

Health related quality of life among Saudi children and adolescents with celiac disease

Norah D. Al Nofaie, Jawaher R. Al Ahmadi¹, Omar I. Saadah²

Joint Program of Family and Community Medicine, Ministry of Health, ¹Department of Family Medicine, Faculty of Medicine, King Abdulaziz University, ²Department of Paediatrics, Paediatric Gastroenterology Unit, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

Abstract

Background/Aims: Celiac disease (CD) is an immune-mediated enteropathy triggered by gluten ingestion in genetically susceptible individuals. This study reports on the quality of life (QOL) of Saudi children and adolescents with CD.

Patients and Methods: This is a case control study that included Saudi patients with CD, aged 9-18 years, who attended CD Clinic at KAU between February 2017 and July 2018. The study was conducted using the Short-Form (SF-36) questionnaire for all candidates, CD-specific QOL questionnaire for the CD patients group, and CD screen questionnaire for the control group.

Results: Overall, 354 subjects were studied (111 CD patients and 243 control). Female subjects constituted 56.8% of both patient and control groups. In the generic SF-36 questionnaire, QOL was comparable between patients and controls in all domains except for the general health domain, which showed difference in favor of the controls (55.01 ± 26.41 and 62.96 ± 18.16 , $P = 0.005$). We also found that males have lower QOL scores in the domains comprising health change ($P = 0.02$), physical functioning ($P = 0.04$), role functioning/emotional and emotional well-being ($P = 0.049$). The CD-specific QOL showed excellent and good scores for 79.3% of patients overall in the tested domains. Patients with poor adherence showed poor QOL in all generic (SF-36) domains but not in CD-specific domains.

Conclusion: The HRQOL for Saudi CD children on GFD is generally comparable to the healthy control with exception of the general health domain. Adherence to the GFD improves the generic (SF-36) QOL domains.

Keywords: Adherence, celiac, children, quality of life, Saudi Arabia

Address for correspondence: Prof. Omar I. Saadah, Paediatric Gastroenterology Unit/Department of Paediatrics/Faculty of Medicine, King Abdulaziz University, P.O. Box 80215 Jeddah - 21589, Saudi Arabia.
E-mail: osaadah@kau.edu.sa

INTRODUCTION

Celiac disease (CD) is an immune mediated enteropathy, triggered by gluten ingestion in genetically susceptible individuals. Both human leukocyte antigen (HLA) and non-HLA genetics have been implicated in its susceptibility.^[1-4] The global prevalence of CD in children has

been estimated to be approximately 0.9%.^[5] Seroprevalence rates of 2.8% and 2.2%, respectively, have been reported for school-aged children and adolescents in the Kingdom of Saudi Arabia.^[6,7] CD is a chronic disease that requires lifelong restriction of gluten intake, and consumption of a gluten-free diet (GFD), which may have an impact on

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the quality of life in children and adolescents with CD. Untreated or poorly controlled CD patients may have different gastrointestinal and non-gastrointestinal symptoms that may impair the quality of life (QOL).^[8,9] Strict adherence to the GFD is the recommended therapeutic approach that can lead to mucosal healing and resolve symptoms resulting in overall improvement of the QOL.^[10] However, some patients, especially adolescents, may have difficulty coping with the dietary restriction of a gluten-free diet, which may adversely affect their QOL.^[11,12] Such emotional and social effects of the diet may counteract the positive effect of mucosal healing.

Several tools have been used to assess QOL. The most widely used instrument is the RAND Short-Form survey (SF-36) which has been used in several clinical studies.^[13-15] The SF-36 was developed from a larger survey in the Medical Outcomes Study (MOS).^[16,17] 2471 participants older than 14 years have been included from the MOS to develop the scoring system and to determine the reference standard values.^[18] The result of the SF-36 has been used as a control reference (RAND control) in several studies.^[13,19]

To the best of our knowledge, only one study has been published from Saudi Arabia that looks at health-related quality of life (HRQOL) using a SF-36 questionnaire in patients with CD.^[19] This study reports the HRQOL of Saudi children and adolescents with CD in comparison with age- and sex-matched healthy controls, utilizing both the SF-36 questionnaire and the celiac specific quality of life questionnaire (CD-QOL). The control subjects were chosen from the local population rather than RAND control.

PATIENTS AND METHODS

This is a case control study that included Saudi patients with biopsy proven CD, aged 9-18 years, who attended CD Clinic at King Abdulaziz University in the period between February 2017 and July 2018. Patients with other chronic illnesses were excluded to ensure the accuracy and validity of the results.

The control groups of children and adolescents were chosen from the general school by a random selection technique. Consent and assent were taken from these participants. We used our controls from the same population rather than use the RAND controls. Before participation, controls were assessed by using a locally validated CD screening questionnaire.

Adherence to the GFD was assessed by combined utilization of self-reported rating of adherence from

KINDL[®] questionnaire (yes/no)^[20] and demonstration of a decline in the level of tissue transglutaminase (tTG) antibody to normal or near-normal level.

Instrument and measures

The study was conducted using the interviewing Short-Form survey (SF-36) questionnaire for all candidates, the CD-QOL questionnaire for CD patients, and the celiac screen questionnaire for controls.

The SF-36 is a 36-question survey used for both patients and controls. It comprises of 2 primary domains, physical and mental, which measure the presence and the severity of symptoms and their limitation on daily activities. It is sub-divided into various secondary domains, including physical functioning, role functioning due to physical health problems, role functioning due to emotional health problems, energy and fatigue, emotional well-being, social functioning, bodily pain, general health, and health changes. Scores range between 0 and 100, with a higher score indicating a better HRQOL. SF-36 was tested and showed reliability and validity as a measurement of quality of life.^[18] An Arabic translated form of SF-36 showed validity, reliability, and equivalence to the original version.^[21]

The CD quality of life survey (CD-QOL) is a reliable and valid CD specific instrument.^[22] It comprises of 20 questions across 4 clinically relevant domains (limitations, dysphoria, health concerns, and inadequate treatment). The instrument assesses the presence of CD-related symptoms in the last 30 days. The questions were expressed in a 5-point Likert scale and the response labeled as poor, good, and excellent after reverse coding. This instrument has high reliability and validity.

Celiac screen questionnaire is a locally validated instrument that includes 15 questions about general health, usually used for the controls to identify individuals with symptoms suggestive of CD. Individuals scoring 25 or above must be excluded from the study.

Ethical considerations

The study was approved by the Research Committee at the Unit for Biomedical Ethics at Faculty of Medicine, King Abdulaziz University (Reference NO 531-18). Informed consent was obtained from all the participants' parents or legal guardians.

Statistical analysis

The statistical analysis was performed using the Statistical Package for the Social Science (SPSS) software, Version 21 for Windows, Descriptive statistics were reported as proportions for qualitative variables such as frequencies

and percentages of QOL scales among controls and cases. Group comparison (CD patients vs. controls and CD patients with good adherence vs. poor adherence) was performed using an independent *t*-test for numerical data. The results were considered significant when the *P* value was less than 0.05.

RESULTS

A total of 354 subjects were included in this study (111 CD patients and 243 controls). Out of the initial number of controls of 284 individuals, 41 were excluded through the CD screening questionnaire and referred to the hospital for further investigations, and 243 individuals were included in the study. Female subjects constituted 56.8% of both cases and controls.

The CD cases and controls were matching in the baseline general characteristics (age, gender, and level of education) with no statistically significant differences between both groups [Table 1].

Comparing our study controls with the RAND control regarding QOL, our study controls had good quality of life and a higher score in more sub-classes than RAND control. The difference was more obvious in the following domains: Energy/fatigue, role functioning and physical, general health, health change, and pain. This makes our study controls more ideal to compare with than RAND control.

Only the general health domain showed significant differences between CD patients and controls in the mean score \pm SD (55.01 ± 26.41 vs. 62.96 ± 18.16 , $P = 0.005$), indicating poor QOL of CD patients in this domain. In the domains emotional well-being and energy/fatigue, though the mean score was lower than that of the control group, the difference was not statistically significant [Table 2].

Concerning the effect of gender on QOL for CD patients, we found that males have lower QOL scores in the following domains: health change ($P = 0.02$), physical functioning ($P = 0.04$), role functioning/emotional ($P = 0.04$) and emotional well-being ($P = 0.049$) [Table 3].

Table 1: Characteristics of the participants

Categories		Patients (n=111)	Controls (n=243)	<i>P</i>
Age (mean) (SD)		14.8 (2.2)	14.9 (2.6)	0.7*
Gender (n, %)	Male	48 (43.2%)	105 (43.2%)	0.3**
	Female	63 (56.8%)	138 (56.8%)	
Education level (n, %)	Primary school	34 (30.6%)	77 (31.7%)	0.2**
	Intermediate school	21 (18.9%)	65 (26.7%)	
	High school	56 (50.5%)	101 (41.6%)	

* *t*-test, ** χ^2 test

Table 2: Comparison between the QOL domains in CD cases and control group

QOL domains	CD cases Mean (SD) (n=111)	Controls Mean (SD) (n=243)	<i>P</i>
Physical functioning	68.5 (30.6)	65.9 (27.4)	0.43
Role functioning/physical	63.7 (46.3)	65.8 (31.2)	0.67
Role functioning/emotional	63.4 (45.6)	55.5 (38.7)	0.12
Energy/fatigue	58.6 (24.0)	60.4 (23.2)	0.51
Emotional well-being	63.0 (20.8)	66.4 (22.7)	0.18
Social functioning	73.5 (26.0)	72.9 (25.0)	0.83
Pain	82.1 (21.1)	77.1 (24.2)	0.61
General health	55.0 (26.4)	63.0 (18.2)	0.01
Health change	70.5 (25.3)	71.6 (26.8)	0.72

QOL: Quality of life; CD: Celiac disease; * *t*-test

Table 3: Gender comparison of CD patients in the main QOL domains

QOL domains	Males mean (SD) n=48	Females mean (SD) n=63	<i>P</i>
Physical functioning	62.6 (31.7)	74.2 (28.5)	0.04
Role functioning/physical	55.9 (48.3)	71.4 (43.3)	0.08
Role functioning/emotional	54.6 (46.1)	72.0 (44.0)	0.04
Energy/fatigue	55.0 (22.5)	62.1 (25.1)	0.12
Emotional well-being	60.4 (19.1)	65.4 (22.4)	0.21
Social functioning	68.6 (26.8)	78.4 (24.5)	0.049
Pain	79.0 (21.4)	85.2 (20.5)	0.12
General health	55.1 (26.5)	55.0 (26.6)	0.97
Health change	65.0 (24.3)	75.9 (25.2)	0.02

QOL: Quality of life; CD: Celiac disease. * *t*-test

When general QOL domains were analyzed based on the level of adherence to the GFD in CD patients, children with good adherence showed significantly better quality of life compared to children with poor adherence in all domains ($P < 0.001$) [Table 4].

Only 20.7% of the CD patients reported a poor response in all CD-specific domains, while 79.3% reported a good or excellent response in overall sum of the four tested domains [Table 5]. Stratifying responses by the level of adherence to the GFD showed no difference. Furthermore, there was no gender difference in CD patients regarding the level of adherence (good adherence was documented in 38 [69%] males vs. 42 [75%] females, $P = 0.49$).

DISCUSSION

In this study, the effect of CD on the QOL of children and adolescents in Saudi Arabia was addressed against healthy controls. The HRQOL is a multidimensional concept that covers various domains including physical, emotional, social, and cognitive aspects. What matters about HRQOL is the patient's perception about their functioning.^[23] We used both, a generic instrument for assessment of HRQOL (SF-36) and a CD-specific instrument. The generic instrument allows for comparison of patients with healthy controls, whereas a CD-specific instrument

Table 4: QOL of CD patients categorized according to the degree of adherence to the GFD

Domain	Good adherence Mean (SD) n=80	Poor adherence Mean (SD) n=31	P	Beta	OR	95 th CI
Physical functioning	78.1 (23.7)	48.3 (29.1)	<0.001	0.47	1.6	(19.2-40.4)
Role functioning/physical	78.1 (39.9)	26.6 (41.3)	<0.001	0.50	1.7	(34.6-68.4)
Role functioning/emotional	78.3 (37.9)	24.8 (41.2)	<0.001	0.50	1.7	(37.3-69.9)
Energy/fatigue	65.6 (2.5)	40.7 (21.0)	<0.001	0.54	1.7	(16.0-33.9)
Emotional well-being	69.4 (17.3)	46.3 (20.0)	<0.001	0.47	1.6	(15.5-30.7)
Social functioning	81.3 (22.5)	53.2 (24.1)	<0.001	0.50	1.64	(18.0-37.2)
Pain	88.1 (18.1)	67.0 (21.1)	<0.001	0.48	1.6	(13.0-28.9)
General health	62.5 (22.7)	35.7 (25.7)	<0.001	0.49	1.6	(16.9-36.7)
Health change	77.28 (23.6)	53.2 (21.2)	<0.001	0.43	1.6	(14.3-33.6)

QOL: Quality of life; CD: Celiac disease; GFD: Gluten free diet; * t-test

measures various problems relevant to the disease.^[24] The control group was carefully selected among healthy children and adolescents using a locally validated questionnaire to exclude individuals with potential or undiagnosed CD.

Few studies have investigated HRQOL in children with CD and they report conflicting results.^[25-29] The discrepancy in these reported results may be attributed to the different instruments used for assessment of HRQOL, along with the different age groups and ethnicity of the study population.

When comparing the HRQOL between children and adolescent with CD and the controls, we found comparable results in all domains with exception of general health, and a trend for lower scores in the role functioning/emotional and emotional well-being domains. However, the study cohort included all patients regardless of their adherence level to the GFD. Further categorization of patients according to the adherence level showed significant difference in QOL domains between both groups,

Table 5: Comparison between CD-QOL domains in children with CD according to the degree of adherence to the GFD

CD-QOL domains	Good adherence	Poor adherence	Total (n, %)	P
Overall sum				
Poor	16	7	23 (20.7%)	0.62*
Good	15	8	23 (20.7%)	
Excellent	49	16	65 (58.6%)	
Dysphoria				
Poor	17	7	24 (21.6%)	0.68*
Good	20	10	30 (27%)	
Excellent	43	14	57 (51.4%)	
Inadequate treatment				
Poor	8	4	12 (10.8%)	0.09*
Good	23	15	38 (34.2%)	
Excellent	49	12	61 (55%)	
Health concern				
Poor	16	8	24 (21.6%)	0.65*
Good	15	7	22 (19.8%)	
Excellent	49	16	65 (58%)	
Limitation				
Poor	16	6	22 (19.8%)	0.73*
Good	13	7	20 (18%)	
Excellent	51	18	69 (62%)	

CD-QOL: Celiac disease-quality of life; GFD: Gluten free diet; * χ^2 test

indicating better QOL in CD patients with good adherence as compared to patients with poor adherence. These findings are consistent with previous reports indicating better HRQOL (SF-36) in patients with better adherence to the GFD.^[30-33] Other studies reported disagreement on the effect of adherence on the QOL.^[30,34,35]

Unlike other studies that reported lower perception of QOL in female CD patients for both, children^[26,28] and adults,^[10,36] our result showed the opposite, which may be related to cultural differences between the Saudi and the Western community, since young females in the Saudi community are less likely to spend as much of their time outdoors with their peers in the Western community. Therefore, they may have less impact on the quality of life in relation to dining outside or keeping self-esteem, compared to their male counterparts.

Some studies reported no difference according to the adherence level. The reasons for such differences may be related to different methods used to assess the dietary adherence, which included questionnaires, self-reporting, CD serology, and biopsy. These methods are considered relatively inaccurate to assess gluten ingestion.^[37]

Dietary adherence to GFD in older children and adolescents was related to the presence of gastrointestinal symptoms, age of the child, and their ethnic and social background, rather than overall perception of HRQOL.^[38]

The CD-specific QOL analysis results demonstrated that more than 80% of children and adolescents in this study showed excellent and good scores in all domains of QOL. Only less than 20% reported poor QOL for all domains. This suggests that most children and adolescents with CD have good QOL as measured by the CD-specific QOL questionnaire.

Comparing the CD-specific QOL domains according to the adherence level to the GFD, no differences were found [Table 5], unlike the result obtained when analyzing

the domains of the generic HRQOL instrument [Table 5]. This may be attributed to the composition of the CD-specific questionnaire that relies mainly on perception of the CD as a chronic illness and various limitations related to the GFD and the disease complications. These concerns will be shared by both symptomatic and asymptomatic patients. Studies showed that screening-identified asymptomatic CD may be less willing to adhere to a GFD.^[11,39] However, in another study by Mahadev *et al.*, using a CD-specific QOL questionnaire has shown no difference in QOL and adherence level between symptomatic and screen-detected asymptomatic patients.^[40]

The study is limited by its design and lack of QOL assessment before starting the GFD for comparison.

In conclusion, HRQOL for Saudi CD children on the GFD is generally comparable to the healthy controls with exception of the general health domain, when assessed by the generic SF-36 and CD-specific instruments. Children with better adherence to the GFD have better QOL in all SF-36 domains, but not in the CD-specific domains. Further studies are required to minimize the difference in QOL scores related to adherence level between assessment, using SF-36 or CD-specific questionnaires.

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Conflicts of interest

There are no conflicts of interest.

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