

ABSTRACT

This study evaluated the oral health-related quality of life (OHQoL) in children with neutropenia. Twenty-seven children with neutropenia were compared to 33 healthy, age-matched control subjects. Previously validated age-specific, multidimensional and self-reporting child OHQoL questionnaires were used. Overall and subscale scores were compared between the two groups. Respondents in the group of children with neutropenia reported that their disease had a significant impact on their oral health in terms of oral symptoms ($p < 0.0001$), functional limitations ($p < 0.0001$), and social well-being ($p < 0.0001$). In global ratings, they rated their oral health to be markedly worse than that of the healthy subjects ($p < 0.0001$). However, there was no difference between the groups in the extent to which their oral condition affected their lives overall. These results, along with responses to individual measures of social and emotional well-being, suggest that children in this group with neutropenia have psychologically adapted to the oral health challenges they experience because of their condition.

KEY WORDS: children, neutropenia, oral health-related quality of life

Oral health-related quality of life of children with neutropenia

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Introduction

The most common infectious diseases of man are dental caries and periodontal diseases. These ailments are in part caused by the oral bacterial flora which forms a complex biofilm. In an immunocompetent individual, standard oral hygiene measures along with regular professional preventive dental procedures are sufficient to maintain long-term oral health. However, congenital or acquired defects in the oral tissues or in the physiologic processes that protect these tissues, such as innate immunity, can result in significant oral disease including periodontal infections and oral ulcers.^{1,2} A rare, aggressive and highly destructive form of periodontal disease (early-onset periodontitis)³ has been described in children with neutropenia.^{4,6}

Neutropenia is characterized by a decrease in circulating neutrophils, the most numerous innate defense cells in the periodontal sulcus. Neutrophils play a critical role in protecting the periodontium against bacterial and fungal infections.^{7,8} Several forms of neutropenia are recognized in children.^{9,10} Past evidence shows that patients with neutropenia are susceptible to oral problems secondary to their innate immune defect.¹ Administering granulocyte colony-stimulating factor (G-CSF) to patients with neutropenia can consistently lead to an increase in circulating neutrophil counts.¹¹⁻¹⁴ There is no evidence, however, that treatment of neutropenia with G-CSF will lead to a resolution of the oral lesions, even if an improvement in the general health of the patient is observed.^{15,16}

Not long ago, the United States Surgeon General released a landmark report entitled "Oral Health in America: A Report of the Surgeon General".¹⁷ The report emphasized the high level of oral diseases among certain pediatric population groups, including those with systemic health conditions. The surgeon general called for greater efforts to promote oral health in these populations who have conditions that have the potential to compromise oral function, well-being and quality of life.¹⁷ A health-related quality of life perspective is a novel concept of health which has the advantage of being multidimensional and considering an individual's biological, psychosocial and behavioral concerns.^{18,19} By integrating body, individual and society into broad explanatory frameworks, we can begin to identify strategies that have the potential to improve the quality of clinical and psychosocial care of those with health conditions.^{20,21} There are no studies reporting the oral health-related quality of life in children with neutropenia.

Measures which address oral health-related quality of life are being used with increasing frequency in oral health surveys and clinical trials in dentistry.²² Child oral health-related quality of life questionnaires (COHQoL) have been developed and validated.^{22,23} This paper compares the oral health-related quality of life of children with neutropenia using age-specific child perception questionnaires.

Materials and methods

Study subjects

Participants in the study included children aged 8 to 18 years with neutropenia as defined by an absolute neutrophil count (ANC) below the threshold value of $1.5 \times 10^9/L$. They were recruited during their regular appointments at the Bone Marrow Failure and Myelodysplasia Clinic of the Hospital for Sick Children, Toronto. Child siblings accompanying patients with neutropenia to their appointment and independent control subjects were enrolled in the study and served as hematologically healthy, age-matched controls. Data were obtained from 60 participants (41 males, 19 females) following procurement of informed consent. The group of participants with neutropenia consisted of 24 males and three females, while in the healthy control group there were 17 males and 16 females. The neutropenic group consisted of children with a variety of inherited marrow failure syndromes which included isolated neutropenia: Kostman's syndrome and cyclic neutropenia or neutropenia associated with other hematological or non-hematological manifestations, aplastic anemia, Fanconi anemia, Shwachman-Diamond syndrome, Barth syndrome, dyskeratosis congenita and Diamond Blackfan anemia. None of the patients suffered from an infection at the time the questionnaire was completed. The mean ages of the participants with neutropenia and the healthy group were $13.5 \pm 3.7SD$ and $11.2 \pm 2.7SD$, respectively. The protocol was approved by the Research Ethics Board of the Hospital for Sick Children.

Data collection

Data were collected using the COHQoL for children aged 8 to 10 years (COHQoL₈₋₁₀) and the COHQoL₁₁₋₁₄ for children aged 11 to 18 years.^{22,23} These questionnaires have been designed to assess the impact of oral health and orofacial conditions on the quality of life of children. The COHQoL is a self-completed survey administered at the time of visits to the Bone Marrow Failure Clinic at the Hospital for Sick Children. The

Table 1. COHQoL overall and domain scores by clinical group.

	Neutropenic (n=27)		Control (n=33)		p*
	Mean	Median	Mean	Median	
Overall scale	14.22	14.00	2.55	1.00	<.0001
Subscales:					
Oral symptoms	5.26	6.00	0.94	0.00	<.0001
Functional limitations	4.30	3.00	0.39	0.00	<.0001
Emotional well-being	2.22	1.00	0.70	0.00	NS †
Social well-being	2.44	2.00	0.52	0.00	<.0001
*p-values obtained from Mann-Whitney tests					
†Not statistically significant					

Table 2. Percentage reporting "sometimes" or "more frequently" to the social well-being questionnaire items.

In the past four weeks (8-10)/three months (11-18), how often have you ... because of your teeth, mouth, lips or jaws...			
	Neutropenic (n=27)	Control (n=33)	p*
Missed school ^a	18.5	0.0	<.0001
Had difficulty paying attention in school ^b	11.1	3.0	<.017
Had difficulty doing homework ^a	7.4	3.0	<.012
Avoided reading/speaking in class ^a	3.7	0.0	NS †
Avoided social activities ^b	0.0	0.0	NS †
Avoided smiling ^b	7.4	3.0	<0.013
Avoided other children ^b	3.7	0.0	NS †
Avoided talking to other children ^b	0.0	0.0	NS †
Been teased by other children ^c	3.7	3.0	NS †
Been asked questions by other children ^c	0.0	0.0	NS †
*p-values obtained from Mann-Whitney tests; †Not statistically significant			

Table 3. Percentage reporting "sometimes" or "more frequently" to the oral symptoms questionnaire items.

In the past four weeks (8-10)/three months (11-18), how often have you had ... in your teeth, mouth, lips or jaws...			
	Neutropenic (n=27)	Control (n=33)	p*
Pain	29.6	6.1	<.0001
Sore spots	22.2	6.1	<.0001
Food stuck	48.1	12.1	<.0001
Bad breath	51.8	0.0	<.0001
*p-values obtained from Mann-Whitney tests			

COHQoL₈₋₁₀ and the COHQoL₁₁₋₁₄ have 25 questions in common falling into four domains: 1) oral symptoms, 2) functional limitations, 3) emotional well-being, and 4) social well-being (Tables 1-4). The

latter consists of questions pertaining to schooling, peer relationships and leisure activities (Table 2). Questions in the COHQoL₁₁₋₁₄ ask about the frequency of events in the past three months while

questions in the COHQoL₈₋₁₀ ask about the frequency of events in the past four weeks to accommodate age-dependant comprehension and development differences. An example of how the questions are worded in the COHQoL₁₁₋₁₄ is, "In the past three months, how often have you felt unsure of yourself because of your teeth, lips, jaws or mouth?" The wording in the COHQoL₈₋₁₀ is as follows: "Have you missed school because of your teeth or mouth in the past four weeks?" The response options are: Never (0); Once or twice (1); Sometimes (2); Often (3); Everyday or almost everyday (4). Global ratings of oral health and the impact of oral disease on the child's overall well-being were obtained as well (Table 5 and 6). The higher the cumulative score, the more the respondents' condition affects their quality of life.

A supplementary Oral Health Questionnaire (OHQ) was administered concurrently to the COHQoL where the subjects indicated whether they were followed by a dentist, the frequency of their dental visits, whether they had dental insurance and if the cost of dental care was a factor in the frequency of their dental care visits. Furthermore, they were asked if their medical doctor and nurses stress the importance of oral health or oral hygiene (Table 7). These aforementioned questionnaires were completed, when required, with the help of a parent or guardian.

Data analysis

The overall and domain COHQoL scores of children with neutropenia were compared with those of healthy, age-matched controls. The two groups were also compared with respect to their responses to individual questions comprising the COHQoLs and to global ratings of oral health and overall well-being. Differences between groups were assessed using non-parametric (Mann-Whitney *U* test) statistics and considered significant if *p*<0.05.

Results

COHQoL overall and domain scores

The possible maximum COHQoL score

Table 4. Percentage reporting "sometimes" or "more frequently" to the functional limitations questionnaire items.

In the past four weeks (8-10)/three months (11-18), how often have you ... because of your teeth, mouth, lips or jaws...			
	Neutropenic (n=27)	Control (n=33)	<i>p</i> *
Had pain when drinking cold drinks or eating hot foods	25.9	0.0	<.0001
Taken longer than others to eat a meal	22.1	0.0	<.0001
Had a hard time biting or chewing hard foods (apple, steak, corn on the cob)	25.9	3.0	<.0001
Had trouble eating foods you like	22.2	0.0	<.001
Had trouble saying some words	7.4	0.0	<.009
Had a problem sleeping at night	14.8	9.7	<.036
* <i>p</i> -values obtained from Mann-Whitney tests			

Table 5. Global ratings of oral health in participants in the control group and those with neutropenia (%).

	Neutropenic (n=27)	Control (n=33)
Excellent	7.4	54.5
Very good	25.9	36.4
Good	51.9	6.1
Fair/Poor	14.8	3.0

was 100 where a higher score indicates that the respondents' systemic disease has a more severe impact on their quality of life. The overall scores ranged from 1 to 58 for the respondents with neutropenia and 0 to 24 in the healthy control group. The mean overall score in the group with neutropenia was 14.2±11.7SD and significantly higher than in the healthy group which produced a mean overall score of 2.5±4.7SD (*p*<0.0001) (Table 1).

The mean and median COHQoL overall domain scores for the oral symptoms, functional limitations, emotional well-being and social well-being domains for each clinical group are listed in Table 1. There were significant differences between the groups for the oral symptoms (*p*<0.0001), functional limitations (*p*<0.0001), and social well-being (*p*<0.0001) domains (Tables 2-4). Regarding the emotional well-being domain scores, no difference was established between the two groups (*p*<0.06) (Table 1).

Table 6. Global ratings of the extent to which life overall was affected in participants in the control group and those with neutropenia (%).

	Neutropenic (n=27)	Control (n=33)
Not at all	25.9	36.4
Very little	51.9	57.6
Some	14.8	3.0
A lot	7.4	0.0
Very much	0.0	3.0

Responses to individual COHQoL items

When responses to individual questions were examined, the participants with neutropenia had significantly higher scores than the healthy control group for all of the oral symptom domain questions. These were: pain in your teeth, lips, mouth or jaws (*p*<0.0001); sores in your mouth (*p*<0.0001); food stuck in your teeth (*p*<0.0001); and bad breath (*p*<0.0001) (Table 3). As for the functional limitations domain questions, the respondents with neutropenia had higher scores than the healthy control group for all of the questions in this category which were: pain when you drink cold drinks or eat hot foods (*p*<0.0001); taking longer than others to eat a meal (*p*<0.0001); difficulty biting or chewing foods like apples, corn on the cob or steak (*p*<0.0001); difficulty eating foods you would like to eat (*p*<0.001); trouble

Table 7. Distribution of responses (%) to OHQ questions.

	Neutropenic (n=27)		Control (n=33)	
	Yes	No	Yes	No
Doctor stresses the importance of oral health	44.4	55.6	86.7	13.3
Are you followed by a dentist?	85.2	14.8	100.0	0.0
Do you have dental insurance?	59.3	40.7	86.7	13.3
Do you visit the dentist on average every 12 months?	33.3	66.7	33.3	66.7
Do you visit the dentist on average every six months?	37.0	63.0	60.0	40.0
Do you visit the dentist on average every three months or less?	11.1	88.9	0.0	100.0
Is cost a factor in the frequency of your dental visits?	40.7	59.3	13.3	86.7

saying some words ($p<0.009$); difficulty sleeping at night ($p<0.036$) (Table 4). Furthermore, the group of patients with neutropenia had significantly higher scores than the healthy control group for three emotional well-being domain questions which were: been upset ($p<0.009$); felt irritable or frustrated ($p<0.002$); been concerned with what other people think ($p<0.014$) because of your teeth, mouth, lips or jaws. Finally, regarding the social well-being domain questions, the participants with neutropenia had significantly higher scores than the control group in four of the 10 questions which asked how often they had missed school ($p<0.0001$), if they had a hard time doing homework ($p<0.012$) or paying attention in school ($p<0.017$), or if they tried not to laugh or smile when with other children ($p<0.013$) because of their teeth, mouth, lips or jaws (Table 2).

Global ratings of oral health and well-being

There was a significant difference between the two groups in their global ratings of the health of their teeth and mouth; the group with neutropenia perceived it as significantly worse than the healthy control group ($p<0.0001$) (Table 5).

However, there was no difference between the two groups in their ratings of the extent to which their oral or orofacial conditions affected their life overall (Table 6).

Oral health questions

Only 11.1% of the subjects with neutropenia reported regular dental visits every three months or less and 37.0% and 33.3% admitted to visiting a dentist only every six and 12 months respectively, leaving 18.6% of the group without regular oral and dental care. In the control group, 60.0% and 33.3% visited the dentist every six and 12 months respectively, leaving only 6.7% without regular dental check-ups at least every 12 months. Also, 40.7% of the subjects with neutropenia and only 13.3% of the control subjects stated that cost was a factor in the frequency of their dental visits. Finally, 44.4% of the participants with neutropenia and 86.7% of the control group participants stated that their medical doctor and nurses did not stress the importance of oral health during their visits (Table 7).

Discussion

The purpose of this study was to provide insight into the oral health-related quality of life (OHQoL) for children with neutropenia compared to hematologically healthy age-matched control subjects.

Analysis of the scores from the child oral health-related quality of life questionnaires (COHQoLs) demonstrated that, overall, the OHQoL of children with neutropenia was worse than that of hematologically healthy controls. This proves that the oral condition of children with neutropenia has a significant nega-

tive effect on the quality of their lives. This agrees with past studies^{6,8,24} that have shown that oral diseases are prevalent in children with neutropenia. However, based on the responses to the two questions measuring global ratings of oral health and well-being, in this study children with neutropenia have adapted to their neutropenia-related worsened oral condition.

It is the scores in the oral symptoms and functional limitations domain questions that contributed the most to the differences observed between the groups. Perhaps the increased prevalence of oral disease and dysfunction stated by the patients with neutropenia in this study can be explained by the responses to certain questions in the oral health questionnaire (OHQ). Only 11.1% of the subjects with neutropenia reported regular dental visits every three months or less and 37.0% and 33.3% admitted to visiting a dentist only every six or 12 months respectively, leaving 18.6% of the group without regular oral and dental care and supervision by a clinician. As previously stated, neutropenia is generally associated with an increased prevalence of oral infections and periodontal diseases. Moreover, there is ample evidence proving that intense management of oral hygiene is useful in the protection against the development of oral and periodontal disease for patients with neutropenia.^{4,25} A case study showed that dental appointments once or twice a year are not enough to maintain periodontal health without progressive attachment loss in patients with cyclic neutropenia. The authors further demonstrated that regular monthly professional interventions proved to be beneficial in maintaining oral health in this group, a recommendation to which only three out of our 27 patients with neutropenia adhered (Table 7).²⁶ Past studies^{27,28} have shown that physical well-being and psychosocial functioning are not a direct product of the nature or severity of the underlying health condition. Instead, levels of disadvantage in chronic health conditions are directly related to the material, social and psychological resources available to these

patients and their families and the way these are used in dealing with the problems brought about by their condition.²⁰ For instance, most patients with neutropenia in our study group did not seek professional oral and dental care as often as they should have. This may have resulted in their stated worse oral status, thus affecting their oral health-related quality of life. Or perhaps the worse oral condition stated by the patients with neutropenia in this study may be partially explained by the following facts: Firstly, fewer than half of the patients with neutropenia admitted that their medical doctors and nurses stressed the importance of oral hygiene and health during their clinic visits and although 59.3% were covered by dental insurance, 40.7% confessed that the cost of dental care was a factor in the frequency of their visits with the dentist. These results prove that we need to continue to provide information on the susceptibility to oral disease of patients with neutropenia so that we can improve patient outcomes and arm dentists with enough evidence to justify treatment decisions to insurance companies that deny treatment claims that do not follow “typical patient” profiles.

Scores on the emotional and social well-being domains suggest that, despite the physical implications of their condition, children with neutropenia display emotional resilience and coping characteristics. This supports past findings²⁹ proving that disabilities related to chronic conditions are not the most influential factor on emotional well-being. Most of our participants with neutropenia reported having to miss school quite often because of their teeth or mouth, which may explain why many of them admitted to having a hard time doing their homework or focusing in class. However, other than reporting their reluctance to smile around other children because of their oral status, their replies to all of the remaining measures of social well-being indicated that most of the subjects in this study have psychologically adapted to the challenges of their condition. Even though most of them reported feeling upset and frus-

trated about their oral health — which they perceived to be markedly worse than that of the control subjects — only a few of them admitted to feeling concerned with what other people thought of their appearance in relation to their oral condition. What’s more, when asked if they were worried about the way their oral condition made them look, the group of patients with neutropenia showed no significant concern. In fact, the healthy participants exhibited a higher level of concern than the subjects with neutropenia. This may be explained by a certain psychological robustness and emotional maturity that comes along with living with a chronic disease. On the other hand, perhaps these findings can be explained by the fact that oral symptoms of neutropenia do not typically have a visible impact on appearance. Furthermore, it is well established that males and females perceive their health status differently.^{30,31} Many epidemiological studies have indicated that females report more pain experiences and more negative responses to pain compared to males.³² And in a study evaluating gender differences in the psychological adjustment to type 1 diabetes mellitus, they found that men had a more positive appraisal of their condition, similar to the coping style differences observed in the general population.^{33,34} Only 11% of our group of patients with neutropenia was made up of female subjects, unlike our healthy control group, whose males and females were represented more equitably.

Summary

The responses to questions in the COHQoL suggest that the children with neutropenia may have developed coping methods which allowed them to adapt psychologically and to become emotionally resilient to oral health challenges engendered by their condition. This may explain why their global rating of life overall was no different than that of the healthy children, despite rating their overall oral health as being significantly poorer than that of the latter group.

The present study had some method-

ological shortcomings mainly explained by the rarity of the condition studied (sample size, gender distribution non-optimal, mostly independent controls). Further work must be attempted with larger sample sizes. Additionally, longitudinal research involving the measurement of change in the COHQoL scores can be of interest to study the effect of factors that may account for the variation in the oral health-related quality of life.

Conclusion

The quality of life of children with neutropenia suffers significantly because of an increased prevalence of oral disease. Greater efforts should therefore be made to educate healthcare professionals about the oral health issues related to neutropenia, as it may contribute to preventing many of the severe oral complications associated with this disease and improve patient well-being and quality of life. Nevertheless, as already stated, how we handle the consequences of illness is more important than the label itself. In this study, it seems that the psychosocial care available to the children with neutropenia and their families in dealing with these consequences are contributing to a fairly good emotional and life adjustment, in spite of the oral health challenges they experience as a result of their condition.

Acknowledgements

We thank the Bone Marrow Failure Clinic doctors, nurses and patients at the Hospital for Sick Children. We also thank Shwachman-Diamond Syndrome Canada for a research grant.

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