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Original Research

Inter-observer agreement in grading oral epithelial dysplasia – A systematic review

Gifrina Jayaraj*, Pratibha Ramani, Herald J. Sherlin, Priya Premkumar, N. Anuja

Department of Oral and Maxillofacial Pathology, Saveetha Dental College and Hospital, Chennai 600077, India

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ABSTRACT

Introduction: Oral epithelial dysplasia does not follow a predictable sequential progression from mild to moderate to severe dysplasia and in rare cases may revert to normal. It is not uncommon for a mild dysplasia to rapidly progress to an invasive carcinoma; however, not all epithelial dysplasia develops into carcinoma. Over the past decades, numerous grading systems have been proposed. However, dysplasia grading is still highly subjective with lack of objective criteria. This systematic review assesses the extent of inter-observer agreement in grading epithelial dysplasia of the upper aerodigestive tract.
Materials and methods: Articles were searched in on-line databases, such as PUBMED, EMBASE and MEDLINE with key words "grading oral epithelial dysplasia, inter-observer agreement, reliability." Manual search of Journals were also done. Articles were reviewed and analysed.
Results: Of the 11 relevant articles, two were excluded and the remaining nine were reviewed. Only three studies showed substantial inter-observer agreement, three showed moderate agreement, and three showed fair agreement.
Conclusion: We recommend standardisation and practice of a universal grading system to achieve better inter-observer agreement in the future. Future systematic reviews based on such a system would probably be more homogeneous.

1. Introduction

Oral squamous cell carcinoma (OSCC) is a major health problem world-wide, especially in the developing countries. Squamous cell carcinoma (SCC) is the most common oral cancer in India with an incidence rate as high as 30–40% [1]. These alarming figures emphasise the need for an early diagnosis and careful evaluation of the potentially malignant disorders that are precursors for malignancy. Histologically, precancerous state is characterised by epithelial dysplasia. The malignant transformation rate of epithelial dysplasia is 36.4% [2].

Oral epithelial dysplasia is graded as mild, moderate and severe based on the likelihood risk of malignant transformation [3]. However, oral epithelial dysplasia does not follow a predictable sequential progression from mild to moderate to severe dysplasia and in rare circumstances can revert to apparently normal state. It is not uncommon for a mild dysplasia to rapidly progress to an invasive carcinoma; and not all epithelial dysplasia develops into carcinoma. This makes identification and appropriate grading of epithelial dysplasia very crucial in the treatment planning. However, dysplasia grading has been a tedious task due to a lack of considerable inter-observer agreement. Previous studies [4–6] have established only a slight to fair inter-observer agreement in grading dysplasia. Recently, the WHO has proposed a 5-point ordinal scale grading system based on cytological and architectural features [7]. Kujan et al. [8] employed a binary grading system that resulted in a considerable inter-observer agreement though it needs validation by a larger sample size. The prevailing endless list of grading systems clearly underscores that the dysplasia grading lacks unanimity, objectivity and predictive value.

Unanimous diagnoses and identification of key histological features that predict malignant transformation are important so that a lesion is not undertreated or overtreated. A review of the current scenario is mandatory so as to identify the pitfalls and make the necessary amendments. Hence, this systematic review assesses

☆ Asian AOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

* Corresponding author at: Department of Oral and Maxillofacial Pathology, Saveetha Dental College, Poonamallee High Road, Velappanchavadi, Chennai 600077, India. Tel.: +91 995209611.
E-mail address: gifrinaj@gmail.com (G. Jayaraj).

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the extent of inter-observer agreement in grading oral epithelial dysplasia from the various studies in the literature.

2. Materials and methods

2.1. Search strategy for identification of studies

The search strategy was in accordance with the Cochrane guidelines for systematic reviews. Articles were searched and selected using PUBMED, MEDLINE and EMBASE. Owing to scarcity of inter-observer agreement studies in grading dysplasia, we wished to exhaust all the possible articles; therefore a timeline was not included in the search. The article search included only those published in the English literature. An Internet search was also done with the key words "grading oral epithelial dysplasia". This was later refined to include inter-observer agreement and reliability. Journals evaluating inter-observer agreement were also cross referenced.

2.2. Selection criteria

The title of the articles and abstracts was reviewed. Articles that considered grading of upper aerodigestive tract only on histopathological basis without the use of markers were selected for further perusal. In studies that were stratified, only the collapsed inter-observer agreement in dysplasia grading was taken into consideration. Studies that compared the WHO grading systems with other grading systems were also taken into consideration. Articles representing agreement in laryngeal dysplasia using Ljubljana classification system were included in the review, as the histological criteria of this system were also adapted in grading oral epithelial dysplasia. Articles that were retracted were excluded. The process is shown in Fig. 1.

2.3. Data extraction and analysis

Once a final conclusion was arrived at regarding the articles to be reviewed, data extracted from each article were tabulated and was later cross checked.

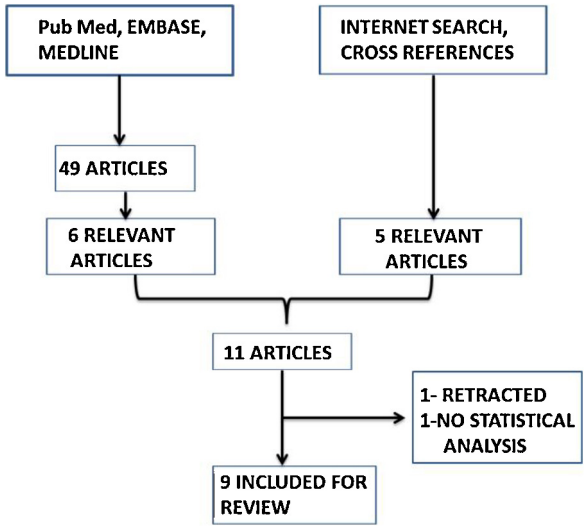

Fig. 1. Flow chart for study selection.

2.4. Outcomes

The current status of inter-observer agreement in histopathological grading of dysplasia using routine microscopy was analysed.

3. Results

3.1. Methods of review

The selection and exclusion criteria of the reviewed studies are shown in Fig. 1. The search strategy identified nine studies that evaluated inter-observer agreement using different grading systems. The descriptions of the individual studies are shown in Table 1 and those of the excluded studies in Table 2. The kappa values for the presence or absence of epithelial dysplasia are listed in Table 3.

Table 1
Description of included studies.

Study design	Examiners	No. of cases	Grading system	Results	Citation
Retrospective study	2-General Pathologists 2-Oral Pathologists	100 slides	No, mild, moderate, severe dysplasia, carcinoma in situ	0.27–0.45 (unweighted κ)	Karabulut et al. [4]
Retrospective study	6 Board-Certified Oral Pathologists	120 slides	No dysplasia–carcinoma in situ compared with the sign out diagnosis	0.15–0.41 (unweighted κ)	Abbey et al. [5]
Retrospective study	6 Board-Certified Oral Pathologists	120 slides with clinical details	No dysplasia–carcinoma in situ compared with the sign out diagnosis	0.17 (unweighted κ)	Abbey et al. [6]
Retrospective study	3 Oral Pathologists	64 slides	5 Point Ordinal Scale	0.74 (weighted κ) CI (0.64–0.85) 0.37, CI (0.32–0.42)	Brothwell et al. [9]
Retrospective prospective study	Local Pathologist Central Pathology Committee	96 slides	Collapsed into mild, moderate, severe	0.70 CI (0.45–0.72) weighted κ	Fischer et al. [18]
Retrospective study	3 Oral Pathologists and 1 General Pathologist	68 slides	WHO system Binary system	0.06– 0.43 (unweighted κ) 0.45 –0.77 (weighted κ) 0.35–0.67 (unweighted κ)	Kujan et al. [8]
Retrospective study design	Scottish Pathology Consistency Group	100 slides	2-grade system	0.52	Mc Laren et al. [10]
Retrospective study design	14 Participants	42 slides	WHO, Ljubljana (LC) and Squamous Intraepithelial Neoplasia (SINC)	WHO 0.42 ± 0.10 LC 0.41 ± 0.12 SIN 0.37 ± 0.07	Sarioglu et al. [11]
Retrospective study design	3 Pathologists	110 slides	WHO, Ljubljana (LC) and Squamous Intraepithelial Neoplasia (SINC)	SINC κ 0.28 LC κ 0.50 Weighted κ-values with all 3 classification systems did not exceed 0.55	Fleskens et al. [12]