J. Oral Diag. 2024;09:e20240232.

REVIEW ARTICLE

Necrotizing sialometaplasia: systematic review and meta analyses over the past 46 years

Júlia dos Santos Vianna Néri [1,2]
Viviane Palmeira da Silva [1,3,4]*
Nara Santos Araújo [1]
Thiago Alexsander Oliveira Gomes [4]
Mayana Barreto do-Nascimento [1]
Maria Cristina Teixeira Cangussu [1]
Luciana Maria Pedreira Ramalho [1]
Jean Nunes dos Santos [1]

Abstract:

Objectives: The aim of this study was to characterize the main characteristics of this disease in relation to diagnosis, clinical aspects, progression and treatment as well as correlating them with remission time. **Material and Methods:** A systematic search was performed following the guidelines given by PRISMA and the Joanna Briggs Institute. *PubMed*, Web of Science and Scopus were the databases used. **Results:** The final analysis resulted in 108 articles with 173 clinical cases. The longest remission time for signs and symptoms (>7 weeks) was registered among male patients ($p = 0.02$) and outside the oral cavity; however no significant correlation was observed ($p>0.05$). A high risk of bias was the most common rating among the articles analyzed (55%); followed by moderate (27%) and low (18%). The lack of standardization in clinical case report descriptions made it difficult to gain a thorough knowledge of the essential characteristics of the NS pathological processes. **Conclusion:** It is recommended that publications follow the standards recommended by the literature; in addition, studies using advanced technologies to better understand NS's pathological path are recommended so as to propose effective treatments for this disease.

Keywords: Necrotizing sialometaplasia; Salivary Glands; Diagnosis; Pathology, Oral; Evidence-Based Dentistry.

[1] Universidade Federal da Bahia, Programa de Pós-graduação em Odontologia e Saúde, Salvador, Bahia- Brasil.
[2] Faculdade Adventista da Bahia, Cachoeira, Bahia, Brasil.
[3] Escola Bahiana de Medicina e Saúde Pública, Salvador, Bahia, Brasil.
[4] Centro Universitário UNIFTC, Salvador, Bahia, Brasil.

Correspondence to:
Viviane Palmeira da Silva .
E-mail: vivianesilva@bahiana.edu.br

Article received on August 11, 2023.
Article accepted on August 21, 2023.

DOI: 10.5935/2525-5711.20230232

INTRODUCTION

First described by ABRAMS et al.[1], necrotizing sialometaplasia (NS) is characterized as being a rare inflammatory condition[1–3]. Although its etiology is not yet fully defined, it is known to be related to traumatic factors that may cause vascular obstruction, with consequent infarction and ischemic necrosis of the minor salivary glands[4]. Therefore, it is believed that NS goes through histopathological stages, which are: infarction, sequestration, ulceration, repair and healing[5].

The histological and clinical aspects of NS can be easily confused with malignant lesions, such as mucoepidermoid carcinoma and squamous cell carcinoma[1–3]. The histopathology is marked by the presence of squamous metaplasia of the acini and salivary ducts, aiming to promote repair of the affected region. However, the maintenance of the lobular architecture of the salivary glands stands out as it is an essential characteristic for the differentiation of NS with malignant lesions[1]. Classically, the clinical aspect shows the presence of consistent nodules or crateriform ulcers surrounded by an erythematous halo and, on rare occasions, there may be destruction of the underlying palatine bone[6].

The natural history of this disease leads to a repair process, therefore the ideal treatment for NS is to wait for the remission of clinical signs and symptoms. This can mean treatment time intervals *of* days, months and years. However, the scientific literature shows cases in which partial surgical interventions were performed, like incisional biopsies, and total ones, such as excisional biopsies or complete removal of the lesion, as well as the use of anti-inflammatory drugs. We hypothesized that such procedures could be considered potentially harmful agents and as a consequence, they activate the healing and repair signaling pathways of the affected area and decrease the remission time for the clinical signs and symptoms of NS. On the other hand, it is not yet known whether the clinical aspects of this lesion have an influence on the total repair of the lesion. However, in vitro and in vivo study models responding to this hypothesis are complex to develop, due to the poorly recognized nature and the rare involvement of the disease. Therefore, it is considered that analyzing clinical cases already published represents a valuable path to answering such questions. Thus, this paper aims to conduct a systematic review of clinical cases of NS and correlate aspects of clinical behavior and prognosis, to better understand the stages of progression of this disease.

METHODOLOGY

Eligibility Criteria

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Joanna Briggs Institute[7]. The acronym PECOS (Population, Exposition, Comparison, Outcomes, Studies) was used to formulate this systematic review: P) Patients with necrotizing sialometaplasia in the head and neck; E) Clinical aspects, medication use, surgical intervention; C) Type of clinical aspect, type of medication used and type of *surgical procedure; O) Decreased the lesion remission time; S) Case reports and case series* in humans with necrotizing head and neck sialometaplasia. Only articles published in the English literature were included in this study. Clinical case series articles that did not differentiate between individual patient data were excluded because they did not allow clinical analysis of the data. Conference abstracts, editorials, scientific review articles, observational studies, and unavailable texts were also excluded from this analysis. There was no delimitation of publication year, age, gender or race.

Search strategies and information

The electronic databases PubMed, Scopus and Web of Science were used. The following search term was used to perform the search: "necrotizing sialometaplasia" OR "necrotizing adenometaplasia" OR "adenometaplasia" AND "salivary gland". The research period was from February to August 2019. The references of the selected articles were also evaluated manually.

Study Selection

All selected articles were tabulated in Microsoft Excel (version 2010) and duplicates were removed manually. In the first stage, two previously trained reviewers (J.V.N. and M.B.N.) read the titles and abstracts and applied the exclusion and inclusion criteria. In the second stage, the full texts were read. Articles that generated disagreement were reviewed and discussed with a third reviewer (V.P.S.).

Data extraction

Data concerning year of publication, first author, gender, age, location, clinical aspects, time of lesion evolution, use of medications, type of surgical intervention, time to lesion remission, incorrect diagnosis and number of biopsies performed were extracted.

Bias risk assessment

An adaptation of the critical appraisal items recommended by the Joanna Briggs Institute for clinical cases was used[7]. As they did not fit the descriptions of most necrotizing sialometaplasia clinic al cases, the prognostic criteria, color and previous treatments in item one, as well as the psychosocial history of the patient and family members, found in item two, were removed. The case series were analyzed by individual clinical case. In the final analysis, cases were categorized as "high ROB (Risk of Bias)" when the study achieved up to a 49% "yes" score; "Moderate ROB" when the study reached a 50% to 69% "yes" score; and "low ROB" when the study reached a score of 70% "yes" or higher[8].

Data synthesis and analysis

For a better understanding of the clinical aspects of NS, a detailed description of the data, from each selected article, was initially carried out, with frequencies and percentages and means and standard deviations for continuous variables, using the following descriptions: gender (male or female) and age (0-10, 11-20, 21-30, 31-40, 41-50, 51-60, >61) of patients; localization of lesion (mouth floor /tongue / lip, nasal cavity, palate, parotid gland, pharynx / larynx, and other sites); clinical aspects (edema, nodule, ulcer, +1 of one aspect), lesion evolution in weeks (0-2 weeks, 2.1-4 weeks, 4.1-6 weeks, >6.1 weeks), use of antibiotic / anti-inflammatory (yes, no), type of surgical intervention (total or partial) and time to lesion remission (0-2 weeks, 2.1-4 weeks, 4.1-6 weeks, >6.1 weeks).

For the bivariate analysis, cases with three or more missing variables were excluded from the database. In addition, the variables were recategorized into dichotomy. The median parameters were used for the age variables (≤41 and ≥43); evolution time in weeks (≤2 and ≥4) and remission time in weeks (≤6 and ≥7). The localization was categorized as "oral cavity" or "not oral cavity", while clinical aspect was categorized as "ulcerated" "not ulcerated". A Fisher's exact test or Chi-squared test was used to assess the variables associated with remission time. Next, a backwards stepwise logistic regression was used, adjusting for the covariates that showed $p \leq 0.10$ in the bivariate model (patient gender and localization of lesion). The odds ratios (OR) and 95% confidence intervals (CI) were then calculated. Data analysis was performed using SPSS software version 25.0 (SPSS Inc. Chicago, IL, USA). *P*-values of <0.05 were considered statistically significant.

RESULTS

Initially, a total of 725 articles were found, of which 361 were duplicates and 263 did not fall within the inclusion criteria (1 systematic review; 3 complete description of the case not provided; 6 abstracts / conferences; 9 animal cases; 9 surveys; 9 in the format of a quiz; 13 letters to the editor; 30 written in other languages; 55 off-topic; 33 bibliographic reviews; and 95 without access via the internet). In the end, 101 articles were selected and 7 were added through references, totaling 108 articles and 173 cases (Figure 1). One hundred and eight studies (99 case reports and 9 case series) were selected for evaluation, totaling 173 patients assessed, with a mean age of 43.6 years.

Descriptive Analysis (general description)

General descriptions of this systematic review's main findings are shown in Complementary Figure 1. It is observed, that, since the 1990s, reports of clinical cases of necrotizing sialometaplasia have been on the rise, with the highest peak in the 2010s (Figure 2). The frequency and detailed percentages of the analyzed variables are described in Table 1. It should be noted that for the category "other sites" in the localization variable, the following areas were included: trachea (3), maxillary sinus (1), lacrimal sac (1), bronchus (1), carotid artery (1), turbinate (1), vocal cord (1), periorbital space (1) and other regions (1): mandibular molars (2), canines (1), preauricular (1), intra-articular (1) and subglottic (1). Regarding the use of medications, in addition to anti-inflammatories and antibiotics (Table 1), the use of other drug classes, such as antifungal, antiviral, and herbal, among others, were also cited (described in Complementary Figure 1).

Forty-three cases reported at least one misdiagnosis prior to NS, except for the study by CARLSON et al.[8] which obtained two different diagnoses. In total, there were 45 diagnostic errors (Figure 3). Twenty-eight (62.2%) of the errors found were related to tumors, among which were: 28 (50%) squamous cell carcinomas; 10 (35.8%) mucoepidermoid carcinomas; 1 (3.6%) adenoid cystic carcinoma; 1 (3.6%) fibrohistiocytic tumor; 1 (3.6%) papilloma; and 1 (3.6%) pleomorphic adenoma. Inflammatory processes were the second most common type of diagnostic error, with a total of 11 cases (25.4%), subdivided into: 4 (36.4%) abscesses; 4 (36.4%) ulcers; 1 (9.1%) inflammatory granulomatous tissue; 1 (9.1%) acute inflammation and fibrovascular proliferation; 1 (9.1%) laryngeal perichondritis. Autoimmune diseases (1

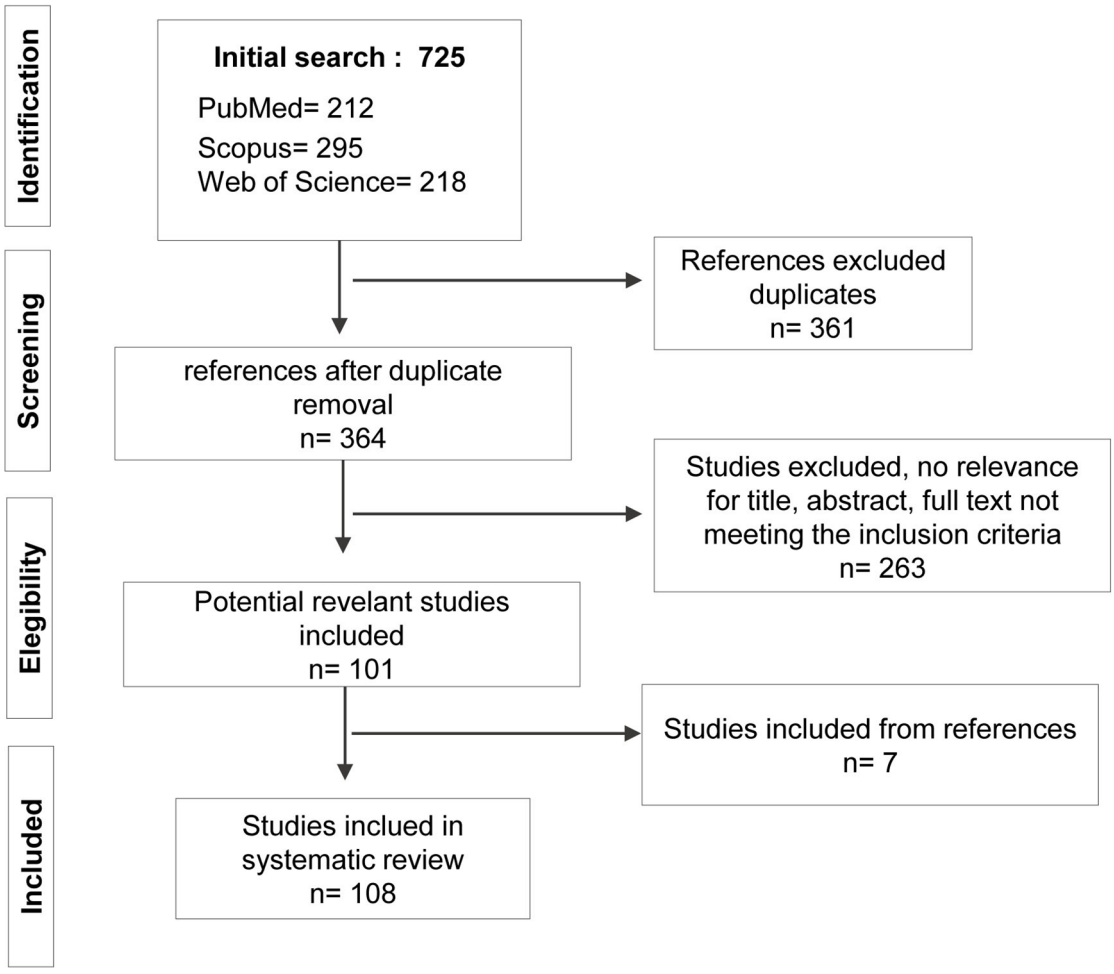

Figure 1. Search Flow Diagram and Selection Criteria.

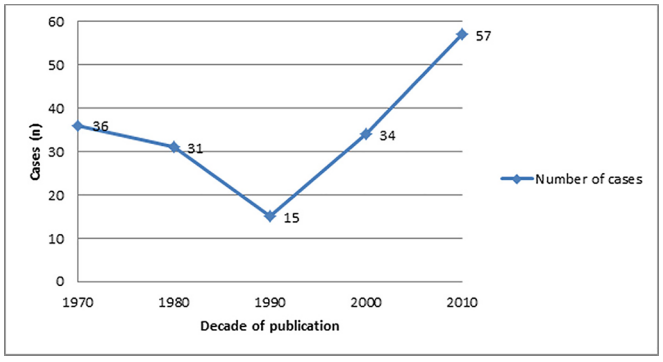

Figure 2. Graph of the number of necrotizing sialometaplasia cases published per decade.

granulomatous disease and 1 Wegener's granulomatosis) and other lesions (2 mucoceles, 1 local necrosis and 1 non-specific submucosal fibrosis) were also diagnosed. 22 cases reported that the final diagnosis was reached after two biopsies; 2 studies required three biopsies.

Statistical analyses

For bivariate analysis, 97 cases were considered (Table 2). The analysis showed that a higher (≥ 7 weeks) remission time was significantly more frequent among male patients (61.8%, OR= 3.1, 95% CI= 1.2-8.1, p=0.02) and in cases of lesions outside the oral cavity (22.2%, OR= 10.5, 95% CI= 1.2-89.4, p= 0.01). However, regardless of the time to remission (≤ 6 or ≥ 7 weeks), there were no significant differences in the ulcerated clinical aspect (≥80%, OR=1.3, 95% IC= 0.38-4.30, p=0.67), evolution time ≤4 weeks (≥ 67%, OR=1.8, 95% IC= 0.54-6.02, p=0.32), use of anti-inflammatories (≥65%, OR=0.8, 95% IC= 0.18-3.67, p>0.05) or partial surgical intervention (≥79%, OR=0.5, 95% IC= 0.12-2.47, p=0.48). In the regression analysis including the gender and localization variables, they were not significantly associated with a remission time ≥ 7 weeks (p>0.05) (Table 3).

Table 1. Frequency distribution of the demographic and clinical characteristics of the clinical cases included in the systematic review.

	n	%
Gender	**172**	**100**
Male	93	54.07
Female	79	45.93
Age (year)	**172**	**100**
0-10	1	0,6
11-20	7	4.1
21-30	39	22.7
31-40	32	18.6
41-50	35	20.3
51-60	31	18
61-70	18	10.5
71-80	6	3.5
81-90	3	1.8
Localization	**172**	**100**
Mouth floor /Tongue / Lip	15	8.8
Nasal cavity	5	2.9
Pharynx / Larynx	5	2.9
Parotid Gland	10	5.8
Others	17	10
Palate	120	69.8
Evolution time (week)	**94**	**100**
0-2	27	28.7
2.1-4	52	55.3
4.1-6	13	14
>6	2	2
Clinical aspect	**151**	**100**
Edema	17	11.26
Nodule	20	13.25
Ulcer	97	64.24
+1	17	11.26
Antibiotic and anti-inflammatory consumption	**43**	**100**
No	14	32.56
Yes	29	67.44
Surgical intervention	**106**	**100**
Partial	66	62.26
Total	40	37.74
Remission Time	**99**	**100**
0-2 weeks	12	12.12
2,1-4 weeks	23	23.23
4,1-6 weeks	24	24.24
>6,1 weeks	40	40.40

Bias risk outcomes for selected studies

Of the total 173 evaluated cases, a higher proportion of cases with a high risk of bias (n = 95, 54.9%), followed by moderate risk (n = 47, 27.2%) and finally low risk (n = 31, 17.9 %) was observed (Table 4).

DISCUSSION

NS was first described by ABRAMS, MELROSE and HOWELL in 1973[1]. However, it was not until the 1990s that there was a rise in the publication of case reports, with the highest peak in the 2010s. Given the inclusion criteria of this work, to date, 173 cases of necrotizing sialometaplasia have been described since 1973. It is important to mention that 43.9% of the analyzed papers had three or more missing variables. This denotes an impoverishment of the database for the analysis of logistic regression in this systematic review. In addition, it has been observed that most articles are at a high risk of bias (55%). These data emphasize the need to improve the quality of clinical report publications on NS.

NS has peculiarities in its pathogenesis that are still not full understood, a fact that turns it into a pathology of complex clinical. This systematic review was carried out in order to understand the influence of clinical aspects and interventions in on the remission time for its signs and symptoms. It was possible to verify that, although the literature and the total number of our cases suggested that there is a higher prevalence of NS in the female gender and localization within the oral cavity, the longest time to remission of signs and symptoms (≥7 weeks) was in male patients (p=0.02) and located outside the oral cavity (p=0.01). The possible factors that explain these results are not amenable to analysis in view of the proposed study model. However, it is important to mention that this result proposes an expansion of the clinical view in relation to the monitoring of these patients, indicating the relevance of a long observation period.

It is known that the stimulation generated by a surgical procedure can induce physiological activation of growth factors to promote healing and repair of the affected region[9]. To analyze the possibility of such procedures interfering with the remission of NS, the relationship between surgical procedures/symptom remission was evaluated; no statistical association was found. On the other hand, NS is known for a tendency

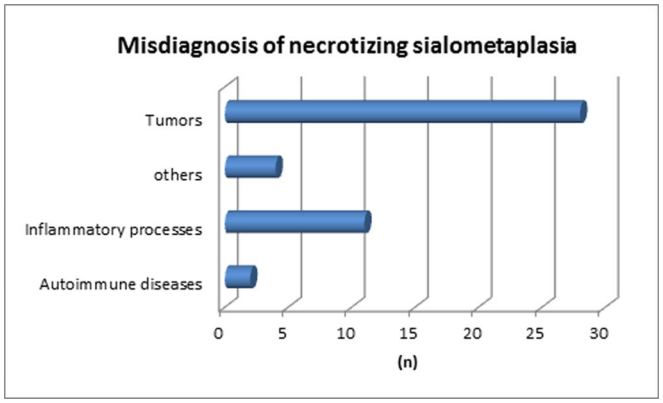

Figure 3. Graph of the number of misdiagnoses during the necrotizing sialometaplasia diagnosis process.

to spontaneously auto-regress. This may be related to the chronicity of its etiology, size and the presence or absence of bone perforation[10]. Due to the descriptions of the cases studied, it was not possible to evaluate the correlation of etiology, size and presence of bone perforation with the time necessary for lesion remission.

The etiology and pathogenesis of NS is still poorly understood, but it is believed that they are due to the compromised vascular supply of the salivary glands, which results in infarction and necrosis of the affected region[11]. However, the etiological factors are expected to vary according to the primary site of the lesion. Trauma during dental procedures is the most common source in cases of palate SN and postoperative vascular lesions are the main cause in cases of parotid glands[12]. Local radiotherapy, cocaine use, smoking, anorexia and bulimia nervosa may also influence the development of this lesion[13,14]. During this clinical case review process, it was difficult to find a description of the previous medical history of the cases, which limited this review's ability to examine what may be the most prevalent etiological factor in the NS case literature.

Although occurring elsewhere, the typical site for manifestation of NS in the head and neck is the palate[15]. The results of this study demonstrated that 88.6% of the cases occurred in the oral cavity and among them 69.8% were in the palate. Such result are in agreement with the case series published by BRANNON et al. (1991)[16], demonstrating similar proportions of occurrence of SN in the palate (72-70%, respectively), as well as their distribution among their microregions, with greater preference for the hard palate (44.5-40.57%, respectively), followed by the palatal junction (8-10% respectively) and soft palate (9-13% respectively). This can be explained by the fact that the blood supply for this region is only provided via one branch of the major palatal artery. As

Table 2. Bivariate analysis considering the remission time of patients with necrotizing sialometaplasia, n = 97.

Variables	Remission time in week					
	n	≤6	≥7	OR	95% CI	P
Gender				3.17	1.18-8.14	0.02[a]
Female	38	25 (65.8%)	13 (38.2%)			
Male	34	13 (34.2%)	21(61.8%)			
Localization				10.57	1.25-89.49	0.01[b]
Oral cavity	65	37 (97.4 %)	28 (77.8%)			
No oral cavity	9	1 (2.6 %)	8 (22.2%)			
Clinical aspect				1.29	0.38-4.30	0.67[a]
Ulcerated	59	31 (83.8%)	28 (80%)			
No ulcerated	13	6 (16.2%)	7 (20%)			
Evolution time in week				1.81	0.54-6.02	0.32[a]
≤ 4 weeks	42	23 (79.3%)	19 (67.9%)			
> 4 weeks	15	6 (20.7%)	9 (32.1%)			
Use of anti-inflammatory				0.85	0.18-3.67	1.00[b]
Yes	22	13 (65%)	9 (69.2%)			
No	11	7 (35%)	4 (30.8%)			
Surgical intervention				0.54	0.12-2.47	0.48[b]
Partial	44	23 (79.3%)	21 (87.5%)			
Total	9	6 (20.7%)	3 (12.5%)			

[a] Chi-squared; [b] Fisher's exact test, CI = confidence interval, OR = odds ratio, n = number of individuals who present the condition within the group

Table 3. Logistic regression for the relationship between remission time and gender and localization.

Variable		
	OR (95% IC)	**p value**
REMISSION TIME		
Gender		
Femele	1	
Male		
Localization	2.08 (0.74-5.87)	0,16
Oral Cavity	1	
No oral cavity	7.38 (0.80-68.12)	0,07

CI Confidence interval, OR odds ration.

Table 4. Risk of bias analysis of the articles selected in the systematic review, an adaptation of the critical assessment list recommended by the Joanna Briggs Institute for clinical cases.

	n	HIGH ROB	MODERATE ROB	LOW ROB
1 case	81	25	32	24
> 1 case	92	71	15	7
All	173	96	47	31

the surrounding bony and mucosal areas are provided for by more than one artery, they are less prone to ischemic events when compared to the palate[17].

Although clinical features are classically described as ulcers and/or nodules, an incisional biopsy is absolutely necessary, as this lesion may mimic malignant neoplasms. The need for a repeat biopsy was found in 14% of the cases and 26% had a misdiagnosis prior to NS, among which the most common was squamous cell carcinoma (50%) and mucoepidermoid carcinoma (36%). The similarity between carcinomas and NS can lead to a misdiagnosis that impacts decision making regarding treatment type and the patient's quality of life[18]. To lessen the effects of these errors, complementary exams such as immunohistochemistry may be used to make a differential diagnosis. Characteristically, in NS the Ki-67 and p53 show low reactivity and focal or absent immunoreactivity, respectively[19,20]. While in squamous cell and mucoepidermoid carcinomas, such markers are highly active[21,22]. Other immunomarkers can be used to define the nature of the lesion, such as AE1-AE3, CK7, S-100 or SMA, however there are no specific markers for NS.

It should be made clear that case reports are not at the top of the scientific evidence chain in contributing to the understanding of the pathological, clinical and therapeutic processes of a given disease[23]. However, it is noteworthy that NS is a disease that has elements that hinder the feasibility of scientific research, such as rarity, poorly recognized etiology and variable clinical processes. The minimum number of scientific research articles (n = 9) present in the literature regarding NS reflects the need to recognize the behavioral patterns of this disease. By so doing it will become possible to outline strategies for research in order to deepen our understanding of this pathology. According to this review of clinical cases, it can be inferred that NS is a lesion of unrecognized etiology, mostly affecting the male gender, with a peak in occurrences seen between 21-30 years of age, in addition to a higher occurrence in the palate, and that remission time is variable between patients. In order to gather further information, it is necessary to improve the quality of the information published in clinical case reports.

Disclosure statement

The authors report no conflict of interest

Ethical approval

Due to the nature of the present study with no patients' involvement, ethical committee approval was not sought.

Informed consent

To perform the present study, informed consent was not required.

REFERENCES

1. Abrams AM, Melrose RJ, Howell FV. Necrotizing sialometaplasia a disease simulating malignancy. Cancer. 1973 Jul;32(1):130-5.
2. Donath K, Seifert G. Tumour-simulating squamous cell metaplasia (SCM) in necrotic areas of salivary gland tumours. Pathol Res Pract. 1977;193(10):689-93.
3. Giles AD. Necrotizing sialometaplasia. Br J Oral Surg. 1980 Jun;18(1):45-50.
4. Daudia A, Murty G. First case of full-thickness palatal necrotizing sialometaplasia. J Laryngol Otol. 2002 Mar;116(2):219-20.
5. Anneroth G, Hansen LS. Necrotizing sialometaplasia. The relationship of its pathogenesis to its clinical characteristics. Int J Oral Surg. 1982;11(5):283-91.
6. Yagihara K, Ishii J, Katsurano M, Tsuchida E, Okamura T, Ishikawa A. A case of necrotizing sialometaplasia clinically mimicking a malignant tumor of the palate. Oral Sci Int. 2018 Jul;15(2):73-7.
7. Joanna Briggs (JBI). Home page [Internet]. Adelaide (AU): Faculty of Health and Medical Sciences The University of Adelaide; [access in 2017 Sep 29]. Available from: https://jbi.global/
8. Carlson DL. Necrotizing sialometaplasia: a practical approach to the diagnosis. Arch Pathol Lab Med. 2009 May;133(5):692-8.

9. Allon I, Kaplan I, Allon DM, Vered H, Shlomi B, Hirshberg A. HIF-1α, VEGF, and EGFR: Contributing factors in the pathogenesis of necrotizing sialometaplasia. Oral Dis. 2014 Jul;20(5):440-5.
10. Kim YH, Joo YH, Oh JH. A case of necrotizing sialometaplasia involving bilateral parotid glands. Am J Otolaryngol. 2013 Mar/Apr;34(2):163-5.
11. Randhawa T, Varghese I, Shameena P, Sudha S. Nair RG. Necrotizing sialometaplasia of tongue. J Oral Maxillofac Pathol. 2009 Jan;13(1):35-7.
12. Aydin O, Yilmaz T, Ozer F, Saraç S, Sökmensüer C. Necrotizing sialometaplasia of parotid gland: a possible vasculitic cause. Int J Pediatr Otorhinolaryngol. 2002 Jun;64(2):171-4.
13. Femopase FL, Hernández SL, Gendelman H, Criscuolo MI, Blanc SA. Sialometaplasia necrotizante: presentación de cinco casos clínicos. Med Oral Patol Oral Cir Bucal. 2004 Aug/Oct;9(4):304-8.
14. Keogh PV, O'Regan E, Toner M, Flint S. Necrotizing sialometaplasia: an unusual bilateral presentation associated with antecedent anaesthesia and lack of response to intralesional steroids. Case report and review of the literature. Br Dent J. 2004 Jan;196(2):79-81.
15. Lynch DP, Crap CA, Martinez MG. Necrotizing sialometaplasia. A review of the literature and report of two additional cases. Oral Surg Oral Med Oral Pathol. 1979;47:63-9.
16. Brannon RB, Fowler CB, Hartman KS. Necrotizing sialometaplasia. A clinicopathologic study of-sixty-nine cases and review of the literature. Oral Surg Oral Med Oral Pathol. 1991 Sep;72(3):317-25.
17. Bascones-Martínez A, Muñoz-Corcuera M, Cerero-Lapiedra R, Bascones-Iludáin J, Esparza-Gómez G. Case report of necrotizing sialometaplasia. Med Oral Patol Oral Cir Bucal. 2011 Sep;16(6):e700-e3.
18. Senapati S, Samal SC, Kumar R, Patra S. Necrotizing sialometaplasia: manifestation of a localized unclassified vasculitis. Indian J Pathol Microbiol. 2016 Apr/Jun;59(2):232-4.
19. Alves MGO, Kitakawa D, Carvalho YR, Cabral LAG, Almerida JD. Necrotizing sialometaplasia as a cause of a non-ulcerated nodule in the hard palate: a case report. J Med Case Rep. 2011;5:406.
20. Krishna S, Ramnarayan BK. Necrotizing sialometaplasia of palate: a case report. Imaging Sci Dent. 2011 Mar;41(1):35-8.
21. Almangush A, Heikkinen I, Mäkitie AA, Coletta RD, Läärä E, Leivo I, et al. Prognostic biomarkers for oral tongue squamous cell carcinoma: a systematic review and meta-analysis. Br J Cancer. 2017 Sep;117(6):856-66.
22. Alves FA, Pires FR, Almeida OP, Lopes MA, Kowalski LP. PCNA, Ki-67 and p53 expressions in submandibular salivary gland tumours. Int J Oral Maxillofac Surg. 2004 Sep;33(6):593-7.
23. Evans D. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. J Clin Nurs. 2003 Jan;12(1):77-84.
24. Aframian D, Milhem I, Kirsch G, Markitziu A. Necrotizing sialometaplasia after silastic ring vertical gastroplasty: case report and review of literature. Obes Surg. 1995 May;5(2):179-82.
25. Alande C, Fénélon M, Catros S, Fricain JC. Persistent ulceration of the oral floor: a case of necrotizing sialometaplasia of the sublingual gland? Med Buccale Chir Buccale. 2017;23(4):188-9.
26. Almazrooa SA, Ouano J, Woo S Bin. Unusual large tongue ulcer. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013 Jul;116(1):4-8.
27. Arguelles MT, Viloria Junior B, Talew MC, McCory TP. Necrotizing sialometaplasia. Oral Surg Oral Med Oral Pathol Oral Radiol. 1976 Jul;42(1):86-90.
28. Arpaci RB, Kara T, Porgali C, Serinzsoz E, Polat A, Vayisoglu Y, et al. Two rare entities in the same palate lesion: hyalinizing--type clear cell carcinoma and necrotizing sialometaplasia. Case Rep Dent. 2014 May;25(3):e-235-7.
29. Balaji SM, Balaji P. Surgical management of necrotizing sialometaplasia of palate. Indian J Dent Res. 2015 Sep/Oct;26(5):550-5.
30. Bernardo T, Tente D, Oliveira P, Helena D, Ribeiro D, Gerós S, et al. Benign or malignant? Case report. Eur Ann Otorhinolaryngol Head Neck Dis. 2012 Oct;129(5):275-7.
31. Birkholz H, Brownd CL. Necrotizing sialometaplasia: report of an ulcerative case. J Am Dent Assoc. 1981 Jul;103(1):48-50.
32. Wenig BM. Necrotizing sialometaplasia of the larynx a report of two cases and a review of the literature. Am J Clin Pathol. 1995 May;103(5):609-13.
33. Buller DL. Nodular and ulcerated lesions of the hard palate. J Am Dent Assoc. 1980 Nov;101(5):823-4.
34. Chakravorty RC, Yoneyama T, Makooi C. Necrotizing sialometaplasia of palate. Br J Surg. 1979 Apr;66(4):283-4.
35. Chen KT. Necrotizing sialometaplasia the nasal cavity. Am J OtoIaryngol. 1982 Nov/Dec;3(6):444-6.
36. Close LG, Cowan DF. Recurrent necrotizing sialometaplasia of the nasal cavity. Otolaryngol Head Neck Surg. 1985;93(3):422-5.
37. Correll RW, Wescott WB, Pierce GL. Asymptomatic, nonulcerated swelling of the posterior hard palate. J Am Dent Assoc. 1982 Sep;105(3):512-3.
38. Devine M, Sammut S, Conn B, Lopes V. Necrotising sialometaplasia in the floor of mouth. Oral Maxillofac Surg. 2014 Mar;18(1):119-21.
39. Dominguez-Malagon H, Mosqueda-Taylor A, Cano-Valdez AM. Necrotizing sialometaplasia of the palate associated with angiocentric T-cell lymphoma. Ann Diagn Pathol. 2009 Feb;13(1):60-4.
40. Dunlap CL, Barker BF. Necrotizing sialometaplasia report of five additional cases. Oral Surg Oral Med Oral Pathol. 1974 May;37(5):722-7.
41. Dunley RE, Jacoway JR. Necrotizing sialometaplasia. Oral Surg Oral Med Oral Pathol. 1979 Feb;47(2):169-72.
42. Farina D, Gavazzi E, Avigo C, Borghesi A, Maroldi R. Case report. MRI findings of necrotizing sialometaplasia. Br J Radiol. 2008 Jun;81(966):e173-e5.
43. Fechner RE. Necrotizing sialometaplasia: a source of confusion with carcinoma of the palate. Am J Clin Pathol. 1977 Apr;67(4):315-7.
44. Forney SK, Foley JM, Sugg Junior WE, Oatis Junuor GW. Necrotizing sialometaplasia of the mandible. Oral Surg Oral Med Oral Pathol. 1977 May;43(5):720-6.
45. Fowler CB, Brannon RB. Subacute necrotizing sialadenitis: report of 7 cases and a review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000 May;89(5):600-9.

46. Fujii T, Ohnishi Y, Minamino Y, Watanabe M, Gotoh M, Wato M, et al. A case of necrotizing sialometaplasia with bone resorption at the hard palate. J Oral Maxillofac Surg Med Pathol. 2014 Apr;26(2):245-8.
47. Gad A, Willén H, Willén R, Thorstensson S, Ekman L. Necrotizing sialometaplasia of the lip simulating squamous cell carcinoma. Histopathology. 1980 Jan;4(1):111-21.
48. Gadkaree SK, Fuller JC, Sadow PM, Deschler DG, Richmon JD. Necrotizing sialometaplasia of the hypopharynx. Ear Nose Throat J. 2019 Oct/Nov;98(9):138-41.
49. Garcia NG, Oliveira DT, Faustino SES, Azevedo ALR. Necrotizing sialometaplasia of palate: a case report. Case Rep Pathol. 2012;2012:679325.
50. Gatti A, Broccardo E, Poglio G, Benech A. Necrotizing sialometaplasia of the hard palate in a patient treated with topical nonsteroidal anti-inflammatory drug. Case Rep Dent. 2016;2016:9545861.
51. Gavron JP, Ardito JA, Curtis AW. Necrotizing sialometaplasia. Laryngoscope. 1981 Jul;91:1176-80.
52. Gilowski L, Wiench R, Polakiewicz-Gilowska A, Dwornicka K. Necrotizing sialometaplasia of the palatal mucosa in patient with history of anorexia: review and case report. Am J Otolaryngol. 2014 May/Jun;35(3):400-1.
53. Gomez A, Gladstone G. Necrotizing sialometaplasia of the lacrimal sac mimicking squamous cell carcinoma: necrotizing dacyocystometaplasia. Orbit. 2016;35(1):48-50.
54. Granich MS, Pilch BZ. Necrotizing sialometaplasia in the setting of acute and chronic sinusitis. Laryngoscope. 1981 Sep;91(9 Pt 1):1532-5.
55. Granick MS, Solomon MP, Benedetto AV, Hannegan MW, Sohn M. Necrotizing sialometaplasia masquerading as residual cancer of the lip. Ann Plast Surg. 1988 Aug;21(2):152-4.
56. Haen P, Ben Slama L, Goudot P, Shouman T. Necrotizing sialometaplasia of the parotid gland associated with facial nerve paralysis. J Stomatol Oral Maxillofac Surg. 2017 Feb;118(1):63-5.
57. Imai T, Michizawa M. Necrotizing sialometaplasia in a patient with an eating disorder: palatal ulcer accompanied by dental erosion due to binge-purging. J Oral Maxillofac Surg. 2013 May;71(5):879-85.
58. Imbery TA, Edwards PA. Necrotizing sialometaplasia: literature review and case reports. J Am Dent Assoc. 1996 Jul;127(7):1087-92.
59. Indirani VL, Ramesh G, Mishra G, Raj A. Histopathology and its role in diagnosing necrotizing sialometaplasia: a report of three cases. Int J Oral Maxillofac Pathol. 2013;4:33-6.
60. Janner SF, Suter VG, Altermatt HJ, Reichart PA, Bornstein MM. Bilateral necrotizing sialometaplasia of the hard palate in a patient with bulimia: a case report and review of the literature. Quintessence Int. 2014 May;45(5):431-7.
61. Jeong CW, Youn T, Kim HS, Park KH, Huh JK. Contralateral recurrence of necrotizing sialometaplasia of the hard palate after five months: a case report. J Korean Assoc Oral Maxillofac Surg. 2015 Dec;41(6):338-41.
62. Johnston WH. Necrotizing sialometaplasia involving the mucous glands of the nasal cavity. Hum Pathol. 1977 Sep;8(5):589-92.
63. Joshi S, Halli R, Koranne V, Singh S. Necrotizing sialometaplasia: a diagnostic dilemma! J Oral Maxillofac Pathol. 2014 Sep/Dec;18(3):420-2.
64. Kandula S, Manjunatha BS, Tayee P, Astekar M. Bilateral necrotising sialometaplasia. BMJ Case Rep. 2016;2016:bcr2015211348. DOI: https://doi.org/10.1136/bcr-2015-211348
65. Kaplan I, Alterman M, Kleinman S, Reiser V, Shuster A, Dagan Y, et al. The clinical, histologic, and treatment spectrum in necrotizing sialometaplasia. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012 Nov;114(5):577-85.
66. Kizilay A, Erdem T, Bayindir T, Ozturan O. A case of necrotizing sialometaplasia in the upper lip. Kulak Burun Bogaz Ihtis Derg. 2003 May;10(5):213-5.
67. Kominek P, Blasch P. Necrotizing sialometaplasia: a potential diagnostic pitfall. Ear Nose Throat J. 2006 Sep;85(9):604-5.
68. Kumar S, Qayyum A, Bhat N. Necrotizing sialometaplasia of the nasopharynx with parapharyngeal extension: case report and brief review of the literature. Ear Nose Throat J. 2014 Dec;93(12):e25-e7.
69. Kumar LB, Muthukrishnan A, Gopalakrishnan S. Necrotising sialometaplasia at multiple sites: a therapeutic challenge to oral physicians. BMJ Case Rep. 2016;2016:bcr2016216621. DOI: https://doi.org/10.1136/bcr-2016-216621
70. Lambert PM. Necrotizing sialometaplasia: report of two cases. Spec Care Dent. 1987;7(2):78-80.
71. Lamey PJ, Lewis MA, Crawford DJ, MacDonald DG. Necrotising sialometaplasia presenting as greater palatine nerve anaesthesia. Int J Oral Maxillofac Surg. 1989 Apr;18(2):70-2.
72. Ledesma-Montes C, Garcés-Ortíz M, Salcido-García JF, Hernández-Flores F. Review of the literature on necrotizing sialometaplasia and case presentation. Quintessence Int. 2015 Jan;46(1):67-72.
73. Lee DJ, Ahn HK, Koh ES, Rho YS, Chu HR. Necrotizing sialometaplasia accompanied by adenoid cystic carcinoma on the soft palate. Clin Exp Otorhinolaryngol. 2009 Mar;2(1):48-51.
74. Madala J, Guttikonda V, Korlepara R, Yeluri S. Necrotizing sialometaplasia: a diagnostic dilemma. Oral Health Dent Manag. 2014 Sep;13(2):687-9.
75. Maisel RH, Johnston WH, Anderson HA, Cantrell RW. Necrotizing sialometaplasia involving the nasal cavity. Laryngoscope. 1977 Mar;87(3):429-34.
76. Mandel L, Kaynar A, DeChiara S. Necrotizing sialometaplasia in a patient with sickle-cell anemia. J Oral Maxillofac Surg. 1991 Jul;49(7):757-9.
77. Matilla A, Flores T, Nogales Junior F, Galera H. Necrotizing sialometaplasia affecting the minor labial glands. Oral Surg Oral Med Oral Pathol. 1979 Feb;47(2):161-3.
78. Matsumoto T, Kuwabaral N, Shiotsul H, Fukuda Y, Yanai A, Ichikawa G. Necrotizing sialometaplasia in the mouth floor secondary to reconstructive surgery for tongue carcinoma. Acta Pathol Jpn. 1991 Sep;41(9):689-93.
79. Merwin GE, Duckert LG, Pollak K. Necrotizing sialometaplasia of the nasopharynx. Ann Otol Rhinol Laryngol. 1979 May/Jun;88(3 Pt 1):348-51.
80. Mitchell RD. Necrotizing sialometaplasia. Case report. Aust Dent J. 1985 Jun;30(3):181-4.
81. Murphy J, Giunta J, Meyer I, Robinson K. Necrotizing sialometaplasia. Oral Surg Oral Med Oral Pathol. 1977 Sep;44(3):419-24.
82. Myers EN, Bankaci M, Barnes EL. Necrotizing sialometaplasia report of a case. Arch Otolaryngol. 1975 Oct;101(10):628-9.
83. Newland J. Bilateral presentation of necrotizing sialometaplasia - a case report. Dent Update. 2007 Nov;34(9):586-8.

84. Niedzielska I, Janic T, Markowski J. Bilateral localization of necrotizing sialometaplasia: a case report. Cases J. 2009 Sep;2:9068.
85. Nilsen R, Bernhoft CH, Gilhuus-Moe O. Necrotizing sialometaplasia. Int J Oral Surg. 1978;7:580-4.
86. Sarioğlu S, Pabuççuoğlu U, Ecevit C, Ceryan K, Paksoy S, Ada E. Sialometaplasia arising in the ectopic salivary gland ductal inclusions of multiple intraparotid lymph nodes. J Clin Pathol. 2004 Dec;57(12):1335-7.
87. Pagni F, Zàrate AF, Urbanski SJ. Necrotizing sialometaplasia of bronchial Mucosa. Int J Surg Pathol. 2010 Feb;18(1):64-5.
88. Philipsen HP, Petersen JK, Simonsen BH. Necrotizing sialometaplasia of the palate Ulcerative or necrotizing stage of leukokeratosis nicotina palati? Int J Oral Surg. 1976 Dec;5(6):292-9.
89. Prabhakaran VC, Flora RS, Kendall C. Pressure-induced necrotizing sialometaplasia of the parotid gland. Histopathology. 2006 Mar;48(4):464-5.
90. Pulse CL, Lebovics RS, Zegarelli DJ. Necrotizing sialometaplasia: report of a case after lower lip mucocele excision. J Oral Maxillofac Surg. 2000 Dec;58(12):1419-21.
91. Raugi GJ, Kessler S. Necrotizing sialometaplasia a condition simulating malignancy. Arch Dermatol. 1979 Mar;115(3):329-31.
92. Ravn T, Trolle W, Kiss K, Balle VH. Adenosquamous carcinoma of the larynx associated with necrotizing sialometaplasia – a diagnostic challenge. Auris Nasus Larynx. 2009 Dec;36(6):721-4.
93. Romagosa V, Bella MR, Truchero C, Moya J. Necrotizing sialometaplasia (adenometaplasia) of the trachea. Histopathology. 1992 Sep;21(3):280-2.
94. Rossie KM, Allen CM, Burns RA. Necrotizing sialometaplasia: a case with metachronous lesions. J Oral Maxillofac Surg. 1986 Dec;44(12):1006-8.
95. Rushinek H, Keshet N, Aframian DJ. Necrotizing sialometaplasia related to vomiting and silastic ring vertical gastroplasty. Quintessence Int (Berl). 2016;47:147-50.
96. Russell JD, Glover GW, Friedmann I. Necrotizing sialometaplasia. J Laryngol Otol. 1992;106(!):569-71.
97. Sandmeier D, Bouzourene H. Necrotizing sialometaplasia: a potential diagnostic pitfall. Histopathology. 2002 Feb;40(2):200-1.
98. Santis HR, Kabani SP, Roderiques A, Driscoll JM. Necrotizing sialometaplasia: an early, nonulcerative presentation. Oral Surg Oral Med Oral Pathol. 1982;53(4):387-90.
99. Sasindran V, Mathew N. Necrotizing sialometaplasia of parotid. Oral Maxillofac Pathol J. 2018;9(1):36-8.
100. Schoning H, Emshoff R, Kreczy A. Necrotizing sialometaplasia in two patients with bulima and chronic vomiting. Int J Oral Maxillofac Surg. 1998 Dec;27(6):463-5.
101. Scully C, Eveson J. Sialosis and necrotising sialometaplasia in bulimia; a case report. Int J Oral Maxillofac Surg. 2004;33:808-10.
102. Shetty A, Chowdappa V, Devasamudra CR, Janardhan JV. Necrotizing sialometaplasia of the hard palate: A rare entity of dilemma on cytology, confirmatory on histopathology. J Clin Diagn Res. 2015;9(12):ED01-ED02.
103. Silva AD, Silva CAB, Furuse C, Nunes e Souza RC, Costa MHM, Araújo VC, et al. Necrotizing sialometaplasia in a patient who is HIV positive: a case report. Spec Care Dent. 2010 Jul/Aug;30(4):160-2.
104. Solomon LW, Merzianu M, Sullivan M, Rigual NR. Necrotizing sialometaplasia associated with bulimia: case report and literature review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007 Feb;103(2):39-42.
105. Spark RP, Duncan DG. Necrotizing sialometaplasia a self-limited pseudotumoral palatal ulcer. Ann Otol Rhinol Laryngol. 1978 May/Jun;87(3 Pt 1):409-11.
106. Speechley JA, Field EA, Scott J. Necrotizing sialometaplasia occurring during pregnancy: report of a case. J Oral Maxillofac Surg. 1988 Aug;46(8):696-9.
107. Suomalainen A, Törnwall J, Hagström J. CT findings of necrotizing sialometaplasia. Dentomaxillofacial Radiol. 2012 Sep;41(6):529-32.
108. Swarup N, Nayak MT, Chowdhary Z, Chandarani S. Necrotising sialometaplasia: a diagnostic perplexity? An innocent entity to malignant masquerade. J Exp Ther Oncol. 2018 May;12(3):185-8.
109. Tsuji T, Nishide Y, Nakano H, Kida K, Satoh K. Imaging findings of necrotizing sialometaplasia of the parotid gland: case report and literature review. Dentomaxillofac Radiol. 2014 Jul;43(6):20140127.
110. Uppal N, Baliga M. Necrotizing sialometaplasia: a rare lesion that mimics oral cancer clinically and histopathologically. Otolaryngol Pol. 2014 May/Jun;68(3):154-6.
111. Walker GK, Fechner RE, Johns ME, Teja K. Necrotizing sialometaplasia of the larynx secondary to atheromatous embolization. Am J Clin Pathol. 1982 Feb;77(2):221-3.
112. Ylikontiola L, Siponen M, Salo T, Sándor GKB. Sialometaplasia of the soft palate in a 2-year-old girl. J Can Dent Assoc. 2007 May;73(4):333-6.
113. Yoshioka T, Harada M, Umekita Y, Taguchi S, Higashi M, Nakamura D, et al. Necrotizing sialometaplasia of the parotid gland associated with angiocentric T-cell lymphoma: a case report and review of the literature. Pathol Int. 2010 Apr;60(4):326-9.
114. Zhurakivska K, Maiorano E, Nocini R, Mignogna MD, Favia G, Troiano G, et al. Necrotizing sialometaplasia can hide the presence of salivary gland tumors: a case series. Oral Dis. 2019 May;25(4):1084-90.