What is the burden of illness in patients with reflux disease in South Africa?

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ABSTRACT
Objectives: To describe the impact of heartburn on patients’ Health-Related Quality of Life (HRQL) in South Africa.
Design: Survey of patient-reported outcomes and physician-assessed symptoms.
Setting: South African, major referral gastroenterology clinic.
Subjects: Consecutive patients with predominant symptoms of heartburn.
Outcome measures: Patients completed the Afrikaans versions of the Gastrointestinal Symptom Rating Scale (GSRS), the Quality of Life in Reflux and Dyspepsia questionnaire (QOLRAD) and the Short Form Health-36 (SF-36). Physician-assessed frequency and severity of heartburn during the previous 7 days were also recorded.
Results: 125 patients with symptoms of heartburn (age: M=46.0 [±12 years]; female= 74%, 87% mixed race) completed the Afrikaans translation of GSRS, the QOLRAD and the Short-Form-36 (SF-36). Patients were bothered most by symptoms of reflux (mean GSRS score of 4.9, on a scale of 1 [not bothered] to 7 [very bothered]), indigestion (4.0) and abdominal pain (4.0). As a result of their symptoms, important reflux related aspects of life, such as problems with food and drink (3.5), emotional distress (3.6), impaired vitality (3.7), sleep disturbance (3.8) and impaired physical/social functioning (4.3) were experienced (QOLRAD scores where 1 represents the most severe impact on daily functioning and 7 no impact). Overall HRQL measured by the SF-36 was poor across all domains and was significantly lower compared to the UK general population.
Conclusions: There is consistent evidence that GERD symptoms substantially impair all aspects of HRQL in this mixed race South African population referred to this central clinic.

Keywords: Burden of illness, Heartburn, Health-Related Quality of Life, South Africa

INTRODUCTION
Gastroesophageal reflux disease (GERD) is characterized either by symptoms alone, without verifiable erosion in the esophagus (non-erosive gastroesophageal reflux disease, NERD) or by esophageal mucosal damage related to abnormal reflux of gastric contents into the esophagus. Its most common manifestations, regardless if it is NERD or GERD, are heartburn and/or acid regurgitation.¹ Symptoms can also be associated with a number of extra-esophageal conditions, including asthma, chest pain, sleep disturbance and otolaryngologic disorders. GERD is one of the most common diseases in western countries with an increasing incidence and prevalence in recent decades, that may partly be explained by the attention dedicated to its study.²⁻⁵ Up to 40% of the adult Western population is affected by GERD⁶, not all of whom seek help from their general practitioner.⁷ Nevertheless, heartburn and acid regurgitation are among the most common reasons for consultation in general practice.⁷,⁸

A number of well-controlled clinical studies have been conducted in South Africa recently, providing evidence that GERD suffers are seeking care and can be successfully treated.⁹⁻¹² However, it is unclear what the exact prevalence of GERD is in South Africa. A recent review suggested that GERD may be less frequent in the sub-Saharan African region than in the Western world, but pointed out the possible reasons for underreporting such as: patients may not present to hospitals; endoscopic services may be inadequate; and the average life expectancy in sub-Saharan Africa is much lower than in industrialized countries.¹³

The impact of GERD on patients’ health-related quality of life (HRQL) is of particular concern because it is generally diagnosed on the basis of patient-reported symptoms alone.¹⁴⁻¹⁵ This is because the majority of patients who seek the assistance of a general practitioner for symptoms of GERD lack signs of esophageal mucosal injury¹⁶ and, in any case, endoscopy is rarely available in primary care, where GERD diagnosis and treatment most often takes place.

Although the impact of GERD on HRQL in Europe and North America is well documented¹⁴,¹⁷,¹⁸ these studies use different

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methodologies in different countries, making international comparisons of the impact of GERD problematic. A series of studies were therefore undertaken using a standardized methodology to assess the impact of heartburn on patients’ HRQL in South Africa, Italy, Spain, Germany, Poland and Hungary. This paper reports the results of the study that used translations of validated generic and disease-specific instruments to measure patient-reported outcomes in South Africa.

RESULTS

Demographic and clinical characteristics

Patient population

Patients with current or previously verified predominant symptoms of heartburn were eligible for entry into the study. Heartburn was defined as ‘a burning feeling rising from the stomach or lower part of the chest towards the neck’. Exclusion criteria included concurrent diagnosis of Irritable Bowel Syndrome or peptic ulcer disease, a major psychiatric illness or dementia, or any other significant medical or surgical disease. Patients treated for peptic ulcer with anti-secretory or anti-Helicobacter pylori therapy were referred for follow-up endoscopy, or those using acetyl salicylic acid (ASA) or other nonsteroidal anti-inflammatory drugs (NSAIDs) daily were also excluded. Patients had to be able to complete the patient-reported outcome instruments themselves, as no proxy assessment or interpreter was allowed. The study was conducted between September 2002 and September 2003 in one centre, at a major referral gastroenterology clinic. Good Clinical Practice was followed; written informed consent was obtained from the patient, and the study protocol and consent form was approved by independent local Ethics in accordance with the revised Declaration of Helsinki and the patients were free to discontinue participation in the study at any time.

The impact of gastrointestinal symptoms on HRQL

HRQL can be measured with generic or disease-specific questionnaires.19 Generic instruments are comprehensive and allow comparison of HRQL across diseases, treatments and populations. Disease-specific instruments, which capture details about specific symptoms, are more sensitive than generic instruments, and are therefore more responsive to treatment and other changes over time.19

Patients completed four instruments: the Gastrointestinal Symptom Rating Scale (GSRS)20; the heartburn version of Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire21, which has excellent psychometric characteristics in clinical trials22,23; and the Short-Form Health 36 (SF-36).24 All instruments have been tested in terms of validity and reliability.21,26 They were translated into Afrikaans by MAPI research institute26 and linguistically validated according to international guidelines.27

GSRS is a disease-specific instrument comprising 15 items combined into five symptom clusters, three (reflux, abdominal pain, indigestion) relevant to GERD and two (diarrhoea and constipation) representing other gastrointestinal symptoms. It uses a seven-point Likert-type scale from 1 (absence of bothersome symptoms) to 7 (very bothersome symptoms). Its reliability and validity are well documented20 and norm values for a general population are available in some countries.29 An Afrikaans translation of GSRS was psychometrically validated in the same study population.29

The other disease-specific instrument, the heartburn version of QOLRAD includes 25 items combined into five dimensions: emotional distress, sleep disturbance, vitality, food/drink problems and physical/social functioning. The questions are rated on a seven-point Likert scale in which, in the reverse of GSRS, lower values indicate a more severe impact on daily functioning. QOLRAD has been extensively documented in international studies in patients with heartburn with regard to reliability, validity and responsiveness to treatment.18,21 Its factor structure has been replicated in several translations.23 The Afrikaans translation of QOLRAD was psychometrically validated in this study population.29

SF-36 is an extensively used generic HRQL questionnaire, its 36 items clustered in eight dimensions: bodily pain, general health, mental health, physical functioning, emotional role, physical role, social functioning and vitality. Item scores for each dimension are coded, summed and transformed into a scale from 0 (worst measurable health state) to 100 (best measurable health state). This study used the Afrikaans acute version of SF-36, which covers a one-week recall period. The reliability and validity of SF-36 is well documented in many languages.29 The mean scores of heartburn patients in each domain of the SF-36 were compared to previously determined United Kingdom norm values.32 Afrikaans norm values to the knowledge of the authors are not available.

The patient, using paper and pencil, completed all questionnaires. All study personnel were trained to instruct the patients in a standardized way in order to minimize bias and enhance compliance.

Statistical methods

Statistics were calculated with SAS version 8.02.31 Pearson correlation coefficients were used to assess convergent and discriminant validity, and p-values were adjusted for multiplicity (Bonferroni: 0.05/165).34 If data was missing from one or more assessment, the mean of the completed items in the same dimension was used, provided that more than 50% of the items in that dimension had been completed.35 Missing values were less than 5% and patients in that group were not significantly different from the rest of the study population.

RESULTS

Demographic and clinical characteristics

A total of 125 patients entered the study. Their demographic and clinical characteristics are shown in Table 1. The age of the study population ranged from 18 to 78 with a mean age of 46
±12.3) years and 74% were female. Over half were married (55%) and most were of mixed race (87%). The majority were either employed full-time (40%) or described as a homemaker/student/retired (36%). Most patients (91%) had experienced heartburn symptoms for over a year and in two thirds (66%), the duration of the current episode was 6 months or less. Over half of patients (54%) had experienced symptoms on five or more occasions in the previous 7 days. Most patients (62%) described their symptoms as being severe during this period.

The impact of gastrointestinal symptoms on HRQL

Gastrointestinal Symptom Rating Scale and Quality of Life in Reflux and Dyspepsia

Patients with heartburn were most bothered by the GSRS symptom clusters related to GERD: reflux (GSRS score of 4.9 on a scale of 1 [not bothered] to 7 [very bothered]), indigestion (GSRS = 4.0) and abdominal pain (GSRS = 4.0). These symptoms were reflected in all five dimensions of QOLRAD, with patients experiencing food and drink problems (QOLRAD score of 3.5 on a scale of 1 to 7, where 1 is most severe), emotional distress (3.6), impaired vitality (3.7), sleep disturbance (3.8) and impaired physical/social functioning (4.3).

Short Form-36

Scores for the individual domains of SF-36 are shown in Figure 1. The lowest scores (<50) were reported for physical role, bodily pain, general health, and vitality. A five score difference between the domains of the studied population and the general norm values are considered to be clinically relevant, that was the case in all domains compared to the UK norm scores.

Correlations between patient-reported outcome instruments

The relevant symptom clusters of GSRS symptom scale (reflux, abdominal pain, and indigestion) were significantly correlated (p<0.0003) with all five dimensions of the QOLRAD, the disease-specific HRQL measure (Table 2). As expected, the strongest correlations were found with

### Table 1. Patient demographics and clinical data (N=125).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean (SD) years</td>
<td>46.0 (12.3)</td>
</tr>
<tr>
<td>Sex: Female</td>
<td>74.4</td>
</tr>
<tr>
<td>Race: Mixed</td>
<td>87.2</td>
</tr>
<tr>
<td>Marital status: Married</td>
<td>55.2</td>
</tr>
<tr>
<td>Employment status: Full-time</td>
<td>40.0</td>
</tr>
<tr>
<td>Employment status: Part-time</td>
<td>5.6</td>
</tr>
<tr>
<td>Employment status: Unemployed</td>
<td>16.0</td>
</tr>
<tr>
<td>Employment status: Homemaker</td>
<td>36.0</td>
</tr>
<tr>
<td>Duration of current episode: &lt;1 month</td>
<td>24.8</td>
</tr>
<tr>
<td>Duration of current episode: 1-6 months</td>
<td>41.6</td>
</tr>
<tr>
<td>Duration of current episode: &gt;6 months</td>
<td>33.6</td>
</tr>
<tr>
<td>Duration of disease: &lt;1 year</td>
<td>8.8</td>
</tr>
<tr>
<td>Duration of disease: 1-5 years</td>
<td>48.0</td>
</tr>
<tr>
<td>Duration of disease: &gt;5 years</td>
<td>43.2</td>
</tr>
<tr>
<td>Severity of symptoms, last 7 days: Mild</td>
<td>11.2</td>
</tr>
<tr>
<td>Severity of symptoms, last 7 days: Moderate</td>
<td>27.2</td>
</tr>
<tr>
<td>Severity of symptoms, last 7 days: Severe</td>
<td>61.6</td>
</tr>
<tr>
<td>Frequency of symptoms, last 7 days: 1-2 days</td>
<td>18.4</td>
</tr>
<tr>
<td>Frequency of symptoms, last 7 days: 3-4 days</td>
<td>28.0</td>
</tr>
<tr>
<td>Frequency of symptoms, last 7 days: ≥5 days</td>
<td>53.6</td>
</tr>
<tr>
<td>Previous peptic ulcer and/or ulcerative reflux esophagitis: Yes</td>
<td>32.8</td>
</tr>
<tr>
<td>Doctor visit because of emotional problems during the past 5 years: Yes</td>
<td>25.6</td>
</tr>
</tbody>
</table>

### Table 2. Correlation coefficients (Pearson) between GSRS, QOLRAD and SF-36 domains, and physician-assessed frequency and severity of symptoms

<table>
<thead>
<tr>
<th>Instruments</th>
<th>GSRS Reflux</th>
<th>GSRS Abdominal pain</th>
<th>GSRS Indigestion</th>
<th>GSRS Diarrhoea</th>
<th>GSRS Constipation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 Bodily pain</td>
<td>-0.27</td>
<td>-0.40</td>
<td>-0.39</td>
<td>-0.32</td>
<td>-0.35</td>
</tr>
<tr>
<td>SF-36 General Health</td>
<td>-0.17</td>
<td>-0.30</td>
<td>-0.32</td>
<td>-0.20</td>
<td>-0.24</td>
</tr>
<tr>
<td>SF-36 Mental Health</td>
<td>-0.31</td>
<td>-0.36</td>
<td>-0.31</td>
<td>-0.23</td>
<td>-0.36</td>
</tr>
<tr>
<td>SF-36 Physical functioning</td>
<td>-0.11</td>
<td>-0.27</td>
<td>-0.27</td>
<td>-0.29</td>
<td>-0.10</td>
</tr>
<tr>
<td>SF-36 Role - Emotional</td>
<td>-0.13</td>
<td>-0.17</td>
<td>-0.26</td>
<td>-0.20</td>
<td>-0.20</td>
</tr>
<tr>
<td>SF-36 Role - Physical</td>
<td>-0.18</td>
<td>-0.27</td>
<td>-0.30</td>
<td>-0.19</td>
<td>-0.22</td>
</tr>
<tr>
<td>SF-36 Social Functioning</td>
<td>-0.27</td>
<td>-0.23</td>
<td>-0.32</td>
<td>-0.26</td>
<td>-0.28</td>
</tr>
<tr>
<td>SF-36 Vitality</td>
<td>-0.23</td>
<td>-0.39</td>
<td>-0.38</td>
<td>-0.18</td>
<td>-0.38</td>
</tr>
<tr>
<td>QOLRAD Emotional distress</td>
<td>-0.61</td>
<td>-0.57</td>
<td>-0.55</td>
<td>-0.27</td>
<td>-0.47</td>
</tr>
<tr>
<td>QOLRAD Food/drink problems</td>
<td>-0.55</td>
<td>-0.52</td>
<td>-0.49</td>
<td>-0.39</td>
<td>-0.48</td>
</tr>
<tr>
<td>QOLRAD Physical/social functioning</td>
<td>-0.56</td>
<td>-0.54</td>
<td>-0.50</td>
<td>-0.35</td>
<td>-0.45</td>
</tr>
<tr>
<td>QOLRAD Sleep disturbance</td>
<td>-0.64</td>
<td>-0.54</td>
<td>-0.54</td>
<td>-0.33</td>
<td>-0.47</td>
</tr>
<tr>
<td>QOLRAD Vitality</td>
<td>-0.60</td>
<td>-0.60</td>
<td>-0.55</td>
<td>-0.37</td>
<td>-0.48</td>
</tr>
<tr>
<td>Physician-assessed symptoms</td>
<td>0.55</td>
<td>0.44</td>
<td>0.36</td>
<td>0.17</td>
<td>0.29</td>
</tr>
<tr>
<td>Frequency of heartburn symptoms</td>
<td>0.75</td>
<td>0.51</td>
<td>0.42</td>
<td>0.24</td>
<td>0.38</td>
</tr>
<tr>
<td>Severity of heartburn symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: Correlation coefficients in bold are statistically significant p<0.0003.
Correlations between patient-reported outcomes and physician-rated symptom assessments

Finally, physician-assessed severity and frequency of heartburn symptoms correlated significantly with the three GERD-related GSRS domains (reflux, abdominal pain and indigestion). Of the remaining GSRS domains, the only significant correlation was between constipation and physician-assessed severity of symptoms.

DISCUSSION

This study demonstrates that the burden of illness in patients with predominant symptoms of heartburn is substantial in the South African, primarily mixed race Afrikaans speaking population studied, as measured by disease-specific and generic HRQL instruments. As expected patients reported that they largely experience worse pain, social functioning and emotional well-being than those with diabetes, hypertension and hypercholesterolemia. However, patients with recent studies.15,39 In general, patients with heartburn experience worse pain, social functioning and emotional well-being than those with diabetes, hypertension and hypercholesterolemia. These aspects of patients' lives are impaired whether or not heartburn is associated with erosive esophageal lesions.4,17,41 A recent study corroborates that the severity of gastrointestinal symptoms is the most important factor in affecting health status.45 Similarly, Irvine concluded that besides disease severity, anxiety and comorbid conditions are also strongly related to impaired HRQL.43

The conclusion that reflux, indigestion and abdominal pain are the most bothersome symptoms of GERD is supported also by previous studies.17,19,44 The impact of GERD on sleep disturbance seen in these patients is the focus of considerable research,46-47, but remains poorly recognized in primary care. The HRQL effects of GERD, including emotional distress, may account for the relatively high prevalence of anxiety and depression seen in other studies.48 However, with effective symptom resolution patients lives are restored to the level observed in the general population.15 In addition, previous research has shown that both the severity and the frequency of symptoms increase the likelihood to consult46 and that when symptoms are sufficiently treated well-being is restored.18,44,50-52

Primary care physicians, are largely unaware of the associated burden of esophageal and extra-esophageal complications, and the pain and distress it can cause52, despite the recent interest in the substantial impact of GERD on patients' HRQL. This is particularly pertinent, given that effective treatment the one starting with the most effective acid suppression, i.e. a step down regimen, with proton pump inhibitors, for example, leads to significant improvements in HRQL.45,50,54 This is also more cost-effective in maintaining quality of life.55-58 For instance, esomeprazole 20 mg once daily (either continuous or on-demand) was significantly and clinically superior to ranitidine 150 mg twice daily in maintaining quality of life and achieving an optimal level of patient satisfaction.54 According to a recent expert review, PPI therapy should be initiated regardless of whether the heartburn symptoms are associated with esophagitis or not.4 In addition to the patient's perspective HRQL is one of the major endpoints in medical research that will help provide more selective treatment regimens for patients.57 Current treatment guidelines discuss this issue in more detail.2,58

In conclusion, both generic and disease-specific patient-reported instruments provided clear and consistent evidence that patients with heartburn are bothered and incapacitated by their symptoms, and that their HRQL is impaired as a result. Continuing education of primary care and specialist physicians is required to mitigate the impact of this widespread and under-treated condition.

REFERENCES

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