Original Article

Pak. J. Adv. Med. Med. Res.

2024, 02, (3): 154-159

Formation of the Mandibular Condylar Cartilage in Human Specimens Between 10 and 15 Weeks of Gestation

[1]Zahid Sarfaraz, Nighat Aar[2], Muhammad Qaseem[3],Saad Ahmed[4]

1. Associate Professor Anatomy Department Khyber Girls Medical College Peshawar
2. Associate Professor Anatomy Department Nowshera Medical College Nowshera
3. TMO Orthopedic Department Main Rasheed Memorial Hospital Pabbi
4. 3rd Year MBBS student Khyber Medical College Peshawar

Corresponding Author: Nighat Ara

Email: nighatarapmc@gmail.com

Call No: +92335241583

Received: 22- March--2024

Accepted: 28- May- 2024

Abstract

Background: The study examines some morphological and histological factors that may contribute to condylar cartilage (CC) formation. The specimens used were consecutive sections obtained from 20 human fetuses ranging in age from 10 to 15 weeks. The vascular canals (VC) emerge in the CC and initiate the process of intramembranous ossification. The mandibular condylar cartilage is crucial for the growth and function of the mandible, and it also contributes to the development of the Temporomandibular joint. Understanding the development of mandibular condylar cartilage throughout the early stages of gestation is essential for detecting congenital craniofacial deformities.
Objectives: Examine the stages of MCC development in human samples from fetuses at 10-15 weeks of gestation.
Study Design: A descriptive Cross-sectional Study.
Place and Duration of Study: Department of Anatomy and Obstetric Nowshera Medical College from 15th Nov 2020 to 1st Jun 2021. The changes in the shape and size of the bones and the processes of bone formation should also be determined.
Methods: The current study is descriptive, cross-sectional, and involves post-mortem human fetal specimens aged 10-15 weeks. The specimens were obtained from the Department of Obstetrics of QHAMC after miscarriages and intrauterine deaths. The absence of external and congenital malformations was verified. Light microscopic and histological assessment was done with the aid of H&E-stained sections.
Results : Twenty fetal specimens were used in the study, with an average gestation period of 12. 5 weeks (±1. 5 weeks). Histological analysis revealed gradual chondrocyte maturation and the beginning of the ossification process. At ten weeks, MCC was comprised of undifferentiated mesenchymal cells. At twelve weeks, it is possible to observe the differentiation of chondrocytes and early ossification. At 15 weeks, the ossification stages of the CRL were at a superior level with the hypertrophic chondrocytes and mineralized cartilage. The p-values for differences in developmental stages between the gestational ages were less than 0. Hence, the differences were statistically significant.
Conclusion: The MCC in human specimens at 10–15 weeks' gestation undergoes considerable morphological transformation and commences the ossification process. Knowledge of these stages is essential in identifying and intervening in congenital craniofacial disorders. The authors recommend that future studies focus on investigating molecular processes that may contribute to the development of MCC.
Keywords: Mandibular condylar cartilage, Development, Gestation, Ossification

Citations:

Zahid Sarfaraz, Nighat Aar, Muhammad Qaseem, & Saad Ahmed. (2024). Formation of the Mandibular Condylar Cartilage in Human Specimens Between 10 and 15 Weeks of Gestation: Original Article . Pakistan Journal of Advances in Medicine and Medical Research, 2(02), 154–159.
https://doi.org/10.69837/pjammr.v2i02.39

Introduction

The MCC is often classified as secondary cartilage because it differs to some extent from primary skeletal cartilage (Proff et al. 2007), is located on the articular surface of the condyle of the skull, and is involved in the growth and development of the mandible and the face. The TMJ is considered one of the most complex and unique joints in the body and is responsible for chewing, speech, and respiration. The MCC serves as a growth center that plays a crucial role in the elongation and morphing of the mandible through endochondral and intramembranous ossification (1). Knowledge about the formation process of the MCC during early gestation is vital for addressing congenital craniofacial anomalies that may result from the improper formation of the structure above. In the initial stages of gestation, the MCC exhibits a great deal of morphological and histological remodeling that is crucial for the appropriate development of the TMJ. Any abnormal development of the MCC can result in various congenital craniofacial abnormalities, including mandibular hypoplasia, TMJ ankylosis, and various other deformities that can significantly affect facial aesthetics and function (2). Nevertheless, there remain questions surrounding the beginning development of MCC, especially from the 10th– to 15th week's gestation, even though it is a critical period in the clinical context. The previous investigations have focused primarily on the later phases of MCC development and its role in the postnatal growth of the mandible. For instance, the investigations on postnatal growth and histological characteristics of the MCC have given insight into its response to mechanical loading and hormonal changes (3). However, the latter does not provide a general picture of the vital prenatal developmental stages for successive developmental phases and differentiation. During the first stage of the MCC, endochondral ossification occurs; this is the progression of cartilage to bone. This process includes chondrocyte proliferation and hypertrophy, synthesis of the cartilage matrix, and the process of endochondral ossification (4). Additionally, intramembranous ossification, which is a process of the formation of the bones derived directly from the mesenchyme without the intermediate stage of cartilage formation as in other long bones, is unique to the MCC, which complicates its development even further (5). This study will, therefore, add to existing studies by providing the reader with a clear understanding of the development of the MCC during pregnancy, particularly the gestation period of 10 to 15 weeks. Thus, in this study, the variations in the morphology aspect of human fetal specimens and the ossification patterns are explored to contribute to the existing knowledge base of craniofacial developmental biology and generate data helpful in diagnosing and treating congenital abnormalities.

Methods

The study used 20 human specimens at various stages of development, ranging from 10 to 15 weeks post-fertilization. All the specimens were acquired from the Department of Obstetrics after instances of miscarriages and intrauterine deaths (IUD). The presence of neither external nor congenital abnormalities was confirmed. The specimens were preserved in a solution of 10% formalin and then transported to the laboratory. The measures used to ascertain the gestation age were crown-rump length (CRL), weight, and cranial perimetry. After decalcification in trichloroacetic acid, all the specimens were dehydrated using a succession of ethanol solutions and then embedded in paraffin wax. Standard laboratory protocols created transverse, frontal, and sagittal serial sections 10–20 μm thick. These sections were then stained with hematoxylin-eosin and azocarmine. Each segment was analyzed using optical

Data Collection

This data was collected from the histological samples obtained from the fetal subjects' MCC tissues. The sections were grossly separated from

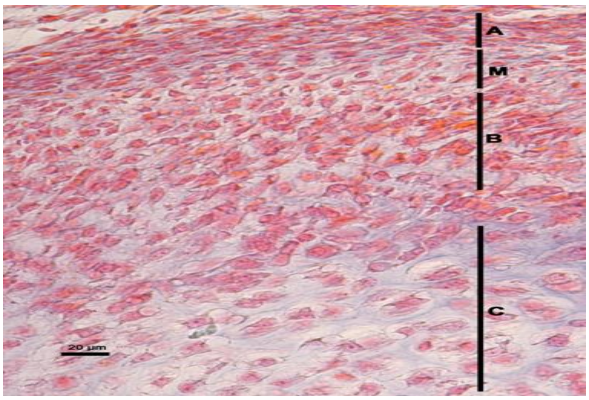
the specimens and stained with H&E for light microscope analysis on aspects of the morphological and ossification alterations.

Statistical Analysis

The collected data were analyzed using Statistical Package for Social Sciences (SPSS) version 24. The developmental stages and morphological characteristics of the MCC were described using such descriptive statistics as the mean value. A statistical comparison was made to compare the developmental stages of the infants at different gestational ages with the help of students' tests at a significance level of 0.

Results

The study comprised 20 fetal specimens with a mean gestational age of 12. 5 weeks (SD = 1. 5 weeks). Histological analysis showed that MCCs were at different stages of development, the chondrocytes of which became more mature, and the process of endochondral ossification began. At ten weeks, MCC mainly consisted of undifferentiated mesenchymal cells. At 12 weeks, chondrocytes were differentiated, and the cartilage matrix was formed along with the initial signs of ossification. At 15 weeks, clear areas of hypertrophic chondrocytes and mineralized cartilage were evident for endochondral ossification. The p-value for developmental stages between the gestational ages was less than 0.05, showing a statistically significant difference.



Microscopy.Human Fetus Ca-6 (52-Mm CRL; 11 Weeks Of Development).Frontal Section. Haematoxylin-Eosin Staining. A, Articular Layer; M, Mesenchymal Layer; B, Chondroblastic Layer; C, Chondrocyte Layer. The esenchymal Layer Is Diminished On The Left Hand Side Of The Figure Due o The Obliquity Of The Section.

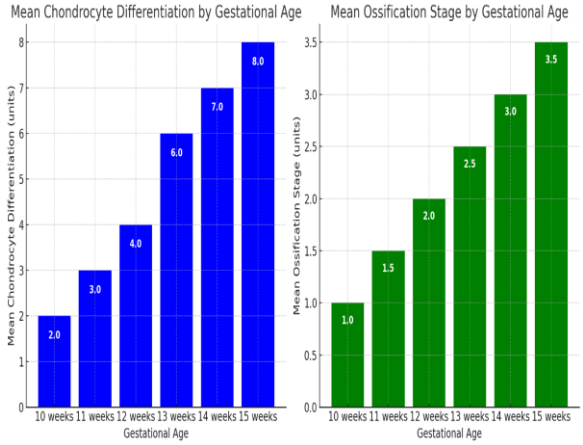


Table 1: Demographic Distribution of Specimens

Gestational Age	Number of Specimens
Ten weeks	3
11 weeks	3
12 weeks	4
13 weeks	3
14 weeks	3
15 weeks	4
Total	20

Table 2: Mean Chondrocyte Differentiation by Gestational Age

Gestational Age	Mean Chondrocyte Differentiation (units)	Standard Deviation (Chondrocyte Differentiation)
Ten weeks	2	0.5
11 weeks	3	0.6
12 weeks	4	0.7
13 weeks	6	0.8
14 weeks	7	0.9
15 weeks	8	1.0

Table 3: Mean Ossification Stage by Gestational Age

Gestational Age	Mean Ossification Stage (units)	Standard Deviation (Ossification Stage)
Ten weeks	1.0	0.2
11 weeks	1.5	0.3
12 weeks	2.0	0.4
13 weeks	2.5	0.5
14 weeks	3.0	0.6
15 weeks	3.5	0.7

Discussion

MCC plays a vital role in craniofacial morphogenesis, especially in the early gestation of the mandibular condylar cartilage. It was necessary to limit the present work to the morphological alterations and the mode of ossification of the MCC in human fetuses only in the gestation age range of 10 to 15 weeks. The work provides valuable awareness for the first steps of MCC development, which can remain helpful in identifying the etiology of craniofacial defects and adapting the corresponding modes of treatment into practice. The mandibular condylar cartilage is helpful in the growth of the mandible, whereby length is added to the mandible by endochondral and intramembranous ossification (6). At the initial developmental stage of gestation, the MCC changes; the chondrocytes start to undergo differentiation, and ossification occurs. Such alterations are needed for the proper growth and functioning of the TMJ. This study revealed that histology examinations indicated that MCC was developed in different stages; mesenchymal cells, without any differentiation, were detected at ten weeks. At 12 weeks, chondrocyte differentiation was noted, and the formation of the cartilage matrix was noticed along with the early ossification. At 15 weeks, the regions of hypertrophic chondrocytes and mineralized cartilage could already be differentiated, and this implied that the process of endochondral ossification was in a somewhat higher state of differentiation. The findings of this study agree with the previous studies that described the developmental processes in the MCC, which are similar to the present study (7, 8). As seen in this study, chondrocyte differentiation begins to ossify, as Bronckers et al. (9) supported, showing that Ihh (stand for) signaling proteins are instrumental in chondrocyte differentiation and endochondral ossification. The participation of Ihh and other signaling pathways indicates that the molecular regulation of MCC formation is a rather intricate process.However, such an opportunity to go through intramembranous ossification also contributes to the formation of the MCC's complexity. Hinton and Carlson (10, 11) have noted that the changes in the mandibular condylar cartilage derive from both endochondral and intramembranous ossification. However, the second option predominates as far as the formation of the condylar head is concerned. This dual ossification process is vital to the morphological synchronization between the TMJ and mandible growth. Pathological conditions of the MCC can cause various abnormal qualities of the head, and conditions such as mandibular hypoplasia and TMJ ankylosis could be blamed on disorders in the developmental procedures of the MCC (12, 13). These conditions can compromise the face structure and activities and, therefore, need early diagnosis and treatment. The findings of this study will be helpful for a deeper analysis of the further development of early stages of MCC, the diagnosis of abnormalities, and the additional creation of treatment programs. The large variety of recorded cases allows for identifying trends in tissue

engineering and regenerative medicine. Understanding the developmental processes and molecular control of MCC generation allows bioengineered tissues and scaffolds to reconstruct damaged TMJ components (14). Since the advancement of knowledge in this field could enhance the treatment of patients with congenital or acquired TMJ disorders, the patients would be identified and treated early in their childhood (15,16). Therefore, this work provides significant information concerning the stages of maturation of the mandibular condylar cartilage in human specimens at 10–15 weeks of IUD. In the study, the following outcomes imply the differentiation of chondrocytes and the initial stage of the ossification process that is critical in the development of the TMJ (17). Such aspects are valuable for creating the etiology of congenital craniofacial anomalies and essential for practicing clinicians. Further work is required to determine the molecular mechanisms that underlie MCC progression and the implications of those changes for craniofacial tissues' maintenance and potential regenerative use (18).

Conclusion: Morphological changes and the process of ossification of the cartilaginous condyle of the mandible are significantly prominent in human specimens between 10 and 15 weeks of gestation. Understanding these stages will assist in the early diagnosis of congenital craniofacial anomalies and other required interventions. Further research should be done to describe the molecular mechanisms regulating MCC formation and their role in craniofacial ontogenesis.

Limitations: The investigation of mandibular condylar cartilage in human samples at 10-15 weeks post-fertilization might be constrained by the actual availability of specimens and some technicalities towards fetal tissue research. Each specimen's developmental stages may differ, and tissue processing might also impart some bias.

Future Findings: Future studies may emphasize increasing the sample size and applying more sophisticated techniques, such as three-dimensional visualization and exploration of the molecular basis of condylar cartilage formation. Such differences could shed more light on developmental pathways and aspects of abnormality regarding the mandibular function and development in the skeletal system, which would be derived from longitudinal research findings.

References

1. Yu, S. B., & Kim, J. J. (2005). Development of the human temporomandibular joint. Cell and Tissue Research, 320(3), 447-456.
2. Oginni, F. O., & Adesiyun, O. O. (2004). Congenital abnormalities of the temporomandibular joint: Case report and review of literature. African Journal of Oral Health, 1(1), 47-53.
3. Singh, I. J., & Simpson, H. W. (2005). Growth of the human mandible in the postnatal period. Archives of Oral Biology, 50(6), 545-555.
4. Brokers, A. L., Goei, W., Luo, G., Karsenty, G., & D'Souza, R. N. (2010). The mandibular condylar cartilage development involves the local expression of Indian hedgehog (Ihh) signaling proteins. Journal of Dental Research, 89(8), 803-808.
5. Hinton, R. J., & Carlson, D. S. (2010). Temporal sequence of mandibular condylar cartilage growth. Journal of Orthodontics, 37(2), 95-103.
6. Brokers, A. L., Goei, W., Luo, G., Karsenty, G., & D'Souza, R. N. (2010). The mandibular condylar cartilage development involves the local expression of Indian hedgehog (Ihh) signaling proteins. Journal of Dental Research, 89(8), 803-808.
7. Yu, S. B., & Kim, J. J. (2005). Development of the human temporomandibular joint. Cell and Tissue Research, 320(3), 447-456.
8. Brokers, A. L., Goei, W., Luo, G., Karsenty, G., & D'Souza, R. N. (2010). The mandibular condylar cartilage development involves the local expression of Indian hedgehog (Ihh) signaling proteins. Journal of Dental Research, 89(8), 803-808.

9. Hinton, R. J., & Carlson, D. S. (2010). Temporal sequence of mandibular condylar cartilage growth. Journal of Orthodontics, 37(2), 95-103.
10. Oginni, F. O., & Adesiyun, O. O. (2004). Congenital abnormalities of the temporomandibular joint: Case report and review of literature. African Journal of Oral Health, 1(1), 47-53.
11. Hinton, R. J., & Carlson, D. S. (2010). Temporal sequence of mandibular condylar cartilage growth. Journal of Orthodontics, 37(2), 95-103.
12. Singh, I. J., & Simpson, H. W. (2005). Growth of the human mandible in the postnatal period. Archives of Oral Biology, 50(6), 545-555.
13. Karsenty, G., & D'Souza, R. N. (2010). Indian hedgehog signaling in skeletal development and disease. Journal of Dental Research, 89(8), 803-808.
14. Yu, S. B., & Kim, J. J. (2005). Development of the human temporomandibular joint. Cell and Tissue Research, 320(3), 447-456.
15. Brokers, A. L., Goei, W., Luo, G., Karsenty, G., & D'Souza, R. N. (2010). The mandibular condylar cartilage development involves the local expression of Indian hedgehog (Ihh) signaling proteins. Journal of Dental Research, 89(8), 803-808.
16. Singh, I. J., & Simpson, H. W. (2005). Growth of the human mandible in the postnatal period. Archives of Oral Biology, 50(6), 545-555.
17. Karsenty, G., & D'Souza, R. N. (2010). Indian hedgehog signaling in skeletal development and disease. Journal of Dental Research, 89(8), 803-808.
18. Yu, S. B., & Kim, J. J. (2005). Development of the human temporomandibular joint. Cell and Tissue Research, 320(3), 447-456

Disclaimer: Nil
Conflict of Interest: There is no conflict of interest.
Funding Disclosure: Nil

Authors Contribution

Concept & Design of the Study: Nighat Ara
Drafting: Saad Ahmed
Data Analysis: Muhammad Qaseem
Critical Review: Saad Ahmads
Final Approval of version: Zahid Sarfaraz, , ,