

## Applicability of Petro-Occipital Fissure Ossification Pattern for Identification of Age and Sex of Skull base Remnants

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**Abstract:** Objectives: To morphologically and radiologically investigate the ossification pattern of petro-occipital fissure (POF) in dried crania of adults so as to determine the developmental changes and their value in age assessment and to evaluate its applicability for identification of age and sex of unknown forensic specimens. Materials & Methods: The study comprised 75 dry skulls (39 males & 36 females) with a mean age of  $62.2 \pm 15.2$  years, at the time of death. Skulls were staged for ossification at the POF midpoint, i.e., between foramen lacerum (FL) and jugular foramen (JF), description of the stage of POF ossification was defined numerically from least ossified (stage 1) to complete fissure ossification (stage 6). Also, plain-film radiographs of 15 cadaveric skulls were taken in the submentovertex position in order to evaluate the degree of POF ossification. The POF ossification pattern was applied for age and sex identification of 60 skull base parts with known age and sex, collected in Forensic museum. Results: Morphological description of POF ossification reported stage I ossification in 5 skulls, stage II in 9 skulls, stage III in 11 skulls, stage IV in 17 skulls, stage V in 26 skulls and only 7 masculine skulls had stage VI ossification. There was a significant increase of the stage of POF ossification in fissures of masculine skulls in comparison to that detected in feminine skulls with a positive significant correlation between chronological age of examined skulls and determined stage of POF ossification both in males and females. Such positive correlation was non-significant till fifties and thereafter was significant to reach a higher significance at above eighties in masculine skulls and return to be non-significant above eighties in feminine skulls. Analysis of radiographic findings defined the presence or absence of POF ossification in skulls but it was difficult to fix the anatomical limits of the fissure precisely and the relative degree of POF ossification. Statistical analysis revealed that the used staged pattern showed specificity for masculine skull identification with  $AUC=0.704$  and for skull age with  $AUC=0.498$ , but showed high specificity for older skull remnants. Conclusion: Evaluation of stage of ossification of POF of dried skulls revealed an age-dependent ossification that started to complete above sixties in both sexes and become sex-dependent thereafter and that stages of POF ossification could be applied for forensic identification of sex and age of skull remnants of unknown identity.

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### 1. Introduction

Anatomically, the skull base or chondrocranium separates the neurocranium from the viscerocranium and serves as an important interface between the soft and hard tissue of the head and neck. Phylogenetically, the skull base is one of the oldest skeletal components, sharing features with the skull bases of earlier vertebrate progenitors. Developmentally, the skull base is relatively stable as compared to the rapidly expanding face and calvaria due to the transit of major blood vessels, nerves, and spinal cord into the head (Verma et al., 2011).

The cranial base is of crucial importance in integrated craniofacial development. As distinct from facial bones, it is formed through endochondral ossification. The posterior and anterior cranial bases are derived from distinct embryologic origins and grow independently--the anterior cranial base solely from the neural crest, the posterior cranial base from the paraxial mesoderm. The anterior cranial base has more prolonged and active growth and exerts more influence

on facial growth than does the posterior cranial base. Cranial base angulation is a unique feature in human beings. Cranial base anomalies have been identified in many genetic and developmental disorders (Nie, 2005; Marom, 2011).

The cranial base is a critical anatomical juncture between soft and hard tissues responsible for vocalization, hearing, breathing, and deglutition and is the major transit point for critical nerves and blood vessels into and out of the head. Forces are transmitted through the vertebral column to the occipital condyles and occipital bone. The connective tissue within the POF may act to dampen the transmission of these forces from the more lateral structures of the basicranium, thereby acting as a protective device of the cochlear apparatus in the young; when the POF ossifies that dampening affect of the soft tissue is lost and the resulting undampened mechanical forces that impact the inner and middle ear and may be a factor in age-related hearing loss. Of further clinical interest, the ossification of the POF may be a factor in a number of

clinicopathologies such as age-related malocclusion, upper respiratory dysfunction, and apnea, (Iseli et al., 2012; Lin et al., 2012).

Primary neoplasms of the petrous apex are rare and include eosinophilic granuloma, chondroma, chondrosarcoma, chordoma, and schwannoma (Villavicencio et al., 2001). The petro-occipital fissure (POF) is clinically important as it is often associated with skeletal myxoid chondrosarcomas of the skull base; while these tumors may be found in various soft tissues throughout the body, 66% of cranial base chondrosarcomas occur within the POF (Sandberg & Bridge, 2003). Histologically, chondrosarcomas tumors lie between the benign chondroma and malignant sarcomas and its prognosis can be correlated with histologic grading (Kveton et al., 1986). Chondrosarcomas of the POF can be painless and locally invasive tumors that present particular problems to the patient and treating clinician due to the complex anatomical architecture of this region of the cranial base (Prades et al., 1994). The contiguous petrous apex of the temporal bone may become involved if POF chondrosarcomas become invasive (Goiney et al., 2011).

Determination of sex from human skeletal remains plays a very important role in establishing the identity of any individual. It is said that very high prediction accuracy can be reached if a well-preserved entire skeleton is available. But many times the pelvis, skull, or other bony parts that point to fairly accurate conclusions regarding sex may be absent (Mo et al., 2009). Thus, understanding of the age- and sex-related morphological changes to the POF may further improve understanding the basic biological processes underlying important clinicopathologies of the head and neck (Seo et al., 2010).

This study aimed to morphologically and radiologically investigate the ossification pattern of petro-occipital fissure (POF) in dried crania of adults so as to determine the developmental changes and their value in age assessment and to evaluate its applicability for identification of age and sex of unknown forensic specimens.

## 2. Materials and Methods

This study was conducted at Department Anatomy, Faculty of General Health & Health Informatics, Um-El Qurra University, Mekkah and Northern Border University, Faculty of Medicine, ArAr, KSA. The study comprised 75 dry skulls with a known age and sex. The age of these skulls ranged between 36 and 89 years. Skulls were staged for ossification at the POF midpoint, i.e., between foramen lacerum and jugular foramen, description of the stage of POF ossification was defined numerically from least ossified (stage 1) to complete fissure ossification (stage 6) as follows:

- Stage 1: The medial and lateral walls of the POF are in close approximation but there is no contact at any point along the length of the fissure. The bony surface along the medial and lateral walls is described as having a textured appearance with high relief due to numerous projections extending into the fissure. The depth of the fissure appears shallow ectocranially to endocranially.
- Stage 2: The medial and lateral walls of the fissure are in close approximation and block a clear view into the endocranium. There is a marked reduction in the high-relief appearance of the fissure walls. The overall depth of the fissure is increased due to bony deposition.
- Stage 3: Bony spicules extend across the fissure, giving an appearance of bridging between the lateral and medial walls of the fissure. This bridging trait is more pronounced in males than females and males tend to exhibit greater bony deposition ectocranially to endocranially.
- Stage 4: The medial and lateral walls of the fissure are abutting, often with large bony protrusions extending up through the fissure space.
- Stage 5: The medial and lateral walls of the fissure show a nearly complete ossification.
- Stage 6: The medial and lateral walls of the fissure are completely ossified. There is little gross difference between the POF and the surrounding bony landscape. The POF is obliterated, <sup>(16)</sup>.

Also, 15 human cadavers were used in the present work for radiographic study of POF (the age of the cadaver was ranged from 24 to 82 years as shown in the sheets of these cadavers). The crania were removed from the body at the level of the axis vertebra (C2) and the mandibles were also removed to facilitate radiographic study of the POF. The dissected crania were tilted back so that orbital-meatal line was parallel to the x-ray film. Plain-film radiographs of the cadaver skull were taken in the submentovertex position with the central ray directed perpendicular to the film.

The POF ossification pattern was applied for age and sex identification of 60 skull base parts with known age and sex, collected in Forensic museum, Faculty of Medicine, Benha University but the forensic analyst was blinded about such data so as to evaluate its applicability for forensic identification

### Statistical analysis

Obtained data were presented as mean±SD, ranges, numbers and ratios. Results were analyzed using Wilcoxon Z-test for unrelated data and Chi-square test. Possible relationships were investigated using Pearson linear regression. Specificity of staged POF ossification pattern as predictor for age and sex identification of unknown specimens was evaluated using the receiver operating characteristic (ROC) curve analysis judged by the area under the curve (AUC). Statistical analysis was conducted using the SPSS

(Version 15, 2006) for Windows statistical package. P value <0.05 was considered statistically significant.

### Results

The study included 75 dried skulls of 39 males (52%) and 36 females (38%) with mean age of  $62.2 \pm 15.2$ ; range: 35-89 years. The mean age of masculine skulls was  $62.1 \pm 16.8$ ; range: 36-89 years and mean age of feminine skulls of  $62.3 \pm 13.5$ ; range: 35-89 years with a non-significant ( $Z=1.069$ ,  $p>0.05$ ) difference between age of included specimens according to gender distribution and between distribution of dried skulls according to chronological age among both sex groups, (Table 1).

Morphological description of POF ossification (Table 2) showed that in 5 skulls (3 males & 2 females) fissure ossification was of stage I, (Fig. 1), in 9 skulls (6 males & 3 females) fissure ossification was of stage II, (Fig. 2), 11 skulls (4 males & 7 females) fissure ossification was of stage III, (Fig. 3), in 17 skulls (7 males & 10 females) fissure ossification was of stage IV, (Fig. 4), in 26 skulls (12 males & 14 females) fissure ossification was of stage V, (Fig. 5) and only 7 masculine skulls had fissure ossification of stage VI, (Fig. 6).

Totally, there was a positive significant correlation between chronological age of examined skulls and determined stage of POF ossification both in males ( $r=0.846$ ,  $p=0.001$ ) and females, ( $r=0.758$ ,  $p=0.005$ ). However, the correlation between chronological age of skull and stage of POF ossification was non-significant till fifties but was significant in age-groups above sixties to reach a higher significance above eighties in masculine skulls and return non-significant in feminine skulls older than eighties as men older than 80 years had complete ossification of POF and classified as Stage IV of POF ossification, while in women older than eighties no skull showed complete ossification or classified as Stage VI of POF ossification, (Table 3).

Morphological changes of the POF were demonstrated in human cadaveric material using plain-film radiographs that defined the presence (Fig. 7a) or absence (Fig. 7b) of POF ossification in skulls of age 82-years old and 24-year-old, respectively. The presence of both hard and soft tissue within the POF made it difficult to define the anatomical limits of the fissure precisely and the staging of POF ossification by using plain-film radiographs.

Using ROC curve analysis for applicability of staged system of POF point ossification for sex and age identification of unknown skull base samples revealed that it could identify parts of masculine skulls with high specificity with  $AUC=0.704$ , (Fig. 8a) and could identify chronological age of skull parts with  $AUC=0.498$ , (Fig. 8b). For age differential identification; for age <50  $AUC=0.344$  (Fig. 9a), for age range of 50-60  $AUC=0.390$  (Fig. 9b), for age range

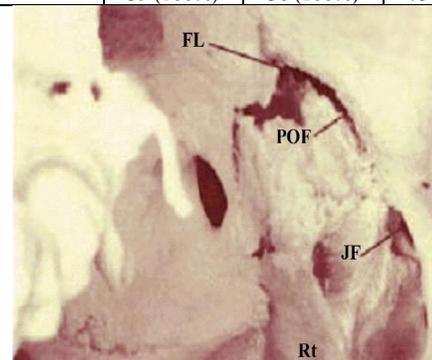
of 60-70  $AUC=0.472$  (Fig. 9c) and for age >80  $AUC=0.550$ , (Fig. 9d).

**Table (1):** Distribution of dried skulls according to age among both sexes

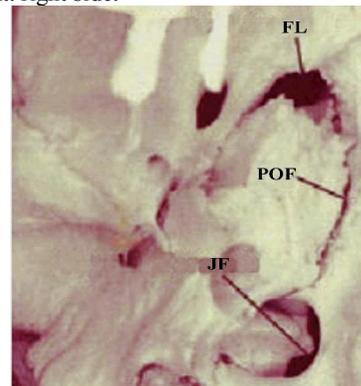
Age group	Males	Females
>30-	7 (17.9%)	4 (11.1%)
>40-	3 (7.7%)	4 (11.1%)
>50-	5 (12.8%)	6 (16.7%)
>60-	9 (23.1%)	8 (22.2%)
>70-	9 (23.1%)	11 (30.6%)
>80-	6 (15.4%)	3 (8.3%)
Total	39 (100%)	36 (100%)

**Table (2):** Distribution of dried skulls according to age among both sexes

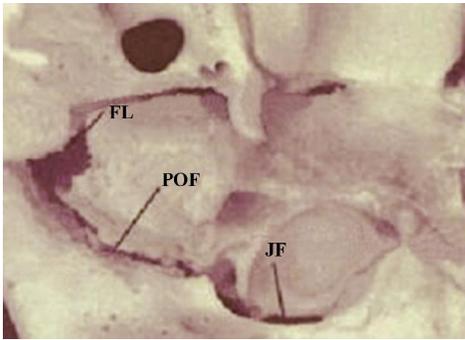
Stage of POF ossification	Males	Females	Total
I	3 (7.7%)	2 (5.6%)	5 (6.6%)
II	6 (15.4%)	3 (8.3%)	9 (12%)
III	4 (10.3%)	7 (19.4%)	11 (14.7%)
IV	7 (17.9%)	10 (27.8%)	17 (22.7%)
V	12 (30.8%)	14 (38.9%)	26 (34.7%)
VI	7 (17.9%)	0	7 (9.3%)
Total	39 (100%)	36 (100%)	75 (100%)



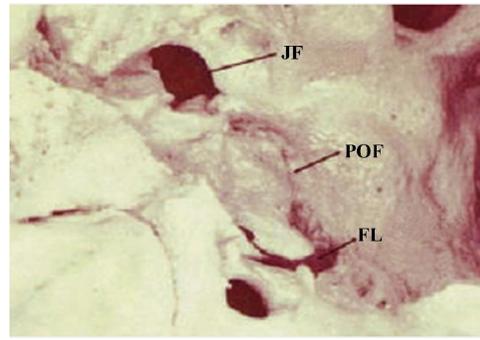
**Fig. (1):** A photograph showing stage I POF ossification with no contact at any point along the length of the fissure; FL: foramen lacerum, POF: petro-occipital fissure, JF: jugular foramen, Rt: right side.



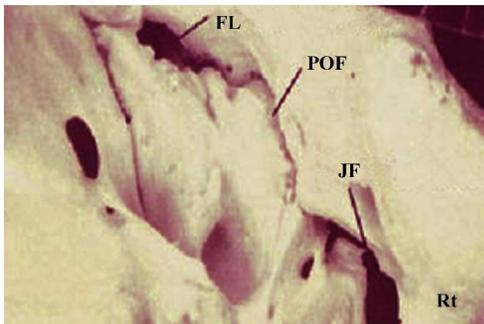
**Fig. (2):** A photograph showing stage II POF ossification: the medial and lateral walls of the fissure are in close approximation with a marked reduction in the high-relief appearance of the fissure walls and the overall depth of the fissure is increased due to bony deposition; FL: foramen lacerum, POF: petro-occipital fissure, JF: jugular foramen.



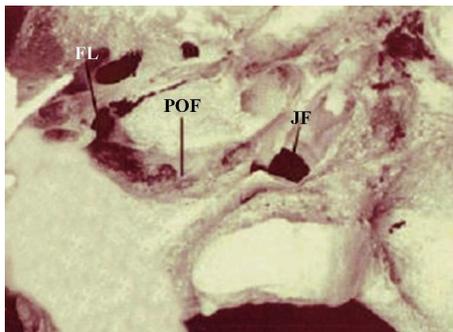
**Fig. (3):** A photograph showing stage III POF ossification: bony spicules extend across the fissure, giving an appearance of bridging between the lateral and medial walls of the fissure; FL: foramen lacerum, POF: petro-occipital fissure, JF: jugular foramen.



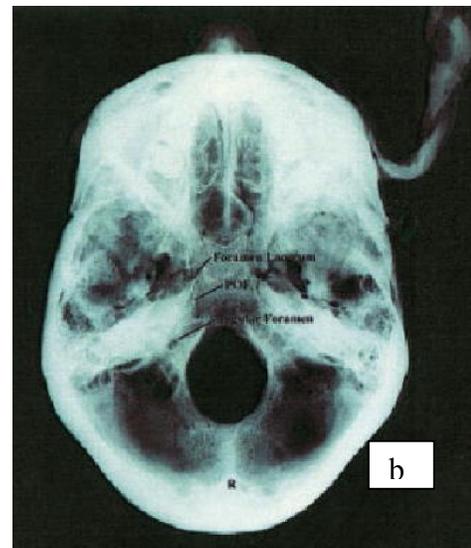
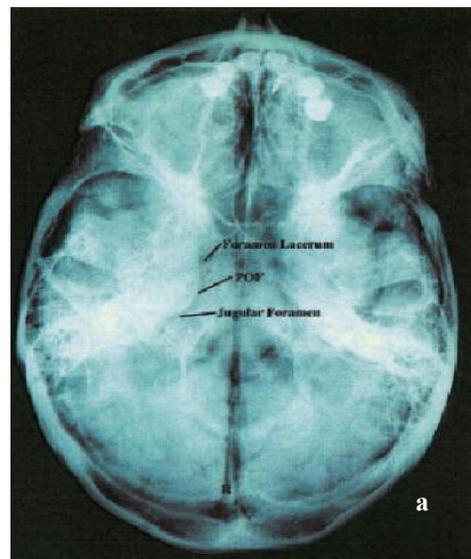
**Fig. (6):** A photograph showing stage VI POF ossification: the medial and lateral walls of the fissure are completely ossified and the POF, much like fully ossified cranial sutures, is obliterated; FL: foramen lacerum, POF: petro-occipital fissure, JF: jugular foramen.



**Fig. (4):** A photograph showing stage IV POF ossification: large bony protrusions extending up through the fissure space; FL: foramen lacerum, POF: petro-occipital fissure, JF: jugular foramen, Rt: right side.



**Fig. (5):** A photograph showing stage V POF ossification: show a nearly complete ossification; FL: foramen lacerum, POF: petro-occipital fissure, JF: jugular foramen.

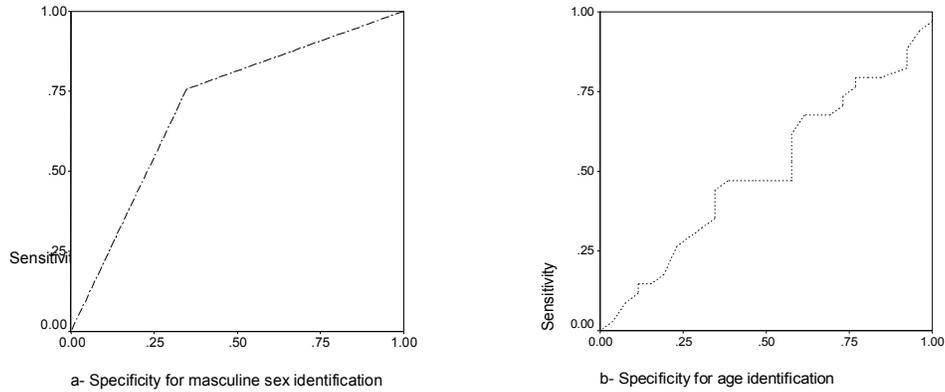


**Fig. (7):** Plain radiographic examination of cadaveric skulls showing absence of POF ossification in young-aged skull (a) and presence of ossification in old-aged skull (b).

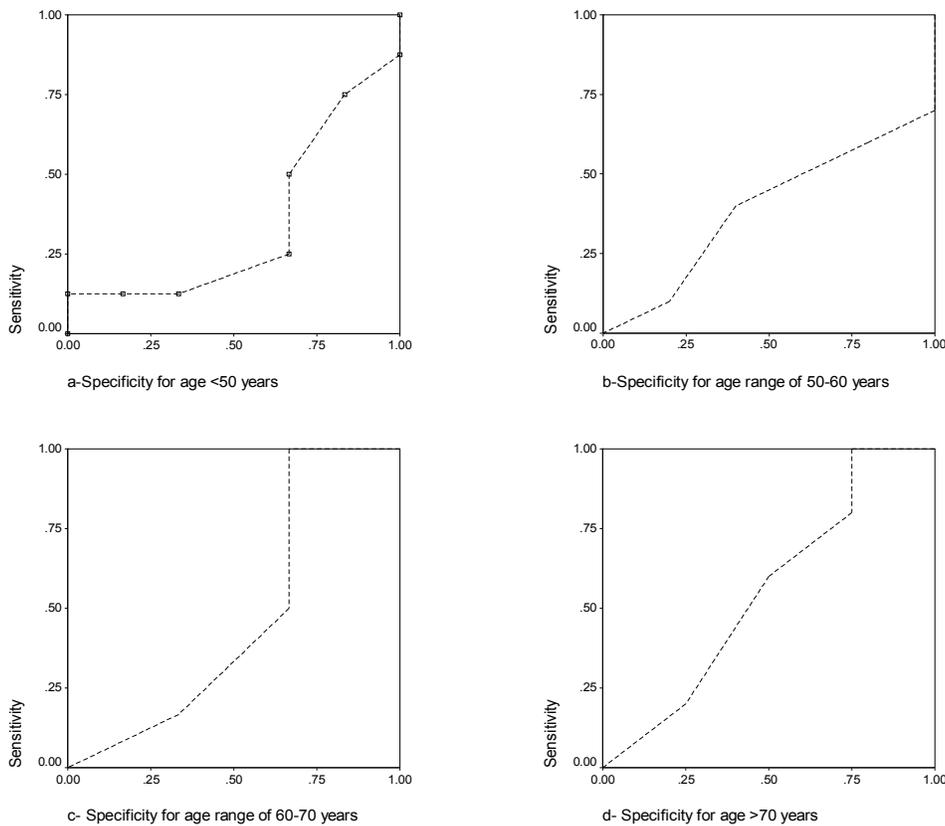
**Table (3):** Correlation coefficients between chronological age of skulls and stage of POF ossification according to the sex of the skull

Age group	Male		Female	
	"r"	p	"r"	P
>30-	0.447	>0.05	0.410	>0.05
>40-	0.500	>0.05	0.470	>0.05
>50-	0.561	>0.05	0.531	>0.05
>60-	0.750	0.032*	0.835	0.019*
>70-	0.831	0.011*	0.694	0.026*
>80-	0.970	0.001*	0.500	>0.05
Total	0.846	<0.001*	0.758	<0.005*

\*: significant correlation; significant value was at p<0.05



**Fig. (8):** ROC curve of applicability of staged system of POF point ossification for sex (a) and age (b) identification of unknown skull base specimens



**Fig. (9):** ROC curve of applicability of staged system of POF point ossification for differential age identification of unknown skull base specimens

### 3. Discussion

Mechanical interactions between the bony skull base and the muscles, ligaments, and dense connective tissue of the upper respiratory tract are observed to occur within the POF. Accordingly, morphological changes that occur within this complex of hard and soft tissue may be related to the interaction of basic biomechanical and molecular forces during growth. An understanding of the normal morphological processes within the POF may provide important clues to the

development of clinicopathologies (Konig et al., 2005).

The POF shares structural similarities to cranial sutures in that both are comprised of fibrous connective tissue that ossifies during adulthood. Accordingly, these structural similarities and the intimate connection between the underlying dura and the POF may indicate a similar molecular mechanism for its ossification (Joo et al., 2012).

Although the precise molecular mechanisms for POF ossification are not completely understood, there

is strong evidence in the literature regarding the ossification of cranial sutures via molecular signaling from the dura. In cranial sutures, the dura mater is believed to regulate suture fusion through multiple pathways, including signaling by transforming growth factor  $\beta_1$  and fibroblast growth factor-2. Identifying the molecular pathways involved in suture ossification has proven an important step in identifying the genesis of the human Apert and Crouzon syndromes, a syndromic craniosynostoses (**Ogle et al., 2004, Feng et al., 2012**).

The present study aimed to morphologically investigate the ossification pattern of POF in adults in dried crania so as to determine the developmental changes and their value in age assessment and also, to evaluate the applicability of radiologic cranial examination for determination of such ossification patterns in preserved human cadavers.

Morphological examination of dried skulls detected varying stages of POF ossification. No feminine skull had reached stage VI ossification while 7 masculine skulls showed ossification stage VI. Thus, indicating the progress of ossification process in males in age older than seventies, but the maximum ossification level in females was stage V in age group older than seventies with no difference compared to skull aged eighties or older.

These findings agreed with previous studies in literature; **Dellinger & Le Minor, (1993)** who reported that age-related changes occur in the hard tissue of the cranial base during early growth and development. Also, the obtained results go in hand with the clinical studies of **Monocoddecicki et al., (1985), Reis, (1994)** and **Cruickshanks et al., (1998)** who reported that regardless of age or occupation, data seem to indicate that men are more likely than women to develop hearing loss. Similarly, the present results agreed with that of **Cruickshanks et al., (2003)** who performed a longitudinal study of the incidence of age-related hearing loss and demonstrated that 21% of adults aged 48–59 and 90% of adults over 80 had hearing loss.

Moreover, the POF is comprised of dense connective tissue and cartilage that physically isolates the petrous portion of the temporal bone from the basicranium (**Opperman, 2000**). Complete POF ossification is primarily observed only in humans older than 60 years of age (**Pierot et al., 2002**). Thus, ossification of the POF and the resultant alteration of the bony landscape of the cranial base may alter CSF flow around the cochlear aqueduct and reduce vibrational dampening of the petrous portion of the temporal bone, thereby exacerbating high-frequency hearing loss in older adults (**Pelosi et al., 2010**).

Morphological changes to the POF were demonstrated in human cadaveric material using plain-film radiographs; however, plain-film radiographic analysis of the POF could only differentiate between the presence and absence of POF ossification in skulls

and could not elucidate the stage of ossification. This finding goes in hand with **Sgouros et al., (1999 a & b)** who found plain radiographs of skull for evaluation of skull base growth in childhood or in cases with craniostenosis is inconclusive and better results were obtained with three-dimensional visualization techniques. Also, **Chong et al., (2002)** and **Sure et al., (2002)** found computed tomography and magnetic resonance imaging are better and complementary to examine skull base to differentiate osseous and cartilaginous components of skull base fissures and to delineate them so as to allow surgical decision making in related pathologies.

**Eskandry et al., (2009)**, documented that CT scans is an accurate and suitable source of anthropometric evaluation of body dimensions and found that the most frequent skull type is dolichocephalic followed by mesocephalic, which seems to be closer to the Anglo-Saxon population considering the rates of dolichocephaly and mesocephaly.

In hand with these data; **Razek & Huang, (2012)**, recently documented that because the petrous apex is not amenable to direct examination, cross-sectional imaging with CT and MR imaging plays an important role in diagnosis and characterization of lesions occurring there.

It could be concluded that evaluation of stage of ossification of POF of dried skulls revealed an age-dependent ossification that started to complete above sixties. Ossification of POF was incomplete in females and progressed in males to complete closure of the fissure.

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