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Basal growth patterns in actinic cheilitis: a proposed classification and comparison with degrees of dysplasia

Padrões de crescimento basal na queilite actínica: uma proposta de classificação e comparação com graus de displasia

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Abstract
Introduction: *Actinic cheilitis (AC) is a potentially malignant disorder caused by intense and prolonged exposure to ultraviolet radiation. This study aimed to analyse the clinical and histopathological features of actinic cheilitis, as well as to evaluate the degrees of dysplasia by the World Health Organisation (WHO) system, the Kujan binary system, and for the first time, the basal growth pattern (Schmitz grading system).* ***Methods:*** *fifty-nine cases of actinic cheilitis were analysed, with clinical data obtained from archived biopsy request forms. Histological specimens were assessed to determine the degree of dysplasia, alongside evaluation of cytological and architectural alterations. Statistical comparisons were conducted using the Chi-square test or Fisher's exact test ($p < 0.05$).* ***Results:*** *histological grading according to the WHO system revealed a predominance of mild dysplasia (47.5%). The Kujan binary system classified most cases as low risk (86.4%), while the Schmitz grading system predominantly identified cases as grade II (60.8%). Statistically significant associations were observed between the WHO and Schmitz systems, as well as between the binary and Schmitz systems ($p < 0.05$). Additionally, an association was identified between the Schmitz system and the microscopic finding of epithelial projections in a drop pattern ($p = 0.007$). A significant correlation was also found between the binary and the WHO systems ($p < 0.05$).* ***Conclusions:*** *the Schmitz grading system appears to be a valuable tool for risk analysis in actinic cheilitis, effectively complementing established grading systems. Its straightforward application and simplicity enhance its practicality and reliability for evaluating these cases.*
Keywords: *actinic cheilitis; lip diseases; oral pathology.*

Resumo
Introdução: *a queilite actínica é uma desordem potencialmente maligna causada pela exposição intense e prolongada à radiação ultravioleta. Este estudo objetivou analisar as características clínicas e histopatológicas da queilite actínica, assim como avaliar os graus de displasia pelo sistema da Organização Mundial da Saúde (OMS), o sistema binário de Kujan, e, pela primeira vez, o padrão de crescimento basal (sistema de gradação de Schmitz).* **Metoodologia:** *cinquenta e nove casos de queilite actínica foram analisados, com dados clínicos obtidos de formulários de biópsia arquivados. As amostras histológicas foram avaliadas para determinar o grau de displasia, juntamente com a avaliação das alterações arquiteturais e citológicas. As comparações estatísticas foram conduzidas usando o teste do Qui-quadrado ou o teste exato de Fisher ($p < 0,05$).* **Resultados:** *a gradação histológica de acordo com o sistema da OMS revelou uma predominância de displasia leve (47,5%). O sistema binário de Kujan classificou a maioria dos casos como baixo risco (86,4%), enquanto o sistema de gradação de Schmitz predominantemente identificou casos como grau II (60,8%). Associações estatisticamente significativas foram observadas entre os sistemas da OMS e de Schmitz, assim como entre os sistemas binário e de Schmitz ($p < 0,05$). Adicionalmente, uma associação foi identificada entre o sistema de Schmitz e o achado microscópico de projeções epiteliais em um padrão de gota ($p = 0,007$). Uma correlação significativa foi também encontrada entre os sistemas da OMS e o binário ($p < 0,05$).* **Conclusões:** *o sistema de gradação de Schmitz parece ser uma ferramenta relevante para a análise de risco da queilite actínica, complementando efetivamente os sistemas de gradação estabelecidos. Sua aplicação direta e simplicidade aumentam sua praticidade e confiabilidade na avaliação desses casos.*
Palavras-chave: *queilite actínica; doenças labiais; patologia bucal.*

INTRODUCTION

Actinic cheilitis (AC) is a chronic inflammatory condition caused by intense and prolonged exposure to ultraviolet (UV) radiation, classified as a potentially malignant disorder (PMD)[1-3]. AC primarily affects fair-skinned individuals who participate in outdoor occupational activities, typically between 40 and 60 years of age[2-4]. Most cases of this PMD occur on the lower lip, due to its anatomical projection, which increases its exposure to UV radiation from sunlight. This exposure induces genetic damage in epithelial cells, raising the likelihood of malignant transformation into squamous cell carcinoma (SCC)[2-4].

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Microscopically, AC can present several alterations in the epithelial lining, including hyperkeratosis, atrophy, and hyperplasia, as well as various degrees of dysplasia. Additional histological findings, such as inflammatory infiltrate, hyperemia, and basophilic degeneration of collagen fibres (solar elastosis), are observed in the connective tissue, with solar elastosis being a fundamental characteristic for diagnosing the lesion[2,5-7]. The World Health Organisation (WHO) established a histological grading system in 2005, based on cytological and architectural criteria of the epithelium. In this system, dysplasia is classified into three grades: 1) mild, when restricted to the lower third of the epithelium; 2) moderate, when it reaches the middle third of the epithelium; and 3) severe, when it extends beyond the middle third of the epithelial lining. However, this definition, based on the involvement of epithelial thirds, oversimplifies the complexity of this classification[7-10].

Although widely used, this system is subjective and leads to significant variability among oral pathologists. To reduce intra- and inter-examiner variability, Kujan et al.[8] (2007) proposed a binary grading system for epithelial dysplasia based on the WHO criteria, classifying lesions as low or high risk for malignant transformation. This classification evaluates architectural and cytological parameters, considering a lesion to be low risk if it exhibits fewer than four architectural alterations and fewer than five cytological alterations. In contrast, lesions are deemed high risk if they display at least four architectural alterations and five cytological alterations[8].

More recently, Schmitz et al.[11] (2018) introduced a new method for assessing epithelial dysplasia in cases of actinic keratosis (AK), cutaneous lesions with malignant potential. This method identifies three basal-layer growth patterns of atypical keratinocytes: crowding, budding, and papillary sprouting. The authors underscore the importance of a thorough examination of the basal layer, as it is believed to represent the beginning for cellular proliferation into deeper layers[11]. Nevertheless, no studies have yet evaluated this grading scheme in cases of AC. Therefore, this study aimed to analyse the clinical and histopathological characteristics of AC, as well as to evaluate the WHO system and the Kujan system, and for the first time, the basal growth pattern (Schmitz grading system). Additionally, a comparison was made between conventional grading systems and the newly proposed method by Schmitz.

Methods

Analysis of clinical and morphological data

This study was conducted with approval from the Ethics and Research Committee of the College of Nursing and Medicine Nova Esperança (Protocol CAAE 04148518.4.0000.5179), in accordance with the Helsinki Declaration. The research analysed 59 cases of AC obtained from the Oral Histopathology Laboratory at the Department of Dentistry, State University of Paraíba (UEPB), Campina Grande, Paraíba, Brazil. Clinical data regarding patients (gender, age, and skin colour) and lesions (location, clinical presentation, colour, size, symptoms, duration, and type of biopsy performed) were obtained from biopsy request forms archived in the Oral Histopathology Laboratory at UEPB. Cases of AC previously treated with vitamin-based cream or topical corticosteroid were excluded from this study.

Regarding the morphological aspects of AC, histological sections stained with hematoxylin and eosin were examined under light microscopy (K223, Kasvi, Brazil). Histopathological analyses were conducted by two experienced oral pathologists, and any disagreements were resolved through discussion until consensus was reached. Three systems were employed to grade epithelial dysplasia: the WHO, the Kujan binary, and the Schmitz grading systems[8,10,11].

According to the WHO system, lesions were classified as mild dysplasia (dysplastic changes confined to the lower third), moderate dysplasia (dysplastic changes extending to the middle third), or severe dysplasia (dysplastic changes exceeding the middle third)[10].

In the binary grading system proposed by Kujan et al.[8] (2007), lesions were classified as high risk (at least four architectural alterations and five cytological alterations) or low risk (fewer than four architectural alterations or five cytological alterations). Architectural and cytological alterations were also evaluated as isolated histopathological parameters. Additional epithelial characteristics were assessed, including mucosal thickness, type and intensity of keratinisation, and the thickness of epithelial ridges. In the connective tissue, parameters such as subepithelial hyalinisation, the intensity of solar elastosis, inflammatory infiltrate, and vascularisation were analyzed[8].

In the grading of dysplasia using the Schmitz system[11], the growth pattern of the basal layer in the specimens was evaluated, with attention to the proposed parameters: I – crowding (atypical keratinocytes clustered in the basal layer, making it more basophilic), II –budding (atypical keratinocytes grouped forming projections towards the lamina propria that do not exceed the epithelial thickness), or III – papillary sprouting (accumulated atypical keratinocytes in the basal layer form projections towards the lamina propria that exceed the thickness of the epithelium).

Statistical analysis

The results obtained were entered into an Excel file (Microsoft Office 2010®) and subsequently exported to the Statistical Package for the Social Sciences program (version 22.0; SPSS Inc., Chicago, IL, USA). Depending on the distribution of the data, either the Chi-square test or Fisher's exact test was used, considering a significance level of 5% ($p < 0.05$).

Results

The cases of AC in this study mainly affected male individuals (n = 42, 71.2%), caucasians (n = 32, 54.2%), and those aged 60 years or older (n = 34, 59.6%). Regarding anatomical location, 58 cases (98.3%) were found on the lower lip, while only 1 case (1.7%) was on the upper lip. Clinically, most cases appeared as plaques (n = 25, 42.4%) and patches (n = 21, 35.6%), with a white colouration (n = 27, 45.8%). Overall, the lesions were predominantly smaller than or equal to 1 cm (n = 32, 54.2%) and asymptomatic (n = 36, 61%) (Table 1).

Table 1 – *Distribution of the sample according to clinical parameters.*

Parameter	n (%)
Gender	
Male	*42 (71.2)*
Female	*17 (28.8)*
Age	
≤ 60 years old	*34 (59.6)*
> 60 years old	*23 (37.0)*
Not reported	*2 (3.4)*
Skin color	
White	*32 (54.2)*
Non white	*16 (27.1)*
Not reported	*11 (18.6)*
Biopsy	
Incisional	*31 (52.5)*
Excisional	*19 (32.2)*
Not reported	*9 (15.3)*
Location	
Lower lip	*58 (98.3)*
Up lip	*1 (1.7)*
Clinical presentation	
Plaque	*25 (42.4)*
Patch	*21 (35.6)*
Ulceration	*3 (5.1)*
Nodule	*3 (5.1)*
Not reported	*7 (11.9)*
Color	
White	*27 (45.8)*
Erythematous	*6 (10.2)*
White-erythematous	*16 (27.1)*
Others	*8 (13.6)*
Not reported	*2 (3.4)*
Size	
Equal to or less than 1 cm	*32 (54.2)*
Greater than 1 cm	*20 (33.9)*
Not reported	*7 (11.9)*
Symptomatology	
Absent	*36 (61.0)*
Present	*(11.9)*
Not reported	*16 (27.1)*
Duration	
1 year or less	*22 (37.3)*
More than one year	*12 (20.3)*
Not reported	*25 (42.4)*

Source: research data

Morphological analysis revealed that orthokeratinization (n = 36, 61%) and moderate solar elastosis (n = 27, 45.8%) were common findings in actinic cheilitis (AC) cases. In the lamina propria, inflammation was most often classified as absent (n = 22, 37.3%) or mild and diffuse (n = 17, 28.8%). Additionally, regarding histopathological characteristics, subepithelial hyalinisation was absent in the majority of cases (n = 54, 91.5%), and vascularisation was considered normal in most cases (n = 37, 62.7%). Regarding cytological alterations, the most frequent findings were anisonucleosis (n = 43, 72.9%), nuclear pleomorphism (n = 46, 78%), increased nuclear size (n = 39, 49.2%), and hyperchromasia (n = 36, 61%). In contrast, mitotic alterations were rare (n = 3, 5.1%). Concerning the classification based on the grading systems, most cases exhibited mild dysplasia (n = 28, 47.5%), low risk of malignant transformation (n = 51, 86.4%), and grade II (n = 31, 60.8%) (Table 2) (Figure 1).

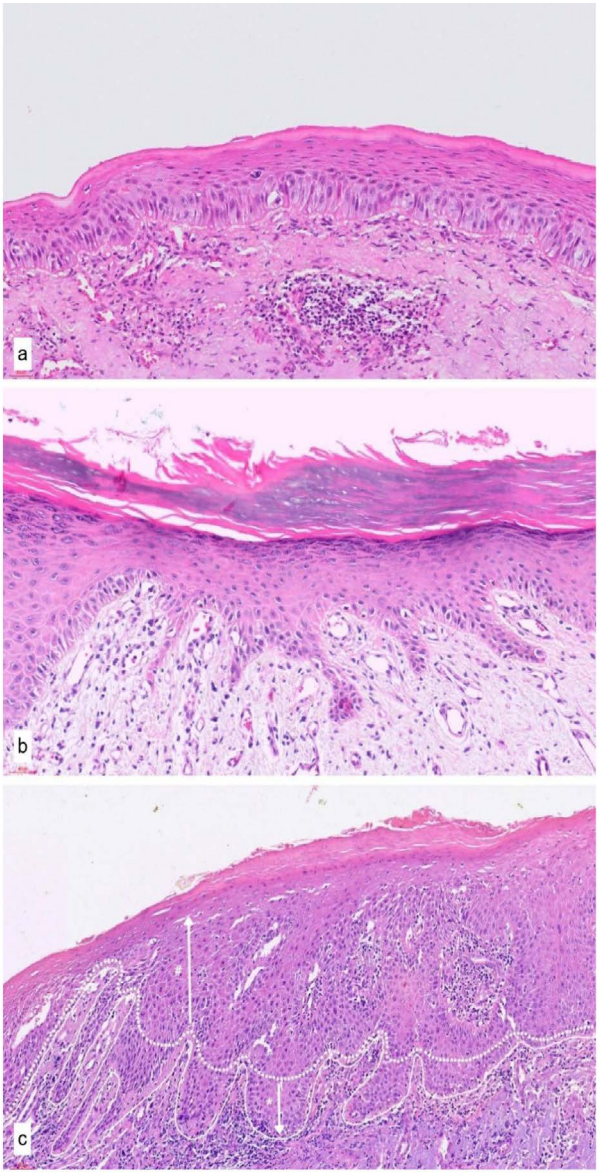
Table 2 – *Distribution of the sample according to morphological parameters and grading systems.*

Parameter	n (%)
Thickness	
Normal	*29 (49.2)*
Hyperplastic	*19 (32.2)*
Atrophic	*11 (18.6)*
Keratinization	
Orthokeratinization	*36 (61.0)*
Parakeratinization	*16 (27.1)*
Both	*7 (11.9)*
Solar elastosis	
Mild	*23 (39.0)*
Moderate	*27 (45.8)*
Severe	*9 (15.3)*
Inflammation	
Absent	*22 (37.3)*
Mild and focal	*17 (28.8)*
Mild and diffuse	*6 (10.2)*
Moderate	*6 (10.2)*
Intense	*8 (13.6)*
Vascularization	
Normal	*37 (62.7)*
Moderate	*20 (33.9)*
Intense	*2 (3.4)*
Subepithelial hyalinization	
Absent	*54 (91.5)*
Moderate	*4 (6.8)*
Intense	*1 (1.7)*
Anisonucleosis	
Absent	*16 (21.1)*
Present	*43 (72.9)*
Nuclear pleomorphism	
Absent	*13 (22.0)*
Present	*46 (78.0)*
Anisocytosis	

Absent	*34 (57.6)*
Present	*25 (42.4)*
Cellular pleomorphism	
Absent	*30 (50.8)*
Present	*29 (49.2)*
Increased N:C ratio	
Absent	*31 (52.5)*
Present	*28 (47.5)*
Increased nuclear size	
Absent	*30 (50.8)*
Present	*39 (49.2)*
Atypical mitoses	
Absent	*56 (94.9)*
Present	*3 (5.1)*
Hyperchromatism	
Absent	*23 (39.0)*
Present	*36 (61.0)*
Increased number and size of nucleoli	
Absent	*41 (69.5)*
Present	*18 (30.5)*
Irregular epithelial stratification	
Absent	*43 (72.9)*
Present	*16 (27.1)*
Loss of polarity of basal cells	
Absent	*16 (27.1)*
Present	*43 (72.9)*
Epithelial projection in a drop pattern	
Absent	*42 (71.2)*
Present	*17 (28.8)*
Increased number of mitoses	
Absent	*54 (91.5)*
Present	*5 (8.5)*
Surface mitoses	
Absent	*58 (98.3)*
Present	*1 (1.7)*
Dyskeratosis	
Absent	*48 (81.4)*
Present	*11 (18.6)*
Keratin pearl	
Absent	*56 (94.9)*
Present	*3 (5.1)*
WHO System	
Hyperkeratosis	*8 (13.6)*
Mild dysplasia	*28 (47.5)*
Moderate dysplasia	*19 (32.2)*
Severe dysplasia	*4 (6.8)*
Kujan Binary System	
Low risk	*51 (86.4)*
High risk	*8 (13.6)*
Schmitz System	
Grade I	*7 (13.7)*
Grade II	*31 (60.8)*
Grade III	*13 (25.5)*

Source: research data

Figure 1 – *Histological grading of actinic cheilitis using the WHO system[10], the binary system[8] and the adaptation of the system proposed by Schmitz et al.[11] (2018), according to the growth pattern.* **(A)** *Mild dysplasia, low risk and pro I (keratinocyte crowding in the basal layer);* **(B)** *Moderate dysplasia, high risk and pro II (budding); and* **(C)** *Severe dysplasia, high risk and pro II (budding), with the thickness of papillary projection (*) of atypical keratinocytes not exceeding that of the overlying epithelium (#), dashed line for pattern assessment adapted from Schmitz et al.[11] (2018).*



Source: Authors

No statistically significant associations were found between clinical parameters and grades of epithelial dysplasia, regardless of the system used (p > 0.05). Among the evaluated histological parameters, a statistically significant association was observed between cases of absent or mild inflammation and those characterised as hyperkeratosis and mild dysplasia, as defined by the WHO (p = 0.026). Similarly, a statistically significant association

was found between the absence of anisonucleosis (p = 0.015), nuclear pleomorphism (p = 0.001), anisocytosis (p = 0.001), cellular pleomorphism (p = 0.012), increased N:C ratio (p = 0.007), and cases classified as hyperkeratosis and mild dysplasia according to WHO (Table 3).

There was a statistically significant association between cases with absence of anisocytosis (p = 0.008), cellular pleomorphism (p = 0.026), atypical mitoses (p = 0.002), subepithelial hyalinisation (p = 0.001), and cases considered low risk according to the Kujan binary system. Additionally, a statistically significant association was found between cases with the absence of an increased number and size of nucleoli (p = 0.021), irregular epithelial stratification (p = 0.024), epithelial projections in a drop pattern (p = 0.010), and cases of hyperkeratosis and mild dysplasia, as classified by the WHO. Similarly, it was observed that cases with absence of increased number and size of nucleoli (p = 0.007), irregular epithelial stratification (p = 0.003), and epithelial projection in a drop pattern (p = 0.005) also presented a statistically significant association with low-risk cases according to the binary system (Table 3).

Furthermore, a statistically significant association was observed between cases with the absence of an increased number of mitoses (p = 0.001), dyskeratosis (p = 0.004), keratin pearls (p = 0.002), and low-risk cases, as defined by the Kujan binary system. Regarding the Schmitz system, a statistically significant association was found between the absence of epithelial projection in a drop pattern (p = 0.007), normal vascularisation (p = 0.020), and grade 0, I, and II cases of the system (Table 3). The comparison between the WHO and Schmitz systems showed a statistically significant association between hyperkeratosis and mild dysplasia, as well as grades 0, I, and II of the Schmitz system (p = 0.010) (Table 4). Similarly, a statistically significant association was found between the low-risk classification of the Kujan binary system and grades 0, I, and II (p = 0.014) of the Schmitz system. Finally, a statistically significant association was found between the Kujan binary system and the WHO system (p = 0.004) (Table 5).

Table 3 – Analysis of the association between morphological parameters of actinic cheilitis and histological grading systems.

Parameter	WHO System			Kujan Binary System			Schmitz System		
	Hyperkeratosis + Mild dysplasia **n (%)**	*Moderate dysplasia + Severe dysplasia* **n (%)**	*p**	*Low risk* **n (%)**	*High risk* **n (%)**	*p**	*0, I and II* **n (%)**	*III* **n (%)**	*p**
Thickness									
Atrophic	*5 (45.5)*	*6 (54.5)*	*0.241[a]*	*9 (81.8)*	*2 (18.2)*	*0.635[b]*	*9 (81.8)*	*2 (18.2)*	*1.000[b]*
Normal + Hyper	*31 (64.6)*	*17 (35.4)*		*42 (87.5)*	*6 (12.5)*		*36 (75.0)*	*12 (25.0)*	
Keratinization									
Orthokeratinization	*21 (58.3)*	*15 (41.7)*	*0.597[a]*	*30 (83.3)*	*6 (16.7)*	*0.464[b]*	*25 (69.4)*	*11 (30.6)*	*1.000[b]*
Parakeratinization + Both	*15 (65.2)*	*8 (34.8)*		*21 (91.3)*	*2 (8.7)*		*20 (87.0)*	*3 (13.0)*	
Solar elastosis									
Mild	*16 (69.6)*	*7 (30.4)*	*0.282[a]*	*21 (93.3)*	*2 (8.7)*	*0.464[b]*	*21 (91.3)*	*2 (8.7)*	*0.057[b]*
Moderate + Severe	*20 (55.6)*	*16 (44.4)*		*30 (83.3)*	*6 (16.7)*		*24 (66.7)*	*12 (33.3)*	
Inflammation									
Absent + Mild	*31 (68.9)*	*14 (31.1)*	***0.026[a]***	*41 (91.1)*	*4 (8.9)*	*0.081[b]*	*37 (82.2)*	*8 (17.8)*	*0.054[a]*
Moderate + Severe	*5 (35.7)*	*9 (64.3)*		*10 (71.4)*	*4 (28.6)*		*8 (57.1)*	*6 (42.9)*	
Vascularization									
Normal	*25 (67.6)*	*12 (32.4)*	*0.181[a]*	*33 (89.2)*	*4 (10.8)*	*0.455[b]*	*30 (81.1)*	*7 (18.9)*	***0.020[a]***
Moderate + Severe	*11 (50.0)*	*11 (50.0)*		*18 (81.8)*	*4 (18.2)*		*15 (68.2)*	*7 (31.8)*	
Subepithelial hyalinization									
Absent	*33 (61.1)*	*21 (38.9)*	*1.000[b]*	*5 (100.0)*	*0 (0.0)*	*1.000[b]*	*41 (75.9)*	*13 (24.1)*	*1.000[b]*
Present	*3 (60.3)*	*2 (40.0)*		*46 (85.2)*	*8 (14.8)*		*4 (80.0)*	*1 (20.0)*	
Anisonucleosis									
Absent	*14 (87.5)*	*2 (12.5)*	***0.015[b]***	*16 (100.0)*	*0 (0.0)*	*0.093[b]*	*14 (87.5)*	*2 (12.5)*	*0.310[b]*
Present	*22 (51.2)*	*21 (48.8)*		*35 (81.4)*	*8 (18.6)*		*31 (76.1)*	*12 (27.5)*	
Nuclear pleomorphism									
Absent	*13 (100.0)*	*0 (0.0)*	***0.001[b]***	*13 (100.0)*	*0 (0.0)*	*0.180[b]*	*10 (76.9)*	*3 (23.1)*	*1.000[b]*

Present	*23 (50.0)*	*23 (50.0)*		*38 (82.6)*	*8 (17.4)*		*35 (76.1)*	*11 (23.9)*	
Anisocytosis									
Absent	*27 (79.4)*	*7 (20.6)*	***0.001***[a]	*33 (97.1)*	*1 (2.9)*	***0.008***[b]	*29 (85.3)*	*5 (14.7)*	*0.057*[a]
Present	*9 (36.0)*	*16 (64.4)*		*18 (72.0)*	*7 (28.0)*		*16 (64.0)*	*9 (36.0)*	
Cellular pleomorphism									
Absent	*23 (76.7)*	*7 (23.3)*	***0.012***[a]	*29 (96.7)*	*1 (3.3)*	***0.026***[b]	*26 (86.7)*	*4 (13.3)*	*0.406*[a]
Present	*13 (44.8)*	*16 (55.2)*		*22 (75.9)*	*7 (24.1)*		*19 (65.5)*	*10 (34.5)*	
Increased N:C ratio									
Absent	*24 (77.1)*	*7 (22.6)*	***0.007***[a]	*29 (93.5)*	*2 (6.5)*	*0.134*[b]	*25 (80.6)*	*6 (19.4)*	*0.542*[a]
Present	*12 (42.9)*	*16 (57.1)*		*22 (78.6)*	*6 (21.4)*		*20 (71.4)*	*8 (28.6)*	
Increased nuclear size									
Absent	*21 (70.0)*	*9 (30.0)*	*0.150*[a]	*27 (90.0)*	*3 (10.0)*	*0.472*[b]	*25 (83.3)*	*5 (16.7)*	*0.406*[a]
Present	*15 (51.7)*	*14 (48.3)*		*24 (82.8)*	*5 (17.2)*		*20 (69.0)*	*9 (31.0)*	
Atypical mitoses									
Absent	*36 (64.3)*	*20 (35.7)*	*0.054*[a]	*51 (91.1)*	*5 (8.9)*	***0.002***[b]	*44 (78.6)*	*12 (21.4)*	*0.137*[b]
Present	*0 (0.0)*	*3 (100.0)*		*0 (0.0)*	*3 (100.0)*		*1 (33.3)*	*2 (66.7)*	
Hyperchromatism									
Absent	*17 (73.9)*	*6 (26.1)*	*0.104*[a]	*21 (91.3)*	*2 (8.7)*	*0.464*[b]	*20 (87.0)*	*3 (13.3)*	*0.209*[b]
Present	*19 (52.8)*	*17 (47.2)*		*30 (83.3)*	*6 (16.7)*		*25 (69.4)*	*11 (30.6)*	
Increase in number and size of nucleoli									
Absent	*29 (70.7)*	*12 (29.3)*	***0.021***[a]	*39 (95.1)*	*2 (4.9)*	***0.003***[b]	*33 (80.5)*	*8 (19.5)*	*0.407*[a]
Present	*7 (38.9)*	*11 (61.1)*		*12 (66.7)*	*6 (33.3)*		*12 (66.7)*	*6 (33.3)*	
Irregular epithelial stratification									
Absent	*30 (69.8)*	*13 (30.2)*	***0.024***[a]	*41 (95.3)*	*2 (4.7)*	***0.003***[b]	*34 (79.1)*	*9 (20.9)*	*0.495*[a]
Present	*6 (37.5)*	*10 (62.5)*		*10 (62.5)*	*6 (37.5)*		*11 (68.8)*	*5 (31.2)*	
Loss of polarity of basal cells									
Absent	*12 (75.0)*	*4 (25.0)*	*0.236*[b]	*15 (93.8)*	*1 (6.2)*	*0.427*[b]	*14 (87.5)*	*2 (12.5)*	*0.310*[b]
Present	*24 (55.8)*	*19 (44.2)*		*36 (83.7)*	*7 (16.3)*		*31 (72.1)*	*12 (27.9)*	
Epithelial projection in a drop pattern									
Absent	*30 (71.4)*	*12 (28.6)*	***0.010***[a]	*40 (95.2)*	*2 (4.8)*	***0.005***[b]	*36 (85.7)*	*6 (14.3)*	***0.007***[a]
Present	*6 (35.3)*	*11 (64.7)*		*11 (64.7)*	*6 (35.3)*		*9 (52.9)*	*8 (47.1)*	
Increased number of mitoses									
Absent	*35 (64.8)*	*19 (35.2)*	*0.070*[b]	*50 (92.6)*	*4 (7.4)*	***0.001***[b]	*42 (77.8)*	*12 (22.2)*	*0.583*[b]
Present	*1 (20.0)*	*4 (80.0)*		*1 (20.0)*	*4 (80.0)*		*3 (60.0)*	*2 (40.0)*	
Surface mitoses									
Absent	*36 (62.1)*	*22 (37.9)*	*0.390*[b]	*51 (87.9)*	*7 (12.1)*	*0.136*[b]	*44 (75.9)*	*14 (24.1)*	*1.000*[b]
Present	*0 (0.0)*	*1 (100.0)*		*0 (0.0)*	*1 (100.0)*		*1 (100.0)*	*0 (0.0)*	
Dyskeratosis									
Absent	*31 (64.6)*	*17 (35.4)*	*0.241*[a]	*45 (93.8)*	*3 (6.2)*	***0.004***[b]	*38 (79.2)*	*10 (20.8)*	*0.432*[b]
Present	*5 (45.5)*	*6 (54.5)*		*6 (54.5)*	*5 (45.5)*		*7 (63.6)*	*4 (36.4)*	
Keratin pearl									
Absent	*36 (64.3)*	*20 (35.7)*	*0.054*[b]	*51 (91.1)*	*5 (8.9)*	***0.002***[b]	*44 (78.6)*	*12 (21.4)*	*0.137*[b]
Present	*0 (0.0)*	*3 (100.0)*		*0 (0.0)*	*3 (100.0)*		*1 (33.3)*	*2 (66.7)*	

Legend: [a]Pearson's chi-square; [b]Fisher's Exact.
Values of p in bold indicate statistically significant results.

Source: research data

Table 4 – *Analysis of the association between the WHO system[10] and the Schmitz system[11].*

WHO System	Schmitz Grading System		
	0, I and II	III	p*
Hyperkeratosis + Mild Dysplasia	32 (88.9)	4 (11.1)	**0.010[b]**
Moderate Dysplasia + Severe Dysplasia	13 (56.5)	10 (43.5)	
Kujan Binary System			
Low risk	3 (37.5)	5 (62.5)	**0.014[b]**
High risk	42 (82.4)	9 (17.6)	

Legend: [a]Pearson's chi-square test; [b]Fisher's exact test.
Values of p in bold indicate statistically significant results.

Source: research data

Table 5 – *Analysis of the association between the Kujan binary system[8] and the WHO system[10].*

Kujan Binary System	WHO System		
	Hyperkeratosis + Mild Dysplasia	Moderate Dysplasia + Severe Dysplasia	p*
Low risk	35 (68.6)	16 (31.4)	**0.004[b]**
High risk	1 (12.5)	7 (85.5)	

Legend: [a]Pearson's chi-square test; [b]Fisher's exact test.
Values of p in bold indicate statistically significant results.

Source: research data

DISCUSSION

The degree of epithelial dysplasia is an important indicator of the transformation of a potentially malignant lesion. Therefore, establishing the degree of epithelial dysplasia in actinic cheilitis (AC) becomes a priority in the histopathological diagnostic process[6,7,12]. It is essential that the grading accurately reflects the dysplastic condition of the lesion; however, some systems used in laboratory routines, such as the WHO system[10], may lead to diagnostic disagreements among professionals[6]. Thus, new grading systems that prioritise simplicity and accuracy should be explored as alternatives to, or complements of, conventional systems. In this context, the method proposed by Schmitz et al.[11] (2018) for analysing basal growth patterns is promising. Our study evaluates this system for the first time in actinic cheilitis (AC), suggesting that it may serve as another simple and useful tool for assessing the risk level of these lesions.

Clinically, the condition may present as excessive dryness, changes in lip colour, white plaques, and a loss of the boundary line between the skin and lip mucosa. Atrophy and oedema of the lips are also common findings[2,3,13,14]. In this study, the analysed cases mainly affected the lower lip (98.3%), while the clinical presentation was mainly characterised by the presence of leukoplakic plaques (42.4%). These findings are supported by the results observed by Lopes et al.[15] (2015), where 97.5% of 161 cases analysed occurred on the lower lip. Additionally, in the same study, 33.6% of AC cases presented with leukoplakic plaque formation[15].

In this study, AC cases were evaluated according to the degree of epithelial dysplasia, based on the WHO, Kujan, and Schmitz grading systems[8,10,11]. Regarding the WHO system, the results demonstrated a higher frequency of cases with mild dysplasia (47.5%), followed by moderate dysplasia (32.2%) and severe dysplasia (6.8%). These findings are supported by the results observed by Arnaud et al.[16] (2014), who conducted a histopathological analysis of 44 AC cases, in which 36.3% were classified as mild dysplasia, 20.4% as moderate dysplasia, and only 11.3% as severe dysplasia. In contrast, Abrantes et al.[6] (2021) observed that the majority of AC cases were classified as severe dysplasia. Overall, these findings suggest that AC cases frequently exhibit some degree of epithelial dysplasia.

Furthermore, according to the new WHO classification[17], another limitation of the histopathological grading system based on epithelial thirds should be noted. Certain individual features, such as bulbous epithelial projections, disorganisation, and basal cell budding, can indicate significant cytological atypia confined to the basal third of the epithelium. In these cases, these features may justify a classification of severe dysplasia, despite being restricted to the basal third, thus challenging the existing grading criteria[17].

Regarding the classification using the Kujan binary system[8], our study found a predominance of cases considered at low risk for malignant transformation (86.4%), which aligns with the findings of Lopes et al.[15] (2015), who also employed this system for analysing AC. However, a contrasting result was observed in the study by Pilati, Bianco, Vieira, Modolo[18] (2017), which compared the WHO system with the Kujan binary system in 58 AC cases and 70 SCC cases. In their analysis, 63.8% of specimens were classified as high risk for malignant transformation. Notably, 87.5% of cases classified as severe dysplasia by the WHO system were categorised as high risk for malignant transformation by the Kujan binary system[18]. These findings reinforce that moderate epithelial dysplasia (ED) is difficult to classify within the subjective WHO system, as it contains cytological and/or architectural characteristics that can overlap with those seen in mild and severe ED classifications, as noted by Câmara et al.[19] (2016).

Our results showed a statistically significant association between the absence of certain epithelial alterations and a lower severity of dysplasia, according to the grading parameters of the WHO and Kujan systems. This suggests that fewer cytological alterations in the epithelium are associated with lower degrees of dysplasia. These findings are consistent with Câmara et al.[19] (2016), who proposed that the degree of dysplasia becomes more severe as the cytological and architectural alterations in the epithelium increase. Furthermore, regarding the association between

the WHO system and the Kujan binary system, our study aligns with the results observed by Câmara et al.[19] (2016), who also found a statistically significant association between the two grading systems. They suggested that the Kujan binary system might be more accurate for AC cases, as it demonstrated a significant correlation between various cytological and architectural alterations, which correspond to the evolution of dysplasia.

In the study conducted by Schmitz et al.[11] (2018), a new histopathological classification for AK cases was proposed. Based on the histopathological findings, AK cases were classified according to the system described by Röwert-Huber et al.[20] (2007). Likewise, AK cases were also analysed by the parameters of the new proposed system, which aimed to assess the basal growth pattern of lesions. In this new system, lesions are classified into three grades: grade I (crowding), grade II (budding), and grade III (papillary sprouting). Analysing 246 AK cases, Schmitz et al.[11] (2018) found that 26.4% were classified as grade I, 49.6% as grade II, and 17.9% as grade III.

In the present study, a similar trend was observed, with most cases (60.8%) classified as grade II (budding). However, 25.5% were categorised as grade III (papillary sprouting), and 13.7% as grade I (crowding). These findings suggest some alignment with Schmitz et al.[11] (2018), although no previous studies have applied this classification system specifically to AC cases. Schmitz et al.[11] (2018) concluded that their grading system, which emphasises basal growth patterns, may offer valuable insights into the histopathological assessment of AK and help improve the accuracy of risk stratification in these cases.

Schmitz et al.[11] (2018) concluded that their proposed new grading system (I-III), based on basal growth patterns, does not correlate with the conventional grading systems already applied in AK cases. However, they suggested that the systems could be applied complementarily for grading dysplasia. Furthermore, they emphasised the importance of analysing the basal layer's features, as it may be a key site for cell proliferation and, therefore, malignant progression. Given its simplicity and applicability, the new system is considered a viable alternative for assessing AK lesions.

Schmitz et al.[11] (2018) also recommended reformulating the conventional grading system for AK to incorporate evaluation of the basal growth pattern. In our study, the Schmitz system showed a statistically significant association with both the WHO and the Kujan binary systems, as well as with the microscopic finding of epithelial projection in droplet shape. This suggests that the Schmitz system could be effectively applied to AC cases. Its simplicity and relevance in assessing the basal growth pattern, which may correlate with the risk of malignant progression, make it a useful tool alongside other established systems. However, since this application in AC cases is unprecedented, we recommend further studies with a larger sample size and extended follow-up duration to validate its effectiveness.

CONCLUSIONS

The findings of this study underscore the importance of accurately assessing the degree of epithelial dysplasia in AC, given its potential for malignant transformation. The WHO, Kujan, and Schmitz grading systems all provide valuable insights into the progression of AC, although some limitations exist in their diagnostic accuracy, particularly regarding moderate dysplasia. Our results highlight the usefulness of the Schmitz system, based on basal growth patterns, in conjunction with conventional grading methods.

This system demonstrated a statistically significant association with both the WHO and Kujan binary systems, suggesting its potential as a complementary tool for more reliable risk assessment in AC cases. Despite its promising applicability, the Schmitz system requires further validation through larger, longitudinal studies to establish its role in clinical practice. Ultimately, improving the accuracy of dysplasia grading systems will aid in better monitoring and management of AC, enhancing early detection and prevention of squamous cell carcinoma development in these lesions.

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