

Desquamative Gingivitis- Clinical and Epidemiological Findings in Patients from Northern Greece

SUMMARY

Background/Aim: Desquamative gingivitis (DG) is a clinical feature-sign associated with other several mucocutaneous or systemic diseases and disorders. The aim of this research was to present the clinical and epidemiological characteristics (prevalence, age, sex, extend of lesions, coexistence with underlying pathologies) of a cohort of 200 patients from Northern Greece that exhibited clinical appearance of DG. **Material and Methods:** 200 patients with DG were referred to the Department of Oral Medicine/Pathology, School of Dentistry, Aristotle University of Thessaloniki during the years 2004-2014. The patients were examined clinically, and a biopsy was performed to settle the diagnosis of any possible underlying disease. The epidemiologic parameters being studied were the gender and age, and the investigated clinical characteristics contained the localization of the lesions and the prevalence in relation to coexisting pathologies, habits etc. Statistics were performed by SPSS 22.00 by chi-square test ($p= 0,05$) and STATA14 program. **Results:** Clinically, most DGs cases (81%) were accompanied by erosions-vesicles mainly in buccal mucosa (68%), tongue (29, 5%) and lips (27%). The most common underlying disorders were immune-related mucocutaneous diseases including OLP (55,5%) and MMP (29,5%), followed by erythema multiforme (7%), and pemphigus vulgaris (6%). Overall, most patients (76%) had a localized form of DG at the gingiva of anterior teeth. This finding was more prominent in OLP. Interestingly, the diffuse DG form was mostly found in males. **Conclusions:** DG constitutes an early or the only clinical sign, mostly indicative for immune-related mucocutaneous disorder. Indeed, a properly taken biopsy can validate an earlier diagnosis and treatment. This would be crucial in order to avoid patient's discomfort and underlying diseases' complications.

Key words: Desquamative Gingivitis, Mucocutaneous diseases, Oral Lichen Planus, Mucous Membrane Pemphigoid

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ORIGINAL PAPER (OP)

Balk J Dent Med, 2023;148-153

Introduction

Desquamative gingivitis (DG) is likely to be a descriptive term used to give a combined clinical appearance composed of oedema, erythema, epithelial desquamation as the result of vesicles and erosions of the attached and marginal gingiva¹. Desquamative gingivitis (DG) is likely to be a descriptive term used to give a combined clinical appearance composed of oedema,

erythema, epithelial desquamation as the result of vesicles and erosions of the attached and marginal gingiva". Regarding the etymology of the term "desquamation" which originates from the latin "desquamare", it means "to remove fish scales" or in terms of oral epithelium it could describe the partial or complete loss (exfoliation) of the oral epithelium or oral mucous membrane².

DG was described for the first time by Tomes and Tomes in 1894. but was not until 1932 that Prinz used the

term to outline the picture mentioned before^{3,4}. Later in 1960 McCarthy et al suggested that DG is rather a clinical sign than a disorder itself, and this suggestion was confirmed by Glickman and Smulow in 1964 throughout their study of several mucocutaneous disorders that presented among other symptoms, desquamation of the gingiva⁵. Since then, scientists agree that DG is more a clinical feature and not a definite diagnosis itself. The infected gingiva becomes edematous, fragile and is prone to exfoliation even with the slightest friction or trauma (positive Nikolsky sign). In some cases extended area of ulceration may be observed giving rise to patient's complains of pain, discomfort or moderate bleeding of the gums^{4,6}. As mentioned above, DG is a clinical feature that is often promptly associated with disorders such as oral lichen planus (OLP), mucous membrane pemphigoid (MMP), and less frequently pemphigus vulgaris (PV), paraneoplastic pemphigus, Linear IgA disease, erythema multiforme, epidermolysis bullosa or even systematic endocrine (Testosterone imbalance, Hypothyroidism, Estrogen deficiencies) etc^{4,7}. A possible explanation of the desquamation is that autoantibodies are directed against molecules such as desmoglein 3, integrin, desmoplakin II and others in the basement membrane of the epithelium causing the lysis of intercellular connections and thus a friable epithelial lining. Other etiologic factors of DG constitute genetic predisposition (DG lesions associated with HLA-B7, metabolic disorders such as diabetes, medication such as NSAIDS or even infections such as those caused by hepatitis C virus (HCV) or hepatitis B virus (HBV)⁸.

The objectives of the study were to evaluate in a quantitative manner certain clinical and epidemiological characteristics of DG in a sample of 200 patients from Northern Greece and to compare the findings with those of international literature. These characteristics were: age, gender, clinical form (localized or diffuse), whether DG was the only clinical sign in oral mucosa, the relation of habits such as smoking or alcohol consumption with DG, and the possible implication of DG with underlying pathologies mainly immune-related mucocutaneous disorders such as oral lichen planus mucous membrane pemphigoid etc.

Material and Methods

A series of 200 DG patients being examined in the Department of Oral Medicine/Pathology of the School of Dentistry, Aristotle University of Thessaloniki, Greece in a period of ten years (2004-2014) have been investigated. A detailed medical record of all the patients was taken including medication received, coexisting pathology (Hypertention, thyroid disorders, anemia, immune-related mucocutaneous disorders). Epidemiologic parameters such as age, gender, habits including smoking and alcohol consumption were also recorded.

Thorough clinical examination was performed. Clinical inclusion criteria consisted of the presence of erythema, edema, the presence of vesicles, ulceration, erosions, detachment of the epithelial lining after mild pressure of phenomenally normal oral mucosa ("Nikolsky" sign). Biopsy and/or immunofluorescence were performed when deemed necessary in order to confirm the existence of autoimmune mucocutaneous disorders in which the desquamative gingivitis appears to be a certain clinical characteristic.

All patients were informed consent when they were examined giving written agreements Those forms were approved by the School of Dentistry Aristotle University of Thessaloniki, Greece and were in accordance to Helsinki Declaration for research and patients' ethics.

The statistical analysis was performed in a descriptive and a comparative basis. Descriptive analysis was fulfilled with the aid of SPSS 22.00 and the use of chi-square test and a confidence interval of 0,05. The comparative analysis was performed using the STATA14 (StataCorp LLC 4905 Lakeway Drive College Station, Texas USA) program and the chi-square test

Results

Most patients in the present study were women (158/200, 79%) and only 42/200 patients (21%) were men. Their mean age was over 60 years. Women were elder than men with a mean age of 59,58y vs 51, 93 respectively. In addition, DG appeared more often in oral lichen planus (observed in 55,5% of the patients), followed by mucous membrane pemphigoid (29,5%), erythema multiforme (7%), and pemphigus vulgaris (6%).

Several other findings coming up from the comparative analysis presented a statistical interest. More specifically, 24% of the patients were observed with diffuse desquamative gingivitis (DDG) in the gingival tissues while in the majority of them (76%) DG had a more localized form as shown in Table 1. According to the same table males present 2x fold of risk of presenting diffuse DG than females.

Table 1. Correlation between sex and extend of lesions in the gingival tissues

| Sex | Extend of pathology | | | | Total | |
|--------------|---------------------------------|-----------|-----------------------------------|-----------|------------|------------|
| | Diffuse desquamative gingivitis | | Localized desquamative gingivitis | | | |
| | No | % | No | % | No | % |
| Males | 17 | 40.48 | 25 | 59.52 | 42 | 100 |
| Females | 31 | 19.62 | 127 | 80.38 | 158 | 100 |
| Total | 48 | 24 | 152 | 76 | 200 | 100 |

Risk ratio: 2.1 (CONFIDENCE INTERVAL 1.3-3.3)

P= 0.00049

DG was the only clinical sign in 38 out of 200 patients (19%). Furthermore, 29 out of 39 were women (76.31%) and only 9 men were observed with DG as the only clinical manifestation (23.68%, $p < 0.001$, Table 2.)

Table 2. Distribution of DG as the only clinical sign among the sexes of the patients that present it as the only clinical manifestation

| sex | DG AS THE ONLY CLINICAL SIGN | |
|--------|------------------------------|-------|
| | No | % |
| male | 9 | 23.68 |
| female | 29 | 76.31 |
| total | 38 | 100 |

Moreover, it seems to be clear that desquamative gingivitis is accompanied by erosions and vesicles in other than gingiva locations of the oral cavity, in the vast majority of patients (162/200, 81%, Table 3.). The most common location of these lesions was the buccal mucosa 68%, followed by the tongue (29/200, 5%) and the lips 27% of the patients.

Table 3. The location of the lesions accompanying DG

| | Lesions only in gingival tissues | | Lesions affecting gingiva and other locations in oral cavity | | Total | |
|--|----------------------------------|----|--|-----|-------|-----|
| | No | % | No | % | No | % |
| | patients | 38 | 19 | 162 | 81 | 200 |

$P < 0.001$

In addition, DG was found to constitute the only clinical sign in 12/38 (31.57%) of the patients with oral lichen planus lesions and in 26/38 (68.43%) of the patients with mucous membrane pemphigoid disorder (Table 4.).

Table 7. Correlation between sex –hypothyroidism and DG as a clinical sign of autoimmune disorders

| SEX | Patients with Hypothyroidism | | | | | | | | Total | |
|--------|------------------------------|------|----------------------------|------|---------------|-------|---------------------------------|-------|-------|-----|
| | Lupus erythematosus | | Mucous membrane Pemphigoid | | Lichen Planus | | Patients without Hypothyroidism | | | |
| | No | % | No | % | No | % | No | % | | |
| Male | 0 | 0 | 0 | 0 | 0 | 0 | 42 | 100 | 42 | 100 |
| Female | 2 | 1.26 | 10 | 6.33 | 24 | 15.19 | 122 | 77.22 | 158 | 100 |
| total | 2 | 1 | 10 | 5 | 24 | 12 | 164 | 82 | 200 | 100 |

Risk Ratio 0 (Confidence interval not defined)
 $P = 0.0006$

Table 4. Correlation between prevalence of DG as the only clinical sign and disorder in which it is observed

| Disorder | Lesions limited in gingival tissue (No/%) | |
|----------|---|-------|
| | No | % |
| OLP | 12 | 31.57 |
| MMP | 26 | 68.43 |
| Total | 38 | 100 |

The study also examined the extend of desquamative gingivitis (localized or diffuse form) in different underlying diseases and the possible statistical correlation. Table 5. shows that in cases of OLP, there is a 2-fold increased possibility for localized form of DG.

Table 5. Correlation between Lichen Planus and extend of DG

| | Extend of lesions | | | | Total | |
|----------------|-------------------|----|--------------|-------|-------|-----|
| | Diffuse DG | | Localized DG | | | |
| | No | % | No | % | No | % |
| Lichen Planus | 16 | 33 | 95 | 63 | 69 | 100 |
| Rest disorders | 32 | 57 | 57 | 40.42 | 141 | 100 |
| Total | 48 | 24 | 152 | 76 | 200 | 100 |

Risk ratio 0.53 (95% COF INTERVAL 0.35-0.81)
 $P = 0.0004$

However, in cases of mucous membrane pemphigoid, the patients present the same predisposition of having both diffuse and localized form of DG as seen in Table 6.

Table 6. Correlation between mucous membrane pemphigoid and extend of DG

| | Extend of lesions | | | | Total | |
|----------------------------|-------------------|----|--------------|----|-------|-----|
| | Diffuse DG | | Localized DG | | | |
| | No | % | No | % | No | % |
| Mucous membrane pemphigoid | 15 | 31 | 44 | 29 | 69 | 100 |
| Rest disorders | 33 | 69 | 108 | 71 | 141 | 100 |
| Total | 48 | 24 | 152 | 76 | 200 | 100 |

Risk ratio 1.1(CONF.INTERVAL 0.66-1.76) $P = 0.76$

Desquamative gingivitis does not seem to be related to smoking or alcohol consumption in the sample of patients that were examined ($p>0.05$). Considering the same group of patients, it was noticed that patients with Oral Lichen Planus and hypothyroidism manifesting DG were exclusively women (Table 7.).

Discussion

According to the findings of this study DG is presented in women of middle age and it is mostly seen in patients with OLP compared to those suffering of MMP. Moreover, DG proved to be the only clinical sign in almost 20% of the patients included in the study and this finding is more frequent in MMP. Regarding topographical distribution DG can be presented as localized or diffusely. The first showed a strong predilection in the cases of OLP in contrast to the almost equal distribution of the two forms as seen in cases of MMP. Finally, in the present study DG did not seem to be correlated with smoking or alcohol consumption but in contrast it did presented in as strong relation to hypothyroidism in patients diagnosed with OLP.

In the literature some of these findings were also confirmed. For example, according to Robinson *et al.* in 2003 and Arduini *et al.* in 2017. suggested that DG is more often diagnosed in middle aged than elder women^{9,10}. Regarding age-gender, Willis *et al.* in 2017 found a peak incidence of DG between 40 and 60 years of age with a higher prevalence in women¹¹.

All reports so far agree that DG is rather a clinical sign than a specific diagnosis itself and as such it comprises a clinical part of another disorder. Arduino *et al.* examined 382 cases of DG and found out that oral lichen planus proved to be the most frequent diagnosis followed by mucous membrane pemphigoid, pemphigus vulgaris and epidermolysis bullosa¹⁰. Lo Russo *et al.* described the diseases related to DG in 125 patients. Among them oral lichen planus was the most frequent one representing 2/3 of the cases¹. Similarly, Leao *et al.* referred to 132 patients out of 187 with DG diagnosed with oral lichen planus. In the same research only a small portion of the patients suffered from mucous membrane pemphigoid and even fewer from pemphigus vulgaris¹². In contrast, there are reports indicating MMP (ranged from 41,6% to 63,6%) to be the most common underlying disease related to DG compared to OLP (ranged from 25% to 6,8%)^{13,14}.

DG may be found as localized or diffuse. Diffuse form of DG appears to be related to more severe cases of the underlying diseases¹¹. In our study the majority of patients presented a diffuse form of DG. Lo Russo *et al.* stated that the main feature of DG is an extensive desquamation and /or erosion affecting mostly the buccal aspect of the gingiva of anterior teeth. According

to the same study, DG can also involve restricted areas of gingiva usually in the early phases of a disease¹⁵. In addition, Leao *et al.* described 134 cases (out of 187) with localized gingival involvement¹². In all these researches there is no direct correlation between the extent of the DG lesions and the underlying disease. However, according to the Lo Russo *et al.*, 58% of all DG cases presented a diffuse DG character and 75% of the patients were diagnosed with oral lichen planus. This finding was not confirmed in our study. It is necessary not to omit the fact that in OLP, exclusive gingival involvement is observed only in 10% of the patients¹⁶. As far as it concerns MMP patients, it is important to notice that gingiva is involved in every case, but most of the times DG is not the only clinical manifestation^{17,18}. On the other hand, there is no assignment about the form (diffuse or localized) of DG that prevails in cases of MMP. In our analysis the two forms of DG have the same probability of appearing in cases MMP.

Very few reports correlate DG in patients with OLP and MMP to hypothyroidism^{19,20} whereas there are studies that support a strong correlation between mucous membrane pemphigoid and lichen planus to autoimmune hypothyroidism^{17,21}. For example, serum antibodies to thyroglobulin and thyroid microsomal antibodies are found to patients with OLP with DG^{21,22,23}. It has been proposed that thyroid cells produce several cytokines including interleukin-6 (IL6) and tumor necrosis factor (TNF) and stimulated thyroid follicular cells producing certain growth factors and adhesion molecules. These cytokines and relevant cells (Langerhans cells and T-lymphocytes and mastocytes) are involved in the pathogenesis of OLP and show increased levels in cases of hypothyroidism. In addition, mast cells release interleukins and TNF, both of which compose pro-inflammatory mediators. The second plays a pivotal role in regulating endothelial cell adhesion molecules, and so allows leukocytes to adhere to the vessel wall. These mechanisms are common in OLP and hypothyroidism enhancing the evidence of a strong relation between the two entities^{24,25,26}. A very recent study orientated the number of patients with DG being positive to anti-Tg and antithyroid microsomal antibodies. Almost half of the patients were found positive for anti-Tg and antithyroid microsomal antibodies^{27,28}. Considering this study, it becomes clear enough that there is a strong correlation of thyroid diseases expressed by hypofunction and DG in a background of lichen planus, OLP and lichen sclerosus²⁷.

As far as it concerns the relation of MMP and DG with hypothyroidism a recent study found out that 32% of MMP patients had hypothyroidism and interestingly 83% of them were females¹⁹. As it is mentioned MMP cases always are accompanied by DG. This means that there will always be a potential association of DG with hypothyroidism in patients suffering from hypofunction of thyroid gland and MMP. These observations should

alert the dental clinician in cases of OLP and MMP and a possibly not-diagnosed thyroid disorder.

The limitations of our study are the unknown role of HPV, the role of dental metal or resin restorations in terms of quantity and quality (especially in Lichen Planus) and the analytical medical history concerning the dose and duration of drug administration that were not taken into consideration and may play a crucial role in the presence of immune-related mucocutaneous diseases.

Conclusions

In a large number of patients of our study, DG seems to prefer middle aged women, being correlated more likely to OLP and less often to MMP, PV or erythema multiforme. It can present by either localized or diffuse form related to early/mild or late/severe stage of the underlying disease, respectively. In our research males developed 2-fold risk of having diffuse DG than females. In addition, in OLP the possibility of finding localized DG was also 2-fold higher compared to diffuse form. In contrast, this finding was not observed in MMP patients which had equal probability for the two forms. DG is usually accompanied by the characteristic manifestations of the underlying diseases in other areas of oral mucosa including buccal mucosa and less frequently tongue. Last but not least, a relation of both OLP and MMP to hypothyroidism was detected in our study. It is well understood that DG as a clinical sign can be a useful tool for the early diagnosis of a possible mucocutaneous disorder.

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Received on Jun 2, 2023.

Revised on July 10, 2023.

Accepted on September 20, 2023.

Conflict of Interests: Nothing to declare.

Financial Disclosure Statement: Nothing to declare.

Human Rights Statement: All the procedures on humans were conducted in accordance with the Helsinki Declaration of 1975, as revised 2000. Consent was obtained from the patient/s and approved for the current study by national ethical committee.

Animal Rights Statement: None required.

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