Original Article

Histopathological Osteomyelitis Evaluation Score (HOES): Pioneering precision for diagnosing jaw osteomyelitis

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Abstract

Background: Osteomyelitis is an inflammatory condition of bone that may arise in response to a foci of infection. A multidisciplinary approach is necessary between the clinician, pathologist, and radiologist to give an early diagnosis for initiating early treatment to prevent lifelong debility.

Objective: The objectives of this study were to analyze the applicability of Histopathological Osteomyelitis Evaluation Score (HOES) in diagnosing different stages of jaw osteomyelitis and to compare the HOES method with preoperative and conventional histopathological diagnosis.

Method: In this retrospective study, 40 slides of preoperatively diagnosed cases of osteomyelitis were evaluated semiquantitatively using HOES criteria for acute (A1, A2, and A3) and chronic (C1 and C2) cases based on histopathological changes in the bone, soft tissue, and inflammatory infiltrate. The results obtained were compared and correlated to preoperative diagnosis and conventional histopathological diagnosis by using Chi-square and Spearman's correlation coefficient.

Result: Out of 40 cases, 26 (65%) were men and 14 (35%) were women, with a mean age of 45.1 years (range: 7 to 70 years). The frequency of occurrence was found to be 68% in mandible and 32% in maxilla. Significant association was observed between HOES and conventional histopathological diagnosis ($\chi^2 = 15.91, P < 0.001$), as well as HOES and preoperative diagnosis ($\chi^2 = 12.69, P < 0.005$). The results of Spearman's correlation revealed 50% correlation of HOES with conventional histopathological diagnosis and 43% with preoperative diagnosis.

Conclusion: HOES serves as a systematic and precise method for classification and differentiation of different stages of osteomyelitis which aids in the stratification of patients for their treatment needs, preventing and halting the progression of disease at an early stage.

Keywords: Diagnosis, Histopathological Osteomyelitis Evaluation Score (HOES), jaw osteomyelitis, osteomyelitis

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INTRODUCTION

Osteomyelitis is an inflammatory condition of bone that may arise in response to a foci of infection (due to trauma, surgery, or prosthesis), secondary to vascular insufficiency, or could be hematogenous in origin.[1] While osteomyelitis can affect bones throughout the body, its

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occurrence in the jaw is particularly concerning due to its proximity to important anatomical structures like teeth, nerves, muscles, and blood vessels along with the effects of oral microbial flora on disease progression and remission. It typically presents with localized pain, swelling, trismus, and systemic signs such as fever in acute stages. Chronic cases may feature persistent pain, fistula formation, necrotic bone, and intermittent swelling. The disease progresses from acute inflammation with vascular compromise to chronic stages marked by fibrosis, necrosis, and biofilm-protected bacterial colonies, complicating treatment and leading to prolonged morbidity. Until now histologic examination of bone specimens coupled with bone cultures is considered as the "gold standard" for the diagnosis of osteomyelitis. Bone culture is a highly reliable diagnostic modality; however, in practice, preprocedural antibiotic administration, salivary contamination of bone sample, soft tissue contamination, sampling errors, low pathogen count and culture failure limit the use of bone cultures.[2,3] Microbiological analysis of sample can be influenced by multiple clinical factors too; therefore, it is important to search for a more reliable and objective histopathological diagnostic method for osteomyelitis. As the disease progresses from an early infection to a chronic form, it undergoes various histopathological changes to prevent the progression or an attempt to repair the bone; all these histopathological changes can be analyzed and employed for diagnosing and classifying osteomyelitis. Though various classifications of jaw osteomyelitis (OJ) have been proposed, among which Zurich classification is the most widely used classification which primarily classifies it into three distinct types: acute osteomyelitis, secondary chronic osteomyelitis, and primary chronic osteomyelitis. However, it has certain limitations as it relies heavily on clinical presentation, which is subjective and can vary significantly among patients, often leading to overlaps between categories. Moreover, the classification lacks standardized histopathological criteria, which are critical for objectively confirming and staging osteomyelitis, especially in complex cases. It also fails to address refractory or recurrent cases comprehensively and is less applicable to noninfectious causes of bone inflammation. In 2014, Tiemann *et al.* described a criteria based system known as Histopathological Osteomyelitis Evaluation Score (HOES) which relies on quantifiable histopathological parameters for diagnosis and scoring of osteomyelitis.[4,5] This study is particularly significant as it is the first to employ the HOES system specifically for diagnosing jaw osteomyelitis, a condition with unique challenges due to the complex anatomy of the jaw and its exposure to diverse oral microbial flora.

METHODOLOGY

This study included a retrospective analysis of 40 histopathologically diagnosed (conventional histopathological diagnosis) cases of jaw osteomyelitis obtained from the archives of the Department of Oral and Maxillofacial Pathology at a dental institute in Gujarat.

The cases were preoperatively/provisionally diagnosed as osteomyelitis by clinician based on clinical and radiological assessment as mentioned in the records. The slides were reviewed and assessed by experienced pathologist who was blinded to the provisional clinical and conventional histopathological diagnoses to ensure unbiased evaluation using the HOES criteria proposed by Tiemann *et al.*[4] which is presented in two formats [Tables 1 and 2]: A tabular form for systematic evaluation and a written graduated form for detailed diagnostic interpretation. Table 3 provides the final assessment criteria, linking overall HOES scores to specific osteomyelitis diagnoses. This dual approach ensures clarity and adaptability in clinical and research applications [Flowchart 1].

The data obtained were analyzed using SPSS Software Version 26.0 (IBM Corp., Armonk, NY). The Chi-square

Table 1: Depicting acute and chronic HOES criteria given by Tiemann *et al*. (Tabular Form)[4]

Stages	Microscopic findings
A1	Osseonecrosis (0/1/2/3)
A2	Soft tissue necrosis (0/1/2/3)
A3	Granulocyte infiltrate (0/1/2/3)
C1	Bone neogenesis/fibrosis (0/1/2/3)
C2	Lymphocyte/macrophage infiltrate (0/1/2/3)

Where, 0=Nonexistent, 1=Mild (1/3rd of the section is involved), 2=Moderate (2/3rd of the section is involved), and 3=Severe (entire section is involved)

Table 2: Depicting written graduated form of HOES criteria given by Tiemann *et al*.[4]

Grades	Interpretation
I	Signs of an acute osteomyelitis
II	Signs of a chronically florid (that is to say active) osteomyelitis
III	Signs of a chronic osteomyelitis
IV	Signs of a subsided (calmed) osteomyelitis
V	No indication of osteomyelitis

Table 3: Assessment of overall HOES value and assignment of the written form after evaluation

OVERALL SCORE	INTERPRETATION
Sum of A1 to A3: ≥4	Signs of an Acute Osteomyelitis
Sum of A1 to A3 and C1 to C2: ≥6	Signs of a Chronically Florid (i.e., Active) Osteomyelitis
Sum of C1 to C2: ≥4	Signs of a Chronic Osteomyelitis
Sum of C1 to C2: ≤4	Signs of a Subsided (calmed) Osteomyelitis
Sum of C1 to C2: ≤1	No indication of Osteomyelitis

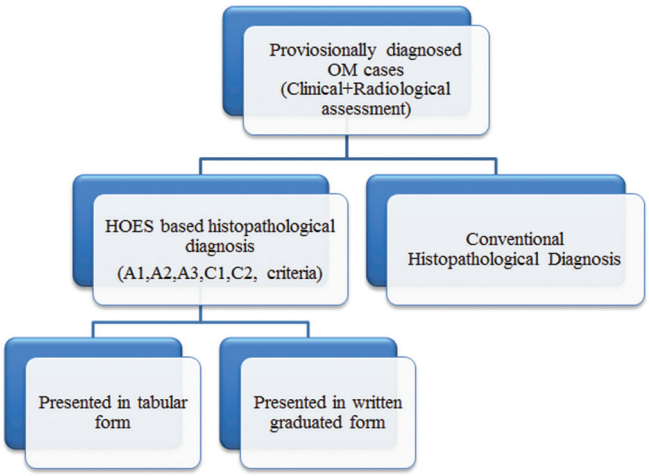
test was employed to determine the association between the variables and Spearman's correlation analysis determined the strength and direction of correlation of HOES with preoperative and conventional histopathological diagnosis. The level of statistical significance was set at a $P < 0.05$.

As the study involved retrospective analysis of the slides retrieved from the achieves of the department, institutional clearance and approval was obtained from the head of the institute.

RESULT

Out of 40 cases, 26 (65%) were males and 14 (35%) were females, with a mean age of 45.1 years (range: 7 to 70 years). Mandible and Maxilla were involved in 68% and 32% of cases, respectively. According to preoperative diagnosis, 65% cases were chronic and 35% were acute in nature. On conventional histopathological examination, 72.5% cases were diagnosed as chronic and 27.5% cases were diagnosed as acute osteomyelitis. Furthermore, when the same sections were classified according to HOES criteria, 57% cases were found to be Chronically Florid (active) Osteomyelitis, 23% cases were of Chronic Osteomyelitis, 2% cases of Acute Osteomyelitis, and 8% were Subsided cases of Osteomyelitis [Figures 1 and 2].

Significant association was observed between HOES and conventional histopathological diagnosis ($\chi^2 = 15.91$, $P < 0.001$), as well as HOES and preoperative diagnosis ($\chi^2 = 12.69$, $P < 0.005$). The results of Spearman›s correlation revealed 50% correlation with conventional histopathological diagnosis and 43% with preoperative diagnosis [Table 4].



Flowchart 1: Workflow of the study

DISCUSSION

Osteomyelitis, an inflammatory bone infection, encompasses both bacterial and nonbacterial etiologies. Among bacterial causes, Staphylococcus species is involved in approximately 75% of cases, with 30–60% cases attributed specifically to *S. aureus*.[6] This pathogen exhibits a multifaceted approach to bone colonization and persistence by interacting and binding to extracellular proteins, subsequently forming microcolonies termed as Staphylococcal Abscess Communities (SACs).[6-8] Furthermore, *S. aureus* exhibits the capability to create a fibrin network surrounding SACs, which serves as a shield against host immune responses, contributing to the persistence of the bacterial colonies.[9-11]

Its virulence extends into osteocyte-lacunae canaliculi networks, producing exfoliative toxins, pore-forming toxins, and super-antigens, which helps in surviving intracellularly and impeding immune responses.[12,13] These virulence strategies collectively contribute to the chronicity and recurrence of osteomyelitis cases, compounded by host factors such as immune-compromised states, systemic conditions like diabetes mellitus, trauma, compromised oral hygiene, and the presence of prosthetic devices.

The diagnosis of osteomyelitis poses significant challenges due to the absence of a standardized classification system.

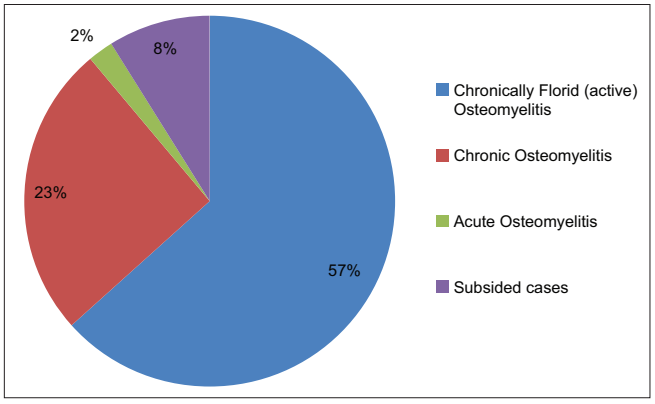


Figure 1: Pie chart depicting distribution of cases according to HOES classification

Table 4: Chi-Square and Spearman's correlation of HOES with provisional and conventional histopathological diagnosis respectively

Histo-pathological osteomyelitis evaluation score	Provisional diagnosis				Conventional histopathological diagnosis			
	χ^2	Sig*	Spearman's Correlation coefficient	Sig*	χ^2	Sig*	Spearman's Correlation coefficient	Sig*
	12.69	0.005	0.43	0.005	15.91	0.001	0.50	0.001

*Significant at $P<0.05$

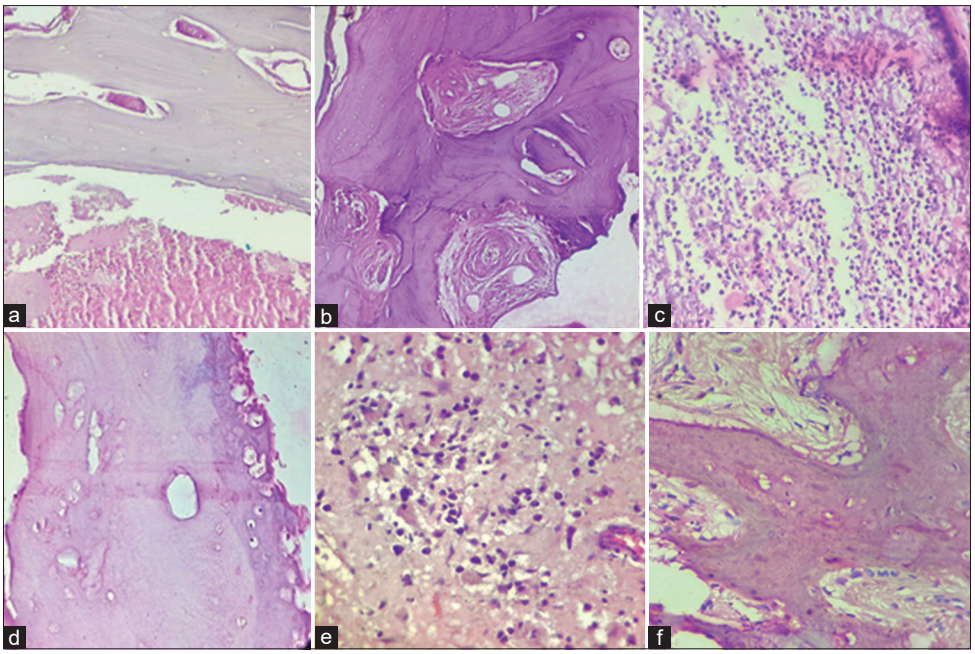


Figure 2: Photomicrograph showing features of HOES in graduated form. (a) Acute Osteomyelitis showing extensive osteonecrosis, microsequestra, and hemorrhagic areas. (b and c) Chronically florid osteomyelitis showing extensive osteonecrosis, fibrosis in intertrabecular area, mixed inflammatory infiltrate. (d and e) Chronic osteomyelitis showing partially necrotic bone with reparative osteogenesis and chronic inflammatory infiltrate. (f) Subsided osteomyelitis showing less necrosis with osteoblastic rimming and fatty marrow (H&E x100)

According to Zurich classification, OJ can be categorized into acute and chronic forms. Chronic form can be further subdivided as primary and secondary chronic osteomyelitis. Secondary chronic osteomyelitis and acute osteomyelitis represent different stages of same disease, associated with bone infection, while primary chronic osteomyelitis (PCO) is mostly not associated with bone infection, rather includes SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis), chronic recurrent multifocal osteomyelitis (CMRO), and juvenile mandibular chronic osteomyelitis (JMCO). Histopathological evaluation and microbiological investigations are the gold standards for diagnosing osteomyelitis. However, microbiological investigation encounter several issues, such as low pathogen counts, risk of contamination, prolonged processing time (up to 2 weeks), chances of false negative results, sample transportation to laboratory, and stringent aseptic practices while obtaining deep bone biopsies.[14,15] Lucidarme *et al*.[16] recommended collection of at least 5 bone samples for diagnosis. Complementary laboratory techniques, including PCR, demonstrate high sensitivity but carry risks of false positives, leading to overdiagnosis. Advanced methodologies, such as genomics, mass spectrometry proteomics (MALDI-TOF), prove invaluable in identifying difficult-to-cultivate opportunistic organisms and detecting antibacterial resistance.[17] However, their widespread application is hindered by cost constraints, requirement of laboratory infrastructure, and skilled technical personnel.

This study presents a comparative analysis of HOES in relation to preoperative and conventional histopathological diagnoses [Table 5]. Tiemann *et al*.[4] reported 68% correlation between HOES and preoperative diagnoses. In contrast, Stupina TA *et al*.'s[5] finding yielded a comparatively weaker correlation of 53.3%. The current study found even weaker correlation of 43.3% between HOES and preoperative diagnoses that may be attributed to the differences in the location and quality of bone biopsies that may lead to underrepresentation of certain disease features, such as fibrosis or granulocyte infiltration, crucial for HOES scoring. While 50% correlation was found between HOES and conventional histopathological diagnoses. Conventional diagnosis may rely heavily on the pathologist's interpretation, while HOES offers a more structured and semiquantitative approach based on histopathological assessment by dissecting the progression of disease into different stages which provides precise diagnosis and classification[5] and stands out as a cost-effective and practical method for systematically classifying osteomyelitis and accurately staging its progression. Its implementation requires minimal additional resources, as standardized grading can be seamlessly integrated into routine histopathological workflows. Furthermore, training pathologists on the HOES scoring system is straightforward and economically feasible. Unlike advanced molecular or imaging modalities, HOES does not necessitate significant infrastructure upgrades, making it particularly advantageous in resource-limited environments. This simplicity and

Table 5: Comparison of previously done studies based on HOES criteria

Study	Total cases	AOM	CFOM	COM	CALMED OM	No OM	Correlation between
Tiemann *et al*.[4]	52	10	5	37	0	0	HOES & Preoperative D/D- 68% Pre-operative & Microbiological diagnosis - 57%
Stupina *et al*.[5]	30	0	4	12	14	0	HOES & Clinical diagnosis- 53.3%
Present study	40	5	23	9	3	0	HOES & Provisional D/D – 43% HOES & Conventional Histopathological D/D – 50%

AOM: Acute Osteomyelitis, CFOM: Chronically Florid Osteomyelitis, COM: Chronic Osteomyelitis, Calmed OM: Calmed/subsided Osteomyelitis, No OM: No Osteomyelitis

adaptability underline the potential of HOES to improve diagnostic precision and disease management.

In terms of microbiological assessment, Tiemann found significant agreement between microbiological investigation and acute osteomyelitis but not in case of subsided and chronic osteomyelitis. In Tiemann's study, 51.4% of cases yielded positive microbiological reports, indicating challenges in detecting pathogens in provisional diagnoses of chronic osteomyelitis; however, acute osteomyelitis demonstrated positivity in 14 out of 15 cases.[4] Stupina T.A *et al*.'s[5] findings revealed positive microbiology reports in all samples, with 16 cases indicating polymicrobial infection and 14 cases caused by a single organism.

Hackenberg *et al*. also proposed a scoring system for osteomyelitis based on MRI, microbiology, and histopathology.[18,19] In their study, it was found that histopathology gave 100% accuracy. However, the inherent challenge of obtaining representative samples introduces an element of caution. Variability in sample quality may arise due to procedural factors or specimen location, potentially leading to misinterpretation or oversight.

Schmidt *et al*. came up with another 'Osteomyelitis diagnostic score' an integrative model that incorporates five key parameters which includes evaluation of clinical history and risk factors, clinical examination and laboratory results, diagnostic imaging modalities (ultrasound, radiology, CT, MRI, nuclear medicine, and hybrid methods), microbiological assessments, and histopathological analyses.[20,21]

As this study did not include microbiological investigation, the future research can be focused on combining HOES with microbiological analysis, imaging modalities, and clinical history which could yield a more comprehensive diagnostic framework. Moreover, expanding the sample size and involving more pathologists in subsequent investigations would enhance the overall understanding and generalizability of the findings. Future studies should also focus on differentiating bacterial and nonbacterial forms of osteomyelitis, recognizing the potential variations in treatment modalities dictated by the nature of the underlying infection.[18,22]

CONCLUSION

Pathophysiology of osteomyelitis is a complex phenomenon. HOES helps in dissecting the disease into several stages and understanding disease progression without the need of any additional diagnostic tools, revolutionizing simplicity in histopathological assessments. Amalgamation of understanding of osteomyelitis pathophysiology coupled with the precision offered by HOES in its systematic approach in disease staging can help to increase diagnostic precision and reproducibility.

Ethical approval

Institutional clearance for utilizing the archives for research purpose and publication was obtained.

Informed consent

As it was a retrospective study based on the achieves of the department, informed consent was not required.

Consent for publication

For this type of study consent for publication is not required.

CRediT authorship contribution statement

Shireen Ali: Writing – original draft, Formal analysis, Conceptualization, Data curation. **Piyush Asnani:** Formal analysis, Data curation, Writing. **Sima Odedra:: Slide analysis,** Writing – review and editing, Validation. **Jayasankar Pillai:** Writing – review and editing, Data analysis. **Namrata Jayasheel:** Writing – review and editing. **Sanjay Yadav:** Writing – review and editing

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Conflicts of interest

There are no conflicts of interest.

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