

Determination of Mandibular Condylar Uptake in Asymptomatic Population

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ABSTRACT

Objective: To determine mandibular condylar uptake values in normal population through quantitative analysis employing Tc-99m MDP SPECT/CT.

Study Design: Cross-sectional study.

Place and Duration of study: Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi, Pakistan, from Jul 22 to Jul 23.

Methodology: A total of 129 individuals, both genders aged 10 to 40 years, with no known skull pathology, were included in the study. Quantitative analysis of Tc-99m MDP SPECT/CT bone scan of asymptomatic population was used to calculate mandibular condyle to clivus ratio. A percentage uptake difference less than or equal to 10 % between both mandibular condyles was considered acceptable.

Result: The study cohort comprised 129 subjects (n=129), with 72(55.8%) males and 57(44.1%) females. Age ranged from 12 to 40 years (Mean±SD: 25.70±8.49). The mean mandibular condyle-to-clivus ratio on the right side was 0.97±0.12 and on the left was 0.98±0.13, which showed low variability (CV ~ 12 - 13%). However, the mean percentage difference in condylar uptake on both sides was 4.13±2.64 %, which showed very high variability (CV=63.92%). Gender-based comparison showed a significantly higher right condyle to clivus ratio in females (1.00±0.10) compared to males (0.94±0.12), with a *p*-value of 0.005 and a moderate effect size (Cohen's *d* = -0.33).

Conclusion: Determination of normal mandibular condylar uptake values in our population will contribute to enhanced diagnostic accuracy in maxillofacial applications of nuclear medicine, like condylar hyperplasia or Temporomandibular joint (TMJ) abnormalities.

Keywords: Computed Tomography, Facial Asymmetry, Mandibular Condylar Hyperplasia.

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INTRODUCTION

Skeletal scintigraphy has a pivotal role in the diagnosis of various bone pathologies, especially in the detection of metastatic bone deposits and foci of active bone turnover. Nuclear medicine techniques employ radiotracers, which are taken up by the target organ/tissue and thus help determine their functional status. Tc-99m MDP is the most used radiopharmaceutical for bone imaging, and its skeletal uptake is proportional to local bone perfusion and metabolism. This characteristic helps in qualitative and quantitative assessment of areas of active bone turnover, like epiphyseal end plates, fracture sites, and regions of hyperplasia.¹ Among maxillofacial applications of bone scan, the most common are mandibular condylar hyperplasia and/or Temporomandibular joint (TMJ) abnormalities. Mandibular condylar hyperplasia is a cause of mandibular overgrowth, facial asymmetry, and pain

or dysfunction of TMJ, leading to bone scan referral in young adults.² The exact etiopathogenesis of this phenomenon is still unknown. However, it is postulated that in some endocrine disorders, chondrocytes express more growth factors, which lead to overgrowth of mandibular condyles.³

Like other imaging modalities, where comparison of ipsilateral and contralateral structures is used for diagnosis, bone scan also relies on comparative analysis of bilateral bony structures, with mandibular condylar uptake values frequently used for planar and SPECT/CT interpretation.⁴ This determines normal mandibular condylar uptake values extremely important for the appreciation of asymmetric uptake or bilaterally increased or decreased condylar uptake. Documented qualitative and quantitative scintigraphic methods used by researchers and nuclear medicine consultants include the study of differences in relative uptake of both mandibular condyles and estimation of the condyle to clivus ratio.⁵ Due to limited research on the subject in this part of the world, Medline/PubMed search did not reveal any research study that tried to

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determine normal mandibular condylar uptake values in the asymptomatic population.

This study aims to determine normal Tc-99m MDP uptake in mandibular condyles with uptake in clivus as reference, employing SPECT/CT quantitative analysis in asymptomatic population. The rationale for determination of normal Tc-99m MDP uptake values in condylar hyperplasia and TMJ pathology is the possibility of misinterpretation of bone scan results in cases of bilaterally symmetrical disease and /or equivocal cases where uptake values qualitatively appear normal or near normal.

METHODOLOGY

The cross-sectional study was conducted at Nuclear Medical Centre, Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan, from Jul 22 to Jul 23. A non-probability convenience sampling technique for participant selection was used. Assuming the expected population standard deviation to be 0.17, and employing t-distribution to estimate sample size, a sample size of 127 was calculated, using WHO Calculator, to estimate a mean with 95% confidence and a precision of 0.036. Approval by the Ethical Review Committee, Armed Forces Institute of Pathology (AFIP) Committee, Rawalpindi IRB number FC-NMC21-24/READ-IRB/22/1284 (Date:23-06-2022), was taken before the start of the study.

Inclusion Criteria: All patients of both genders, aged 10 - 40 years who reported for bone scintigraphy for evaluation of suspected or known skeletal conditions other than skull were included in the study.

Exclusion Criteria: Patients with a history of trauma to face, surgery to temporomandibular joint, fracture of mandible, symptoms of compromised joint like pain and jaw movement restriction and the patients with relative mandibular condylar uptake more than 10% were excluded from the study.

After taking a detailed history that included age, gender, history of facial trauma or any known facial or skull pathology, and symptoms of temporomandibular pathology, and performing a clinical examination of the patients that included any facial asymmetry or jaw deviation, Tc-99MDP was injected intravenously at a dose of 08-10 Mega Becquerel/kg (0.216-0.27millicurie). The Pediatric Dosage Card of EANM was used to calculate the injected dose for those less than 18 years old. A bone scan was performed 03 hours after injection. This was followed by SPECT/CT of the skull using a

SPECT/CT hybrid system composed of a dual-head variable-angle planar gamma camera with a Low Energy High Resolution (LEAP) collimator. The peak energy level was set at 140 keV with a 20% window width. A total of 64 projection images of 20 s each were acquired over 180 using a 128×128 matrix and a pixel size of 23mm.² Images were reconstructed with ESoft software (OSEM) with a Butterworth filter.

The whole condylar approach was used to draw the region of interest (ROI) on the transaxial slice where condyles were visualized, and total counts were calculated. An identical ROI was applied to either side of the condyles to obtain the maximum count per pixel. Relative uptake in mandibular condyles was calculated, and keeping in view the published literature value of < or equal to 10% was used for confirmed asymptomatic population for condylar hyperplasia.² The difference in activity between the condyles was calculated by dividing sum counts in both condyles by the ipsilateral condylar count= $\times 100\%$. After that condyle to clivus ratio was calculated by drawing a fixed ROI on both condyles and clivus on a transaxial image. Clivus was taken for internal validation as it is the least metabolically active bone and has no articulation to other bones of the skull. The right and left condylar to clivus ratio was calculated separately in each participant.

The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 27.0. The normality of data for continuous variables was assessed by the Shapiro-Wilk test. Mean and standard deviation were calculated for normally distributed variables such as Rt mandible to clivus ratio and Lt mandible to clivus ratio; hence, for comparisons across age groups, one-way ANOVA was applied, and differences across gender were evaluated using independent samples t-tests of these variables. Median, interquartile range (IQR), and range were calculated for 'percentage condylar uptake difference' as it was non-normally distributed, so to characterize the distribution across gender and age groups, the Mann-Whitney U test and Independent Sample Kruskal-Wallis were used, respectively. Effect sizes were reported as Cohen's d for parametric tests and rank-biserial correlation for non-parametric tests, where applicable. A significance threshold of $p < 0.05$ was used for all statistical tests.

RESULTS

The study cohort consisted of 72(55.8%) males and 57(44.1%) females, aged 12-40 years (mean:

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25.70±8.49 years). The mean right condyle-to-clivus ratio was 0.97±0.12, and the left was 0.98±0.13, both showing low variability (CV~12-13%). The mean percentage difference in condylar uptake was 4.13±2.64% (range: 0-10%), with a higher variability (CV=63.92%). Distribution of the variables in this cohort is summarized in Table-I.

Table-I: Descriptive Statistics Of Participant Demographics and Condylar Uptake Values (n=129)

	Mean±SD (Range)	Median (25th - 75th Percentile)	CV (%)
Rt mandibular condyle to clivus ratio	0.97±0.12 (0.52-1.31)	0.97 (0.89-1.04)	12.37
Lt mandibular condyle to clivus ratio	0.98±0.13 (0.62-1.41)	0.96 (0.89-1.05)	13.26
% Condylar uptake difference	4.13±2.64 (0.00-10.00)	4.00 (2.00 -6.00)	63.92

The right condyle to clivus ratio was significantly higher in females than in males, with a moderate effect size ($p=0.005$, Cohen's $d = -0.51$). The left condyle to clivus ratio showed a trend toward higher values in females compared to males, but this difference was only marginally statistically significant ($p=0.051$), as shown in the figure. The percentage uptake difference in both condyles did not differ significantly between genders, with both groups showing a median difference of 4% and similar interquartile ranges. The rank-biserial correlation indicated a negligible effect size ($r=0.03$) Table-II.

Table-II: Gender Distribution Of Mandibular Condyle-To-Clivus Ratios and Condylar Uptake Difference (n=129)

	Gender		p-value	Effect Size
	Male (n = 72)	Female (n = 57)		
	Mean±SD / Median (IQR) (range)			
Rt mandible to clivus ratio	0.94± 0.12 (0.52-1.22)	1.0± 0.10 (0.80- 1.31)	0.005c	-0.51e
Lt mandible to clivus ratio	0.96±0.13 (0.71-1.41)	1.01± 0.13 (0.62 - 1.32)	0.064c	-0.33e
% Condylar uptake difference	4.00 (4.00) (0.0-10.0)	4.00 (2.00) (1.0-10.0)	0.771d	0.03f

c Independent sample T-test
d Mann-Whitney U test
e Cohen's d
f Rank biserial correlation

Across the 11-20, 21-30, and 31-40 age groups, no significant differences were observed in mandibular condyle-to-clivus ratios or condylar %

uptake difference ($p>0.2$), indicating consistency in uptake across age Table-III.

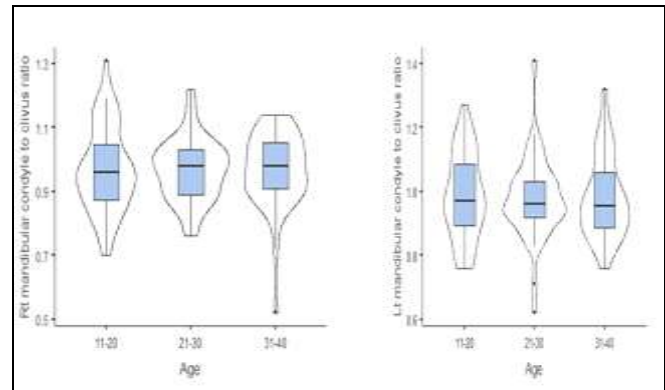


Figure: Condyle to Clivus Uptake Difference Across the Age

Table-III: Comparison of Mandibular Condyle-To-Clivus Ratios and Uptake Differences Across Age Groups (n=129)

	Age (years)			p-value
	11 - 20 (n = 42)	21 - 30 (n = 43)	31 - 40 (n = 44)	
	Mean ± SD / Median (IQR)			
Rt mandibular condyle to clivus ratio	0.97±0.13	0.97±0.10	0.97±0.12	0.993a
Lt mandibular condyle to clivus ratio	0.98±0.13	0.98±0.13	0.98±0.13	0.949a
Condylar % uptake difference	3.00 (2.00- 4.00)	4.00 (3.00- 6.50)	3.00(2.00 - 6.00)	0.087b

aOne-way ANOVA

b Kruskal-Wallis

DISCUSSION

In this study, no significant differences were observed in mandibular condyle-to-clivus ratios or condylar % uptake difference ($p>0.2$), indicating consistency in uptake across age. The study objective was to analyze mandibular uptake ranges across age groups from 11-40, which showed that across the 11-20, 21-30, and 31-40 age groups. Gender based analysis showed that the right condyle to clivus ratio was significantly higher in females (1.00±0.10) than in males (0.96±0.13), with a p -value of 0.005, and a moderate effect size (Cohen's $d=-0.51$). The left condyle to clivus ratio showed a trend toward higher values in females compared to males, but this difference was only marginally statistically significant ($p=0.051$).

Tc-99m radionuclide uptake in mandibular condyles can represent the ongoing growth in it.⁷ A retrospective study conducted by Olate *S et al.*, stated

that the growth process in young adults is strong, especially in age of 10-15 years.⁸ In our study, 42 individuals were within range of 11-20 years. This study suggested it is important to diagnose condylar hyperplasia in its active or inactive phase. So that time and method of intervention that must be applied should be decided. Various diagnostic techniques are used for its evaluation. Planar whole-body bone scintigraphy has its disadvantages, as it may superimpose various other skull bones mimicking mandibular condyles. For this, single photon emission tomography (SPECT/CT) skull is a definite technique in which SPECT is fused with a CT component radiation dosage from this low-dose CT is 20-25% of the normal CT scan.

A national study conducted by Haider *et al.*, (33 patients) showed a comparison of planar and SPECT/CT, concluding that planar bone scan could not accurately differentiate between external auditory meatus and TMJ on 2D images that were further confirmed by SPECT/CT.⁹ In this study, 3D SPECT/CT was only used to minimize the overlapping effect of other skull bones on the TMJ joint.

An international study conducted by Ouyang *et al.*, on 54 Chinese individuals, where the cutoff for positive condylar hyperplasia was taken as 13%.¹⁰ Guennouni *et al.*, reported a case report where the uptake difference for active hyperplasia came out to be 14.29%.¹¹ The data in study by Lopez *et al.*, showed relative percentage uptake values in mandibular condyles used for the asymptomatic population found maximum differences of 6%, 6.2%, 6.7% and 8.7%.¹² In this study maximum percentage difference was found to be 4%.

López *et al.*, further modified by taking the condyle to clivus ratio in patients with facial asymmetry. In females, this ratio was above 1.33, and for males, this ratio was above 2.09.¹³ Our study established ratios in the asymptomatic population by taking a percentage difference of less than 10% as a reference. Niño-Sandoval *et al.*, proposed that structural references be used for comparing MDP radiotracer uptake in mandibular condyles, including cervical 3 vertebrae, Lumbar 4 vertebrae, and clivus. Clivus is more easily visualized within the field of mandibular condyles on SPECT/CT skull, so it is most acceptable reference that could be used for evaluating condylar hyperplasia.¹⁴ De Schepper *et al.*, also used clivus as a reference point.¹⁵ Karssemakers *et al.*, stated

that there could be a difference in uptake values of both condyles due to repeated stress given by mastication; so clivus is a reference point.¹⁶

Hamed *et al.*, used the condyle to L4 ratio to compare planar bone scan with that of SPECT/CT.¹⁷ After different supportive literature, clivus was used as the reference point in this study. CT component of the SPECT/CT is important to draw an exact ROI over mandibular condyles and clivus, also augmented by López *et al.*, that SPECT/CT is more specific (specificity 100%) when compared to SPECT alone, which is only sensitive (sensitivity 80%).¹⁸ SPECT/CT allows a 3D approach to avoid any misinterpretation of overlapping structures.¹⁹ This study showed a relative percentage difference of 4%, while values for mandibular condyles 11-20 years were 0.97 ± 0.13 . This ratio is reduced to 21-30 with again rising trend in 31-40 years, which could be age-related bone remodeling as one possible cause, which is also studied by Agarwal *et al.*,²⁰

This study showed that the right condyle to clivus ratio was significantly higher in females (1.00 ± 0.10) than in males (0.96 ± 0.13), with a *p*-value of 0.05 and a moderate effect size (Cohen's *d* = -0.51) in the asymptomatic population, while the left condyle to clivus ratio showed a trend toward higher values in females compared to males. The gender-based significant difference in right condyle-to-clivus ratios, with higher uptake in females, indicates a potential physiological variation that may have diagnostic relevance.^{21,22}

Although the study highlighted that the left condyle ratio also trended higher in females, it did not reach conventional statistical significance. However, other medical conditions, either local or systemic, should be kept in mind during the treatment of condylar hyperplasia, and patients with uncertain diagnoses should be kept for follow-up.

LIMITATION OF STUDY

Subjects enrolled through a non-probability consecutive sampling technique may not be representative of the entire population. Secondly, this study only included asymptomatic patients referred for bone scan indications other than condylar pathology, but it is not possible to rule out condylar pathology based on history alone.

CONCLUSION

The mean percentage difference in condylar uptake was 4.13 ± 2.64 (range: 0-10%), while across the age groups no significant differences were observed in mandibular condyle-to-clivus ratios or condylar indicating consistency in uptake across age. Gender-based comparison showed a

significantly higher right condyle to clivus ratio in females (1.00 ± 0.10) compared to males (0.94 ± 0.12), with p-value of 0.005 and moderate effect size (Cohen's $d = -0.33$). Determination of these normal values of mandibular condylar uptake in our population enhances diagnostic accuracy in evaluating condylar hyperplasia or TMJ abnormalities, thus contributing to evidence-based decision-making in maxillofacial applications of nuclear medicine.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

RF & FH: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZSD & MIN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RS & MR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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