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Craniosynostosis: Report of cases on dry skulls and review of etiology, normal growth of skull vault and anatomical basis of its variations

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Abstract:

Background: Craniosynostosis involves premature fusion of one or more cranial sutures and can result in various anomalies of soft tissues and bones of the cranium. Asymmetry of the skull shape is called plagiocephaly which can be deformational and synostotic. Craniosynostosis is an isolated rare congenital anomaly which can pose challenge in palaeopathological research due to lack of reference material. Craniosynostosis if left untreated can result on morphological defects leading to impaired brain development and neurological damage. **Methods:** 50 dry skulls were studied for any synostosis and abnormal shape of which 31 are males and 19 are females in the osteological collection of department of anatomy, Yenepoya Medical College, Mangalore and Kanachur Institute of Medical Sciences, Mangalore. All the skulls were in good state without mandible. Origin and chronology of the skull was unknown. **Results:** We report 2 cases of partial and complete craniosynostosis

and associated cranial malformations. Complete synostosis of single or multiple suture was observed in 2 skulls. One skull was scaphocephalic with absence of sagittal suture and other case was of pancraniosynostosis with complete absence of all the sutures of cranial vault. **Conclusion:** Incidence of craniosynostosis in skull in historic population has not been estimated. Cases presented here is the rare findings related to palaeopathological material and provides new set of data for cranial and facial morphology

Key Words: craniosynostosis, plagiocephaly, brain development, facial morphology

Introduction: Cranial sutures belong to the type of fibrous joints with flat bones held together by fibrous tissue. These sutural joints have multifunctional importance i.e. preventing the separation of bones by allowing minimum cranial bone movement [1], growth and development of brain ease during vaginal delivery [2]. Craniosynostosis is a congenital anomaly due to premature closure of one or more sutures of the skull. It occurs in 1 of 2000 live births and accounts for second common cranial malformations after orofacial clefts [3,4]. It can be familial or sporadic in occurrence. If left untreated can lead to increase intracranial pressure and restriction of cranial growth [5]

Craniosynostosis are classified based on the sutural fusion, most common being sagittal synostosis (60%), followed by coronal synostosis (25%), metopic in 15% and last being lambdoid synostosis (2%)[6]. Craniosynostosis is classified based on the underlying mechanisms. If it occurs due to defect in ossification process it is called primary craniosynostosis. Secondary synostosis occurs due to other underlying haematological or metabolic dysfunctions. It can also occur as a part of other syndromes like Apert, Crouzon or Pfeiffer syndromes[7]. It can also develop as an isolated disorder[6]. Predictable pattern of skull deformities that are exhibited with distinct sutural synostosis are:

Scaphocephaly: in this there is early fusion of sagittal suture. Can result in increase in anteroposterior length of skull and decreased intertransverse diameter[8].

Plagiocephaly: involves early fusion of coronal suture. It can be anterior or posterior resulting in frontal or occipital bossing[9].

Trigonocephaly: involves early closure of metopic suture. Here forehead appears to be narrow and pointed with head being triangular[10].

Brachicephaly: when bilateral coronal suture undergoes synostosis , it leads to flattening of occipital and frontal region[9].

Pancraniosynostosis is the most severe form of craniosynostosis characterised by fusion of three or more sutures. It occurs early in postnatal life as clover leaf skull with microcephaly[11]. Reporting of adult cases of craniosynostosis is very rare due to early surgical intervention. In

the present study we report two cases of craniosynostosis with morphological parameters compared to normal skull to analyse the shape, size of skull and its morphological basis.

Materials and methods:

50 dry skulls in the osteological collection of department of anatomy, yenepoya medical college, Mangalore and Kanachur Institute of Medical Sciences, Mangalore was observed for any synostosis and abnormal shape after the clearance from the scientific board. All the skulls were in good state without mandible. Origin and chronology of the skull was unknown. Morphometry of the abnormal skulls were measured with the help of sliding and spreading callipers. Various indices were calculated to compare the shape and size of splanchnocranium and neurocranium. Single reference skull of same sex was measured to find the variation of values. Positive findings of synostosis were documented with the help of digital camera. Complete synostosis of single or multiple suture was observed in 2 skulls. One skull was scaphocephalic with absence of sagittal suture and other case was of pancraniosynostosis with complete absence of all the sutures of cranial vault.

Results:2out of 50 skulls examined 2 skulls showed the total absence of sutures. Brachiocephalic Skull identified was that of male with normal appearance of neurocranium and absence of all cranialsutures. Facial profile is prognathic with upturned nasal spines. the features of the skull are tabulated in table 1. These morphological variations have resulted in abnormal shape of the skull called brachycephaly (Fig)

Table1: Morphological features of skull with pancraniosynostosis

Skull view	Features
Frontal view	Frontal bone vertical with prominent frontal eminences Nasal spine is upturned Most of the dentition lost with presence of second and third molar on right side upper arch. This concludes that the skull was of an adult at the time of death.
Lateral view	Thinning of bone observed along the lateral wall of the orbit and at the roof of the orbit. Bilateral partial and asymmetrical fusion of squamous suture.
Vertical view	Absence of all sutures of the cranial vault with plagiocephaly.

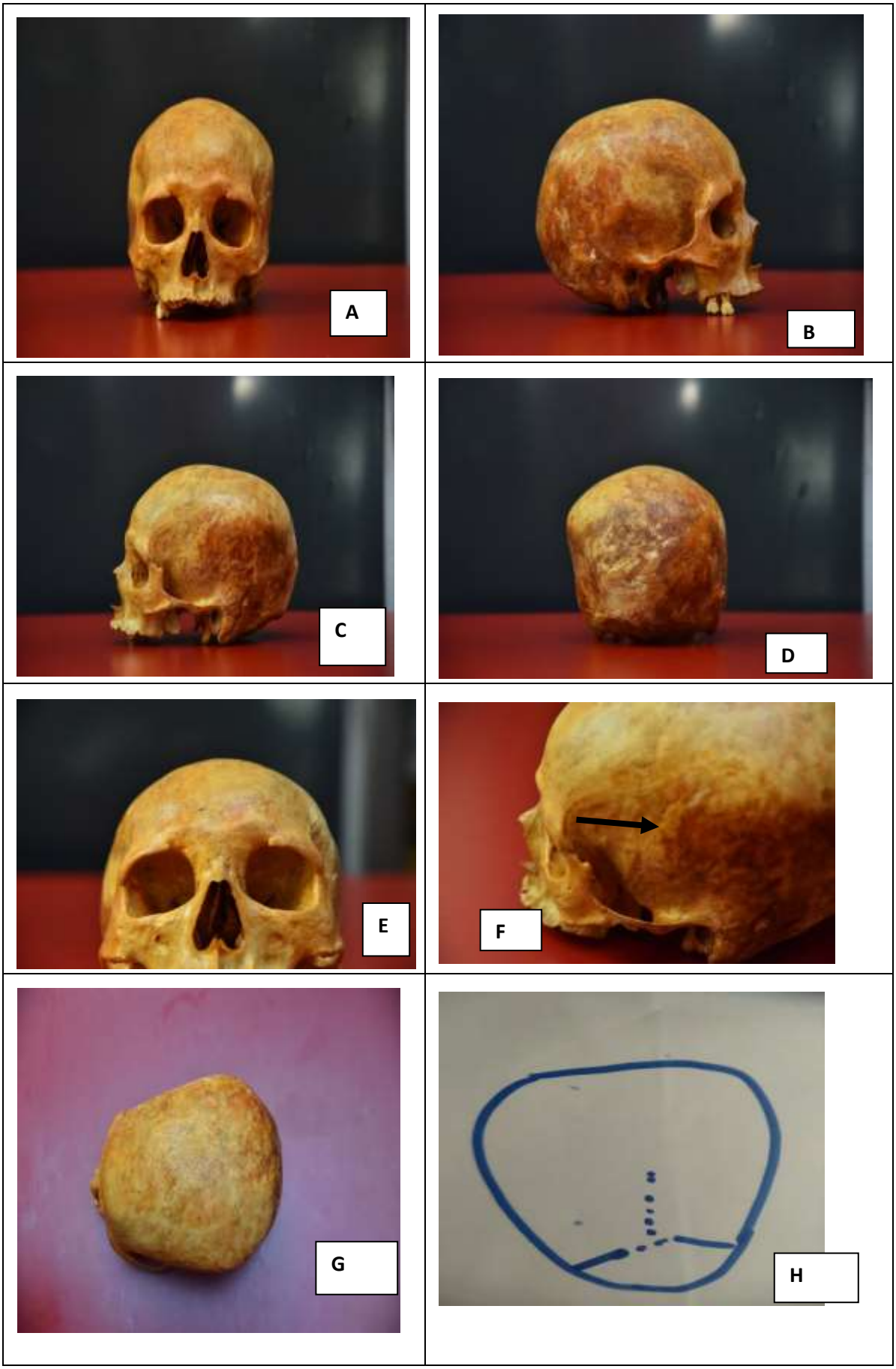
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fig 1: A pancraniosynostotic skull of male A. lateral view B. posterior view C.anterior view D. Superior view E . Close up photograph showing thinning of roof of the orbit.F. Photograph showing thinning of greater wing of sphenoid bone G. skull showing typical deformity of brachycephaly H. schematic representation of brachycephaly.

Table 2: craniofacial measurements of skull with Pan craniosynostosis compared with normal skull

Measurements	Case 1	Reference skull
Maximum cranial length	175mm	184mm
Maximum cranial breadth	136mm	126mm
Bizygomatic breadth	124mm	127mm
Basion bregma height	130mm	133mm
Upper facial height	61.97mm	59.49mm
Nasal breadth	23.73mm	24.32mm
Nasal height	45.53mm	44.91mm
External length of skull base	100mm	104mm
Biasterionic breadth	125mm	104mm
Frontal chord	104mm	110mm
Parietal chord	120mm	118mm
Occipital chord	105mm	91mm
Frontal Arc	115mm	122mm
Parietal Arc	130mm	135mm
Occipital Arc	120mm	110mm
Orbital breadth	37.75 mm®,38.0mm(L)	38.7®,39.63(L)
Orbital height	31.56mm®,30.76(L)	31.73®,32.10(L)
Biorbital breadth	93.54mm	100.35mm
Bimaxillary breadth	90.7mm	70.98mm
Basion prosthion	94.49mm	93.43mm
Foramen magnum length	33.93mm	35.27mm
Foramen magnum breadth	30.09mm	26.58mm
Maximum cranial breadth/ maximum cranial length ×100	77.7	68.4

Maximum cranial breadth was increased in the affected skull compared to normal. This shows that the skull has attained brachycephaly due to remodelling along the frontolateral segments. Increase in facial height in studied skull compared to the reference skull indicates that that there is broadening of upper part of face.Biasterionic breadth was more in the studied skull supporting the fact of remodelling of frontolateral segments and brachycephaly. Occipital chord and arc shows higher measurements compared to the reference skull.

Second skull was of female child. With the absence of third molar in the maxilla and unfused spheno occipital synchondrosis. It can be concluded that cranium 2 belonged to a child. Skull presented with premature fusion of multiple cranial sutures associated with synostotic scaphocephaly and plagiocephaly as shown in Fig 2.

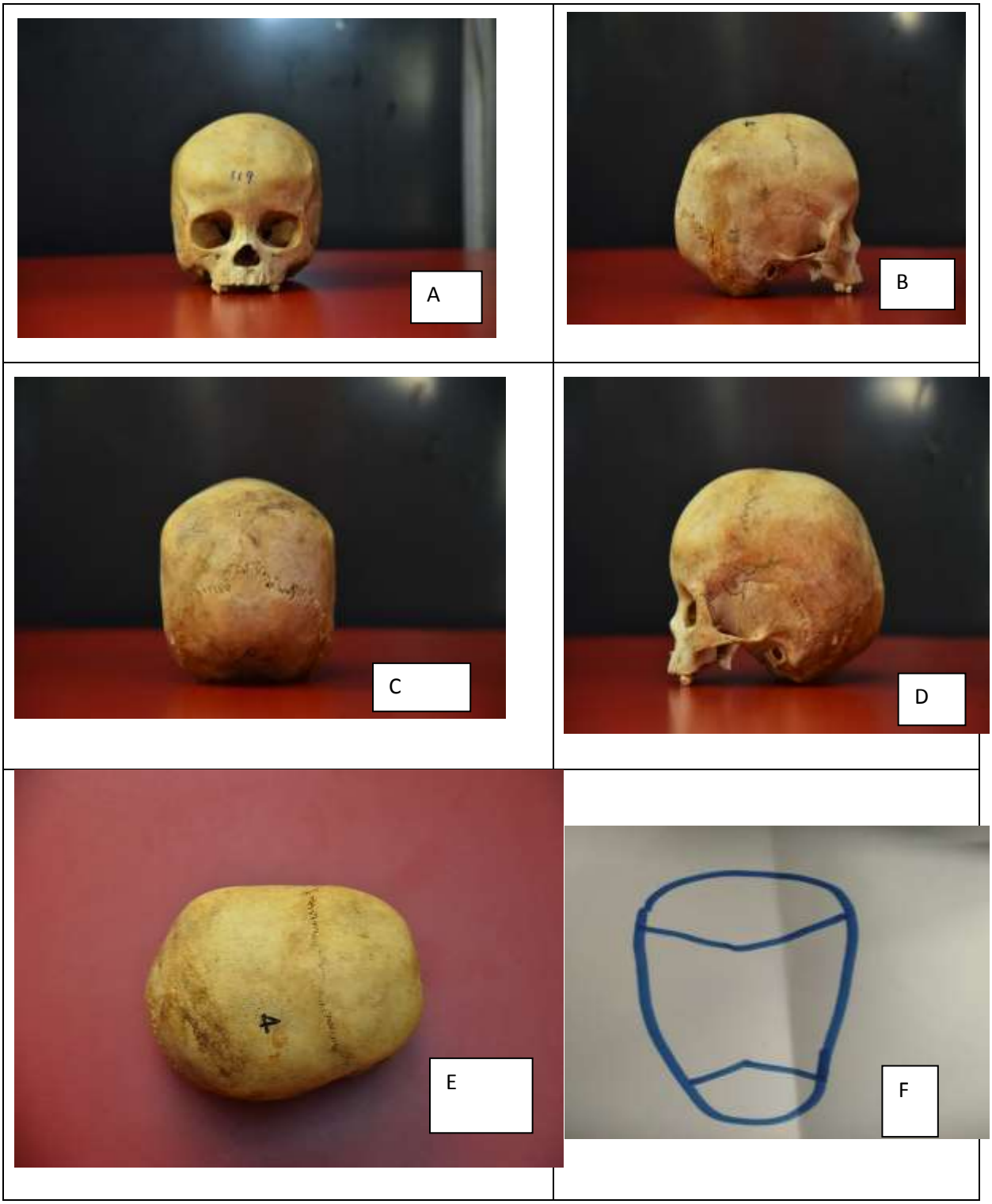

Fig 2: A scaphocephalic skull of female child A.Anterior view B. Right Lateral view C. Posterior view D. Left lateral view E. Superior view F. schematic representation of scaphocephalic skull.

Most prominent feature was narrow brain case with frontal bossing which was evident in maximum cranial length more in scaphocephalic skull and decreased cranial breadth compared to normal skull. Frontal view showed prominentforehead, narrow face and large

orbits. Maximum contrast between measurements of scaphocephalic and normal skull were related to size of parietal and occipital bones. Superior view showed that the skull is narrow with complete absence of sagittal suture and non-obliterated other sutures of the vault.

Craniofacial measurements of scaphocephalic skull compared to the normal skull are presented in Table 2. Maximum cranial length was increased in scaphocephalic skull than normal. Maximum cranial breadth is decreased compared to normal. The values of parietal cord and arc showed more values compared to the reference skull (108 vs 102 mm and 120 vs 114mm). The occipital cord and arc length was decreased compared to normal skull. Occipital nob formation was not formed in the studied skull which can occur due to premature sutural closure.Sagittal elongation of neurocranium is followed by prominent compensatory changes on face measurements. There was significant decrease in upper facial height (42 mm vs 54 mm in reference skull). The nasal height of the investigated skull was smaller only by 5mm when compared to the normal skull. These diameters suggest the abnormal shape of the skull. Cephalic index is significantly lower in the investigated skull

Table 2: Craniofacial measurements (in millimeters) of the scaphocephalic skull compared with the reference skull.

Measurements	Case 2	Single Reference skull
Maximum cranial length	162mm	153mm
Maximum cranial breadth	113mm	123mm
Bizygomatic breadth	94mm	100mm
Basion bregma height	118mm	123mm
Upper facial height	42.04mm	54.98mm
Nasal breadth	19.02mm	24.32mm
Nasal height	32.04mm	37.74mm
External length of skull base	76mm	85mm
Biasterionic breadth	94mm	101mm
Frontal chord	93mm	97mm
Parietal chord	108mm	102mm
Occipital chord	83mm	91mm
Frontal Arc	110mm	114mm
Parietal Arc	120mm	114mm
Occipital Arc	105mm	114mm
Orbital breadth	33.61®,32.69(L)	34.97®,35.70(L)
Orbital height	24.64®,25.43(L)	31.94®,30.92(L)
Biorbital breadth	74.37mm	85.63
Bimaxillary breadth	70.98mm	79.05mm
Basion prosthion	70.55mm	78.59
Foramen magnum length	30.98mm	30.79mm
Foramen magnum breadth	25.29mm	24.49mm
Maximum cranial breadth/ maximum cranial length ×100	69.7	80.3

DISCUSSION:

Variations in skeletal signs, poor preservation techniques and scarcity of literature are of challenge in paleopthological research especially in rare diseases. Asymmetrical deformities of skull are common but reported cases are very few[6]. The studied skulls have undergone critical morphological variations that has led to abnormal shape of the skulls like scaphocephaly and brachycephaly. In case of scaphocephalic skull compensatory growth has occurred perpendicular to the sagittal suture. Sagittal suture will cause the transverse growth of cranium, closure of which has resulted in expansion of skull in anteroposterior direction[12]. Increased parietal cord and arc shows that the bone has expanded in sagittalplane which makes the skull elongated antero posteriorly. In contrast occipital bone showed decreased measurements which is evidenced by the dimensions of occipital cord and arc. In case of pancraniosynostotic skull has attained brachycephaly due to remodelling that has occurred along the frontolateral segments. Albright *et al* explained the mechanism of premature closure of sutures. Signs of sutural closure begins in one part of the suture and will progress along the suture[13]. Abnormality of skull shape is also expressed by cephalic index which is 69 units (vs 80in normal skull) in scaphocephalic skull. Similar observation was reported in other studies where the difference between scaphocephalic skull and reference skull ranged from 3- 17 units[14]. Cranial index was decreased in pancraniosynototic skull compared to the reference skull indicates that the cranial sutures would have closed while the brain has been expanding[15]. Thefacial dimensions were very much decreased in scaphocephalic skull which is in line with the findings of Kohn *et al* that the face dimensions are reduced in scaphocephalic skull [16]. Inpancraniosynostosis all dimensions were reduced including facial dimensions.

Patency of sutures depends on variousextracellular matrixmolecules and various transcription factors[7]. Sutures are fibrous joints among the adjacent skull bones. It helps in the moulding of head during parturition and to make adjustments for the growing brain and to withstand mechanical trauma during childhood[8]. mineralisation of membranous bones of the skull starts by 13 weeks of gestation[9]from paraxial mesoderm. This will be completed by 18 weeks where bones meet with sutural induction. This leads to appositional growth along the suture with deposition of osteoid. This leads to enlargement of skull. Premature fusion of anyone of the suture prevents growth at that locus withcontinued growth at other sutures which can lead to abnormal shape of the skull[9]. Anatomically sutures are designated as a type of fibrous joint having 2 plates of bones separated by a space containing osteogenic stem cells[10].prenatal development of cranial vault can be divided into 3 stages.

Embryonic stage: Up to 4th week of development foetal head has mesenchyme derived from paraxial mesoderm and neural crest cells[21]. Neurocranium develops from first five somites of paraxial mesoderm and also unsegmented somites, viscerocranium from neural crest[17]At the site of development of cranial bones, mesenchymal cells are highly condensed and a membrane is formed due to high vascularity. At the end of 5th week capsular membrane is formed around the developing brain that gives rise to calvaria. These curved plates extend cranially and fuse with each other and also with base of the skull[18].

Foetal stage: capsular membrane is divided into ectomeninx and endomeninx. ossification centres develop in the ectomeninx to form individual cranial bones. woven bone is formed first in the embryo which is replaced by lamellar bone at birth[19]. Bones of the cranial base are formed in cartilage and undergo endochondral ossification[18]. Sutures are formed at the site of major dural reflections. These dural folds divide the cranial cavity and sutures are formed in the same direction. Site of this dural bands acts as the site of slow bone growth at the same time allows the new bone formation at the edges[20].

Bone remodelling: with continued brain growth the osteogenic membrane at the suture produces bone tissue thus enlarging individual bone and also maintains the articular contact[18].

Etiology of craniosynostosis is vague and can be referred to various attributes like haematological causes, genetic factors, hormonal levels and other mechanical causes[17]. Incraniosynostosis cranial sutures are formed normally but mechanical fusion occurs at an early age in an accelerated phase[18]. Early closure of sutures can arrest further bone formation at the site and result in craniofacial anomalies. It can also affect the developing brain[18].According to Skrzat *et al,* sutural closure begins with fusion of 2 diploe and the lamina of the adjacent cranial bones which becomes single unit and there will be degenerative changes in the compact layer[21.] Anderson *et al* showed that the degree of sutural development will be same as adjacent bone but denser. It was observed that stage of sutural closure was not related to the interdigitations of the bone margins[22]. Furuya *et al* stated that with increasing age the sutures are placed closer with initiation of sclerosis and bone mineralisation around the suture which cannot be traced in the absence of suture[15]. During initial stages of sutural closure bony projections are seen in the margins of the suture bridging the gap. Beginning of sutural closure can be on endocranial surface or on the ectocranial surface which can arrest the further bone formation and can result in craniofacial anomalies and effect on developing brain[11].According to Moss, the Basi cranium was the primary site and transmitted tensile forces through the duramater which resulted in craniosynostosis in children[16]. Opperman *et al* identified various signalling factors like transforming growth factor, fibroblast growth factor receptor, TWIST while dura acts like an intermediary source. Mutations in these factors can be an important factor that can result in craniosynostosis[17].The studied skull showed narrow brain case which is reflected in maximum cranial length which is more in scaphocephalic skull and deceased cranial breadth compared to normal skull. Contrast between measurements of scaphocephalic skull and the reference skull were shown by the size of parietal and occipital bones.

Synostosis of single suture are mentioned in the literature. Cases that refer to pan craniosynostosis are very rare and remain as challenge in osteological research due to lack of reference literature. In skull 1 thinning of lateral segments of the bone can be the feature of increased intracranial pressure. It indicates that sutures underwent synostosis later in life with features of increased intracranial pressure and presented with normal size [23]. Modifications in the fronto lateral segments of the skull is the feature of increased intracranial pressure which can be the characteristic sign of Arnold chiari malformation [24]. Postnatal pancraniosynostosis is a condition that can occur later in life where the brain tends to expand even after the closure of cranial sutures (wood). it has a syndromic association as mentioned in table 1

Table 1: Clinical manifestations of syndromic craniosynostosis

Syndrome	Characteristic features
Apert Syndrome	Involves coronal craniosynostosis, fusion of phalanges of digits with mental retardation. Shows autosomal dominant inheritance with advanced paternal age. This condition arises as result of mutation of fibroblast growth factor as suggested by wilkie *et al*[27].
Crouzon Syndrome	There can be variable involvement of sutures with coronal craniosynostosis being dominant. it is associated with brachicephaly, prominence of forehead, hypertelorism, proptosis[28]

Severity of skull deformity points to the lack of surgical intervention in the past historic time. In the present reported cases there is no evidence on its origin. Severe skull deformities can result in cognitive dysfunction, speech and language defects, lack of working memory and attention. Due to abnormal shape of the calvaria, lack of bone growth at the fused suture can affect growth of brain, cortical and subcortical structures [25]. According to the study conducted by Aldridge *et al*. There was elongation of forebrain and hindbrain associated with fusion of sutures which resulted in cognitive defects. It was also shown that morphologicaleffets due to sutural fusion was not restricted to the areas of sutural fusion[26]. Structural defects at the occipital region can result in visual area defects and also children with sutural fusion can result in attention deficit hyperactivity disorder and also dyslexia [27].

Limitations of the study: As the incidence of craniosynostosis is very rare in the present era, the study can be planned on a larger sample from various regions to know the anatomical variations.

Conclusion: Incidence of craniosynostosis in skull in historic population has not been estimated. Cases presented here is the rare findings related to palaeopathologicalmaterial and provides new set of data for cranial and facial morphology. Craniosynostosis is a very rare anomaly which can result in deformities, neurological deficits during the growth of a child. Early treatment of craniosynostosis is utmost important for normal development and aesthetics of the child

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