Craniosynostosis in Africa: Insights from 8 Countries—A Systematic Review and Meta-Analysis

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Key words
- Africa
- Craniosynostosis
- Global neurosurgery
- Pediatric neurosurgery

Abbreviations and Acronyms
CI: Confidence interval
CT: Computed tomography
ICP: Intracranial pressure
OT: Open technique
QOL: Quality of life

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OBJECTIVE: **Craniosynostosis is a congenital skull deformity that impacts development and quality of life of children if left untreated. This study aimed to evaluate literature regarding presentation, treatment, and outcomes of craniosynostosis in Africa.**

METHODS: **A systematic review of the literature using PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar databases was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.**

RESULTS: **Fourteen retrospective/prospective studies with 620 patients and 14 case reports involving 27 cases (8 countries) were included. In 12 articles, 56.6% of patients (317/560) were males, with a mean age of 2.4 years (confidence interval [CI]: 1.1—3.7). Abnormal head shape was the most reported presentation in 77.8% of cases (332/427, 8 articles). Syndromic craniosynostosis was seen in 25.2% (CI: 13.7%—36.6%). Common phenotypes were trigonocephaly in 31.5% (CI: 3.6%—59.4%), anterior plagiocephaly in 23.2% (CI: 5.1%—41.3%), and scaphocephaly in 22.1% (CI: 13.5%—30.8%). Five hundred seventy eight patients, 99.5% (CI: 99.0%—100.0%), underwent surgical treatment. Vault remodeling was performed in 72.9% patients (CI: 47.4%—98.6%). Postoperative complications included cerebrospinal fluid leaks 5.4% (CI: 0.0%—11.6%) and surgical site infections 4.5% (CI: 0.0%—10.8%). Follow-up ranged between 0.2 and 40.9 months; 95.6% of cases (CI: 90.1%—100.0%) exhibited improved deformity and neurological deficits at last follow-up. The mortality rate was 3.1% (CI: 0.0%—6.9%, 2 articles).**

CONCLUSIONS: **Few studies on craniosynostosis in Africa highlight the need for more research. Treatment with open techniques yields few complications and a low mortality rate. Early diagnosis and collaborative data reporting will enhance understanding of its burden and variations across Africa.**

INTRODUCTION

Craniosynostosis is a congenital deformity defined by the premature and erratic fusion or growth arrest of cranial sutures resulting in an abnormal skull shape.[1,2] In severe cases, infants may present with increased intracranial pressure (ICP), facial abnormalities, and respiratory or neurocognitive dysfunction.[1-3] Nonsyndromic craniosynostosis account for 75% of craniosynostosis with the remaining classified as syndromic cases.[3-5] Crouzon, Apert, and Pfeiffer syndromes are the most common among the estimated 180 syndromes associated with craniosynostosis.[3] Etiology of craniosynostosis can be attributed to genetic mutations and maternal and environmental factors but in most cases, it is unknown.[1,2] Approximately 20% of craniosynostosis cases are linked to gene mutations, often inherited through autosomal dominant patterns.[1,2] These mutations typically involve genes related to fibroblast growth factor, fibroblast growth factor receptor, or transforming growth factor beta.[1,2,4,5] The estimated prevalence of craniosynostosis is 1 per 2000 to 2500 live births.[6-8] Shlobin et al. reported 84,665 children worldwide were born with craniosynostosis in 2019 including 72,857 with nonsyndromic craniosynostosis.[9]

While craniosynostosis has been extensively documented in the literature, particularly for patients of European descent, literature regarding the prevalence of craniosynostosis and its types, surgical interventions, and treatment outcomes specifically among the African

population is limited.[9] To address the scarcity of information concerning craniosynostosis in Africa, our systematic review aims to elucidate its prevalence, analyze demographic and clinical profiles, examine features and types of craniosynostosis, evaluate treatment efficacy, and ascertain overall outcomes in this population. Additionally, we delineate country-specific challenges and recommendations for craniosynostosis management, thereby contributing to a more comprehensive understanding of the diverse landscapes across Africa.

METHODS

Search Strategy

A systematic review of the literature was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Figure 1.) A comprehensive search was carried out across electronic databases including PubMed, Scopus, Google Scholar, and Web of Science using key search terms "craniosynostosis AND Africa." Furthermore, we conducted a comprehensive manual review across databases and search engines, including Google and Bing, using the keyword "craniosynostosis" combined with terms such as "[*each African Country*]," "pediatric," "children," "infantile," "child," "presentation," "management," "surgery," "treatment," and "outcome," using Boolean operators (AND/OR). There was no time frame limit to the search strategy. Our primary objective was to use original English articles (retrospective/prospective studies and case reports/series) to investigate patient characteristics, clinical presentation, and diagnosis of craniosynostosis in pediatric patients in all the African countries represented in the literature. Secondary objectives aimed to estimate the features of craniosynostosis including the proportions of common sutures involved, management strategies, postmanagement complications, and outcomes. Exclusion criteria were as follows: non-English articles, literature reviews, correspondences, commentaries, book chapters, animal studies, opinion pieces, systematic reviews, and meta-analyses.

Data Extraction

Three authors (**K. D., U. B.,** and **S. P.**) independently conducted the search and selection process. In instances of disagreements regarding inclusion criteria or collected data, consensus was reached through review and discussion among the authors. Initially, articles were screened based on titles, followed by a review of abstracts and full texts to determine eligibility. Subsequently, 6 authors (**K. D., P. K., B. L., O. O., M. S., and S. P.**) thoroughly examined full texts to finalize inclusion and extract pertinent data. Bibliographies were also meticulously scrutinized to identify articles meeting our inclusion criteria.

The following variables were extracted: 1) demographic information, including age, sex, and preclinical history; 2) underlying conditions and genetic predispositions; 3) diagnostic modalities and sutures involved; 4) management strategies; 5) perioperative complications; 6) length of hospitalization including intensive care unit stay; 7) follow-up time; 8) clinical outcomes at last follow-up; and 9) limitations and recommendations. Moreover, to offer a thorough understanding and context of the extracted articles, bibliometric details including the type of article, journal name, number of reported cases, and country of origin were recorded for each study.

Statistical and Summary of Literature

Statistical analysis was carried out in R Studio (Version 4.3), focusing on predefined characteristics of interest relevant to our primary and secondary objectives. Meta-analysis was conducted with the aid of the packages *metafor*, *meta*, *and metadat*. Given the expected high variability among the individual studies included in this study, data aggregation was achieved using a random effects model. The Cochran Q statistic was employed to evaluate the heterogeneity across studies, while the I^2 test was used to measure the extent of this heterogeneity. We also calculated 95% prediction intervals to provide an estimate of the range within which the true effect size is expected to fall in future studies, accounting for between-study variability for studies with $I^2 > 99$. For visual representation, proportions were depicted in forest plots. Subgroup analysis was completed to explore how different categories within the population might affect the pooled proportions. In addition, our approach to summarizing categorical data involved computing frequencies and percentages for each category, derived from individual studies. For continuous data, we employed a strategy of calculating averages and standard deviations, pooling data from the multiple sources. Our reporting of descriptive statistics is grounded in the data that were accessible within each study. We have maintained transparency by explicitly stating the number of studies from which data extraction was successful and detailing the count of patients for each variable of interest, in the context of the total patient population within each study. A narrative summary was employed in reporting the challenges and proposed solutions extracted from the literature. To provide

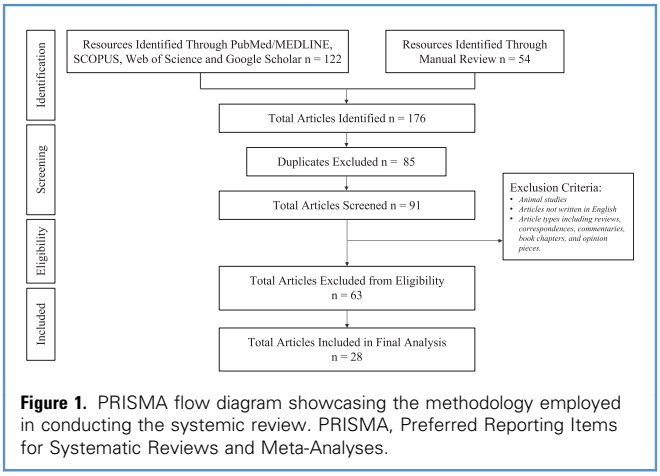

Figure 1. PRISMA flow diagram showcasing the methodology employed in conducting the systemic review. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1. Descriptive Analysis and Pooled Meta-Analyses of Demographics, Preclinical Characteristics, Diagnostics, Management, and Outcomes in the Original Articles

Variable	Percentage (Sum/Number of Patients in Article)	Prevalence (95% CI)	Number of Articles Reporting Variable	I^2
Patient demographics				
Mean age (years): 2.4 (1.1—3.7)			8	99.6
Male	56.6 (317/560)	64.3 (55.1—73.4)	12	78.4
Female	43.4 (243/560)	35.7 (26.6—44.9)	12	78.4
Signs and symptoms				
Head deformity	77.8 (332/427)	71.6 (45.6—97.7)	8	99.5
Visual disturbances/visual defects	52.6 (51/97)	60.8 (23.6—98.1)	3	95.0
Signs of elevated ICP	57.9 (51/88)	71.1 (28.5—100.0)	3	97.8
Abnormal facial appearance	29.8 (37/124)	27.3 (0.0—56.3)	3	94.3
Headache	64 (32/50)	64 (50.7—77.3)	2	0.0
Proptosis	34.7 (25/72)	45 (0.0—112.9)	2	98.3
Hypotelorism	18.5 (12/65)	28.7 (0.0—78.9)	2	94.5
Seizures	11.1 (8/72)	10.3 (3.3—17.3)	2	0.0
Genetic syndromes				
Syndromic synostosis	28.3 (89/315)	25.2 (13.7—36.6)	5	72.6
Crouzon	14.3 (45/315)	13.8 (9.9—17.6)	5	0.0
Apert	11.4 (32/282)	10.9 (7.2—14.5)	3	0.2
Pfeiffer	1.9 (5/266)	1.9 (0.2—3.5)	2	0.0
Saethre-Chotzen	2.3 (5/219)		1	
Carpenter	0.9 (2/219)		1	
Diagnostic modality				
CT scan	100 (175/175)	98.2 (96.3—100.0)	8	0.0
Radiograph	100 (50/50)	98.1 (94.3—100.0)	2	0.0
Cranial phenotype/sutures involved				
Oxycephaly	64 (32/50)	63.6 (0.0—132.2)	2	98.2
Posterior plagiocephaly/lambdoid synostosis	2.6 (7/271)	2.5 (0.7—4.4)	2	0.0
Anterior plagiocephaly/unicoronal synostosis	39 (119/305)	23.2 (5.1—41.3)	4	90.6
Brachycephaly/bi-coronal synostosis	19.4 (34/175)	18.2 (12.3—24.1)	5	6.7
Multiple suture synostosis	31.8 (116/365)	37.4 (8.8—65.9)	6	98.6
Scaphocephaly/sagittal suture synostosis	16.9 (71/420)	22.1 (13.5—30.8)	8	71.9
Trigonocephaly/metopic synostosis	16.7 (69/413)	31.5 (3.6—59.4)	8	99.1
Surgical management				
Surgical	100 (578/578)	99.6 (99.0—100.0)	12	0.0
Open surgery	99 (518/523)	99.5 (98.9—100.0)	10	1.7
Endoscopic technique	0.9 (5/523)	0.5 (0.0—1.1)	10	2.3
Surgical types				
Suturectomy/linear craniectomy/strip craniectomy	29 (139/479)	53.8 (23.4—84.2)	8	99.6
Cranial vault remodeling	81.5 (371/455)	72.9 (47.4—98.6)	6	99.4

CI, confidence interval; ICP, intracranial pressure; CT, computed tomography; CSF, cerebrospinal fluid.

Continues

Table 1. Continued

Variable	Percentage (Sum/Number of Patients in Article)	Prevalence (95% CI)	Number of Articles Reporting Variable	I^2
Fronto-orbital advancement	73.9 (219/296)	60.2 (17.4—100.0)	3	98.7
Distraction osteogenesis	3.3 (9/271)	24.6 (0.0—69.9)	4	99.7
Postoperative complications				
Complications	10.4 (12/115)	8.9 (2.2—15.5)	4	35.3
Surgical site infection	4.7 (2/43)	4.5 (0.0—10.8)	2	0.0
Dural tear	4.7 (2/43)	3.9 (0.0—11.4)	2	26.4
Hypotension	2.3 (1/43)	2.7 (0.0—7.4)	2	0.0
CSF leak	6.9 (3/43)	5.4 (0.0—11.6)	2	0.0
Outcome at last follow-up				
Follow-up range (months): 1—1.42				
Improved	96.2 (50/52)	95.6 (90.1—100.0)	3	0.0
Repeat surgery	7.1 (24/339)	5.9 (2.9—8.8)	5	14.6
Death	2.6 (2/77)	3.1 (0.0—6.9)	4	0.0

CI, confidence interval; ICP, intracranial pressure; CT, computed tomography; CSF, cerebrospinal fluid.

visual representation of the number of countries and craniosynostosis cases reported in the review, we created maps with R Studio using the *ggplot* package.

RESULTS

Electronic Search Yield

Our initial search yielded 176 sources (Figure 1). After removing 85 duplicates and examining 91 sources with our inclusion and exclusion criteria, we included 28 articles in our systematic review: 14 retrospective and prospective studies[10—23] with 620 patients (analyzed in Table 1 and summarized in Supplemental Table 1) and 14 case reports/series[24-37] with 27 patients (analyzed in Table 2 and summarized in Supplemental Table 2) for a total of 647 patients. The 28 studies came from 8 different African countries (Congo, Egypt, Ghana, Morocco, Nigeria, South Africa, Tanzania, and Tunisia) illustrated in Figure 2. Of the contributing countries, South Africa led with the highest number of studies, contributing 14 articles (51.9%), followed by Egypt with 6 publications (22.2%). Morocco and Tunisia each contributed 2 studies, representing 7.4% of the total. Regarding patient cohorts, South Africa accounted for the majority, with 547 of 647 patients (84.5%), while Egypt contributed 91 of 647 patients (14.1%).

Demographics, Clinical Characteristics, Diagnostics, Management Strategies, and Outcomes of Retrospective and Prospective Studies

Supplemental Table 1 provides a comprehensive summary of the demographics, clinical characteristics, diagnostics, management, and outcomes of patients extracted from the 14 retrospective/prospective studies included in our systematic study. Wall et al.[38] presented the largest cohort, with 219 patients, representing 35.3% of patients, on the other hand, the study with the smallest cohort, consisting of 8 patients, was conducted by Kleintjest et al.[39] They both originated from South Africa.

The mean age at presentation of 392 patients from 8 retrospective/prospective studies analyzed was 2.4 years (95% confidence interval [CI]: 1.1—3.7). In 12 articles, the gender distribution was 56.6% (317/560) males and 43.4% (243/560) females (Table 1). Among symptoms reported, abnormal head shape was the most common, reported in 77.8% (332/427) of patients in 8 articles. In 3 articles, visual disturbances were observed in 52.6% (51/97), while headaches were reported in 64.0% (32/50) of patients in 2 articles. Proptosis was identified in 34.7% (25/72) of patients, in 2 studies. Raised ICP was reported in 57.9% (51/88) of the patients across 3 studies. Craniometric data reporting was limited, with few articles providing detailed measurements. One article documented an average head circumference of 32.6 ± 69.36 cm for 47 patients.[15] The mean cephalic index, reported by 3 articles,[16,40,41] was 75.2. Craniometrics for 9 patients[16] in another study showed a mean cranial volume of 943.68 cm^3, with mean anterior and posterior cranial volumes of 298.21 cm^3 and 636.74 cm^3, respectively.

Diagnostic imaging techniques used across the studies included computed tomography (CT) scans for 87.5% of patients (175/200), radiographs in 36.0% of patients (50/139), magnetic resonance imaging in 11.5% of cases (18/157), and ultrasound in 10.3% of cases (16/155). Twelve articles detailed 99.6% (95% CI: 99.0%—100.0%), 578 patients, undergoing surgical treatment. Of the detailed surgical approach, in 10 articles, 99.6% (95% CI:

Table 2. Descriptive Analysis of the 27 Patients Included in the 14 Case Reports

Demographics	
Number of patients	27
Average age (years)	2.0 ± 2.5
Male	14 (51.9%)
Female	12 (44.4%)
	1 N/A
Presenting symptoms/comorbidities (n = 27)	
Abnormal head shape	27 (100.0%)
Average HC (cm)	34.5 ± 6.7
Developmental delay*	11 (40.7%)
Hydrocephalus	4 (14.8%)
Syndactyly	4 (14.8%)
Imaging modality (n = 27)	
CT scan	12 (44.4%)
MRI	7 (25.9%)
X-ray	8 (29.6%)
USG	4 (14.8%)
Surgical management (n = 6)	
Unilateral frontal advancement	2
Bilateral frontal advancement	2
Craniotomy	1
Unspecified	1
Syndromic Craniosynostosis (n = 20)	
Crouzon syndrome	4 (20.0%)
Apert syndrome	1 (5.0%)
Pfeiffer syndrome	3 (15.0%)
Carpenters syndrome	3 (15.0%)
9p Deletion syndrome	9 (45.0%)
Cranial phenotype/sutures involved (n = 24)	
Oxycephaly	1 (4.2%)
Brachycephaly/bi-coronal synostosis	1 (4.2%)
Anterior plagiocephaly/ unicoronal synostosis	7 (29.2%)
Trigonocephaly/metopic synostosis	11 (45.8%)
Scaphocephaly/sagittal suture synostosis	1 (4.2%)
Multiple suture synostosis	3 (12.5%)
Outcomes (N = 6)	
Improve	2
Did not improve	2
Death	2
Length of hospital stay in days†	24.7 ± 24.3
Follow-up period in years	4.1 ± 7.1

N/A, not available; HC, head circumference; 9p, long arm of Chromosome 9; CT, computed tomography; MRI, magnetic resonance imaging; USG, ultrasonography.

*Patients with developmental delay included 9 patients with 9p deletion syndrome and 1 patient with Carpenter syndrome.

†Two patients had extended hospital stays: one was admitted for 20 days due to poor clinical condition, and the other for 51 days. However, no additional details regarding the reasons for the prolonged stay were provided for the latter patient.

98.9%–100.0%) underwent open procedures and in 4 articles, 0.5% (95% CI: 0.0%–1.1%) had endoscopic surgery. In 6 articles, vault remodeling was adopted in 72.9% of patients (95% CI: 47.4%–98.6%). Of the reported vault remodeling procedures, fronto-orbital advancement was adopted in 60.2% (95% CI: 17.4%–100.0%) of cases in 3 articles. In 8 articles, strip craniectomy was adopted in 53.8% of patients (95% CI: 23.4%–84.2%). Adjunct management was reported in 1 study by Labuschagne et al. with 18 patients, all using orthotic helmet devices after endoscopic suture release.[10] One study by Fawzy et al. reported a mean intraoperative blood transfusion volume of 550 mL.[16] The estimated blood loss after surgery varied by type of management as reported by 2 studies.[10,13] In a comparative study conducted by Elhawary et al.,[13] the open technique (OT) and endoscopic technique were compared, revealing estimated blood loss of 55 mL for endoscopic technique and 150 mL for OT. Labuschagne et al.[10] reported a blood loss range of 5 to 30 mL in patients undergoing the flexible endoscope-assisted suture release procedure.

Regarding postoperative complications, cerebrospinal fluid leaks were reported in 5.4% (95% CI: 0.0%–11.6%) and surgical site infections in 4.5% (95% CI: 0.0%–10.8%). Follow-up period ranged between 1 and 1.42 months. Reoperation was necessary for 7.1% of patients (24/339) due to various indications, as reported in 5 articles. Among the articles addressing patient outcomes, 96.2% of cases (50/52 patients across 3 articles) showed improvements in head shape and neurological deficits at the last follow-up. The mortality rate at the last follow-up was 3.1% (95% CI: 0.0%–6.9%, 2 articles). Descriptive analysis on the data extracted from the 27 patients in the 14 case reports/series[24-37] are represented in **Table 2** and **Supplemental Table 2**.

Overall Proportion Estimates of Sutural Involvement

Twelve studies[13,15-17,19,21-23,38-41] met criteria for inclusion in our meta-analysis of sutural involvement (**Figure 3**). Four studies[13,19,22,38] were included in the proportional meta-analysis for anterior plagiocephaly, 8 studies[13,15,17,19,21,22,38,39] for scaphocephaly, 6 articles for multiple suture synostosis,[13,17,19,22,23,38] and 5 articles[15,19,21,38,39] for syndromic craniosynostosis. The pooled estimate of the proportion of anterior plagiocephaly was calculated for 305 patients, multiple suture synostosis for 365 patients, and scaphocephaly for 420 patients. Using the random effects model, the overall pooled estimate of anterior plagiocephaly was 23.2% (95% CI: 5.1%–41.3%, **Figure 3A**), that for multiple suture synostosis was 37.4% (95% CI: 8.8%–65.9%, **Figure 3B**), and scaphocephaly 22.1% (95% CI: 13.5%–30.8%, **Figure 3C**). In 5 studies,[15,17,19,21,22] brachycephaly/bi-coronal synostosis was estimated at 18.2% (95% CI: 12.3%–24.1%) and in 8 articles[13,15-17,21,22,38,39] trigonocephaly/metopic synostosis was estimated at 31.5% (95% CI: 3.6%–59.4%). The pooled estimate of the proportion of syndromic craniosynostosis was estimated at 25.2% (95% CI: 13.7%–36.6%, **Figure 3D**).

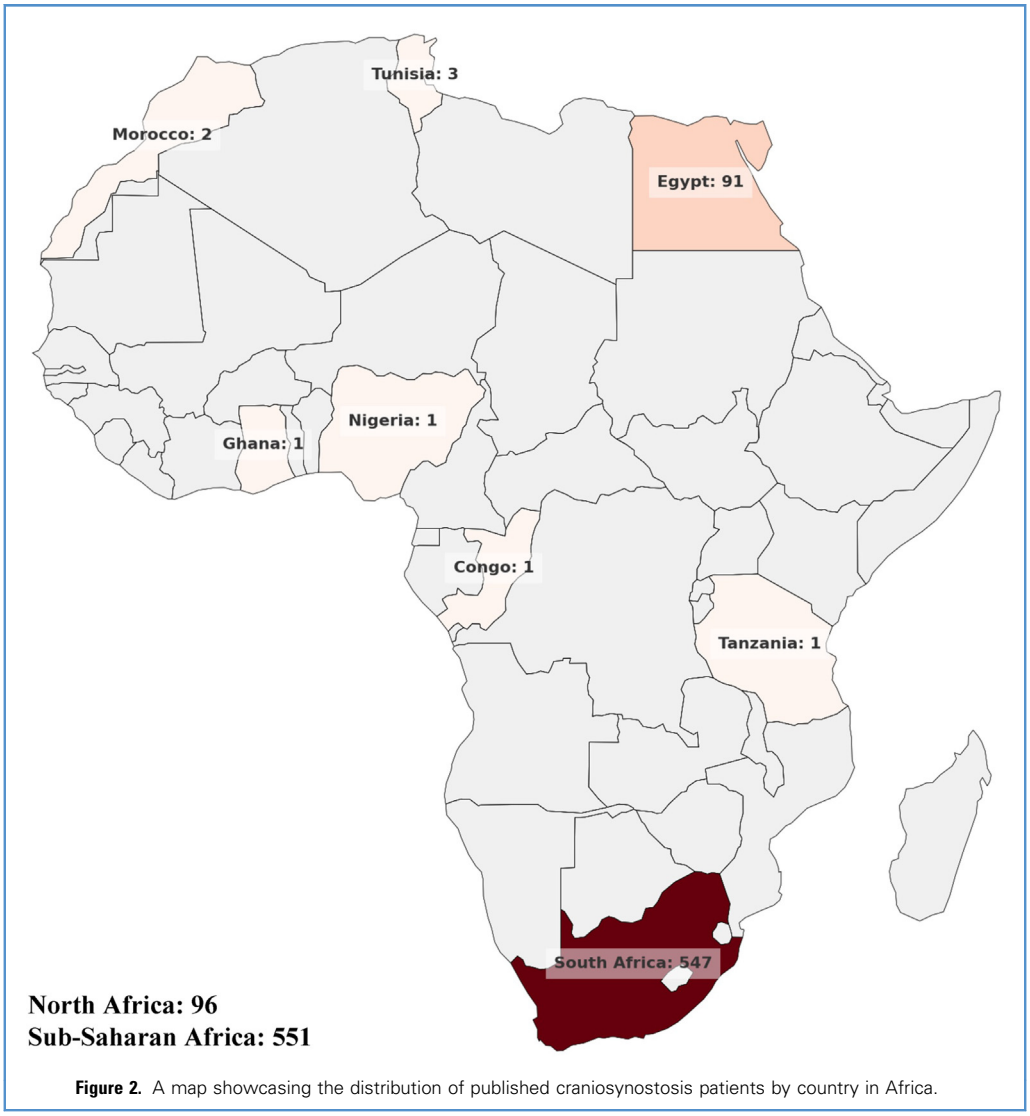

Figure 2. A map showcasing the distribution of published craniosynostosis patients by country in Africa.

Challenges and Proposed Solutions

The management of craniosynostosis in Africa is confronted with diverse challenges across different countries, necessitating tailored solutions to improve outcomes. **Table 3** highlights country-specific challenges and proposed solutions for craniosynostosis patient care across Africa. In Congo, the reported absence of specific genetic data and the difficulty in accessing the region for research highlight the need for targeted genetic studies.[31] In Ghana, the author of a case report highlighted the challenge of malfunctioning diagnostic equipment like CT scanners and buttressed the importance of integrating clinical features with molecular studies for timely diagnosis.[27] Morocco and Tunisia face limited exposure to rare syndromes and complex surgeries, respectively, calling for enhanced diagnostic capabilities and advanced prenatal diagnostic techniques.[24,32] Nigeria's challenges, from insufficient specialist training to inadequate healthcare infrastructure, call for enhanced training, robust data management, and research collaborations, with potential growth in medical tourism to advance management.[26]

In South Africa, the challenges reported are extensive and include difficulties in ensuring regular postoperative attendance and care due to socioeconomic, expertise, and geographical constraints.[1,5] This is further exacerbated by limited access to and understanding of genetic testing, alongside managing the complications of open surgical procedures in a resource-limited setting.[1,5,41] The recommendations for South Africa include adopting less invasive and more cost-effective surgical approaches, improving early detection rates through education on the phenotypic spectrum of craniosynostosis, and considering innovative solutions such as outsourcing the production and fitting of orthotic helmets to reduce overall treatment costs.[1,5,40,41] In the included Tanzanian article, the

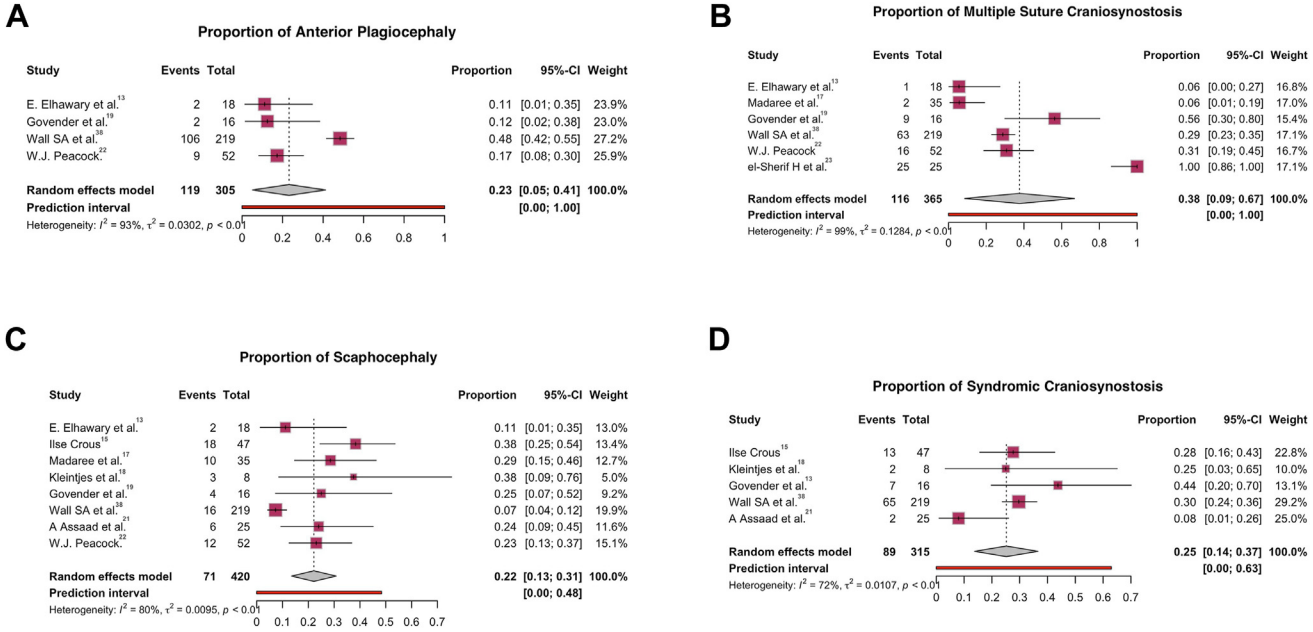

Figure 3. Forest plots for the pooled proportions of (**A**) anterior plagiocephaly, (**B**) multiple suture synostosis, (**C**) scaphocephaly, and (**D**) syndromic synostosis in Africa.

authors report that the country's primary challenge lies within education, marked by an absence of dysmorphology training within the medical curriculum. This deficiency is essential for the early detection and management of complex syndromes like craniosynostosis.[25] The proposed solution emphasizes the importance of a multidisciplinary approach in the management of patients, necessitating the integration of dysmorphology training into the medical education system to equip future healthcare professionals with necessary skills and knowledge.[25] Collectively, these highlight the need for bolstering healthcare infrastructure, enhancing professional training and fostering research to effectively manage craniosynostosis in Africa.

DISCUSSION

Currently, there is a lack of a comprehensive review of craniosynostosis in Africa. Left untreated, this condition greatly impacts neurocognitive development, cosmetic appearance, and overall quality of life (QOL) of children.[42,43] While craniosynostosis is mainly a clinical diagnosis often detected within the first year of life, skull x-ray and cranial CT can be used to confirm diagnosis and help plan surgical reconstruction.[1,2,5] Assessment of genetics is also a crucial step in evaluation when syndromic craniosynostosis is suspected.[44] In addition to improving cosmetic appearance, the goal of surgery is to create sufficient space in the cranial vault to allow for proper brain development.[1] Timely surgical intervention can lead to exceptional outcomes, such as normal brain growth and development.[45] In our review, a significant proportion of patients who underwent surgery showed improvements in both phenotypic and neurological aspects during the last follow-up. Notably, postoperative complications were minimal, with only 2 reported deaths. Despite the challenges encountered in diagnosing and treating craniosynostosis in resource-limited settings, it is imperative to explore potential solutions to enhance patient outcomes. Additionally, there is a need to investigate avenues for developing research in this setting to address the specific needs and challenges faced by patients in resource-limited environments.

In our review, the mean age at diagnosis was estimated to be 2.4 years. In the United States, the mean age at diagnosis is about 4.1 months.[46] With initial suspicions and diagnoses typically made clinically soon after birth, regional differences in the reported ages at diagnosis may stem from various factors, including limited early identification—especially in nonsyndromic cases—and occasionally, missed early signs by pediatricians or neurologists, resulting in delayed referrals to neurosurgeons.[1,47,48] Limited awareness among primary care providers further contributes to these delays, as only a small percentage of initial cases are identified at the primary care level, with many diagnoses ultimately relying on proactive parental concerns.[49] Craniosynostosis syndromes are diagnosed much earlier due to the presence of easily identifiable physical features.[15] In our study, an abnormal head shape was the most common clinical feature, similar to reported findings of Johnson and Wilkie in 2011.[50] Headaches, vomiting, and fatigue are common symptoms of and along with visual disturbances which suggest elevated ICP.[51] Typically, craniosynostosis presents with an abnormal head shape and dysmorphic features; however, in our review, we identified visual disturbances,

headaches, and raised ICP as frequently reported symptoms. These findings, alongside the mean age at presentation, likely reflect the severity of cases in the African context and highlight the challenges in managing these patients. This severity also potentially highlights the limited access to early intervention and less-invasive procedures, which have demonstrated safety and efficacy but may be less accessible, further impacting patient outcomes and management approaches.[52-54] Most craniosynostosis cases are nonsyndromic, with a pooled prevalence of 26% in our study identifying as syndromic; this was consistent with literature, with reported rates of 20%–25%.[1,55] The limited data in this review, however, may result in the underestimation of the true rate of syndromic craniosynostosis in Africa.

Craniometrics play an essential role in the management and follow-up of patients, providing insights into progression and success of treatments. In our study, the mean head circumference was 32.6 cm, a measurement reported by 1 article.[15] Preoperative mean cephalic index was documented in 3 articles, highlighting its use in assessing patients and planning surgery. There was a gap regarding postoperative craniometrics, however. Incorporating craniometric evaluation both before and after surgery helps to enhance patient care and outcomes.[56] In our analysis, CT scans were the most reported diagnostic/preoperative imaging modality adapted. Plain radiographs were reported in 2 studies only,[21,23] both of which reported cases from over 35 years ago. Regarding imaging, the general consensus is to minimize CT use as much as possible in young children due to the risks associated with radiation, at least until after the first year.[57] Magnetic resonance imaging, effective for brain assessment, lacks the precision for cranial sutures offered by CT but offers improved visualization of brain anomalies.[58] Despite this, the reported figures indicate that, in the majority of cases, the appropriate imaging modality is obtained prior to surgical intervention. However, challenges in accessing imaging scanners and the barriers contributing to imaging delays in Africa are beyond the scope of this study but have been well documented in the extant literature. Compared to Boulet et al.[7] where sagittal synostosis prevailed at 40%–60%, our study found anterior plagiocephaly most common. Sagittal synostosis was seen to be the second most common suture involved in our study, aligning with broader literature.[59] Our study observed trigonocephaly third among mono-sutural types, differing from a Dutch study that found sagittal and metopic most common.[60] Unlike Hwang et al.,[44] who noted a 15% prevalence of multiple suture craniosynostosis, our study revealed higher proportion of 38% in the involvement of multiple sutures. The observed discrepancy in the distribution of craniosynostosis subtypes compared to international data likely reflects both under-reporting and a scarcity of available data from African countries. These limited data may be biased toward more severe cases, as these are more likely to be documented and reported.

Renier et al.[61] emphasize that most cases, including scaphocephaly, often require fronto-cranial remodeling, with severe forms needing extensive skull vault reconstruction. Fronto-orbital advancement is particularly effective for correcting anterior cranial vault anomalies and was the most reported vault remodeling surgery in our study, aligning with our reported high numbers of anterior plagiocephaly. Early surgical intervention, ideally between 4 and 8 months for nonsyndromic cases, as suggested by Layliev et al.,[62] leads to better outcomes. Largely however, the type and timing of surgery depend on the age and suture involved.[63-65] Majority of patients had correctional surgery for their synostosis with 578 reported cases. Surgery can be performed either via open or endoscopic approach, each with specific indications and benefits; however, not all craniosynostoses are amenable to endoscopic correction.[52-54] Endoscopic surgery is typically indicated for infants aged less than 6 months with metopic or sagittal craniosynostosis and is associated with minimal blood loss and tissue disruption, shorter hospital stay, and operative times compared to open surgery.[52-54] This approach is particularly beneficial in cases requiring less extensive suture release, such as in single suture synostosis. It is often accompanied by postoperative use of cranial helmets, as seen in one included article,[52] to allow for directed cranial growth. On the other hand, open surgery, traditionally the standard of care, is often reserved for more complex synostoses and older infants.[63,64] Open techniques are usually postponed until the infant reaches 9 to 12 months.[65] While endoscopic surgery offers advantages in some scenarios, its limited use in the reviewed studies highlights several barriers to diagnostics and care. Key challenges include the high cost of the specialized equipment required for endoscopic procedures, limited availability of trained surgeons proficient in these techniques, and inadequate infrastructure to support such advanced surgical approaches.[66] In contrast, open surgery, although associated with longer recovery periods and increased blood loss, is potentially more widely practiced due to its lower resource demands and the broader availability of surgeons trained in traditional methods. Addressing these barriers requires investment in capacity-building initiatives, such as training programs, and improved access to surgical equipment, which could facilitate the adoption of less-invasive techniques in Africa, ultimately improving patient outcomes. This is exemplified by a recent model that resulted in the establishment of a craniofacial practice in southern Ghana, laying a strong foundation for future initiatives.[67] Similar programs are essential to bridging the treatment gap and enhancing the QOL for affected patients. In our study, the average age of the patients and the substantial reporting of multiple suture synostosis are also potential factors probably contributing to the prevalent use of open surgery in cases examined in the review. Both techniques aim to alleviate the constraints on brain growth and improve cranial aesthetics.[63]

The reoperation rate was 7.1%, with a similar rate of 7.2% reported by Sloan et al.[68] but higher than 2.4% reported by Jubbal et al.[69] Reoperation rates reported in literature vary widely, from as low as 1% to 100%.[52,70] The need for subsequent surgery arises from diverse factors, including cosmetic enhancements or to address ICP or brain

Table 3. Challenges and Proposed Solutions for Comprehensive Management of Craniosynostosis in Africa

Country	Challenges	Recommendations and Proposed Solutions
Congo	1. Central African region not previously known as polymorphic in available databases and sequence data from the Congolese population are not available in existing databases.[31] 2. Central African region is poorly accessible for genetic studies.[31]	1. Even in cases of a well-known genetic condition with known spectrum of mutations, it is useful to reach a molecular diagnosis as discovering novel mutations allows for further insight into their pathogenesis.[31]
Ghana	1. Unable to obtain CT head scan at hospital due to equipment malfunction.[27]	1. Combining clinical features and molecular studies can allow for quicker diagnosis, counseling, and management of infants with Pfeiffer syndrome in low-resource settings to offset the risk of abandonment of neonates with dysmorphic features.[27]
Morocco	1. Lack of exposure to rare syndrome.[24]	1. To improve diagnostic ability, may consider prenatal investigations consisting of fetal ultrasound or MRI and genetic testing in addition to postnatal craniofacial CT with 3D reconstruction, brain MRI, and possible preoperative MRI with angiographic sequences to detect venous malformations.[24]
Nigeria	1. Some specialists may not have optimal exposure because of the limited spectrum of practice, while others with international exposure return to Africa with limited and absence of equipment and support staff.[26] 2. Limited staff support—no dedicated pediatric ICU or trained pediatric intensivist.[26] 3. Lack of neurosurgical, imaging, and radiotherapy equipment.[26] 4. Lack of research and innovation.[26]	1. Training a team of neurosurgeons with support staff to enhance the care of patients.[26] 2. Development of functional systems; data storage and retrieval and the use of protocols.[26] 3. Institutional collaboration to improve the quality of research and the ability to place them in more visible journals.[26] 4. Explore sub-Saharan Africa as a site for medical tourism.[26]
South Africa	1. Inability for regular postoperative attendance and care required following less invasive procedures given socioeconomic, lack of expertise, and geographical constraints in lower income and developing countries.[1,5] 2. Genetic testing access is limited in the public sector in South Africa. It is expensive when available and limited understanding of its value reduces utilization.[1,5] 3. Managing complications of open procedures is challenging in low- and middle-income countries due to limited medical resources, lack of expertise and large multidisciplinary teams, and frequently scarce and expensive blood products.[1,5] 4. Universal need to reduce cost of healthcare within low- and middle-income countries.[41]	1. Application of expedient and effective approaches such as open remodeling.[1,5] 2. Education and practice with recognizing the phenotypic spectrum of craniosynostosis will allow for improved, earlier detection rates and may lead to improved patient outcomes.[40] 3. Providers working with limited resources in low- and middle-income countries may consider less invasive techniques for craniosynostosis repair such as either rigid or flexible endoscope-assisted suturectomy.[41] 4. Applying an endoscopic approach and outsourcing orthotic helmet production and fitting to a third party is close to 50% more cost-effective than an open approach.[41]
Tanzania	1. Lack of dysmorphology training within the medical curriculum in low-resource settings.[25]	1. A multidisciplinary approach is vital in the management of patients with Carpenter syndrome.[25]
Tunisia	1. Limited experience with complex surgeries for correction of abnormalities associated with Pfeiffer syndrome.[32]	1. Screen parents for mosaicism if history of prior fetus with Pfeiffer syndrome.[32] 2. Application of fetal ultrasonography exploring the head, face, and extremities in combination of 3-dimensional ultrasound examination, fetal MRI, and molecular biology analysis for prenatal diagnosis.[32]

CT, computed tomography; MRI, magnetic resonance imaging; 3D, 3-dimensional; ICU, intensive care unit.

development issues. This need also depends on the type and extent of the deformity and the specific sutures involved. Staged operations are often recommended, particularly for syndromic patients.[52,70-73] The likelihood of undergoing a second surgery also varies depending on the surgical approach employed, age of patient, and the specific suture affected.[73,74] Additionally, syndromic craniosynostoses are linked to significantly increased reoperation rates.[70] Although craniometric evaluations, neurocognitive development, and QOL are crucial in assessing craniosynostosis outcomes, these metrics were under-reported in the included studies. None assessed QOL or cognitive outcomes as primary endpoints, and only 4 studies[15,16,40,41] mentioned craniometrics all of which are important outcome measures crucial for evaluating patient recovery.[75,76] This reflects a significant gap in the existing literature,

limiting our ability to provide a comprehensive analysis of long-term surgical outcomes. Future research should address these deficiencies to fully capture the impact of surgical interventions on patients' overall well-being and functional development in Africa. Such an approach would provide a more nuanced understanding of treatment efficacy and guide evidence-based improvements in craniosynostosis management.

Limitations

This systematic review on craniosynostosis encountered several limitations, which we delineate to provide a comprehensive and critical evaluation of the evidence. The examined literature exhibited significant heterogeneity, posing challenges in conducting a standardized analysis. Despite our broad search strategy across multiple databases, this yielded few articles on the topic. The exclusion of non-English articles from the analysis, while practical, may have inadvertently led to the omission of significant contributions from non-English–speaking countries. The exclusion of these articles poses a limitation in terms of the representativeness and inclusivity of our findings, potentially overlooking valuable insights and pertinent data. Additionally, the temporal variability among the included studies, as they span several years during which significant advancements in healthcare practices, technology, and craniosynostosis management strategies may have occurred. This variability could affect the relevance and applicability of older study findings in current healthcare settings.

This scarcity of literature reflects the niche nature of the subject and compounds the depth of analysis possible. This was compounded by the geographic coverage of our study with data collected from only 8 African countries, which represents 14.8% of the continent. Specifically, most of the studies originate from South Africa and Egypt. More than 99% of the patients included in this review are from these 2 countries, with 85% from South Africa alone. This skewed distribution introduces a substantial bias toward the healthcare practices and outcomes of these countries, limiting the generalizability of our findings to the entire continent. The disparities in resources, healthcare infrastructure, and medical expertise mean that the conclusions derived from studies included in this review cannot be readily extrapolated to other parts of the continent. It is essential to recognize that the differences in care provision across the continent necessitate cautious interpretation of our findings and highlight the need for more regionally inclusive studies to bridge gaps in the literature and to capture a more comprehensive understanding of this condition across Africa.

While this review provides valuable insights into craniosynostosis in Africa, the limited geographic representation and the significant bias toward 2 country data are critical limitations that restrict the applicability of our conclusions to the entire African continent. Future research should aim to include a more diverse range of studies from various regions across Africa to provide a more comprehensive understanding of craniosynostosis and its management on the continent.

Future Directions

Improving craniosynostosis care in Africa requires specialized infrastructure, supported by international collaborations, targeted investments, and private initiatives. Programs like the WFNS equipment donation highlight scalable models for growth.[77] Developing a skilled pediatric neurosurgical workforce lies at the heart of improving care for these patients and relies on education, international collaboration, and ongoing training. Partnerships with global institutions and local programs to provide expertise and practical skills. Simulation laboratories and localized research foster innovation, ensuring sustainable improvements. Training local professionals reduces dependence on external expertise, while collaborations with high income countries facilitate resource sharing and improved outcomes. These initiatives bridge disparities and extend care to underserved regions.

Moving forward, this review lays the groundwork for future research endeavors in the field of craniosynostosis in Africa. There is a pressing demand for studies delving into the long-term effects of surgical interventions. Such research should encompass not only the evaluation of physical outcomes but also place considerable emphasis on assessing developmental milestones and QOL metrics. Expanding the scope to encompass these will provide a more comprehensive understanding of the efficacy and impact of surgical interventions in craniosynostosis patients. Additionally, comparative studies in African patients between open and endoscopic surgical techniques could offer invaluable insights into the efficacy, safety profiles, and patient outcomes associated with each method, potentially guiding surgical best practices. The future landscape of research on craniosynostosis would benefit immensely from a more rigorous approach to data reporting. Standardizing these data points across studies will enable a more seamless comparison and synthesis of results.

CONCLUSION

There have been few studies on craniosynostosis in Africa, highlighting the need for more research to better understand this condition within the continent. Despite limited resources, treatment of craniosynostosis in Africa using OTs yields few complications and a low mortality rate. Improving patient outcomes relies on expanding neurosurgical training, research, and collaboration.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Kwadwo Darko: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing — original draft, Writing — review & editing. **Sonia Pulido:** Conceptualization, Data curation, Writing — original draft, Writing — review & editing. **Muhammad Ammar Haider:** Conceptualization, Data curation, Writing — original draft. **Milan Sivakumar:** Data curation, Writing — original draft, Writing — review & editing. **Bernice Limann:** Data curation, Formal analysis, Writing — original draft, Writing — review & editing. **Pearl Tenkorang:** Data curation, Methodology, Writing — original draft, Writing — review & editing. **Okikioluwa Odesanya:** Data curation, Writing — original draft, Writing — review & editing. **Peace Odiase:** Conceptualization, Formal analysis, Visualization. **Mark Farid:** Data curation, Formal analysis, Visualization. **Umaru Barrie:** Conceptualization, Data

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REFERENCES

1. Kajdic N, Spazzapan P, Velnar T. Craniosynostosis - recognition, clinical characteristics, and treatment. *Bosn J Basic Med Sci*. 2018;18:110-116.
2. Kabbani H, Raghuveer TS. Craniosynostosis. *Am Fam Physician*. 2004;69:2863-2870.
3. Kimonis V, Gold JA, Hoffman TL, Panchal J, Boyadjiev SA. Genetics of craniosynostosis. *Semin Pediatr Neurol*. 2007;14:150-161.
4. Ciurea AV, Toader C. Genetics of craniosynostosis: review of the literature. *J Med Life*. 2009;2:5-17.
5. Betances EM, Mendez MD, J MD. *Craniosynostosis*. Treasure Island (FL): StatPearls; 2023.
6. Chim H, Manjila S, Cohen AR, Gosain AK. Molecular signaling in pathogenesis of craniosynostosis: the role of fibroblast growth factor and transforming growth factor-beta. *Neurosurg Focus*. 2011;31:E7.
7. Boulet SL, Rasmussen SA, Honein MA. A population-based study of craniosynostosis in metropolitan Atlanta, 1989-2003. *Am J Med Genet*. 2008;146A:984-991.
8. Lajeunie E, Le Merrer M, Bonaiti-Pellie C, Marchac D, Renier D. Genetic study of nonsyndromic coronal craniosynostosis. *Am J Med Genet*. 1995;55:500-504.
9. Shlobin NA, Baticulon RE, Ortega CA, et al. Global epidemiology of craniosynostosis: a systematic review and meta-analysis. *World Neurosurg*. 2022;164:413-423.e3.
10. Labuschagne HC, Moodley H. Risk stratification of hospital admissions for COVID-19 pneumonia by chest radiographic scoring in a Johannesburg tertiary hospital. *J Neurosurg*. 2023;31:71-77.
11. Vensuya Bisetty LL, Harrichandparsad R. Anil madaree morphometric analysis of the cranial fossae in scaphocephalic patients: an anatomical basis. *J Craniofac Surg*. 2022;33:1375-1380.
12. Nivana Mohan LL, Harrichandparsad R. Anil madaree anterior synostotic plagiocephaly: a quantitative analysis of craniofacial features using computed tomography. *J Craniofac Surg*. 2022;33:2339-2349.
13. Mohamed E, Elhawary MA. Mohamed gabr outcomes of surgical management of metopic synostosis : a retrospective study of 18 cases. *J Kor Neurosurg*. 2022;65:107-113.
14. Anil MWMMM. Novel method of lateral vault modification in scaphocephaly. *J Craniofac Surg*. 2021;32:2859-2863.
15. Crous I. *Craniosynostosis in a South African Population*. Faculty of Health Sciences, Division of Human Genetics, University of Cape Town; 2021.
16. Hossam Hassan Fawzy J-WC, Choi JW, Ra YS. One-piece fronto-orbital distraction with midline splitting but without bandeau for metopic craniosynostosis: craniometric, volumetric, and morphologic evaluation. *Ann Plast Surg*. 2019;83:285-292.
17. Anil Madaree WMMM. Use of acellular dermal Matrix in craniosynostosis. *J Craniofac Surg*. 2018;29:126-129.
18. Kleintjes WG. Craniofacial abnormalities in twins at tygerberg hospital, craniofacial unit. *J Craniofac Surg*. 2005;16:169-171.
19. Govender PV, Nadvi SS, Madaree A. The value of transcranial Doppler ultrasonography in craniosynostosis. *J Craniofac Surg*. 1999;10:260-263.
20. Wall JHG SA, Hockley AD, Wake MJ, Poole MD, Briggs M, Briggs M. Fronto-orbital re-operation in craniosynostosis. *Br J Plast Surg*. 1994;47:180-184.
21. A Assaad AAG, Gheita AA. Experience in Egypt with 25 cases of craniosynostosis and forehead advancement. *Child's Nerv Syst*. 1987;3:219-221.
22. Peacoc WJ. The treatment of craniosynostosis. *SAMJ*. 1982;62:49-51.
23. Hassanein El-Sherif ASK, Abou-Senna AM. Adley farid ghaly craniosynostosis in Egypt. *J Neurosurg*. 1970;33:29-34.
24. Bouare F, Noureldine MHA, Hajhouji F, Ghannane H, Jallo GI, Ait Benali S. Complex craniosynostosis in the context of Carpenter's syndrome. *Childs Nerv Syst*. 2022;38:831-835.
25. Lodhia J, Rego-Garcia I, Koipapi S, et al. Carpenter syndrome in a patient from Tanzania. *Am J Med Genet*. 2021;185:986-989.
26. Bot G, Constantini S, Shilong D, et al. Orbital advancement using the modified buttress technique in sub-Saharan Africa: a demonstrative case report. *Ann Med Res Practice*. 2021;2:2.
27. Danso KA, Akuaku RS, Young FNA, Wiafe SA. Pfeiffer syndrome type 3 with FGR2 c.1052C>G (p.Ser351Cys) variant in West Africa: a case report. *Pan Afr Med J*. 2021;40:136.
28. Mohamed AM, Kamel AK, Eid MM, et al. Chromosome 9p terminal deletion in nine Egyptian patients and narrowing of the critical region for trigonocephaly. *Mol Genet Genomic Med*. 2021;9:e1829.
29. Ben Nsir A, Darmoul M, Zemmali M, Slimane A, Hattab N. Plagiocephaly due to frontosphenoidal suture synostosis: report of 2 cases and literature review. *Pediatr Neurosurg*. 2016;51:204-209.
30. Salahiddine S, Anass A. A rare case of a familial form of nonsyndromic trigonocephaly. *PAMJ*. 2015;21, 2015-08-07.
31. Lumaka A, Mubungu G, Mukaba P, et al. A novel heterozygous mutation of three consecutive nucleotides causing Apert syndrome in a Congolese family. *Eur J Med Genet*. 2014;57:169-173.
32. Ben Hamouda H, Tlili Y, Ghanmi S, et al. Pfeiffer syndrome type II discovered perinatally: report of an observation and review of the literature. *Diagn Interv Imaging*. 2012;93:785-789.
33. Hlongwa P. Early orthodontic management of Crouzon Syndrome: a case report. *J Maxillofac Oral Surg*. 2009;8:74-76.
34. Jeftha A, Stephen L, Morkel JA, Beighton P. Crouzonodermoskeletal syndrome. *J Clin Pediatr Dent*. 2004;28:173-176. Winter.
35. Farag HM, Kotb SM, Sweify GA, Fawzy RK, Ismail SR. A diagnostic clinical genetic study of craniofacial dysmorphism. *East Mediterr Health J*. 1999;5:470-477.
36. Samson G, Gardner JC. Craniosynostosis, microcephaly, hydrancephaly, humero-radial synostosis, and thumb aplasia: a new syndrome? *Am J Med Genet*. 1996;61:174-177.
37. Christianson AL, Van Allen MI. Sutural exostoses, rib hyperostoses, craniosynostosis, mental retardation with focal fat deposition: Proteus syndrome? *Am J Med Genet*. 1996;66:150-153.
38. Wall SA, Goldin JH, Hockley AD, Wake MJ, Poole MD, Briggs M. Fronto-orbital re-operation in craniosynostosis. *Br J Plast Surg*. 1994;47:180-184.
39. Kleintjes WG. Craniofacial abnormalities in twins at tygerberg hospital, craniofacial unit. *J Craniofac Surg*. 2005;16:169-171.
40. Bisetty V, Lazarus L, Harrichandparsad R, Madaree A. Morphometric analysis of the cranial fossae in scaphocephalic patients: an anatomical basis. *J Craniofac Surg*. 2022;33:1375-1380.
41. Labuschagne J, Mutyaba D, Ouma J, Dewan MC. Flexible endoscope-assisted suture release and barrel stave osteotomy for the correction of sagittal synostosis. *J Neurosurg Pediatr*. 2023;31:71-77.
42. Speltz ML, Collett BR, Wallace ER, et al. Intellectual and academic functioning of school-age children with single-suture craniosynostosis. *Pediatrics*. 2015;135:e615-e623.
43. Burokas L. Craniosynostosis: caring for infants and their families. *Crit Care Nurse*. 2013;33:39-50. quiz 51.
44. Hwang SK, Park KS, Park SH, Hwang SK. Update of diagnostic evaluation of craniosynostosis with a focus on pediatric systematic evaluation and genetic studies. *J Korean Neurosurg Soc*. 2016;59:214-218.
45. Esparza J, Hinojosa J, Garcia-Recuero I, Romance A, Pascual B, Martinez de Aragon A. Surgical treatment of isolated and syndromic craniosynostosis. Results and complications in 283 consecutive cases. *Neurocirugia (Astur)*. 2008;19:509-529.
46. Seruya M, Oh AK, Boyajian MJ, et al. Age at initial consultation for craniosynostosis: comparison across different patient characteristics. *J Craniofac Surg*. 2013;24:96-98.

47. Nguembu S, Kanmounye US, Tetinou F, Djiofack D, Takoukam R. Barriers to management of nontraumatic neurosurgical diseases at 2 Cameroonian neurosurgical centers: cross-sectional study. *World Neurosurg*. 2020;139:e774-e783.

48. Reddy K, Hoffman HJ, Armstrong D. Delayed and progressive multiple suture craniosynostosis. *Neurosurgery*. 1990;26:442-448.

49. Ivanov VP, Sakhno LP, Shchetinina AM, Kim AV, Trushcheleva SV. Early diagnosis and surgical treatment of craniosynostoses. *Ros Vest Perinatol i Pediatr (Russ Bullet Perinatol Pediatr)*. 2022;67:62-67.

50. Johnson D, Wilkie AO. Craniosynostosis. *Eur J Hum Genet*. 2011;19:369-376.

51. Still MEH, Chidarala S, Alvarado A, Neal D, Governale L, Ching J. Craniosynostosis surgery for increased intracranial pressure. *J Craniofac Surg*. 2022;33:1454-1457.

52. Riordan CP, Zurakowski D, Meier PM, et al. Minimally invasive endoscopic surgery for infantile craniosynostosis: a longitudinal cohort study. *J Pediatr*. 2020;216:142-149.

53. Meier PM, Goobie SM, DiNardo JA, Proctor MR, Zurakowski D, Soriano SG. Endoscopic strip craniectomy in early infancy: the initial five years of anesthesia experience. *Anesth Analg*. 2011;112:407-414.

54. Bonfield CM, Sharma J, Cochrane DD, Singhal A, Steinbok P. Minimizing blood transfusions in the surgical correction of craniosynostosis: a 10-year single-center experience. *Childs Nerv Syst*. 2016;32:143-151.

55. Armand T, Schaefer E, Di Rocco F, Edery P, Collet C, Rossi M. Genetic bases of craniosynostoses: an update. *Neurochirurgie*. 2019;65:196-201.

56. Patel KB, Eldeniz C, Skolnick GB, et al. 3D pediatric cranial bone imaging using high-resolution MRI for visualizing cranial sutures: a pilot study. *J Neurosurg: Pediatrics PED*. 2020;26:311-317.

57. Badve CA, K MM, Iyer RS, Ishak GE, Khanna PC. Craniosynostosis: imaging review and primer on computed tomography. *Pediatr Radiol*. 2013;43:728-742.

58. Arora V, Sidhu BS, Singh K. Comparison of computed tomography and magnetic resonance imaging in evaluation of skull lesions. *Egyptian J Radiol Nuclear Med*. 2022;53:67.

59. Singer S, Bower C, Southall P, Goldblatt J. Craniosynostosis in Western Australia, 1980-1994: a population-based study. *Am J Med Genet*. 1999;83:382-387.

60. Cornelissen M, Ottelander B, Rizopoulos D, et al. Increase of prevalence of craniosynostosis. *J Cranio-Maxillo-Fac Surg*. 2016;44:1273-1279.

61. Renier D, Lajeunie E, Arnaud E, Marchac D. Management of craniosynostoses. *Childs Nerv Syst*. 2000;16:645-658.

62. Layliev J, Gill R, Spear M, Cifuentes J, Wang L, Kelly KJ. The optimal timing for primary cranial vault reconstruction in nonsyndromic craniosynostosis. *J Craniofac Surg*. 2016;27:1445-1452.

63. Hoffman C, Valenti AB, Odigie E, Warren K, Premaratne ID, Imahiyerobo TA. Impact of health disparities on treatment for single-suture craniosynostosis in an era of multimodal care. *Neurosurg Focus*. 2021;50:E13.

64. Tombeng M, Niryana I. Open suturectomy management in craniosynostosis of bilateral coronal and metopic suture. *Neurologico Spinale Medico Chirurgico*. 2021;4:15-18, 03/31.

65. Selber JC, Brooks C, Kurichi JE, Temmen T, Sonnad SS, Whitaker LA. Long-term results following fronto-orbital reconstruction in nonsyndromic unicoronal synostosis. *Plast Reconstr Surg*. 2008;121:251e-260e.

66. Wireko AA, Ahluwalia A, Ali SH, et al. Insights into craniosynostosis management in low- and middle-income countries: a narrative review of outcomes, shortcomings and paediatric neurosurgery capacity. *SAGE Open Med*. 2024;12:20503121241226891.

67. Obiri-Yeboah S, Boakye FN, Nii Lamy Larmie R, et al. Craniofacial surgery in a low-resource setting: the successes, challenges, and prospects. *FACE*. 2024;5:174-181.

68. Sloan GM, Wells KC, Raffel C, McComb JG. Surgical treatment of craniosynostosis: outcome analysis of 250 consecutive patients. *Pediatrics*. 1997;100:E2.

69. Jubbal KT, Agrawal N, Hollier LH Jr. Analysis of morbidity, readmission, and reoperation after craniosynostosis repair in children. *J Craniofac Surg*. 2017;28:401-405.

70. Wong GB, Kakulis EG, Mulliken JB. Analysis of fronto-orbital advancement for Apert, Crouzon, pfeiffer, and saethre-chotzen syndromes. *Plast Reconstr Surg*. 2000;105:2314-2323.

71. Adamo MA, Pollack IF. A single-center experience with symptomatic postoperative calvarial growth restriction after extended strip craniectomy for sagittal craniosynostosis. *J Neurosurg Pediatr*. 2010;5:131-135.

72. Cetas JS, Nasseri M, Saedi T, Kuang AA, Selden NR. Delayed intracranial hypertension after cranial vault remodeling for nonsyndromic single-suture synostosis. *J Neurosurg Pediatr*. 2013;11:661-666.

73. Mossop CM, Rogers G, Boyajian M, Myseros JS, Keating RF. 124 symptomatic recurrence following the open surgical repair of nonsyndromic craniosynostosis: a 16 Year experience. *Neurosurgery*. 2013;60:161.

74. Rattani A, Riordan CP, Meara JG, Proctor MR. Comparative analysis of cranial vault remodeling versus endoscopic suturectomy in the treatment of unilateral lambdoid craniosynostosis. *J Neurosurg Pediatr*. 2020;26:105-112.

75. Jimenez DF, Barone CM. Early treatment of anterior calvarial craniosynostosis using endoscopic-assisted minimally invasive techniques. *Childs Nerv Syst*. 2007;23:1411-1419.

76. Jimenez DF, Barone CM, Cartwright CC, Baker L. Early management of craniosynostosis using endoscopic-assisted strip craniectomies and cranial orthotic molding therapy. *Pediatrics*. 2002;110(1 Pt 1):97-104.

77. Venturini S, Park KB. Evaluating the effectiveness and the impact of donated neurosurgical equipment on neurosurgical units in low- and middle-income countries: the world federation of neurosurgical societies experience. *World Neurosurg*. 2018;109:98-109.

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Supplemental Table 1. Summary of Demographics, Preclinical Characteristics, Management Strategies, and Outcomes of all Retrospective and Prospective Studies

#	Author, Year, Country	Study Aim	Number of Patients	Mean Age in Years, Sex	Presenting Signs and Symptoms Medical Comorbidities	Associated Genetic/ Congenital Conditions	Imaging Modality	Craniometrics, Fusion Characteristics	Management and Postmanagement Complications	Postsurgical Outcomes	Mean Last Follow-Up, Reported Clinical Outcome	Conclusion
1	Labuschagne J, 2023, South Africa[1]	To discuss the experience in treating pediatric patients with sagittal synostosis using minimally invasive flexible endoscopic techniques followed by cranial helmet molding therapy.	18	0.28, 10 M, 8 F	N/A	N/A	CT scan (18)	Mean preoperative CI (67.7) Scaphocephaly (18)	Endoscope-assisted suturectomy (18) No intraoperative complications observed	CI 6 weeks postoperative (77.1), CI 1 year postoperative (76.3)	17 months, All parents were satisfied with the cosmetic outcome of the procedure	In this modest single-hospital series, the authors demonstrated the feasibility of FEASR in treating sagittal synostosis with favorable cosmetic outcomes.
2	Bisetty et al., 2022, South Africa[2]	To analyze and compare the morphometry of the anterior, middle, and posterior cranial fossae in patients with scaphocephaly.	24	2.47, 20 M, 4 F	N/A	N/A	CT scan (24)	Mean CI (67.1 ± 3.51) Scaphocephaly (24)	N/A	N/A	N/A	The morphometric dimensions obtained in the present study indicate a preponderance of deformity in the ACF and PCF, especially with elongation along the AP plane (lengths) in scaphocephalic patients.

M, male; F, female; N/A, not available; CT, computed tomography; CI, Cephalic Index; FEASR, flexible endoscope-assisted suture release; ACF, anterior cranial fossa; PCF, posterior cranial fossa; AP, anteroposterior; CNS, central nervous system; MRI, magnetic resonance imaging; WC, Whitaker classification; LVP, lateral vault panel; ET, endotracheal; CV, cranial volume; ACV, anterior cranial volume; PCV, posterior cranial volume; ADM, acellular dermal matrix; MZ, monozygotic; DZ, dizygotic; TCD, transcranial Doppler; ICP, intracranial pressure; CSF, cerebrospinal fluid.

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Supplemental Table 1. Continued

#	Author, Year, Country	Study Aim	Number of Patients	Mean Age in Years, Sex	Presenting Signs and Symptoms Medical Comorbidities	Associated Genetic/ Congenital Conditions	Imaging Modality	Craniometrics, Fusion Characteristics	Management and Postmanagement Complications	Postsurgical Outcomes	Mean Last Follow-Up, Reported Clinical Outcome	Conclusion
3	Mohan et al., 2022, South Africa[3]	To document and compare the morphometry of the ACF, orbit, and ear on the ipsilateral (synostotic) and contralateral (nonsynostotic) sides using CT) scans	18	1.23, 8 M, 10 F	N/A	N/A	CT scan (18)	Width: Ipsilateral mean (42.8 ± 4.87 mm), contralateral mean (50.7 ± 5.84 mm) Length: Ipsilateral mean (26.6 ± 6.71 mm), contralateral mean (33.1 ± 5.36 mm) Curvature: Ipsilateral mean (61.1 ± 9.81 mm), contralateral mean (79.4 ± 9.65 mm) Volume: Ipsilateral median 15.0 (13.3—16.4) cm^3, contralateral median 16.2 (13.9—18.7) cm^3	N/A	N/A	N/A	There was side-to-side asymmetry in the ACF, orbit, and ear. The volume was the most affected of all the significant ACF parameters.
4	Mohamed E. Elhawary et al., 2022, Egypt[4]	To describe the surgical management and postoperative outcomes in infants with metopic synostosis.	18	0.78, 12 M, 6 F	Hypotelorism (10), prominent metopic suture (8) CNS anomalies (2), cardiac anomalies (1).	N/A	CT scan (18), MRI (18)	Trigonocephaly (18), scaphocephaly (2), anterior plagiocephaly (2), multiple suture synostosis (1)	Cranial vault remodeling (10), suturectomy (3), open surgery (13), endoscopic technique (5), dural tear (2), wound infection (1), seroma (1), hypotension (1), mortality (1)	Class I WC (1), Class II WC (3), Class III WC (1), Class IV WC (3), reoperation (3)	12 months, papilledema resolved in 18 cases.	Regardless of type of surgery, the outcomes of surgical correction of metopic synostosis are excellent with only a few patients requiring revision or developing major complications.

5	Madaree et al., 2021, South Africa[5]	To describe a novel method of LVP remodeling in the treatment of craniosynostosis.	106	0.92, 57 M, 49 F	N/A	N/A	N/A	N/A	Open surgery (106) N/A	Postoperative CI at 1 year ranged from 73 to 82 with a mean of 75%.	N/A	The wedge osteotomy and modification of the LVP is a simple and effective method to increase the biparietal diameter and to improve the cephalic index. It is a quick and expedient technique with satisfactory outcomes.
6	Ilse Crous, 2021, South Africa[6]	To describe the craniosynostosis phenotype in a South African population.	47	1.88, 25 M, 22 F	Visual disturbances/ defects (11), head deformity (10), abnormal facial appearance (27), seizures (4), proptosis (5), hypotelorism (2), global development delay (12), polydactyly (2) syndactyly (5) brachydactyly (1) broad thumbs (5), myelomeningocele (1)	Crouzon syndrome (8), Apert syndrome (4), Pfeiffer syndrome (1)	CT scan (47)	Average head circumference (32.6 cm), scaphocephaly (28), trigonocephaly (6), brachycephaly (6), plagiocephaly (3)	Surgery—unspecified (47), bleeding (1), pressure sore from ET tube (1)	N/A	N/A	Recognizing and understanding the phenotypic spectrum of craniosynostosis will aid in improving the detection rate and allow for earlier diagnosis of complex craniosynostosis which can lead to an improved outcome.
7	Fawzy, H.H et al., 2019, Egypt[7]	To present the technique of 1-piece fronto-orbital distraction with midline splitting osteotomy but without bandeau for the treatment of metopic craniosynostosis.	9	1.14, 6 M, 3 F	N/A	N/A	CT scan (9)	Mean CV (943.7 cm^3), mean CI (90.8), mean ACV (298.2 cm^3), mean PCV (636.7 cm^3) Trigonocephaly (9)	Open surgery (9), distraction osteogenesis (9) N/A	No major complications or mortality.	17 months, satisfactory aesthetic and functional outcomes (9)	The technique of 1-piece fronto-orbital distraction with midline splitting osteotomy but without bandeau is an effective surgical option for the treatment of metopic craniosynostosis.

M, male; F, female; N/A, not available; CT, computed tomography; CI, Cephalic Index; FEASR, flexible endoscope-assisted suture release; ACF, anterior cranial fossa; PCF, posterior cranial fossa; AP, anteroposterior; CNS, central nervous system; MRI, magnetic resonance imaging; WC, Whitaker classification; LVP, lateral vault panel; ET, endotracheal; CV, cranial volume; ACV, anterior cranial volume; PCV, posterior cranial volume; ADM, acellular dermal matrix; MZ, monozygotic; DZ, dizygotic; TCD, transcranial Doppler; ICP, intracranial pressure; CSF, cerebrospinal fluid.

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Supplemental Table 1. Continued

#	Author, Year, Country	Study Aim	Number of Patients	Mean Age in Years, Sex	Presenting Signs and Symptoms Medical Comorbidities	Associated Genetic/ Congenital Conditions	Imaging Modality	Craniometrics, Fusion Characteristics	Management and Postmanagement Complications	Postsurgical Outcomes	Mean Last Follow-Up, Reported Clinical Outcome	Conclusion
8	Madaree et al., 2018, South Africa[8]	To evaluate the use of acellular dermal matrix in diminishing contour irregularities in the frontal region following craniofacial reconstruction for craniosynostosis	35	1.71, 21 M, 14 F	N/A	N/A	N/A	Plagiocephaly (12), brachycephaly (7), scaphocephaly (10), trigonocephaly (4), multiple suture synostosis (2)	Cranial vault remodeling (35), open surgery (35) N/A	Infection (0), seroma (0)	23 months, N/A	As compared with the pre-ADM patients, we have noticed better outcomes and lesser contour problems since we commenced the use of ADMs.
9	Kleintjs, W.G, 2005, South Africa[9]	To correlate the craniofacial and systemic anomalies in twins	8	N/A	Craniofacial abnormalities (12)	Crouzon syndrome (2)	N/A	Plagiocephaly (4), scaphocephaly (3), trigonocephaly (1)	Surgery—unspecified (8) N/A	Cosmetic improvement[8]	N/A	Twins with craniofacial abnormalities are rare. The authors found that MZ twins are affected more and are more likely to have both siblings affected. DZ twins are affected less and are unlikely to have a co-twin affected.
10	Govender P.V et al., 1999, South Africa[28]	To correlate preoperative and postoperative TCD findings with intraoperative ICP measurements as determined by lumbar puncture and with CT features of elevated ICP	16	2.15, 1 M, 4 F	Head deformity (16), increased ICP (16)	Crouzon syndrome (3), Apert syndrome (4)	CT scan (16), TCD (16)	Multiple suture synostosis (9), scaphocephaly (4), anterior plagiocephaly (2), brachycephaly (2)	Open surgery (16), suturectomy (16) N/A	N/A	0.5 months, N/A	The 3 modalities TCD, ICP, and CT showed poor correlation with each other. No single parameter can be used in the assessment of children with craniosynostosis in isolation; a constellation of parameters provides the most useful information.

11	Wall SA, 1994, South Africa[10]	To review all of the cases that had undergone surgery for craniosynostosis in the Birmingham and Oxford units and to document the nature and number of cases that subsequently required further major fronto-orbital revision, which had not been anticipated as part of their initial surgical plan, and to correlate this with the timing of the first procedure.	219	0.95, 105 M, 114 F	Head deformity (219)	Apert syndrome (24), Crouzon syndrome (30), Pfeiffer syndrome (4), Saethre-Chotzen syndrome (5), Carpenter syndrome (2)	N/A	Trigonocephaly (28), scaphocephaly (16), anterior plagiocephaly (106), posterior plagiocephaly (6), multiple suture synostosis (63)	Fronto-orbital advancement (191), suturectomy (28), cranial vault remodeling (1) N/A	Reoperation (15)	41 months	Early craniofacial surgery for craniosynostosis increases the need for a repeat fronto-orbital procedure, as a significantly larger proportion of the children operated on before the age of 6 months needed reoperation
12	Assaad et al., 1987, Egypt[11]	To review the operative procedures in treatment of craniosynostosis with decompression of the brain and improvement of facial appearance as the primary objectives.	25	4.6, 18 M, 7 F	Head deformity (12), visual failure (10), headache (7), facial appearance (3), exophthalmos (17), hydrocephalus (1), ventricular septal defect (1), high arched palate (1), growing skull fracture (1), reduced visual acuity (18)	Crouzon syndrome (2)	X-ray (25), CT scan (25)	Scaphocephaly (6), plagiocephaly (2), trigonocephaly (2), brachycephaly (6), oxycephaly (7)	Fronto-orbital advancement (19), suturectomy (6), open surgery (25), CSF leak (2), surgical site infection (1)	The overall results were satisfactory, CSF leak (1), facial appearance improved in the majority of the cases	Resolved headache (25), improved visual acuity (4)	The addition of strip craniectomies to the forehead advancement technique has been followed by satisfactory improvement of the face and skull shape.
13	W.J. Peacock, 1982, South Africa[12]	To describe the treatment of craniosynostosis and methods used in treating craniosynostosis at Department of Neurosurgery at the University of Cape Town	52	N/A	Craniofacial dysostosis (7)	N/A	N/A	Scaphocephaly (12), anterior plagiocephaly (9), posterior plagiocephaly (1), trigonocephaly (1), brachycephaly (13), multiple suture synostosis (16)	Fronto-orbital advancement (9), suturectomy (43), open surgery (52) N/A	Reoperation (5)	N/A	To achieve acceptable improvement surgery should be performed as early as possible, preferably within the first few weeks of life.

M, male; F, female; N/A, not available; CT, computed tomography; CI, Cephalic Index; FEASR, flexible endoscope-assisted suture release; ACF, anterior cranial fossa; PCF, posterior cranial fossa; AP, anteroposterior; CNS, central nervous system; MRI, magnetic resonance imaging; WC, Whitaker classification; LVP, lateral vault panel; ET, endotracheal; CV, cranial volume; ACV, anterior cranial volume; PCV, posterior cranial volume; ADM, acellular dermal matrix; MZ, monozygotic; DZ, dizygotic; TCD, transcranial Doppler; ICP, intracranial pressure; CSF, cerebrospinal fluid.

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Supplemental Table 1. Continued

#	Author, Year, Country	Study Aim	Number of Patients	Mean Age in Years, Sex	Presenting Signs and Symptoms Medical Comorbidities	Associated Genetic/ Congenital Conditions	Imaging Modality	Craniometrics, Fusion Characteristics	Management and Postmanagement Complications	Postsurgical Outcomes	Mean Last Follow-Up, Reported Clinical Outcome	Conclusion
14	el-Sherif H et al., 1970, Egypt[13]	To investigate craniosynostosis in Egypt through clinical, radiological, and biochemical approaches, focusing on prevalent types and optimal surgical management.	25	6.48, 23 M, 2 F	Headache (16), reduced visual acuity (20), vomiting (7), seizures (4), proptosis (20), optic atrophy (19), nystagmus (5), babinski (5)	N/A	X-ray (25)	Oxycephaly (25)	Suturectomy (25), open surgery (25), CSF leak (1), hyperthermia (2)	Reoperation (1)	36 months, headaches, vomiting, bilateral extensor plantar responses, grand mal seizures, and bladder incontinence disappeared postoperatively (25), improved visual acuity (9)	Unlike the disease in other countries, where sagittal synostosis is the most common variety, oxycephaly represents the most common clinical entity in Egypt.

M, male; F, female; N/A, not available; CT, computed tomography; CI, Cephalic Index; FEASR, flexible endoscope-assisted suture release; ACF, anterior cranial fossa; PCF, posterior cranial fossa; AP, anteroposterior; CNS, central nervous system; MRI, magnetic resonance imaging; WC, Whitaker classification; LVP, lateral vault panel; ET, endotracheal; CV, cranial volume; ACV, anterior cranial volume; PCV, posterior cranial volume; ADM, acellular dermal matrix; MZ, monozygotic; DZ, dizygotic; TCD, transcranial Doppler; ICP, intracranial pressure; CSF, cerebrospinal fluid.

Supplemental Table 2. Summary of Demographics, Preclinical Characteristics, Management Strategies, and Outcomes of all Case Reports

#	Author, Year Country	Study Aim	Age (Years), Sex	Presenting Symptoms Presenting Signs	Associated Genetic/ Congenital Syndromes and Conditions	Imaging Modality	Craniometrics Fusion Characteristics	Management and Postmanagement Complications	Mean Follow-Up (in Months); Reported Clinical Outcome	Conclusion
1	Bouaré F, 2022, Morocco[14]	To report a case of a 12-month-old male who presented with craniofacial deformities and neurological abnormalities.	1, M	Forehead flattening, limb abnormalities, facial deformity, developmental delay, intellectual disability	Carpenter syndrome, congenital heart defects	CT scan	Oxycephaly	Fronto-orbital advancement Massive hemorrhage	2 months, improved	Early corrective surgery is typically done within 6—12 months of age. MRA can detect venous abnormalities that risk bleeding, and 3D CT imaging assesses skull weakening to prevent bone fragmentation during cranial flap creation. Addressing these issues can reduce surgery cancellations and improve outcomes.
2	Lodhia J, 2021, Tanzania[15]	Investigated the first genetically confirmed Carpenter syndrome patient from continental Africa who presented with neurological deficits (including craniosynostosis)	0.6, F	Limb abnormalities, facial deformity	N/A	X-ray, CT scan, USG	Trigonocephaly	Surgical	N/A	The initial diagnosis of CS in this patient was made by physical examination and showed the importance of dysmorphology training as an element in the medical curriculum, even in low-resource settings.

M, male; CT, computed tomography; MRA, magnetic resonance angiography; 3D, 3-dimensional; F, female; N/A, not available; USG, ultrasonography; CS, craniosynostosis; HC, head circumference; 9p, long arm of Chromosome 9; MRI, magnetic resonance imaging; SD, standard deviation; ICP, intracranial pressure; CDSS, Crouzonodermoskeletal syndrome.

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Supplemental Table 2. Continued

#	Author, Year Country	Study Aim	Age (Years), Sex	Presenting Symptoms Presenting Signs	Associated Genetic/ Congenital Syndromes and Conditions	Imaging Modality	Craniometrics Fusion Characteristics	Management and Postmanagement Complications	Mean Follow-Up (in Months); Reported Clinical Outcome	Conclusion
3	Bot G. M., 2021, Nigeria[16]	Documented a case of anterior cranial remodeling and orbital advancement in Nigeria.	1.5, F	Forehead flattening	N/A	CT scan	Anterior plagiocephaly	Unilateral fronto-orbital advancement	Improved	The need for multidisciplinary collaboration, training, and adaptable surgical techniques such as the modified buttress technique is necessary in developing this part of neurosurgery. Therefore, routine craniosynostosis surgery is feasible in sub-Saharan Africa.
4	Danso K. A., 2021, Ghana[17]	Investigated Pfieffer syndrome and its various effects on the body in a neonate from Ghana	N/A, F	Dyspnea, limb abnormalities, facial deformity, macrocephaly, limb abnormalities,	Pfeiffer syndrome	X-ray, USG	HC (38.8 cm)	Conservative	N/A	In terms of clinical practice, this case will aid healthcare providers especially in areas of low accessibility to identify and manage the condition and counsel the families of affected individuals.

5	Mohamed A. M., 2021, Egypt[18]	Delineated the clinical phenotype of patients with 9p deletions, identified the chromosomal breakpoints, and observed the critical region for trigonocephaly, which is a common finding in 9p terminal deletion	0.4, M	Limb abnormalities, facial deformity, developmental delay, intellectual disability, congenital heart defects, limb abnormalities	9p deletion syndrome	CT scan, MRI	−0.5 SD Trigonocephaly	N/A	N/A	Clinical findings reflected the typical phenotype of 9p deletion syndrome which suggested that the genome location of 11,587,302 −11,575,785 in band 9p23 is the critical region for trigonocephaly
			0.9, F	Microcephaly, limb, abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	CT scan, MRI	N/A Trigonocephaly	N/A	N/A	
			9, F	Microcephaly, limb abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	CT scan	−2.9 SD Trigonocephaly	N/A	N/A	
			3, M	Congenital heart defects, limb abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	CT scan, MRI	−3.1 SD Trigonocephaly	N/A	N/A	
			6, F	Congenital heart defects, limb abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	CT scan, MRI	−1 SD Trigonocephaly	N/A	N/A	

M, male; CT, computed tomography; MRA, magnetic resonance angiography; 3D, 3-dimensional; F, female; N/A, not available; USG, ultrasonography; CS, craniosynostosis; HC, head circumference; 9p, long arm of Chromosome 9; MRI, magnetic resonance imaging; SD, standard deviation; ICP, intracranial pressure; CDSS, Crouzonodermoskeletal syndrome.

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Supplemental Table 2. Continued

#	Author, Year Country	Study Aim	Age (Years), Sex	Presenting Symptoms Presenting Signs	Associated Genetic/ Congenital Syndromes and Conditions	Imaging Modality	Craniometrics Fusion Characteristics	Management and Postmanagement Complications	Mean Follow-Up (in Months); Reported Clinical Outcome	Conclusion
			1.8, F	Microcephaly, congenital heart defects, limb abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	MRI	−2 SD Trigonocephaly	N/A	N/A	
			0.3, F	Congenital heart defects, limb abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	CT scan, MRI	−3.2 SD Trigonocephaly	N/A	N/A	
			2.7, M	Congenital heart defects, limb abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	CT scan, MRI	−0.9 SD Trigonocephaly	N/A	N/A	
			0.8, F	Macrocephaly, limb abnormalities, facial deformity, developmental delay, intellectual disability	9p deletion syndrome	N/A	N/A Trigonocephaly	N/A	N/A	

6	Nsir A. B., 2016, Tunisia[19]	Discussed the difference between the frontosphenoidal suture and that of unilateral coronal suture	1.8, M	Forehead flattening, facial deformity	N/A	CT scan	Plagiocephaly	Bilateral fronto-orbital advancement	Improved	Frontosphenoidal synostosis should be suspected and carefully searched when dealing with plagiocephaly with patent coronal suture. Good outcome requires a prompt diagnosis and early correction.
			0.1, F	Forehead flattening, facial deformity	N/A	CT scan	Plagiocephaly	Unilateral fronto-orbital advancement	Improved	
7	Saghir S, 2015, Morocco[20]	Discussed a rare case of familial nonsyndromic trigonocephaly	0, M	N/A	Trigonocephaly	CT scan	HC (34 cm) Trigonocephaly	Conservative	month Improved	N/A
8	Lumaka A, 2014, Congo[21]	Presented a Congolese male patient and his mother who were affected by Apert syndrome of variable severity	0.1, M	Limb abnormalities, facial deformity	Apert syndrome	X-ray	HC (41 cm)	N/A	N/A	Authors discovered a novel and unique mutation involving 3 adjacent nucleotides. The present report underscored the usefulness of reaching a molecular diagnosis, even in cases with a well-known genetic condition and where the spectrum of mutations is known.
9	Hamouda H. B., 2012, Tunisia[22]	Reported a case of Pfeiffer syndrome type II, discovered perinatally, which was distinguished from type III by the skull appearing like a cloverleaf, and the clinical, radiological, and evolutive features and the advantage of prenatal diagnosis of this syndrome with a review of the literature	0, M	Macrocephaly, dyspnea, limb abnormalities, facial deformity, raised ICP	Pfeiffer syndrome	X-ray, CT scan, USG	HC (37 cm) Brachycephaly	Conservative	N/A	Prenatal diagnosis of Pfeiffer syndrome remains difficult and is based on methodical fetal ultrasonography exploring the head, face, and extremities, with, in addition, if there are abnormalities, a 3-dimensional ultrasound examination and fetal MRI with a molecular biology analysis.

M, male; CT, computed tomography; MRA, magnetic resonance angiography; 3D, 3-dimensional; F, female; N/A, not available; USG, ultrasonography; CS, craniosynostosis; HC, head circumference; 9p, long arm of Chromosome 9; MRI, magnetic resonance imaging; SD, standard deviation; ICP, intracranial pressure; CDSS, Crouzonodermoskeletal syndrome.

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Supplemental Table 2. Continued

#	Author, Year Country	Study Aim	Age (Years), Sex	Presenting Symptoms Presenting Signs	Associated Genetic/ Congenital Syndromes and Conditions	Imaging Modality	Craniometrics Fusion Characteristics	Management and Postmanagement Complications	Mean Follow-Up (in Months); Reported Clinical Outcome	Conclusion
10	Hlongwa P. J., 2009, South Africa[23]	Investigated the case of a 7-year-old South African with Crouzon syndrome and the orthodontic measures taken to correct his condition	7, M	Facial deformity	Autosomal dominant mutation in the FGFR2 gene	X-ray	Multiple suture synostosis	Surgery-Multiple craniotomies and conservative physiotherapy/ equipment based (maxillary anterior expansion using removable expansion appliance)	Improved	An understanding of these abnormalities is necessary for the dental team to make the appropriate referrals to ensure the patient receives the best available care. The orthodontist can be an integral part of the multidisciplinary team.
11	Jeftha A, 2004, South Africa[24]	We have recently documented a South African child with the CDSS. In this article, we briefly reviewed the nosology of the disorder and discussed the general orodental management and genetic implications.	2, F	Head deformity, facial deformity, axillary and groin dark skin pigmentation,	Crouzon syndrome	USG, X-ray	HC (34 cm)	N/A	N/A	The delineation of the CDSS as a distinctive entity with a well-defined molecular basis has important implications for prognostication and clinical and genetic management.
12	Farag H. M., 1999, Egypt[25]	Made a diagnostic evaluation of craniofacial anomalies, either isolated or part of a genetic syndrome, and highlighted the importance of using minor features, as well as very apparent ones, to obtain accurate diagnoses	N/A, F	Head deformity	N/A	N/A	Anterior plagiocephaly, trigonocephaly	N/A	N/A	Abnormalities were shown up by G-banding and by flourescence in situ hybridization studies. This proved to be a rapid and efficient method
			N/A, M	Head deformity	Pfeiffer syndrome type 1	N/A	Anterior plagiocephaly	N/A	N/A	N/A
			N/A	Head deformity	Crouzon syndrome	X-ray	Anterior plagiocephaly	N/A	N/A	N/A
			N/A, M	Head deformity	Crouzon syndrome,	N/A	Scaphocephaly	N/A	N/A	N/A
			N/A, M	Head deformity	Carpenter syndrome	N/A	Anterior plagiocephaly	N/A	N/A	N/A

13	Samson G, 1996, South Africa[26]	Reported a possibly new syndrome involving craniosynostosis accompanied by other congenital anomalies	0.1, M	Microcephaly, congenital heart defects, limb abnormalities, facial deformity, developmental delay, intellectual disability, raised ICP	N/A	X-ray, CT scan	HC (22 cm)	Conservative	0.14 months Death	The specific combination of anomalies present in this South African boy appears to be unique and do not match to previously described syndromes. Therefore, we conclude that they represent a hitherto previously undelineated syndrome.
14	Christianson A. L., 1996, South Africa[27]	Discusses a possible case of Proteus syndrome in comparison with another known similar case in literature	3, M	Macrocephaly, limb abnormalities, facial deformity, developmental delay, intellectual disability	Proteus syndrome	X-ray, CT scan	N/A	Conservative	No neurological abnormalities reported	It is unclear if the patient will develop pathognomonic signs of Proteus syndrome or if the manifestations in this child will have a different prognosis. Thus, ongoing monitoring was indicated for this child, and similar patients, because of the concern of tumors and complications of focal overgrowth.

M, male; CT, computed tomography; MRA, magnetic resonance angiography; 3D, 3-dimensional; F, female; N/A, not available; USG, ultrasonography; CS, craniosynostosis; HC, head circumference; 9p, long arm of Chromosome 9; MRI, magnetic resonance imaging; SD, standard deviation; ICP, intracranial pressure; CDSS, Crouzonodermoskeletal syndrome.

REFERENCES

1. Labuschagne HC, Moodley H. Risk stratification of hospital admissions for COVID-19 pneumonia by chest radiographic scoring in a Johannesburg tertiary hospital. *J Neurosurg*. 2023;31:71-77.
2. Vensuya Bisetty LL, Harrichandparsad R. Anil madaree morphometric analysis of the cranial fossae in scaphocephalic patients: an anatomical basis. *J Craniofac Surg*. 2022;33:1375-1380.
3. Nivana Mohan LL, Harrichandparsad R. Anil madaree anterior synostotic plagiocephaly: a quantitative analysis of craniofacial features using computed tomography. *J Craniofac Surg*. 2022;33:2339-2349.
4. Mohamed E, Elhawary MA. Mohamed gabr outcomes of surgical management of metopic synostosis : a retrospective study of 18 cases. *J Kor Neurosurg*. 2022;65:107-113.
5. Anil MWMMM. Novel method of lateral vault modification in scaphocephaly. *J Craniofac Surg*. 2021;32:2859-2863.
6. Crous I. *Craniosynostosis in a South African Population*. University of Cape Town; 2021.
7. Hossam Hassan Fawzy J-WC, Choi JW, Ra YS. One-piece fronto-orbital distraction with midline splitting but without bandeau for metopic craniosynostosis: craniometric, volumetric, and morphologic evaluation. *Ann Plast Surg*. 2019;83:285-292.
8. Anil Madaree WMMM. Use of acellular dermal Matrix in craniosynostosis. *J Craniofac Surg*. 2018;29:126-129.
9. Kleintjes WG. Craniofacial abnormalities in twins at tygerberg hospital, craniofacial unit. *J Craniofac Surg*. 2005;16:169-171.
10. Wall JHG SA, Hockley AD, Wake MJ, Poole MD, Briggs M, Briggs M. Fronto-orbital re-operation in craniosynostosis. *Br J Plast Surg*. 1994;47:180-184.
11. A Assaad AAG, Gheita AA. Experience in Egypt with 25 cases of craniosynostosis and forehead advancement. *Child's Nerv Syst*. 1987;3:219-221.
12. PEACOC WJ. *The treatment of craniosynostosis*. 1982.
13. Hassanein El-Sherif ASK, Abou-Senna AM. Adley farid ghaly craniosynostosis in Egypt. *J Neurosurg*. 1970;33:29-34.
14. Bouare F, Noureldine MHA, Hajhouji F, Ghannane H, Jallo GI, Ait Benali S. Complex craniosynostosis in the context of Carpenter's syndrome. *Childs Nerv Syst*. 2022;38:831-835.
15. Lodhia J, Rego-Garcia I, Koipapi S, et al. Carpenter syndrome in a patient from Tanzania. *Am J Med Genet*. 2021;185:986-989.
16. Bot G, Constantini S, Shilong D, et al. Orbital advancement using the modified buttress technique in sub-Saharan Africa: a demonstrative case report. *Annals of Medical Research and Practice*. 2021;2:2, 04/22.
17. Danso KA, Akuaku RS, Young FNA, Wiafe SA. Pfeiffer syndrome type 3 with FGR2 c.1052C>G (p.Ser351Cys) variant in West Africa: a case report. *Pan Afr Med J*. 2021;40:136.
18. Mohamed AM, Kamel AK, Eid MM, et al. Chromosome 9p terminal deletion in nine Egyptian patients and narrowing of the critical region for trigonocephaly. *Mol Genet Genomic Med*. 2021;9:e1829.
19. Ben Nsir A, Darmoul M, Zemmali M, Slimane A, Hattab N. Plagiocephaly due to frontosphenoidal suture synostosis: report of 2 cases and literature review. *Pediatr Neurosurg*. 2016;51:204-209.
20. Salahiddine S, Anass A. A rare case of a familial form of nonsyndromic trigonocephaly. *PAMJ*. 2015;21, 2015-08-07.
21. Lumaka A, Mubungu G, Mukaba P, et al. A novel heterozygous mutation of three consecutive nucleotides causing Apert syndrome in a Congolese family. *Eur J Med Genet*. 2014;57:169-173.
22. Ben Hamouda H, Tlili Y, Ghanmi S, et al. Pfeiffer syndrome type II discovered perinatally: report of an observation and review of the literature. *Diagn Interv Imaging*. 2012;93:785-789.
23. Hlongwa P. Early orthodontic management of Crouzon Syndrome: a case report. *J Maxillofac Oral Surg*. 2009;8:74-76.
24. Jeftha A, Stephen L, Morkel JA, Beighton P. Crouzonodermoskeletal syndrome. *J Clin Pediatr Dent*. 2004;28:173-176. Winter.
25. Farag HM, Kotb SM, Sweify GA, Fawzy RK, Ismail SR. A diagnostic clinical genetic study of craniofacial dysmorphism. *East Mediterr Health J*. 1999;5:470-477.
26. Samson G, Gardner JC. Craniosynostosis, microcephaly, hydrancephaly, humero-radial synostosis, and thumb aplasia: a new syndrome? *Am J Med Genet*. 1996;61:174-177.
27. Christianson AL, Van Allen MI. Sutural exostoses, rib hyperostoses, craniosynostosis, mental retardation with focal fat deposition: Proteus syndrome? *Am J Med Genet*. 1996;66:150-153.
28. Govender PV, Nadvi SS, Madaree A. The value of transcranial Doppler ultrasonography in craniosynostosis. *J Craniofac Surg*. 1999;10:260-263.