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The views of African and Middle Eastern Gastroenterologists on the management of mild-to-moderate, non-erosive gastro-esophageal reflux disease (GERD)

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ABSTRACT

Introduction: Gastro-esophageal reflux disease (GERD) is a common gastrointestinal disorder that occurs when backflow of the gastric contents into the esophagus results in troublesome symptoms. Though GERD has been extensively studied in Western populations, literature on the management of GERD in patients in Africa and Middle East (AME) is scarce.

Areas covered: In this review, we provide an overview of the management of mild-to-moderate GERD in AME. Here we focus on the efficacy and safety of currently available treatments for GERD to help physicians and community pharmacists appropriately manage patients with mild-to-moderate GERD in the primary healthcare setting, detailing specific situations and patient scenarios that are relevant to the region, including management of GERD during Ramadan and post-bariatric surgery.

Expert opinion: Under-appreciation of the burden of GERD in the region has resulted in a lack of consensus on management. Barriers that currently prevent the adoption of treatment guidelines in the primary healthcare setting may include lack of availability of local guidelines and referral systems, a paucity of region-specific research, and dogmatic adherence to traditional practice. By increasing awareness, strengthening knowledge, and by more effective utilization of resources, physicians and pharmacists could optimize GERD management strategies to better support patients.

1. Introduction

Gastro-esophageal reflux disease (GERD) is a common gastrointestinal disorder that occurs when reflux of the gastric contents into the esophagus and oral cavity results in troublesome symptoms and/or complications [1,2]. A generally accepted definition for mild and moderate GERD is lacking; however, the severity of GERD has been previously evaluated using a 4-point scoring system in which 0 = no symptoms, 1 = mild (symptoms that are present but can be overlooked), 2 = moderate (symptoms that cause discomfort but do not significantly impair quality of life or daily activity) and 3 = severe (symptoms that impair quality of life or daily activity) [3,4]. In addition to symptomatic severity, GERD is also defined according to endoscopic severity. Non-erosive reflux disease (NERD) describes the presence of classic GERD symptoms without endoscopic evidence of esophageal mucosal injury, whilst erosive esophagitis is characterized by the presence of esophageal mucosal lesions [5].

Estimates of the prevalence of GERD in Africa and Middle East (AME) range between 7.6–61.8% [6–15]. The majority of these studies reported prevalence rates based on the frequency of symptoms experienced over the duration of 1 week [6,9–11,14];

however frequency of symptoms was not clear from some investigations [8,12,13,15]. It has been reported that the prevalence of GERD has increased in recent years [13], though there is a profound lack of studies on the prevalence of the disorder in this region, especially in Africa. There is a clear need to carry out further epidemiological studies to better elucidate the burden of disease in the region.

GERD represents a common reason for patient visits to primary care providers [16]. Depending on the severity of GERD, it can impact the quality of life of patients and their emotional, social, and physical functioning, as well as their work productivity [14,17,18]. In a cross-sectional study in students in Saudi Arabia, 17.2% of patients with GERD experienced impacts on their daily functioning [14]. Moreover, a South African study reported that, owing to GERD symptoms, patients experienced issues with food and drink, emotional distress, impaired vitality, sleep disturbance, and impaired physical/social functioning [18].

There is a clear need to develop recommendations to guide community-based healthcare professionals when managing patients with uncomplicated GERD in the region. There is

Article highlights

- There is a paucity of region-specific research on both the epidemiology and management of GERD in patients from AME. However, GERD appears to be highly prevalent in populations in this region. Further well-designed clinical studies are required to fully elucidate the burden of GERD and determine the efficacy and safety of treatments in patients from AME.
- Patients may benefit from a stepwise approach to the management of GERD. Lifestyle modifications remain a key strategy to mitigate the impact of non-communicable diseases such as mild GERD, especially in resource-limited settings.
- Alginates and antacids are effective for the management of occasional reflux symptoms and can be used as an adjunctive therapy to PPIs to manage refractory GERD or rebound symptoms that occur when deprescribing PPIs.
- Treatment with a PPI for 4–8 weeks is recommended for patients with more frequent reflux symptoms. It is essential that patients that do not respond to PPIs are referred for further investigation and that physicians are aware of the potential risks of long-term PPI use.
- Treatment for GERD should be tailored to the individual and it is important that special care is taken when assessing certain populations, such as pregnant women, those fasting during Ramadan, patients with nocturnal symptoms, and patients who have undergone bariatric surgery.
- Appropriate management of GERD at a community level could help improve the quality of life of patients in a cost-effective manner and reduce complications by ensuring referral to secondary care where necessary.

also a need for ongoing education at primary care level regarding GERD management [18], including knowledge of alarm symptoms and referral pathways. Optimal management of GERD at the community level could improve quality of life in a cost-effective manner and ensure appropriate referral to specialist care when needed. This review aims to give an overview of the management of mild-to-moderate GERD at the primary healthcare level in AME. It should be noted that due to the paucity of data on the management of GERD in populations in AME, much of the guidance in this review has been extrapolated from global guidelines and data from Western populations, in order to provide more specific guidance for primary care physicians within the AME region based on the available data. The authors also recognize that the best practices for the diagnosis and management of GERD in AME may differ between regions. However, for the purpose of this review, we have chosen to discuss the AME region as a whole in order to provide top-line and easy to follow guidance to help primary care physicians appropriately manage GERD during the early stages of the treatment pathway.

2. Overview of mild-to-moderate GERD

2.1. Pathophysiology of GERD

GERD is a multifactorial disease with a number of contributing factors [19], including reduced lower esophageal sphincter (LES) pressure, frequent transient lower esophageal sphincter relaxation (TLESR), acid pocket, hiatal hernia, impaired esophageal clearance, increased abdominal pressure, visceral hypersensitivity, impaired mucosal integrity, central sensitization [19], in addition to psychological factors [20]. Meals are the

major aggravating factor for GERD symptoms. Within 15 minutes after eating, secreted acid starts to accumulate on top of stomach contents without mixing, known as the acid pocket [21–23]. The pH of the acid pocket is much lower than the contents of the stomach and can persist on top of the stomach contents for up to 2 hours [22–24], where it acts as a reservoir for post-prandial reflux [22].

Eating food in general induces TLESRs [25]. However, eating a large meal can lead to increased intragastric distention which in turn induces frequent TLESRs, which can lead to symptoms of GERD [26]. Meals consumed within 2–3 hours before going to bed can predispose patients to nocturnal reflux by increasing the availability of acid during the night [25,26]. The acid pocket may persist or expand in the supine position, resulting in nocturnal reflux [27]. Patients may experience worsened symptoms over time when this is combined with the loss of physiological protection that occurs in the sleeping position [27–29].

2.2. Symptomatology

The most common symptoms of GERD are regurgitation and heartburn [9,30]. In a nationwide study carried out in Saudi Arabia, 49.3% and 35.9% of GERD patients reported heartburn and regurgitation, respectively [30], whilst 75.3% and 67.3% of GERD patients experienced these symptoms in a 2020 study carried out in Nigeria [9]. A number of atypical and extra-esophageal symptoms of GERD can also occur, including nausea, epigastric pain, dyspepsia-like symptoms, cough, chest pain, sleep disturbance, and bloating [8,9,15,31].

A high degree of overlap between GERD, functional dyspepsia, and irritable bowel syndrome has been observed in some parts of AME [7,9], which is unsurprising given the high incidence of functional gastrointestinal disorders in the region [32]. This overlap may significantly worsen GERD and health-related quality of life, and therefore must be considered in the clinical management of this population of patients [9].

2.3. Risk factors

Several possible risk factors for GERD have been identified in populations in AME (Figure 1). Several studies have implicated older age as a risk factor for GERD [7–9,11], whilst others have reported no association [6,7]. Use of analgesics [7,9,11,15,33], smoking [11,14,15,33,34], psychological distress [7,14], and consumption of caffeinated beverages [10,11,15,33] have also been associated with GERD, though there are inconsistent findings between studies regarding the role of smoking [8–11,15,33,34] and caffeinated beverages [9–11,15,33,34]. Variation in results is likely due to differences in the populations studied and methodologies adopted between investigations [8].

Urbanization and adoption of a 'Western diet' is an important contributing factor to GERD [7,11,13,15,33,34]. This may also be related to increasing rates of obesity [13,35], which has also been identified as a risk factor for GERD [8,30,33,34], though data on the association between body mass index
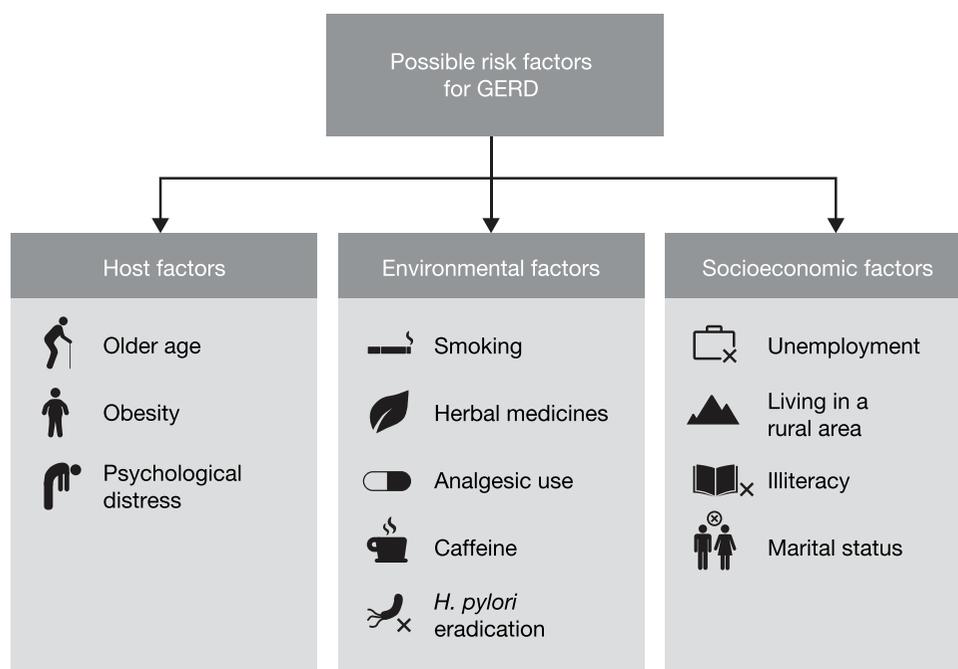
Figure 1. Possible risk factors for GERD.

(BMI) and GERD in the region are inconsistent [7,9,11]. Use of herbal medicines has been associated with an increased risk for GERD in regions such as Nigeria and Iran [7,9]. Socioeconomic characteristics such as unemployment, living in a rural area, illiteracy, and single or widowed marital status have also been associated with GERD [6,7,11], though these associations require further validation [11].

The relationship between *Helicobacter pylori* infection and GERD is controversial [36]. The prevalence of *H. pylori* in AME ranges between 41.0–87.7%, depending on patient age and the region [37,38]. Decreasing infection rates have been observed in some areas [39–41]. Multiple investigations have been unable to find a significant association between *H. pylori* eradication and GERD [42,43], though there is some evidence to suggest that eradication of *H. pylori* may contribute to worsened reflux in GERD patients with antral-predominant infection [44,45]. To our knowledge, this association has not been investigated in populations from AME, reinforcing the need for research into this association in the region.

Section 2: **Key action points**

- GERD is a multifactorial disease with a number contributing factors.
- Data on the symptomatology of GERD in AME are limited. However, studies in patients from the region indicate that heartburn and regurgitation are the most common symptoms. Patients may also experience a number of atypical and extra-esophageal symptoms of GERD, including nausea, epigastric pain, dyspepsia-like symptoms, cough, chest pain, sleep disturbance, and bloating.
- A number of possible risk factors have been identified in patients with GERD in AME. However, there is variability between studies in terms of identified risk factors, likely due to differences between the populations studied.
- Urbanization and adoption of a Western diet may be an important contributing factor for GERD in patients from AME.

3. Management of mild-to-moderate GERD

3.1. A stepwise approach

The primary goals of management of mild-to-moderate GERD in the community include symptom relief, improvement in the health-related quality of life of the patient, and prevention of GERD-associated complications. Management of GERD generally follows a stepwise approach, in terms of the treatments used and onwards referral to relevant healthcare professionals (Figure 2) [1].

3.2. Lifestyle modifications

Lifestyle modifications remain a key strategy to mitigate the impact of non-communicable diseases, including GERD. Lifestyle modifications often have low economic costs and therefore may be especially beneficial in resource-limited settings [1,46]. Patients are often counselled on dietary and lifestyle modifications, including weight loss in obese patients, eating smaller meals more frequently, eliminating possible triggers foods such as caffeine, alcohol, and chocolate, leaving 2–3 hours between evening meals and bedtime, and raising the head of the bed [5,31]. These adaptations alone can often be used for mild and intermittent reflux symptoms (<2 times per week), but also in combination with pharmacotherapy in cases of moderate GERD [1,47].

Weight loss in obese patients, elevation of the head of the bed, and avoidance of late evening meals may all have a beneficial effect on GERD parameters [5]. Though physiological evidence suggests that tobacco, alcohol, chocolate, caffeine, and high fat foods can decrease LES pressure [48], there is limited and conflicting evidence regarding the efficacy of alcohol and smoking cessation and dietary measures in reducing symptoms of GERD [5,46]. However, Katz et al. (2013)
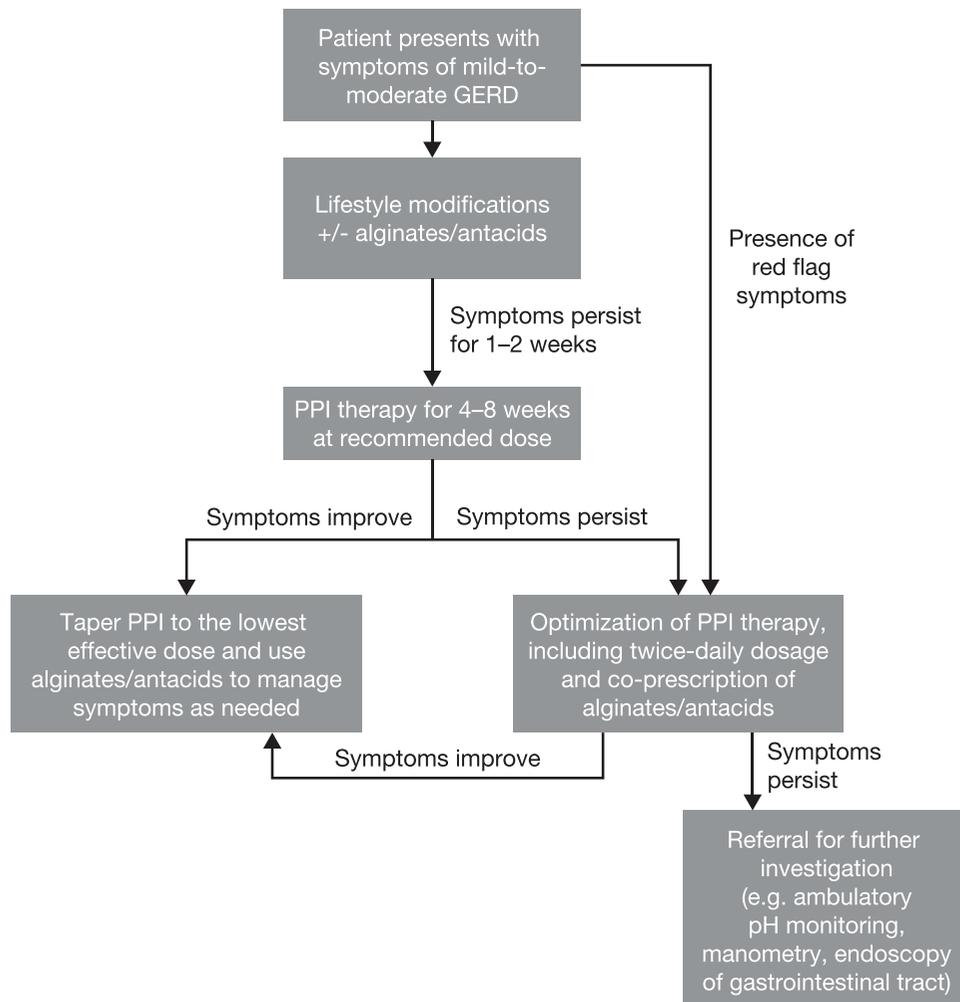
Figure 2. Stepwise approach to the management of mild-to-moderate GERD. **Abbreviation**: PPI: proton pump inhibitor.

noted that selective elimination of some foods may lead to an improvement of GERD symptoms [5].

Patients taking medication for other health conditions should see their physician to find out whether they may be contributing to their symptoms. Some medications can increase acid reflux and cause symptoms of GERD, including antibiotics, nonsteroidal anti-inflammatory drugs, anticholinergics, tricyclic antidepressants, statins, and angiotensin-converting enzyme (ACE) inhibitors [47].

3.3. Alginates and antacids

Intermittent symptoms of reflux occurring less than twice a week can be treated with over-the-counter (OTC) antacids and alginates [1]. Antacids and alginates offer rapid symptom relief and can be taken by patients as required [1,49,50].

As natural polysaccharide polymers that are isolated from brown seaweed (*Phacophycae*) [49,51], alginate-based therapies are generally well tolerated [52,53]. Clinical studies have demonstrated the superiority of alginate-based monotherapies to both placebo [52–56] and antacids [54,56–60] in the reduction of GERD symptoms. In a meta-analysis of 14 randomized controlled trials (RCTs), the odds of resolution of GERD symptoms were

significantly higher for alginate-based therapies compared with placebo or antacids (odds ratio [OR]: 4.42; 95% confidence interval [CI] 2.45 to 7.97; P = 0.001) [56]. Compared with antacids, alginate-based formulations are more effective in controlling post-prandial esophageal acid exposure [61] and in relieving reflux symptoms [56,60], including heartburn and regurgitation [62].

In patients with episodic heartburn, alginate-based formulations can help to achieve a rapid heartburn-free period. Dettmar et al. (2006) reported that sodium alginate was significantly superior to a control, ranitidine and omeprazole, in the immediate reduction of reflux and gastric acidity during the first hour after consuming a meal in patients with occasional reflux [50]. Rapid action (30 minutes or less) was more frequently observed among patients treated with alginate-based therapy compared with antacid (49.4% vs 40.4%; P = 0.0074) [58]. Furthermore, a trend toward a more prolonged duration of action compared with antacids has been reported [58,59]. Giannini et al. (2006) reported a trend towards more prolonged duration of action in patients who received sodium alginate compared with those who received magaldrate anhydrous (median: 16.5 vs 12.7 hours, respectively) [58]. Similarly, Chevrel et al. (1980) found that relief from symptoms lasted for more than 4 hours in 75% of

patients treated with an alginate-based formulation, compared with 23% of patients who received an antacid [59].

The rapid relief of GERD symptoms with alginate-based treatments could be attributed to their physical mode of action. Alginates suppress reflux by creating a physical barrier that floats on top of the liquid contents of the stomach [63,64]. Alginates rapidly react with gastric acid to precipitate into a gel, creating a raft that forms a physical barrier to reflux [57,63,64]. This physical barrier is also important in the prevention of post-prandial reflux, as the raft can localize to the post-prandial acid pocket and displace it below the diaphragm to reduce post-prandial reflux [57,64]. In contrast, antacids increase intragastric pH by neutralizing hydrochloric acid in the stomach [47].

Pepsin and bile acids also have a well-established role in esophageal damage. *In vitro* studies have shown that the alginate-based formulations can suppress pepsin activity [65,66]. Furthermore, alginate-based treatments have demonstrated a considerable ability to delay the diffusion of pepsin and bile acids. Pepsin and bile acids of refluxate could be removed by the alginate raft, thus preventing the aggressors from reaching the esophagus [65]. In both *in vitro* and *ex vivo* models, alginates coat the esophageal mucosa and exert a topical protective effect against gastric acid [67,68].

Both antacids and alginates can be used as an adjunctive therapy to manage intermittent symptoms from incomplete response to proton pump inhibitors (PPIs), or when coming off a PPI [69,70]. Many studies have demonstrated that co-therapy with PPIs and alginates is more beneficial than acid-suppression alone [69,71–73]. Co-therapy of alginates with PPIs is addressed in the *Managing patients with breakthrough symptoms* and *Management of patients tapering down or stopping PPIs* sections below.

3.4. Acid suppressants

Assessment for treatment with an acid suppressant is recommended for patients who have more frequent symptoms [1], or those who do not respond to lifestyle modifications and/or alginates/antacids after 1–2 weeks. PPIs inhibit stomach acid secretion by inactivating the active hydrogen-potassium ATPase proton pump (H+-K+-ATPase) [47].

Treatment with a PPI is warranted in patients who experience troublesome symptoms of reflux two or more times a week [1]. PPIs should be given at the lowest effective dose to relieve symptoms [1], for a period of 4–8 weeks [5, 74, 75]. Patients should be aware that traditional delayed-release PPIs must be administered 30–60 minutes before a meal for optimal symptom control [1,5].

Available PPIs include omeprazole, lansoprazole, pantoprazole, esomeprazole, dexlansoprazole and rabeprazole [47],

Table 1. Standard dosage of currently available PPIs [1].

PPI	Standard dosage
Omeprazole	20 mg
Rabeprazole	20 mg
Pantoprazole	30 mg
Esomeprazole	40 mg
Dexlansoprazole	60 mg

though the availability of PPIs may differ between countries [1]. The standard dosages of currently available PPIs are presented in Table 1. However, the recommended dosage may vary between regions [1], and HCPs should refer to local guidelines in their region. Global guidelines for the management of GERD suggest that patients who do not respond to standard dosing may benefit from twice-daily (BID) dosing [1,5]. BID dosing has been shown to significantly improve gastric acid control in patients with GERD [76]. However, several studies have indicated that this does not translate into a reduction in esophageal symptoms [76]. In a meta-analysis by Zhang et al (2017), it was reported that BID does not significantly improve symptoms of GERD and that further research is required to determine the therapeutic efficacy of this dosing regimen [77].

It is difficult to compare the efficacy of different PPIs because they are often used at different doses [47,78]. Esomeprazole (40 mg) appears to have a stronger effect on acid suppression compared with rabeprazole (20 mg), omeprazole (20 mg), lansoprazole (30 mg), and pantoprazole (40 mg) [79]. However, other comparative studies have failed to show a difference in the efficacy of different PPIs [80,81], especially when they are used at the same dose [78]. Immediate release and dual-delayed release PPIs, such as omeprazole sodium bicarbonate and dexlansoprazole, are also available and may allow for more flexible dosing in comparison to traditional PPIs [5,82].

Potassium-competitive acid blockers (P-CABs) represent a novel group of drugs which reversibly bind to K+ ions and block the H+-K+-ATPase enzyme to prevent production of stomach acid [83,84]. A number of clinical trials have demonstrated the efficacy of vonoprazan in improvement of symptoms of GERD in Japanese patients [85–87]. P-CABs are not currently available in AME [84]. Further human trials will be useful to fully elucidate the therapeutic benefits and safety of P-CAB drugs and determine their usefulness in this population.

3.5. Prokinetics

Prokinetics are drugs which enhance motility through the gastrointestinal tract. Though prokinetics have a potential role as an adjunctive therapy to PPI therapy by enhancing gastric emptying [88], their exact role for treatment of GERD is unclear and use should be reviewed by a gastroenterologist.

3.6. Potential risks associated with PPIs

In general, PPIs have an encouraging short-term and long-term safety profile [89]. The AspECT trial evaluated the safety of esomeprazole (20 and 40 mg) for a minimum of 9 years. Out of 2,535 patients, only 13 (0.5%) had a serious adverse event of Grade 3–5 that was related to esomeprazole [90]. Moreover, analysis of data from the randomized SOPRAN (12-year follow-up; n = 298) and LOTUS (5-year follow-up; n = 514) trials of esomeprazole for the treatment of chronic GERD has not shown major safety concerns [91].

While PPIs have an encouraging safety profile in general, some studies assessing their long-term use have indicated possible side effects, including increased risk of fractures [92], pneumonia [93], *Clostridium difficile* infection [94], hypo-magnesemia [95], folate deficiency [96], chronic kidney disease

[97], and dementia [98]. It should be noted that the majority of these studies are observational, and further investigations are needed to assess the potential risks associated with long-term use of PPIs [99]. However, physicians should be aware of these possible risks when recommending PPIs. The possibility of drug–drug interactions with PPIs also warrants further investigation [100]. However, the populations in these studies do not necessarily represent the population of patients with GERD who are otherwise healthy with no other medical conditions.

3.7. Management of atypical symptoms of GERD

Heartburn and regurgitation are the two most common symptoms of GERD [9,30]; however, patients can also experience extra-esophageal symptoms, such as chest pain and cough [9]. In a study carried out in Nigeria, 34.2% and 26.0% of patients with GERD experienced chest pain and cough, respectively [9]. Another study carried out in Saudi Arabia reported that 24.1%, 11.7%, and 11.3% of GERD patients experienced chest pain, laryngitis or hoarseness, and chronic dry cough, respectively [30].

In patients with typical or atypical symptoms of GERD, a thorough clinical assessment should be carried out to exclude non-GERD causes [1,5], particularly in high-risk patients such as those with diabetes, dyslipidemia, and hypertension. Patients with chest pain should be referred to a cardiologist [101], whilst those with other extra-esophageal symptoms should be referred to Ear, Nose and Throat or a pulmonary specialist [102].

In patients who also have typical symptoms of GERD, a therapeutic trial with PPIs can be recommended to treat extra-esophageal symptoms [5]. For management of non-cardiac chest pain (NCCP), PPIs are very effective and have been found to significantly improve NCCP-associated with GERD compared with placebo (81% vs 44%, respectively; P = 0.03) [103].

However, PPIs may be unsatisfactory in patients with atypical GERD symptoms, such as cough. Patients who do not respond to a PPI should be referred to a higher center for further investigations with impedance-pH testing off therapy [5]. Though uncontrolled studies have demonstrated that PPIs at high doses can relieve symptoms of cough [104], a substantial number of GERD patients with cough did not achieve a satisfactory response to PPI therapy in RCTs [104–106]. A 2011 meta-analysis reported no significant difference between PPIs or placebo in total cough resolution in adults with cough associated with GERD (OR: 0.46; 95% CI 0.19 to 1.15). The authors concluded that there was insufficient evidence to determine whether PPI treatment is beneficial in this population [105]. Moreover, O'Hara et al. (2021) reported that PPIs were not significantly different to placebo in reducing reflux symptom index (RSI) score in patients with persistent throat symptoms in a recent RCT [107].

Alginate-based therapies, as a monotherapy and in combination with PPIs, may be beneficial for the treatment of atypical symptoms of GERD. In a study by Lieder et al. (2011), chronic cough was relieved in 93% of patients who received lansoprazole 15 mg twice daily plus a standard dose of sodium alginate and potassium bicarbonate [108]. Alginate-based therapies were also found to improve global symptoms of GERD, including chest pain, in a meta-analysis by Leiman et al. [56]. Two small-scale pilot studies have demonstrated that alginates can help relieve extra-esophageal GERD symptoms in patients with laryngopharyngeal reflux disease (LPR). McGlashan et al. (2009) reported that treatment with a liquid alginate suspension four times daily significantly reduced RSI scores in patients with LPR at 2 months and 6 months compared with a control group [109]. Wilkie et al. (2018) found that an alginate-based formulation was comparable to an alginate co-prescribed with a PPI in reducing RSI scores, encompassing chest pain and cough, in patients with extra-esophageal symptoms [110].

3.8. Red flag symptoms and onwards referral

Mild-to-moderate GERD can often be managed effectively at a community level. However, there are a number of red flag symptoms which indicate that patients should be referred to secondary care for further investigation, such as gastroscopy. Red flag symptoms include [1]:

- Dysphagia
- Vomiting
- Odynophagia
- Hematemesis
- Unexplained weight loss
- Iron-deficiency anemia
- No response to acid suppressive therapy
- New-onset symptoms at age 45 to 55 years

Section 3: Key action points

- There is a clear paucity of data on the efficacy of treatments for GERD in populations from AME
- However, global guidelines and evidence in other populations suggest that patients may benefit from a stepwise approach to treatment, both in terms of the treatments used and onwards referral to relevant healthcare professionals.
- Lifestyle modifications represent a useful means of managing symptoms of mild GERD in resource-limited settings.
- Alginates and antacids are an effective option for treatment of occasional reflux symptoms and can be used as an adjunctive therapy to PPIs.
- Patients who have more frequent symptoms of reflux should be managed with a PPI for 4–8 weeks. Physicians should follow local guidance when recommending the type and dosage of PPI.
- A thorough clinical examination should be carried out in patients with atypical symptoms of GERD to rule out non-GERD causes.
- It is essential that patients who have red flag symptoms or are refractory to PPIs are referred to secondary care for further investigation.

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4. Management of mild-to-moderate NERD

NERD is defined as troublesome reflux symptoms in the absence of erosive esophagitis (EE) [111]. Currently, differentiation of NERD and EE can only be made using white light endoscopy of the upper gastrointestinal tract [111]. Endoscopic investigation may not be routinely carried out in patients with gastrointestinal symptoms in some regions, particularly in Africa, due to limited access to endoscopy within the primary care setting [112,113]. However, there are several situations where patients should be referred onwards from primary care for further investigation. Red

flag symptoms are addressed in the *Red flag symptoms and onwards referral* section above.

NERD is heterogeneous and has significant overlap with functional gastrointestinal disorders, such as hypersensitive esophagus and functional heartburn [106]. Patients with functional heartburn and hypersensitive esophagus may be less responsive to treatment with antisecretory therapy [106,114–116]. A lack of response to PPIs may therefore be indicative of an alternative diagnosis and should warrant further investigation using gastroscopy and/or ambulatory pH monitoring [5,47,106].

Treatment with PPIs may be less successful in resolving symptoms in patients with NERD compared with those with EE [56,106,117]. In a 2013 guideline, Katz et al. (2013) presented evidence to suggest that ~70–80% of patients with EE will experience complete relief with PPIs compared with ~50–60% of those with NERD [5].

A number of studies have demonstrated the superiority of alginate-based monotherapies compared with placebo or antacids in managing the symptoms of NERD [52,56]. In a meta-analysis by Leiman et al. (2017), treatment with an alginate-based formulation significantly increased the odds of symptom resolution in patients with NERD compared with placebo or antacids (OR: 4.42; 95% CI 2.45 to 7.97; P = 0.001) [56]. In an open-label placebo-controlled study, GERD patients (63% of whom were diagnosed with NERD) reported a significant reduction in reflux after treatment with an alginate-antacid formulation compared with before treatment (p < 0.001) [118] .

Alginate-based monotherapies have been found to have efficacy comparable to that of the PPI omeprazole in the treatment of NERD [119,120]. Saifullah et al. (2018) reported no significant difference in the therapeutic efficacy of omeprazole vs an alginate-based treatment in patients with NERD (60% vs 56.7% for intention-to-treat [ITT], respectively, P = 0.793; and 66.7% vs 65.4% for per protocol, respectively, P = 0.7) [120]. Moreover, a combination of sodium alginate and omeprazole was found to be superior to omeprazole alone for complete symptom resolution (56.7% vs 25.7%, P < 0.05) in a RCT in patients with NERD [73]. However, none of these studies carried out ambulatory pH monitoring as part of the diagnostic procedure for NERD [73,119–121]. pH monitoring can help distinguish patients with 'true NERD' as opposed to those with hypersensitive esophagus or functional heartburn [122], which may be difficult to determine as diagnostic criteria may be questionable [123]. Thus, a lack of pH monitoring can be considered a limitation of these studies as the proportion of patients with functional heartburn or hypersensitive esophagus was not determined [119].

Section 4: Key action points

- NERD is a heterogeneous disorder that has significant overlap with some functional gastrointestinal disorders
- Endoscopic investigation may not be routinely carried out in some parts of AME due to limited accessibility. However, the presence of red flag symptoms and/or a lack of response to PPI therapy warrant further investigation of the upper gastrointestinal tract.
- Treatment with PPIs may not be as effective in patients with NERD compared with those with EE
- Alginate-based therapies have been found to be effective in managing symptoms in patients with NERD, both as a monotherapy and as a co-therapy with PPIs.

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5. Management of GERD during pregnancy

Data on the prevalence of GERD during pregnancy are very limited. In a cross-sectional survey carried out in Nigeria, the prevalence of GERD in pregnant women was 14.5% [124]. A questionnaire-based study carried out in pregnant women visiting a prenatal care facility in Iran reported that the prevalence of GERD was 80.9% [125]. There is a clear need for further investigations into the prevalence of GERD during pregnancy in the region.

Initial treatment for GERD during pregnancy should include dietary and lifestyle modifications [1], addressed previously in the *Lifestyle modifications* section. If these measures are unsuccessful, OTC calcium-based antacids are a suitable first-line pharmacological therapy for GERD during pregnancy [1,126]. Caution should be exerted regarding other formulations [126]. Examples of agents that should not be used include sodium bicarbonate-containing antacids as they can cause alkalosis and fluid retention [126,127], and magnesium trisilicate as it may be harmful for the baby [126,127]. Calcium carbonates and alginates are considered to have an acceptable safety profile [128–130].

Moderate cases may require other lines of treatment, including PPI therapy [127]. The long-term safety of alginates and PPIs in pregnancy is yet to be confirmed. Medication for mild-to-moderate GERD in pregnancy should be used at the lowest effective dose. Although PPIs are used in pregnancy, a stepwise approach is recommended [1], and it is advised that treatment is not started if the symptoms of GERD are manageable [127]. Theoretically, alginates should have a favorable safety profile for the treatment of GERD during pregnancy due to their physical, non-systemic mode of action [49]. Fluid retention is a theoretical concern with alginates containing sodium [131]; however, studies on alginate-based formulations have reported no evidence of edema in pregnant women [131,132].

PPI therapy should only be considered if the patient is experiencing moderate-to-severe symptoms and not adequately responding to alginates. Alginate-based reflux suppressants should be considered for the treatment of heartburn during pregnancy, since evidence from clinical trials has demonstrated that they are as effective as antacids in alleviating pregnancy-related heartburn [128,129].

In a study of 134 women at <36 weeks of gestation comparing an alginate-based reflux suppressant and a magnesium–aluminum antacid gel, the improvement in heartburn frequency was 80% vs 88%, respectively (P = 0.275). Similarly, the secondary outcome measures of 50% reduction in frequency of heartburn and improvement of heartburn intensity, and 50% reduction in heartburn intensity, did not differ significantly between groups. However, the 50% reduction of heartburn intensity was numerically higher in the antacid group (80%) vs the alginate group (68%) (P = 0.075). There were no differences between intervention groups with respect to quality of life or pregnancy and neonatal outcomes [128].

Alginate use for over 4 weeks was also investigated in an open-label, multicenter study in 150 pregnant women. The efficacy endpoints were satisfactory. Safety signals for fetal

distress were reported in three cases, though none of the adverse events affecting the fetus were considered related to the study medication [133]. In another study including 144 patients at ≤38 weeks of gestation from the UK and South Africa, treatment was deemed by the investigators to be a success in 91% of patients. Very few maternal treatment-related adverse events or serious adverse events were reported, which included single occurrences of hypertension, diarrhea, and nausea. Adverse events and fetal/neonatal deaths were consistent with the population incidences in the UK and South Africa, indicating no safety concerns for use during pregnancy [131].

In the 2021 NICE guideline, it was noted that evidence regarding the effects of using antacids and alginate-based reflux suppressants on the baby is lacking. Therefore, hypothetical risks could not be ruled out. Furthermore, the design of the available studies looking into the use of alginates for the treatment of heartburn in pregnancy was mostly focused on assessment of effectiveness, and additional studies might be needed to broaden the reporting of adverse events [134]. Data on the use of GERD medication during lactation are very limited [135].

Section 5: **Key action points**

- Data on the prevalence and management of GERD in pregnant women in AME are very limited.
- Dietary and lifestyle modifications should be recommended for the initial management of GERD during pregnancy.
- If symptoms persist despite these interventions, calcium-based antacids can be recommended as a first-line pharmacological treatment for GERD during pregnancy.
- PPIs should only be recommended where symptoms are moderate-to-severe and cannot be adequately managed with lifestyle modifications or OTC treatments.
- Alginate-based therapies may be as effective as antacids for the treatment of GERD in pregnant women, and should, theoretically, have a good safety profile for use during pregnancy due to their non-systemic mode of action.
- However further clinical studies are required to determine the efficacy and safety of alginates in pregnant women.

6. Management of patients who do not respond to treatment or who experience breakthrough symptoms on PPIs

A substantial number of patients with GERD do not achieve a satisfactory response to treatment despite adequately dosed PPI therapy for the recommended duration of 4–8 weeks [5,74,136,137]. A systematic review showed that 45% (30–60%) of patients reported persistent reflux symptoms while on PPIs, based on observational primary care studies [138].

There are several reasons why a patient may be refractory to PPI treatment. Firstly, there may be an issue with patient adherence to treatment – if the patient is not using the PPI as prescribed, this can cause symptoms to persist [136]. Alternatively, if the PPI dose is too low, this may also cause a lack of response [76]. Indeed, for patients who do not achieve an adequate response to once-daily PPI therapy, the initial response may be to introduce twice-daily dosing [139]. However, in some individuals, persistent reflux symptoms are related to weakly acidic or weakly alkaline reflux episodes, meaning that increasing the dose of PPI may not be effective [138].

An inadequate response to PPI treatment may actually be related to the diagnosis rather than the treatment. A more thorough clinical review of the patient may be of value, to determine whether specialized investigations or referral are required. GERD symptoms have a wide range of causes, including functional heartburn, achalasia, rumination, eosinophilic esophagitis, and gastroparesis [31,136,140]. Thus, further diagnostic testing, such as upper endoscopy (with possible biopsy), esophageal pH monitoring, manometry, or evaluation of gastric emptying may elucidate whether there is an alternative cause for the symptoms [31,76,136,141].

Lifestyle interventions are important to support GERD management and optimize response to treatment [1,5,47]. These modifications should be actively encouraged before any further investigations or therapies are initiated. Potential medication-related effects should also be carefully considered as a possible reason for an inadequate response to PPI therapy [1,47]. Please refer to the *Lifestyle modifications* section above.

The role of PPI metabolism may be an important factor in refractory GERD [142]. PPIs are mainly metabolized by cytochrome P450 2C19 (CYP2C19). GERD patients with the CYP2C19 rapid metabolizer genotype may experience lower efficacy rates when taking PPIs [142]. Therefore, switching to a CYP2C19-independent therapy may be of benefit.

In highly selected cases, certain patients with an inadequate response to treatment may prefer to undergo anti-reflux surgery (fundoplication), although the benefits to a patient's GERD symptoms must be weighed against the risk of post-surgical complications, such as difficult swallowing, excess gas, and an inability to belch that leads to bloating and discomfort [76]. Access to elective surgery may also be difficult in some regions [143]. Ambulatory pH monitoring plus manometry should always be carried out in this group of patients before surgical therapy to rule out alternative diagnoses [5].

In patients with well-defined GERD who have incomplete resolution of reflux symptoms despite treatment with a PPI, consideration should be given to splitting or increasing the dose of the existing PPI, or changing the treatment, including switching to a different PPI or using an add-on treatment to enhance symptom control [1,5,144].

Potential add-on treatments for refractory GERD include alginates [69,76,145]. The addition of an H_2RA to twice-daily PPI in the evening can improve overnight intragastric pH control; however, in most cases, this benefit is only temporary [145,146].

The acid pocket is an important phenomenon in the pathogenesis of breakthrough symptoms of GERD [147]. The strong physical barrier formed by an alginate is vital for the elimination or displacement of the acid pocket, which is particularly important in the prevention of postprandial reflux [22,49,64]. Thus, using an alginate in combination with a PPI can hamper the reflux of gastric content and decrease the burden of breakthrough reflux symptoms in patients with GERD who have an inadequate response to PPIs [69].

Several studies have demonstrated that alginates as an add-on to PPIs can provide improved relief of reflux symptoms in patients with GERD, including those with NERD. Sodium alginate in combination with once-daily omeprazole was superior to omeprazole alone in terms of complete resolution of heartburn for at least 7 consecutive days (56.7% vs 25.7%, respectively; P < 0.05) in patients with NERD, as reported by Manabe et al. (2012) [73]. Ranaldo et al. (2017) demonstrated that in patients with refractory NERD, adding alginate to PPI treatment improved reflux symptoms vs baseline [72]. In a multicenter study of patients with GERD symptoms by Reimer et al. (2016), adding an alginate–antacid suspension to once-daily PPI treatment decreased the severity and frequency of heartburn and regurgitation [69]. In two studies by Coyle et al. (2017) an alginic acid–antacid combination was added to once-daily PPI. Although a significant difference in symptomatic improvement vs placebo was observed in the exploratory study (P = 0.012), there was no significant difference between groups in the confirmatory study (P = 0.5939) [71], suggesting that a proportion of patients may benefit from the addition of an alginate to standard-dose PPI to reduce persistent reflux symptoms.

Section 6: **Key action points**

- A substantial number of patients with GERD continue to experience symptoms of reflux despite adequately dosed PPI therapy for the recommended duration of 4–8 weeks
- Dietary and lifestyle modifications should be actively encouraged to optimize response to PPI treatment before other therapies or investigations are initiated.
- In patients with well-defined GERD who experience refractory symptoms despite treatment with a PPI, consideration should be given to splitting or increasing the dose of the existing PPI, or changing the treatment, including switching to a different PPI or using an add-on treatment to enhance symptom control
- Alginate-based therapies can be used as an add-on treatment to PPIs to improve relief of reflux symptoms in patients with refractory GERD.

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7. Management of patients tapering down or stopping PPIs

For appropriate management of GERD, PPIs should be given for a period of 4–8 weeks [5,74] and then deprescribed in patients who experience symptom resolution [75]. However, physicians may continue to prescribe PPIs for prolonged periods [148–151], and without patient review [152], which presents a barrier to appropriate reflux management. Indeed, up to 96% of patients taking long-term PPIs may not have an appropriate indication for treatment [149,151,153]. Patients should be made aware of both the benefits and potential risks of long-term PPI therapy (refer to the section *Potential risks associated with PPIs* above), and the alternative management options that are available to them. Treating physicians may not be fully aware of the concerns that patients may have about adverse effects when using PPIs for prolonged periods, and how willing they may be to experiment with their treatment regimen [154].

If a patient has a diagnosis that is compatible with long-term PPI therapy, the lowest effective dose to relieve symptoms should be prescribed [5,155,156]. PPIs are regularly prescribed at high doses rather than at the lowest effective dose [153,157]. As well as the potential disadvantage to the patient, over-prescription of PPIs can have serious cost implications for health services [151].

Patients on long-term PPIs may be eligible to reduce or discontinue their PPI dose if they have remained symptom-free [158]. An appropriate step-down treatment approach consisting of the tapering or cessation of PPIs is essential in the long-term period to avoid the risk of adverse effects and to reduce unnecessary treatment. However, there are no clear guidelines on tapering or stopping PPI therapy [158]. Decreasing the treatment to the lowest effective dose could be followed by on-demand treatment if successful symptom control is achieved; PPIs may then be deprescribed in cases where on-demand treatment proves successful and they are no longer needed, although the patient may still require close monitoring [158]. There will likely be cost savings resulting from deprescribing in patients who have had a satisfactory response to PPIs and adopt an on-demand approach to therapy [158]. Reinforcing the adoption of lifestyle modifications should also support the deprescribing of PPIs (refer to the *Lifestyle modifications* section above).

Rebound acid hypersecretion (RAHS) occurs when stomach acid secretion increases above pre-treatment levels upon discontinuation of PPIs. Rebound symptoms caused by RAHS may contribute to increased rates of long-term PPI use as patients who experience RAHS can find it harder to discontinue PPI treatment [158]. Managing rebound symptoms is key to patients being able to reduce or stop PPI treatment; patients should be made aware that such symptoms may arise, that they are likely temporary, and can be treated with alternatives therapies rather than resuming PPI therapy [158]. Alginates may be used concomitantly with PPIs as a short-term rescue therapy to decrease the symptomatic burden [69]. Patients can self-treat as needed with alginates in response to the appearance of acute breakthrough symptoms [70]. Other treatment options include antacids [70,158]. It is worth noting that some medications, such as alginates, may not be available free of cost from primary healthcare services. In regions such as South Africa where alginates are not on the Standard Treatment Guidelines and Essential Medicines List [159], this may represent a barrier to treatment as patients may be unable to pay the retail price for treatment OTC.

Section 7: **Key action points**

- To our knowledge, there are no data on the management of reflux symptoms in patients with GERD from AME.
- It is recommended that PPIs are given for a period of 4–8 weeks and then deprescribed in patients who experience symptom resolution.
- In patients with a long-term indication for PPI therapy, PPIs should be prescribed at the lowest effective dose.
- Effective management of rebound symptoms is crucial to patients being able to reduce or stop PPI therapy.
- Alginates can be used alongside PPIs as a rescue therapy to manage rebound symptoms when deprescribing PPIs.

8. Management of GERD symptoms during Ramadan

Ramadan is a holy month in the Islamic calendar where Muslims are religiously abstained from having food or drink from dawn to sunset. Dietary habits change substantially during this period, as people typically have one meal before dawn (Suhoor) and then break their fast just after sunset by having a larger main meal (Iftar) [160,161].

There is a paucity of data on GERD in fasting subjects during Ramadan. In a longitudinal cohort study of the effects of fasting during Ramadan on GERD symptoms, fasting subjects reported that GERD symptoms were less severe during the month of fasting compared with a non-Ramadan month. GERD symptoms were also less severe in people who were fasting compared with non-fasting subjects [162]. Sadeghpour et al. (2012) found that healthy individuals may experience minor gastrointestinal symptoms such as epigastric pain and heartburn whilst fasting, though reported no serious complications [163]. Further clinical studies are required to elucidate the impact of fasting during Ramadan on the symptoms of GERD.

However, changes in lifestyle and eating patterns during Ramadan may trigger symptoms of reflux. These include eating large volumes of food at meals [25,26,160,164], eating foods that may trigger reflux, such as fatty foods [25,26,160], and eating late at night with a small gap between the meal and going to sleep [25,165]. As the stomach typically requires 2–3 hours to empty its contents [166], these changes may lead to reflux symptoms. A detailed description of the pathophysiology of post-prandial and nocturnal reflux is provided in the *Pathophysiology of GERD* section above.

There are a number of lifestyle modifications that may help patients experiencing symptoms of GERD during Ramadan. When it is time to break their fast, patients may wish to avoid one large meal and try smaller, frequent meals during the sunset to sunrise period [47]. Patients should also be reminded to avoid large meals for 2–3 hours before going to bed [1,5,25,31,165].

Timing of PPI administration should be considered based on the time when symptoms are most prevalent. PPIs taken 30–60 minutes before Suhoor would be acceptable for GERD patients who experience symptoms during fasting [1,5]. However, PPIs cannot be taken before Iftar in patients with post-prandial reflux as those who are fasting are not permitted to ingest anything before breaking the fast. Thus, there may be health implications for fasting patients if their symptoms are not optimally managed during Ramadan [167].

Alginates may be useful as an on-demand treatment when reflux symptoms occur after a large evening meal. It can take between 3–6 hours to raise the intragastric pH above 4 after the first dose of PPIs [168]. Alginate-based therapies may represent a suitable alternative to PPIs for on-demand treatment of symptoms as they can rapidly form a raft-like structure that acts as a physical barrier to reflux [57,63]. Dettmar et al. (2006) reported that treatment with sodium alginate achieved a significantly more rapid reduction in gastric acidity and reflux into the esophagus during the first hour after a meal, compared with omeprazole, ranitidine, and a control [50]. The efficacy of alginate–antacid treatments in suppressing post-prandial reflux has also been demonstrated in a number of human studies [57,63,64]. In addition to forming a physical barrier to reflux, alginate–antacid combinations can increase intragastric pH [61]. De Ruigh et al. (2014) described evidence that an alginate–antacid formulation significantly increased nadir refluxate pH in the 30–150-minute post-prandial period compared with antacid treatment alone (P < 0.05) [61]. Moreover, Wilkinson et al. (2019) evaluated the intragastric neutralization capacity of an alginate–antacid suspension using intragastric pH monitoring in healthy subjects, finding that the formulation was able to maintain intragastric pH at ≥4 for 50.8% of the time during a 30-minute post-prandial period, compared with 3.5% with placebo (P = 0.0051) [169].

Section 8: Key action points

- There is a paucity of data on GERD in fasting subjects during Ramadan. Further clinical studies are required in order to determine the effects of fasting during Ramadan on symptoms of GERD.
- There are a number of lifestyle modifications that may benefit patients experiencing symptoms of GERD during Ramadan, such as eating smaller, frequent meals during the sunset to sunrise period and avoiding large meals for 2–3 hours before going to bed.
- The timing of PPI administration should take into account when symptoms are most prevalent. PPIs can be taken 30–60 minutes before Suhoor, though cannot be taken before Iftar as those who are fasting are not permitted to ingest anything before breaking the fast.
- Alginates may be effective as an on-demand treatment to manage symptoms of post-prandial reflux after eating a large meal.

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9. Management of nocturnal symptoms

Data on the prevalence of nocturnal symptoms of GERD in patients in AME are scarce. One nationwide study in Saudi Arabia reported that 27% of patients experienced nocturnal GERD and sleep disturbances [30]. Patients with night-time symptoms often have significant regurgitation with extra-esophageal symptoms such as cough or choking [170].

A number of predictors of nocturnal symptoms have been identified, including increased BMI, consumption of carbonated soft drinks, snoring and daytime sleeping, asthma, increased blood pressure, and use of benzodiazepines [171]. Patients who suffer with nocturnal symptoms of GERD are more prone to esophageal mucosal damage [172]. Therefore, the presence of nocturnal symptoms should warrant further investigation, including upper gastrointestinal tract endoscopy where appropriate.

There is evidence that use of non-pharmacological interventions, such as avoiding meals 2–3 hours before bed and elevating the head of the bed can help to relieve nocturnal symptoms of GERD [5,173,174]. Improvement in GERD symptoms and esophageal pH values has been observed in three RCTs in which the head of the bed was elevated using foam wedges or blocks [5,173,174].

PPIs can be used to control nocturnal gastric pH in patients with nocturnal symptoms of GERD [5]. Traditional delayed-release PPIs should be taken approximately 30–60 minutes before consumption of the last meal before bed in order to prevent nocturnal symptoms [5]. In some cases, PPIs may need

to be stepped up to twice-daily dosing in order to ensure optimal control of symptoms [5].

Patients may benefit from add-on or on-demand treatments that can be taken after meals or during the night when symptoms arise, such as an alginate-based formulation. In a multicenter RCT by Reimer et al. (2016), patients who were treated with an alginate-based formulation in addition to once-daily PPIs had significantly greater improvements in Heartburn Reflux Dyspepsia Questionnaire (HRDQ) reflux score and the number of days with night-time symptoms compared with patients who received PPIs or the placebo group [69]. Further RCTs looking specifically at alginates for

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Section 9: Key action points

- Evidence regarding nocturnal GERD symptoms in patients from AME is limited, though the available data suggest that nighttime symptoms and sleep disturbances are common.
- The presence of nocturnal symptoms warrants referral to secondary care for further investigation
- PPIs can be recommended for the management of nocturnal symptoms of GERD. Traditional delayed-release PPIs should be taken approximately 30–60 minutes before consumption of the last meal before bed for control of night-time symptoms.
- Non-pharmacological interventions, such as avoiding large meals 2–3 hours before bed and elevating the head of the bed can be recommended to help relieve nocturnal GERD symptoms.
- Patients may benefit from add-on and on-demand treatments such as alginates, although further clinical studies are required to fully elucidate the efficacy of alginates in reducing nocturnal symptoms of GERD.

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night-time symptoms would be useful to determine the efficacy of their monotherapy in management of nocturnal GERD.

10. Management of GERD after bariatric surgery

People who are obese may be at a greater risk of developing GERD, and weight loss resulting from bariatric surgery can often help to relieve GERD symptoms [175].

The most common types of bariatric surgery are laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) [176]. The incidence of post-surgery GERD symptoms depends on the type of procedure. The anti-reflux effect of LRYGB results from reduced acid production in the gastric pouch, and a long Roux limb preventing bile reflux [177]. With LSG, reduced acid production and gastric volume, and accelerated gastric emptying, contribute to an improvement in GERD [176]. However, LSG has been shown to aggravate GERD symptoms, a finding which is supported by a recent retrospective analysis of inpatient data from the Middle East [178]. A review of the relationship between bariatric surgery and GERD in obese patients found that LRYGB was more effective for treating GERD than LSG, and the incidence of *de novo* GERD symptoms after LRYGB was lower than after LSG [179]. In another analysis of patients with GERD, complete resolution of GERD symptoms was observed in 62.8% of patients who underwent LRYGB and 15.9% in those who underwent LSG. There was also an increased need for revisional surgery in LSG patients with preoperative GERD

symptoms, which was not observed in the LRYGB cohort [180]. Careful assessment may be needed before performing LSG in patients with GERD, and there are certain procedural factors that can help to reduce the incidence of postoperative GERD, including consideration of sleeve size and volume, and avoidance of narrowing the gastric body or pylorus [180]. The LSG procedure is less complex than the other surgical techniques [176]; between 2014 and 2018 in the Middle East, only 7.3% of all bariatric procedures were LRYGB, whereas 76.4% were LSG [181].

Patients with reflux should have a preoperative upper gastrointestinal endoscopy prior to bariatric surgery to rule out any incidental disease that may lead to complications, such as duodenal ulcer or *H. pylori* infection [182]. Indeed, endoscopy appears to play a key role in the standard preoperative preparation of patients for bariatric surgery in the Middle East [183]. Endoscopy can also indicate the presence of a hiatus hernia, which may require surgical repair during the bariatric procedure, and guide which technique may be most appropriate for the individual patient [182]. Identification and repair of hiatal hernias before LSG may reduce the risk of postoperative GERD [180].

After bariatric surgery, *de novo* or recurrent reflux may develop and will require close monitoring. Patients presenting with postoperative GERD symptoms should be managed with medical therapy similar to that used in the general population [184]. PPIs are first-line medication; prokinetic agents can also be considered [184]. Alginates can be used as an adjunctive therapy to reduce symptoms of GERD, such as regurgitation [69]; the reduced gastric capacity makes alginates an attractive treatment option due to their mechanism of action in creating a physical barrier on top of the acid pocket [69].

With persistent symptoms that have no identifiable cause, such as uncontrollable reflux, revision surgery may be considered [184]. Conversion of LSG to LRYGB is one option that has proven successful [185]. However, as with

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Section 10: Key action points

- Endoscopy should be carried out prior to bariatric surgery in order to rule out any incidental disease that may result in complications. This is part of the standard preoperative preparation of patients for bariatric surgery in the Middle East.
- Patients with symptoms of GERD after bariatric surgery should be managed in a similar manner to the general population.
- PPIs are recommended as the first-line treatment for management of symptoms of GERD after bariatric surgery.
- Alginates can be recommended as an adjunctive therapy alongside PPIs to reduce symptoms of GERD.

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any surgical procedure, the benefits of having further bariatric surgery must be considered along with the potential risks involved.

Additional self-care measures should always be reinforced after bariatric surgery. For discussion of lifestyle modifications in GERD, refer to the *Lifestyle modifications* section above.

11. Conclusions

Though data on the prevalence of GERD are limited, GERD appears to be a prevalent gastrointestinal problem in AME that can have a significant impact on health-related quality of life and productivity. There is a clear paucity of data on the management of GERD in populations in AME and further well-designed clinical trials are necessary in order to determine the efficacy and safety of various management strategies for GERD in patients from the region. However, based on data extrapolated from Western populations and global guidance, it is recommended that management of GERD should follow a stepwise approach, both in terms of the treatments used and onwards referral to relevant healthcare professionals. Lifestyle modifications represent a useful means of managing symptoms of mild GERD in resource-limited settings. Alginates and antacids are an effective option for treatment of occasional symptoms of reflux and can also be used as an adjunctive therapy to manage intermittent symptoms from an incomplete response to PPI therapy or rebound symptoms that occur when deprescribing PPIs. Patients who have more frequent symptoms of reflux should be managed with a PPI for 4–8 weeks. It is essential that patients who are refractory to PPIs are referred for further investigation and that physicians are aware of the potential risks associated with PPIs. Special care should be taken when assessing certain populations, such as pregnant women, those fasting during Ramadan, patients with nocturnal symptoms, and patients who have undergone bariatric surgery, to ensure that treatment is optimal and tailored to the individual needs of the patient. By managing GERD appropriately at a community level, primary healthcare physicians could help improve the quality of life of patients in a cost-effective manner and reduce complications by ensuring appropriate referral to specialist care where needed.

12. Expert opinion

The research discussed in this article provides clinical evidence and a practical perspective to guide African and Middle Eastern medical practitioners to manage mild-to-moderate GERD in a cost-effective manner that incorporates a stepwise approach to treatment and timely specialist referral. Barriers that currently prevent the adoption of the treatment guidelines for GERD in the primary healthcare setting are multifactorial, but may include lack of availability of local guidelines and referral systems, a paucity of region-specific research, and a dogmatic adherence to traditional practice. Under-appreciation of the burden of GERD in the region has resulted in a lack of policy/consensus on management. However, by increasing awareness and strengthening knowledge, and by more effective utilization of resources, physicians and community pharmacists could provide greater support to patients in optimizing GERD management strategies.

It is hoped that this review will facilitate an improvement in the understanding of the pathogenesis and management of GERD by primary care practitioners, and heighten the recognition of red flags that may necessitate referral. Currently, the availability of and access to expert advice and diagnostic modalities is weaker in some parts of the region compared with others, meaning a potential divergence in care pathways.

There is a pressing need for GERD-related research in AME; the dearth of evidence from this region is likely due to resource limitations and a greater focus on communicable diseases.

In the meantime, ensuring appropriate PPI prescribing for the correct duration, monitoring of treatment outcomes, adoption of lifestyle modifications, and use of antacids and alginates are essential components of optimal GERD management at the community level. Looking ahead, increased access to diagnosis, improved education of HCPs, and the introduction of newer therapies with favorable safety profiles could be cost-effective and improve the quality of life of patients with GERD. Advances in the endoscopic management of reflux may also make it easier to provide definitive treatment that is tailored to the individual needs of the patient. Newly introduced anti-reflux endoscopic techniques such as GERDx, anti-reflux mucosal ablation (ARMA), and anti-reflux mucosectomy (ARMs), though not yet acknowledged in guidelines, have shown promise in preliminary studies and may also be of benefit to patients in the near future. Future research to provide a clearer perspective on real-world GERD epidemiology and outcomes in the AME region is clearly warranted; well-conducted, original research on GERD may also necessitate a more regular updating of treatment guidelines. In addition, investigating cost-effective management strategies, including better resource allocation and treatment de-escalation, and management of GERD in specific population groups, will be beneficial for clinical practice in this region. Healthcare systems are being transformed through constantly evolving technology, and patients are increasingly utilizing digital means to take ownership of their health. Digital health innovations offer a wide range of possibilities for improving healthcare, and physicians in the AME region must welcome these advancements and opportunities that have the potential to promote healthcare system efficiency and reduce costs, and ultimately provide better patient care.

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