevalent among individuals with Down syndrome,[15,18,19] the location of the anterior limit of the anterior cranial base (nasion), which serves as a landmark for the evaluation of sagittal jaw relationship, could be considered defective in Down syndrome due to the reduced length, as observed in this study.

Cranial base modification is not directly within the purview of orthodontic functional/ orthopaedics appliance treatment modality. The growth and dimension of the cranial base is genetically predetermined and an altered genetic influence will affect its dimension, as noted among patients with Down syndrome in this study. However, in the course of correcting the poor skeletal relationships such as skeletal pattern III, some effects have been noticed in the cranial base length and the angular deflection. [26-29] Orthodontists should take into consideration the effect of these appliances on the cranial base when correcting skeletal discrepancies in Down syndrome. A clockwise rotation of the mandible with the use of Frankel regulator II, a cervical pull headgear, has been previously reported.[26-28] The use of these appliances cause the basion to move more posteriorly with further flattening of the cranial base angle [26] Orthodontists should be weary of further flattening the cranial base in individuals with Down syndrome when planning functional and orthopaedic appliance therapy, as this could compress the cerebral tissue posteriorly, resulting in subsequent cerebral dysfunction.

One of the limitations of this study is the small sample size. The sample was conducted among a limited number of Down syndrome participants. The stigmatisation faced by this group of individuals made parents/guardians not so receptive to allowing their children to partake in the study, so only the few who gave their consent were recruited in the study.

Conclusion

This study showed that the cranial base dimension of children with Down syndrome is significantly different from that of controls. It therefore suggests evidence of hypoplasia of cranial base bones and more flattened cranial base among Down syndrome individuals. A decrease in the anterior cranial base length, posterior cranial length, and total cranial base length were observed among the male and female Down syndrome participants. The increased cranial base angle observed in this study gave a flattened cranial base appearance with larger angle among male and female individuals with Down syndrome.

Growth modification therapy for Down syndrome individuals for the purpose of correcting skeletal variation should be embarked upon with great caution to prevent further flattening of the cranial base.

Recommendation

Further studies on the cranial base of Down syndrome involving a large number of participants is therefore recommended, to validate the observations made in this current study.

Also, efforts should be made to stop the stigmatisation of this group of individuals.

Contributors

All the authors contributed to the design, data collection, analysis and write-up of the manuscript.

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Conflict of Interest

Nil

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Instructions for Authors

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Competing interest for a given manuscript exists when the author has ties to activities that could inappropriately influence his or her judgment, whether or not judgment is in fact affected. Financial relationships with industry for example, through employment, consultancies, stock ownership, honoraria, expert testimony, either directly or through immediate family, are usually considered to be the most important competing interests. However, conflicts can

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Original articles should report original research relevant to basic and clinical orthodontics including randomized trials, intervention studies, studies of screening and diagnostic tests, cohort studies, cost effectiveness analyses and case control studies. While reporting randomized controlled trials (RCT), authors must attempt to be in conformity with the consolidated standards of reporting trial.

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Each manuscript should be accompanied with a structured abstract (divided into background, methods, results and conclusions) in no more than 250 words. Four to five key words to facilitate indexing should be provided in alphabetical order along with the abstract. The text should be divided in sections on introduction, methods, results, discussion and conclusion.

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Abstract should be of 100-150 words highlighting the aims, methods and main results along with 3-4 key words.

The text should contain no more than 1500 words, 3 illustrations or tables and up to 20 references, preferably recent publications.

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State-of-the-art review articles or systematic, critical assessments of literature are also published. Normally a review article on a subject already published in the West African Journal of Orthodontics is not accepted for a period of 3 years.

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Clinical cases highlighting uncommon malocclusion condition, orthodontic treatment techniques are published as case reports. Single case reports are usually not accepted, unless some new or unusual aspect regarding aetiopathogenesis, diagnosis or management is brought out that adds to the existing body of knowledge. The text should not exceed 1000 words and is divided into sections, i.e., abstract, introduction, case report and discussion. The number of tables/figures should be limited to 2. Ten recent references are acceptable. A maximum of 3 or 1 author is permitted from the principle and each of the associated departments respectively. Thus, case reports from only one investigative department can have a maximum of 3 authors.

Letter to Editor(s)

Letters commenting upon a recent article in the West African Journal of Orthodontics are welcome.

Such letters should be received within 6 months of the article's publication. At the editorial board's discretion, a letter may be sent to authors! experts for comments and both letter and reply may be published together. Letters may also relate to other topics of interest to orthodontists and others, and/or useful clinical observations. Letters should not be more than 400 words. The number of authors should not exceed 2, including the authors' reply in response to a letter commenting upon an article published in this journal.

Images Section

A short text of about 150 words depicting the condition with color photographs (vide infra) is needed.

Normally only clinical photographs are accepted but accompanying skiagrams or pathological images could also be considered for publication.

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Such articles are published on topical orthodontic issues including social aspects. It is expected that the authors have sufficient credible experience on the subject for giving viewpoints. These should not exceed 1500 words.

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Announcements for conferences, symposia, meetings or courses may be sent for publication in advance. The announcements should provide title, date(s) and place of the event and contact address, telephone, and email

occur for other reasons, such as personal relationships, academic competition and intellectual passion. If any of the authors have accepted reimbursement for attending symposium, a fee for speaking, fee for organizing educational reach, funds for a member of the staff of consultation fees from an organization that may in: way gain or lose financially from the result of the study, review, editorial or letter, a competing interest would be deemed to exist. If any of the authors had been employed by an organization that may in any way gain or lose financially from the publication, or if any of them hold stocks or shares in such an organization, competing interest would be deemed to exist. If competing interest exists, the author(s) must disclose them while submitting the manuscript.

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The second page should carry an abstract in case of original article (250 words), review article (200 words), brief report (100-150 words), and case report (50 words), respectively. For original article and reviews, the abstract should be structured as detailed earlier. For brief reports, the abstract should state the purpose of the study, basic methodology, main findings (giving specific data and statistical significance) and key conclusion(s). Below the abstract, authors should provide 3-5 key words for indexing; terms from the Medical Subject Headings (MESH) list of Index Medicus should be used. The basic structure of a paper follows the well known acronym IMRAD, which stands for Introduction (what questions was asked), Methods (how was it studied), Results (what was found) and Discussion[4].

Introduction

The introduction must clearly state the question that the author(s) tried to answer in the study. It may be necessary to briefly review the relevant literature.

Only cite those references that are essential to justify the proposed study.

Materials and Methods

The methods section should describe, in a logical sequence, how the study was designed (e.g., how randomization was done), carried out (e.g., how subjects were chosen or excluded, ethical considerations, accurate details of materials used, exact drug dosage and form of treatment, etc.) and data were analyzed (e.g., an estimate of the power of the study, exact test used for statistical analysis, etc.).

For standard methods, appropriate references are sufficient, but if standard methods are modified these should be clearly brought out.

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Ethics

When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1964, as revised in 2000.

They should indicate whether the study was approved by the Institutions' Ethical Committee, and whether informed consent was obtained from the study participants. They should not use patients' names, initials, or hospital numbers, especially in illustrative material. This journal reserves the right to reject a manuscript on ethical grounds, on the basis of recommendations of its "Ethical Committee", even if the research has been cleared by the institutional ethical committee. Moreover, when reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.

Statistics

Authors should describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible, they meet to quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Actual P values are provided rather than stating as just <0.05 or >0.05 etc. References for the design of the study and statistical methods should be to standard works when possible (with pages stated) rather than to papers in which the designs or methods were originally reported. Any general-use computer programs used should be specified and statistical terms, abbreviations, and most symbols be defined.

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This section should include only relevant, representative data and not all information collected during the study. Major findings should be presented clearly and concisely. Text, tables, and illustrations should be used sensibly while avoiding repeating in the text all the data depicted in the tables or illustrations and emphasizing or summarizing only important observations. Tables and figures should be restricted to those needed to explain the argument of the paper and to assess its support. It is necessary to cite the tables in the text and type them on separate sheets. It may also be useful to mention what the study did not find.

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Discussion ordinarily should not be more than one third of the total length of the manuscript. This section should include a summary of the major findings, their relationship to other similar studies, limitations of methods and implications of these findings in future research. Conclusions should be linked to the goals of the study. Unqualified statements and conclusions which are not completely supported by the data should be avoided. Authors should also refrain from making statements on economic benefits and costs unless their manuscript includes economic data and analyses.

Acknowledgements

In acknowledgements section, it is suitable to list all contributors who do not meet the criteria for authorship, such as a person who provided purely technical help, writing assistance, or a department head who provided only general support. Financial and material support should also be acknowledged.

Groups of persons who have contributed materially to the paper but whose contributions do not justify authorship may be listed under a heading such as "clinical investigators" or "participating investigators", and their function or contribution should be described, for example, "served as scientific advisers", "critically reviewed the study proposal", "collected data", or "provided and cared for study patients". A written consent is required from all the persons acknowledged, indicating their acceptance for the same.

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Journal Article

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Each table should be typed in double-space on a separate sheet of paper. Tables not submitted as photographs must be numbered consecutively (Arabic numerals) in the order of their first citation in the text, with a brief but self explanatory title for each.
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Statistical measures of variations should be identified such as standard deviation and standard error of the mean.
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Figures should be professionally drawn and photographed; freehand or typewritten lettering is unacceptable. Instead of original drawings, X-ray films, and other material, sharp, glossy, black-andwhite photographic prints of high quality are necessary, usually 127x 173 mm (5x7 in) but no larger than 203x254 mm (8x10 in) For color illustrations negatives or positive transparencies are provided, along with color prints. It is preferable to have the photograph in portrait form rather than in landscape form to fit easily into one column.
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