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RESEARCH

# Oral health-related quality of life in Fanconi anemia: a cross-sectional study

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## Abstract

**Purpose** To evaluate the oral health-related quality of life (OHRQoL) of individuals diagnosed with Fanconi anemia (FA).

**Methods** A cross-sectional study was conducted with FA patients from two Brazilian referral centers. Participants underwent a complete dental, periodontal, and oral mucosa examination, as well as assessment of resting salivary flow. The short version of the Oral Health Impact Profile (OHIP-14) questionnaire was administered. Descriptive and bivariate analyses were performed, followed by multivariate analysis to examine the impact of independent variables on OHRQoL.

**Results** The study included 20 (57.1%) males and 15 (42.9%) females, with a mean age of 18.9 years. Oral leukoplakia (OL) was found in 18 individuals. The overall OHIP-14 score was $9.9 \pm 10.5$. Individuals aged $\geq 16$ years had higher OHIP-14 scores, indicating worse OHRQoL for physical pain ($p = 0.007$), psychological discomfort ($p = 0.001$), physical disability ($p = 0.03$), psychological disability ($p = 0.001$), handicap ($p = 0.004$), and overall score ($p = 0.007$). Females reported more negative OHRQoL than males for physical pain ($p = 0.02$), psychological discomfort ($p = 0.03$), psychological disability ($p = 0.009$), and overall score ($p = 0.02$). Individuals with OL had an overall OHIP-14 score 1.83 times higher than those without OL (95% CI: 1.02–3.28; $p = 0.04$). Lower salivary flow correlated with higher overall OHIP-14 scores (95% CI: 0.14–0.84; $p = 0.01$).

**Conclusion** This study represents the first attempt to evaluate OHRQoL in individuals with FA. The presence of OL and reduced salivary flow were identified as predictors of a negative impact on OHRQoL. It is imperative to integrate patients' quality of life in the clinical treatment protocols for the FA population.

**Keywords** Fanconi anemia · Head and neck squamous cell carcinoma · Oral health-related quality of life · Oral mucosa · Quality of life

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## Introduction

Fanconi anemia (FA) is a rare autosomal recessive disorder [1, 2] with an incidence of 1 in 136,000 live births [1]. Upon receiving a diagnosis of FA, each family is confronted with multifaceted challenges ranging from coping with the emotional distress induced by the news to assuming the intricate task of orchestrating childcare [3]. The impact of FA on families varies according to the developmental stage of the patient and the unique trajectory of the individual's disorder progression [4]. Individuals with FA commonly manifest specific congenital abnormalities, progressive bone marrow failure, and a predisposition to cancer, particularly acute myeloid leukemia and oral squamous cell carcinoma (OSCC) [2, 5].

While significant attention has been directed towards the risk of cancer [2, 5], literature on other oral diseases experienced by individuals with FA remains scarce [5–7]. Exploring how oral manifestations associated with FA affect oral health-related quality of life (OHRQoL) necessitates further investigation. OHRQoL represents a multidimensional construct that delineates the influence of oral health on an individual's overall well-being [8, 9]. It encompasses different dimensions including functional, psychological, social, and pain/discomfort aspects related to oral health [8]. By evaluating the impact of oral health conditions and treatments on daily activities, emotional well-being, social interactions, and overall life satisfaction, OHRQoL emerges as a critical metric for understanding oral health beyond clinical parameters. This underscores the significance of patient-centered care in dentistry [10]. Integrating clinical data with the patient's perspective fosters a comprehensive understanding of individuals, thus enhancing the effectiveness of monitoring and treatment processes [11].

It is acknowledged that low salivary flow and oral diseases, including dental caries, periodontal diseases, OSCC, and oral potentially malignant disorders (OPMD) have a detrimental impact on the quality of life of affected individuals [12, 13]. The most frequent OPMD, oral leukoplakia (OL), harbor a risk of transformation to OSCC and manifest without symptoms in approximately 60% of reported cases, being often detected during routine examinations [14]. However, other oral diseases, such as dental caries and periodontitis can induce acute or chronic pain, bleeding, and discomfort. Left untreated, these conditions can affect different aspects of life, including activities of daily living, sleep, speech, eating, social relations, and self-esteem [12].

The purpose of the present study was to assess the OHRQoL of individuals with FA and its association with oral diseases. It was hypothesized that the detrimental repercussions of FA and oral diseases surpass mere symptoms and functional limitations, potentially also impacting emotional and social well-being.

## Methods

### Study design, participants, and ethical issues

A cross-sectional study was conducted between August 2022 and December 2023. Individuals diagnosed with FA, according to the criteria outlined in the 2020 Fanconi Anemia Clinical Care Guidelines [15], were included. The diagnosis involved testing for chromosome breakage in peripheral blood lymphocytes using DNA cross-linking agents, primarily diepoxybutane or mitomycin C. Patients were recruited from two public referral services supported by the Brazilian Public Health System—Hospital das Clínicas, Universidade Federal de Minas Gerais, in Belo Horizonte, and Hospital das Clínicas, Universidade Federal do Paraná, in Curitiba. Inclusion criteria encompassed individuals of all ages and both sexes. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [16]. Informed consent was obtained from all participants. The study was approved by the Institutional Ethics Committee (No. 66312622.4.1001.5149) and was conducted in accordance with the Declaration of Helsinki.

### Data collection

Information was collected during clinical consultations and/or from medical records. Demographic characteristics included sex and age. Data related to FA comprised age at diagnosis, hematopoietic stem-cell transplantation (HSCT) status, time post-HSCT, and skeletal alterations (i.e., unilateral or bilateral alteration in upper limbs/hands). The distance from residence to the reference center was also recorded.

### Oral condition assessments

The oral mucosa was evaluated by two trained dentists (N.C.M.S. and P.A.S.R.), with the final diagnosis established by a consultant in oral medicine and oral pathology (T.A.S.). This assessment aimed to identify and quantify lesions consistent with OPMD [17]. OPMD comprises a diverse group of conditions (e.g., OL, erythroplakia, oral lichen planus, among others), which are characterized by abnormal clinical appearances of the oral mucosa. These lesions may present as white or red plaques, ulcers, or other mucosal changes [17]. Specifically, the inclusion criteria for OL cases comprised homogenous lesions (thin, flat, uniform white plaques

with at least one well-demarcated area, with or without fissure) and non-homogenous lesions (predominantly white or reddish-white lesions with an irregular, nodular, or exophytic surface) [18]. An incisional biopsy was performed on all identified lesions, and oral epithelial dysplasia (mild, moderate, or severe) was graded [19] by the same consultant (T.A.S.).

The number of decayed, missing, and filled teeth (DMFT) was recorded according to established guidelines [20].

Periodontal examinations were conducted by two trained clinicians (N.C.M.S. and P.A.S.R.). To assess intra- and inter-examiner reliability, periodontal examinations were performed on 10 consecutive individuals. The weighted Kappa test and the intraclass correlation coefficient were used, with dichotomized values for probing depth (< and ≥ 4 mm) and clinical attachment level (CAL) (< and ≥ 3 mm). The Kappa values for probing depth and CAL were greater than 0.87, and the intraclass correlation coefficient values were greater than 0.85. Periodontal status was assessed using a periodontal probe (PCP 15, Hu-Friedy, North Carolina, Chicago, IL, USA). Parameters including plaque index [21], probing depth, CAL, and bleeding on probing (BOP) were recorded. Each tooth was probed on four sites: buccal, mesial, distal, and lingual/palatal. Periodontal disease classification (healthy, gingivitis, and periodontitis) was determined by two periodontists (F.O.C. and A.C.M.C.). Gingivitis was characterized by sites with a probing depth of ≤ 3 mm, ≥ 10% of sites with BOP, and the absence of attachment loss and radiographic bone loss [22]. Patients were considered to have periodontitis if they met one of the following criteria: (i) detectable interdental CAL at two or more non-adjacent teeth, or (ii) detectable buccal or oral CAL of ≥ 3 mm with pocketing exceeding 3 mm at two or more teeth, provided that the observed CAL could not be attributed to non-periodontal causes such as gingival recession from trauma, dental caries extending into the cervical area of the tooth, CAL on the distal aspect of a second molar associated with malposition or extraction of a third molar, an endodontic lesion draining through the marginal periodontium, or a vertical root fracture. Periodontitis was classified according to its stages and grades [23].

Saliva samples were collected in the early morning using unstimulated sialometry. Participants were instructed to refrain from eating, drinking, and brushing their teeth for at least 30 to 60 min prior to the assessment. Subsequently, participants were asked to expel saliva accumulated over a 10-min period [24]. Hyposalivation was defined as unstimulated salivary flow ≤ 0.10 mL/min [25].

### OHRQoL assessment tool

Participants' OHRQoL was evaluated using the short version of the Oral Health Impact Profile (OHIP-14) questionnaire [8], previously validated for use in Brazil [11]. Printed copies of the questionnaire were distributed to participants or the parents/guardians of children by the same researcher (N.C.M.S.) and collected upon completion. The OHIP-14 comprises 14 items covering functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. Each item offers five response options: 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often, and 4 = very often. The total OHIP-14 score ranges from 0 to 56, with individual scores derived for each of the seven items. A higher score indicates a greater negative impact on participants' OHRQoL.

### Statistical analysis

The Statistical Package for the Social Sciences–SPSS (IBM, 22.0; Armonk, NY, USA) was used for analysis. Descriptive statistical analysis was conducted. The Mann–Whitney test and Kruskal–Wallis tests were employed to associate independent variables with the dependent variable (OHIP-14 scores). The chi-squared test was used to compare oral conditions and skeletal alterations. Statistical significance was set at $p < 0.05$. Poisson regression was conducted to determine the impact of each variable on the overall OHIP-14 score. Independent variables were included in the regression model based on their significance level ($p < 0.20$). Within this final model, values of $p < 0.05$ were considered statistically significant.

## Results

### Characteristics of the participants

Out of 41 potentially eligible individuals, 36 responded to the questionnaire, and 35 individuals were included, comprising 22 from Curitiba and 13 from Belo Horizonte. One participant was excluded from analysis due to incomplete data. The mean age of the participants was 18.9 ± 8.5 years, with a range of seven to 42 years. Age at the time of FA diagnosis was 7.5 ± 5.4 years. Twenty (57.1%) individuals were males and 15 (42.9%) were females. Twenty-four (68.6%) patients had undergone HSCT at a mean post-transplant time of 7.9 ± 6.2 years. Twenty-one (60%) participants exhibited unilateral skeletal alterations in their upper limbs/hands, with bilateral occurrences noted in 18 (51.4%) cases. Sixteen (45.7%) individuals were using continuous medication at the time of examination and six (37.5%) used two or more medications. The medications included hormones ($n = 5$), vitamins ($n = 5$) and anxiolytic ($n = 4$), antidepressant ($n = 3$), antipsychotic ($n = 2$), anticonvulsant ($n = 1$), and antihypertensive ($n = 1$) drugs. One patient had undergone

radiotherapy. The mean distance traveled by individuals from their place of residence to the reference center was 1156 ± 1202 km (Table 1).

## Oral conditions

All OPMD cases ($n = 18/51.4\%$) were diagnosed as OL. Histopathological analysis revealed that 15 cases exhibited mild epithelial dysplasia, while three cases exhibited moderate epithelial dysplasia. In eight (22.8%) and five (14.3%) individuals these lesions affected two and three sites, respectively. Two individuals had a previous history of both OSCC and extraoral malignancy. A previous history of oral graft-versus-host disease (GVHD) was positive in five (14.3%) participants (Table 2).

Among 31 individuals, 20 (57.2%) had decayed teeth and six (19.3%) had missing teeth. For most participants (65.7%), oral hygiene was scored as poor or bad. Thirteen (37.1%) individuals had gingivitis, six (17.1%) had periodontitis, while eight (22.9%) exhibited periodontal health. Of these, four (66.6%) individuals presented with stage I periodontitis, while one (16.7%) had stage II, and another individual (16.7%) had stage III. The grade of all cases was classified as A (Table 2).

The median unstimulated salivary flow of FA individuals was 0.45 mL/min (Table 2). Three (8.5%) participants showed hyposalivation (unstimulated salivary flow ≤ 0.10 mL/min). Among the 16 individuals using medications, two experienced hyposalivation, including those prescribed hormones ($n = 2$), an anxiolytic ($n = 1$), and an antidepressant ($n = 1$). Also, the sole individual who underwent radiotherapy displayed hyposalivation. None of the three individuals with hyposalivation had a history of chronic or acute GVHD. The mean salivary flow of individuals with a history of GVHD (0.69 ± 0.50 mL/min) was comparable to that of those without a history of GVHD (0.39 ± 0.19 mL/min) ($p = 0.19$).

Skeletal alterations in the upper limbs and/or hands were significantly associated with compromised plaque control. Specifically, patients with unilateral skeletal alterations ($p = 0.02$) or bilateral skeletal alterations ($p = 0.02$) exhibited poorer plaque control (Supplementary Table 1).

**Table 1** Clinicodemographic analysis of individuals with Fanconi anemia (FA) ($n = 35$)

| Variables | n(%) |
|---|---|
| Sex | |
| Male | 20 (57.1) |
| Female | 15 (42.9) |
| Age (median, mean ± SD, and range) | 16; 18.9 ± 8.5; 7–42 |
| Age at FA diagnosis | 7; 7.5 ± 5.4; 1–33 |
| HSCT | |
| Yes | 24 (68.6) |
| No | 11 (31.4) |
| Time post-HSCT (years) (median, mean ± SD, and range) | 6.5; 7.9 ± 6.2; 0–20 |
| Skeletal alterations | |
| Upper limb/hand alteration (unilateral) | |
| Present | 21 (60) |
| Absent | 14 (40) |
| Upper limb/hand alteration (bilateral) | |
| Present | 18 (51.4) |
| Absent | 17 (48.6) |
| Distance to reference center in km (median, mean ± SD, and range)* | 516; 1156 ± 1202; 1.4–3472 |

*HSCT* hematopoietic stem-cell transplantation, *SD* standard deviation

*Distance from the patient's residence to the reference center where the individual undergoes follow-up

## OHIP-14 scores versus clinicodemographic variables

The median overall OHIP-14 score was 6.0 (mean: 9.9 ± 10.5), with higher scores observed in the categories of physical pain and psychological discomfort (Table 3).

Female individuals reported a more negative perception of OHRQoL compared to males in the subscales of physical pain ($p = 0.02$), psychological discomfort ($p = 0.03$), psychological disability ($p = 0.009$), and in the overall OHIP-14 score ($p = 0.02$). There was a positive correlation between age and scores for physical pain ($p = 0.007$), psychological discomfort ($p = 0.001$), physical disability ($p = 0.03$), psychological disability ($p = 0.001$), handicap ($p = 0.004$), and the overall OHIP-14 score ($p = 0.007$). Individuals aged 16 years and older had higher scores, indicating a worse perception of OHRQoL in these categories. Also, a positive association was noted between age at FA diagnosis and physical pain scores ($p = 0.01$). In contrast, a negative association was observed between age at FA diagnosis and social disability ($p = 0.04$), suggesting that patients diagnosed with FA at a younger age had a worse impact on this aspect compared to those diagnosed at an older age (Supplementary Table 2).

Individuals with FA who exhibited OL reported a more negative perception regarding functional limitation ($p = 0.01$) and social disability ($p = 0.04$) compared to those without oral lesions. Consistently, a higher number of OL sites were significantly associated with a more negative perception of functional limitation ($p = 0.01$), physical disability ($p = 0.03$), and handicap ($p = 0.03$) (Supplementary Table 2).

While the diagnosis of periodontal disease did not impact OHIP-14 outcomes, BOP was significantly associated with a more negative perception of physical pain ($p = 0.002$), psychological discomfort ($p = 0.04$), physical disability ($p = 0.03$), psychological disability ($p = 0.001$), handicap ($p = 0.008$), and the overall OHIP-14 score ($p = 0.006$).

**Table 2** Oral manifestations of individuals with Fanconi anemia ($n=35$)

| Variables | n(%) |
|---|---|
| Oral leukoplakia | |
| Present | 18 (51.4) |
| Absent | 17 (48.6) |
| Oral leukoplakia (number of sites) | |
| None | 17 (48.6) |
| 1 site | 4 (11.4) |
| 2 sites | 8 (22.8) |
| 3 sites | 5 (14.3) |
| 4 sites | 1 (2.9) |
| History of oral chronic graft-versus-host disease | |
| Yes | 5 (14.3) |
| No | 23 (65.7) |
| NA | 7 (20) |
| Number of decayed teeth (median, mean ± SD, and range) | 1; 1.8 ± 2.2; 0–8 |
| Number of missing teeth (median, mean ± SD, and range) | 0.0; 0.4 ± 1.4; 0–6 |
| Plaque index | |
| Poor | 7 (20) |
| Bad | 16 (45.7) |
| Good | 5 (14.3) |
| Excellent | 3 (8.6) |
| NA | 4 (11.4) |
| Periodontal measurements | |
| Probing depth (mm) | 2.7 ± 1.1; 1.4–6.2 |
| Clinical attachment level (mm) | 2.8 ± 1.2; 1.5–6.4 |
| Bleeding on probing (%) | 19 ± 17.6; 0–74 |
| Periodontal status | |
| Healthy | 8 (22.9) |
| Gingivitis | 13 (37.1) |
| Periodontitis | 6 (17.1) |
| NA | 8 (22.9) |
| Periodontal disease | |
| Periodontitis stage IA | 4 (66.6) |
| Periodontitis stage IIA | 1 (16.7) |
| Periodontitis stage IIIA | 1 (16.7) |
| Resting salivary flow (mL/min) | 0.45; 0.5 ± 0.3; 0.1–1.5 |

*NA* not available, *SD* standard deviation

**Table 3** Descriptive analysis of oral health-related quality of life (OHIP-14) scores among Fanconi anemia individuals ($n=35$)

| OHIP-14 | Median; mean ± SD; range |
|---|---|
| Functional limitation | 0.0; 0.8 ± 1.5; 0–6 |
| Physical pain | 2.0; 2.3 ± 1.8; 0–7 |
| Psychological discomfort | 1.0; 2.4 ± 2.8; 0–8 |
| Physical disability | 1.0; 1.5 ± 2.6; 0–7 |
| Psychological disability | 1.0; 1.3 ± 1.8; 0–8 |
| Social disability | 0.0; 0.8 ± 1.7; 0–8 |
| Handicap | 0.0; 0.4 ± 1.2; 0–5 |
| Overall | 6.0; 9.9 ± 10.5; 0–47 |

*SD* standard deviation

Moreover, a lower value of salivary flow was significantly associated with a more negative perception of psychological disability ($p=0.02$). Other variables analyzed, including HSCT, history of oral GVHD, decayed and missing teeth, plaque index, skeletal alterations, and distance travelled by patients to the reference center, did not significantly affect the OHIP-14 outcomes (Supplementary Table 2).

Table 4 displays the results of the regression model. The variables sex, age, BOP, presence of OL, and salivary flow were tested as potential predictors of a negative perception of OHRQoL. Female individuals exhibited an overall OHIP-14 score 1.95 times higher, albeit not significantly, compared to male individuals (95% CI: 0.99–3.84; $p=0.05$). Individuals

**Table 4** Poisson regression explaining the relationship of oral health-related quality of life (OHIP-14) overall score among individuals with Fanconi anemia ($n = 35$)

| | Dependent variable OHIP-14 (overall) | | | |
|---|---|---|---|---|
| | Crude | | Adjusted | |
| | PR (95% CI) | *p* value | PR (95% CI) | *p* value |
| Sex | | | | |
| Male | 1 | **0.01** | 1 | 0.05 |
| Female | 2.28 (1.20–4.31) | | 1.95 (0.99–3.84) | |
| Age (years) | 1.04 (1.01–1.07) | **0.01** | 1.01 (0.95–1.06) | 0.71 |
| Bleeding on probing (%) | 1.01 (1.00–1.02) | **0.01** | 1.01 (0.98–1.03) | 0.36 |
| Oral leukoplakia | | | | |
| Absent | 1 | **0.03** | 1 | **0.04** |
| Present | 1.87 (1.03–3.42) | | 1.83 (1.02–3.28) | |
| Salivary flow (mL/min) | 0.39 (0.11–1.30) | 0.12 | 0.34 (0.14–0.84) | **0.01** |

*CI* confidence interval, *PR* prevalence ratio

Bold indicates statistically significance at $p < 0.05$

with OL had an overall OHIP-14 score 1.83 times higher (indicating a more negative perception of OHRQoL) compared to those without OL (95% CI: 1.02–3.28; $p = 0.04$). The results also demonstrated an association between salivary flow and the overall OHIP-14 score. The lower the salivary flow, the higher the overall OHIP-14 score (95% CI: 0.14–0.84; $p = 0.01$).

## Discussion

FA is an example of a rare disease posing health challenges since infancy [3, 4]. The assessment of OHRQoL in individuals with rare diseases has garnered increasing significance, as it may contribute to healthcare improvement [26]. This study represents the first attempt to evaluate OHRQoL in individuals with FA. Our findings underscore that individuals with OL and reduced salivary flow are more likely to experience a negative impact on OHRQoL. These results suggest that unsatisfactory oral conditions in this population can adversely affect their quality of life. Additionally, while skeletal changes in the upper limbs and/or hands did not directly affect OHRQoL or dental/periodontal parameters, they were associated with a poorer control of dental plaque, suggesting vulnerability of these individuals in oral hygiene self-care.

The overall OHIP-14 scores observed in our cohort were comparable to those reported in German patients affected by rare diseases [27]. Consistently, a recent study by our research group on patients with chemotherapy-induced oral mucositis also showed similar overall OHIP-14 scores as found in the present investigation [28]. However, OHIP-14 scores among individuals with rare diseases can vary significantly; for instance, one study reported mean scores ranging from 15.1 to 19.9 depending on different symptom combinations [26]. Herein, females reported a more negative perception of OHRQoL. Possible explanations for this sex difference may include documented elevated psychological burden among women [29] and socio-cultural influences [30]. An alternative hypothesis posits that men may exhibit greater resilience towards oral diseases and discomfort, potentially influenced by societal expectations of masculinity [31]. Although age did not show a significant impact when analyzed alongside other variables, it proved important in several categories of the OHIP-14 in bivariate analysis. Older individuals perceived worse OHRQoL, reflecting age-related factors influencing oral health perception, chronic diseases emergence, and access to health programs [32]. In FA, advancing age correlates with increased risk of developing OSCC (approximately 20% by age 40), possibly contributing to poorer OHRQoL, especially among those who underwent HSCT [1].

The data from this study demonstrate that the diagnosis of OL negatively impacts quality of life. The systemic conditions inherent to individuals with FA predispose them to develop multiple OL [5–7]. The association between OL presence and poorer OHRQoL outcomes might be linked to both the stigma associated with these lesions and their potential transformation into oral cancer. This is consistent with previous qualitative findings that indicate OL's effects extend beyond physical limitations to affect psychological and social well-being [13]. Additionally, it has been shown that individuals with OL perceive their quality of life more negatively compared to those with OSCC or OSCC recurrence, which is attributed to higher rates of anxiety and fear [33].

A decrease in resting salivary flow significantly worsened the quality of life of individuals with FA in our cohort. Previous research has documented hyposalivation among FA patients [34]. Saliva serves critical functions such as lubricating oral tissues, aiding in chewing and swallowing, buffering acids, and protecting against dental caries and oral infections [35]. The reduced salivary flow observed in this

population may be attributed to the disease pathogenesis, medications, HSCT, radiotherapy, and comorbidities such as GVHD [5, 34–37]. Additionally, a stressful routine can influence salivary flow [35]. In the present study, among the three individuals with hyposalivation, two were using medication and one had undergone radiotherapy. However, a history of GVHD did not show an association with hyposalivation in our sample. The reduction in salivary flow compromises several essential functions, leading to difficulties in chewing, swallowing, and speaking, thereby negatively impacting oral health, overall well-being, and quality of life [36].

Oral diseases such as dental caries and periodontitis can lead discomfort and pain, impairing essential functions like speech, swallowing, and chewing, thereby impacting overall quality of life [12]. Few studies have focused on the oral health of individuals with FA [5–7]. Lyko et al. [7] reported similar rates of missing teeth and dental caries in individuals with FA compared to those without FA. In our study, although OHRQoL was not affected by variables such as decayed or missing teeth and plaque index, oral hygiene was found to be suboptimal, with more than two-thirds of patients exhibiting poor or bad plaque control. Interestingly, we observed a positive association between oral hygiene and the presence of skeletal alterations in the upper limbs and hands. Given that skeletal malformations affecting the thumb, arms, and/or hands are prevalent in approximately 70% of FA patients [38], it is crucial to consider the impact of these abnormalities on oral health when planning dental treatments.

FA is recognized as one of the rare diseases associated with periodontal manifestations, particularly gingivitis [39]. However, the precise impact of FA on the periodontium remains uncertain, with defective hemopoiesis suggested as a potential underlying mechanism [39]. Apart from disease-specific complications, immunosuppressive medication may exacerbate periodontal outcomes in affected individuals [40]. Among the periodontal measurements employed in this study, only BOP was found to significantly influence the perception of OHRQoL. This underscores the significance of factors that are noticed by individuals, such as gingival bleeding, as opposed to less perceptible factors like bone loss and periodontal pocket depth. This finding is consistent with a previous study in which the oral health self-perception of individuals with FA regarding gingival inflammation was linked to their gingival bleeding index [41].

The current study highlights the frequent need for patients to travel long distances to access healthcare services. This factor did not seem to directly interfere with OHRQoL; however, it does raise concerns about consistent access to reference centers [42], which is particularly relevant for an early detection of oral diseases, the monitoring of OPMD, and cancer prevention. This observation aligns with previous research involving individuals diagnosed with aplastic anemia, whose quality of life was not significantly impacted by their distance from reference services [43]. On this basis, rare diseases pose significant challenges for affected individuals and their families, often exacerbated by difficulties in accessing support services due to infrastructural barriers. This aspect is particularly pronounced in rural areas, where long distances constitute a major obstacle [44].

Limitations of the present study include its cross-sectional design, which hinders causal inference, and the potential recall bias associated with the use of a questionnaire. Additionally, the study covered a wide age range and employed a single instrument, the OHIP-14, to measure OHRQoL across all age groups. While the OHIP-14 was initially validated in an older adult population [8], its application among pediatric population is documented [45, 46]. However, administering the OHIP-14 in children and adolescents pose challenges due to the format of response options in an ordinal scale, instead of a simpler method that uses dichotomized responses [45]. Another shortcoming is the lack of a control group without FA, which hampers comparative analyses. However, strengths included a substantial sample of individuals with FA from two referral services in Latin America, one of which has more than 40 years of experience with HSCT for this population [47]. Given the small sample size attributable to the rarity of FA, caution should be taken when interpreting the associations between predictors and OHRQoL. Nevertheless, understanding the impact of FA on OHRQoL is crucial, as preventive measures are often lacking. Future studies are encouraged to explore the family dynamics of this population, covering aspects such as emotional well-being, social interactions, and financial stability.

The present study sheds light on the critical needs of patients with FA, offering valuable insights for dental care practices. Beyond the FA cohort, these findings provide potential guidance for managing oral manifestations in other chronic diseases. The study underscores the scarcity of salivary data in FA literature, highlighting the importance of recognizing the impact of reduced salivary flow on OHRQoL. Additionally, while previous research focuses on the progression of OPMD to OSCC [5], there remains a notable gap in understanding how OPMD presence, particularly OL, affects the quality of life of FA patients. Sensitivity and nuanced communication are crucial in delivering news about OPMD [48], acknowledging the heightened concerns of FA patients regarding OSCC risk. This emphasizes the need for tailored approaches to ensure informed decision-making without exacerbating fear or compromising quality of life.

## Conclusion

Individuals with FA commonly exhibited oral conditions such as decayed and missing teeth, poor oral hygiene, gingivitis, and changes in salivary flow. Among them, patients with

OL or with diminished salivary flow experienced a greater negative impact on OHRQoL. Taken together, the results of the present study underscore the importance of comprehensive healthcare for FA individuals, requiring collaboration between reference centers. It is necessary to increase the awareness of health professionals about oral health care.

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**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Conflict of Interest** The authors declare no competing interests.

**Ethical approval** The study was approved by the Ethics Committee of Universidade Federal de Minas Gerais and Universidade Federal do Paraná (No. 66312622.4.1001.5149).

**Informed consent** Consent was obtained from all participants.

**Consent to publish** The authors confirm that human research participants provided informed consent for the publication of the results.

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