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GASTROESOPHAGEAL REFLUX DISEASE PRESENTING WITH ATYPICAL SYMPTOMS IN CHILDREN- CHALLENGES OF DIAGNOSIS IN SUB-SAHARAN AFRICA: TWO CASE REPORTS

Ikobah, J. M^{1,2}, Uhegbu K.^{1,2}, Ikpeme O.^{1,2}, Adedokun O.², Akpan F.², Ekanem E. E.^{1,2}

¹Department of Paediatrics, University of Calabar, Calabar, Cross River State, Nigeria

²Department of Paediatrics, University of Calabar Teaching Hospital, Calabar, Cross River State, Nigeria



ABSTRACT INTRODUCTION

Gastroesophageal reflux disease (GERD) is the involuntary retrograde movement of gastric contents across the lower oesophageal sphincter (LES) into the oesophagus which is associated with inconvenient symptoms or complications. It is prevalent all over the world but more has been reported in developed countries than in developing countries. This is a report of two cases of GERD in children involving a preterm neonate and an adolescent who presented to the University of Calabar Teaching Hospital with non-specific symptoms. The preterm neonate had repeated apnoea and failure to thrive while the adolescent presented with non-cardiac chest pain and abdominal pain. With review by the Paediatric Gastroenterologist, diagnosis of GERD was made and treatment commenced. Both

patients showed significant improvement in their symptoms; the preterm gained weight and the apnoea stopped, while the adolescent no longer had the chest pain and abdominal pain. These two cases show that there is the need for a high index of suspicion among Paediatricians who see children with non-specific symptoms such as non-cardiac chest pain, failure to thrive and apnoea in the newborn and to refer them to the Paediatric gastroenterologists timely for proper evaluation and treatment.

KEYWORDS

Gastro-oesophageal reflux, Gastro-oesophageal reflux disease, preterm neonates, children, overweight, sub-Saharan Africa

INTRODUCTION

Gastroesophageal reflux (GER) is the involuntary passage of gastric contents into the oesophagus.^{1,2} It is a normal physiologic occurrence mostly observed in infants, but also affects all age group.¹ It frequently occurs postprandial and in infants is associated with visible regurgitation of feeds.^{1,3} Gastroesophageal reflux disease (GERD) occurs

when the involuntary retrograde movement of gastric contents across the lower oesophageal sphincter (LES) into the oesophagus is associated with troublesome symptoms or complications.^{1,4} GER occurs in approximately 50% of infants aged less than three months and in 60% of infants aged three months and above.⁵⁻⁷

CORRESPONDING AUTHOR

Dr Joanah Ikobah
Paediatric Gastroenterology, Hepatology and Nutrition Unit
Department of Paediatrics
University of Calabar/University of Calabar Teaching Hospital,
Calabar, Cross River State, Nigeria
Telephone: +234 905 867 7572
ORCID Number: 0000-0002-0400-2295
email address: ikobah.joan@gmail.com;
joanahikobah@unical.edu.ng

In infancy, the male female ratio of GER is 2:1.7. Approximately, 50% of infants experience regurgitation during at least one feeding session in a 24 hour period by the age of two months and this increases to 60 – 70% at the age of 3 to 4 months and above.⁵⁻⁷ At 12 months of age about 5% of infants could still present with GER.^{6,7} The incidence of GER in preterm neonates delivered before 34 weeks of gestational age is about 22%.⁸ The prevalence of GERD in children 0 to 23 months, 2 years to 11 years, and adolescence aged 12 to 17 years

is approximately 2.2% to 12.6%, 0.6% to 4.1%, and 0.8% to 7.6% respectively.⁹ Globally, an estimated 20–30% of the world's population have symptoms of GERD and about 1% of children aged 14 years or less account for this number.¹⁰ The clinical presentation of GERD in children is non-specific, varies depending on the age of the child and maybe misdiagnosed for other medical conditions. GERD has been widely reported in developed countries in children, however, little is known about GERD in children in sub-Saharan Africa. We report two cases of GERD in children in Calabar, South-South Nigeria illustrating the challenges of diagnosis.

Case one: A preterm infant delivered at a GA of 28 weeks with a birth weight of 1.2kg, length of 35cm and head circumference of 29cm was admitted into the new born unit. Examination findings revealed a preterm male infant, in respiratory distress with oxygen saturation between 40% and 70%. On examination of the respiratory system, respiratory rate was 62 cycles/minute with crepitation in the lower lung zones bilaterally. Heart rate was 164b/min and no murmur heard. He was admitted into the new-born unit and managed as a very low birth weight preterm with respiratory distress syndrome. The oxygen saturation gradually improved within 24 hours of admission to between 96% and 98% in room air. On the 4th day of life, he developed jaundice (total bilirubin of 2.8mg/dl, and unconjugated bilirubin of 1.1mg/dl) and was commenced on phototherapy. He was on nil per os from admission and feeds commenced on the 5th day of life with expressed breast milk given at 2mls two hourly, he however, developed apnoea after feeds with vomiting. Feeds were reduced to one ml every hour, however, vomiting persisted, weight gain was poor, and feeds could not be advanced. Parenteral nutrition is not available in our hospital. The Paediatric Gastroenterologist was called to review patient on account of not tolerating feeds orally and poor weight gain. Weight on the day of review was 2.1kg at 10 weeks of age post-delivery. Oesophageal pH monitoring and upper GI endoscopy could not be done. The hospital has no neonatal endoscope and oesophageal pH monitor is not available.

A diagnosis of GERD was made, patient was managed conservatively, and protein pump inhibitor (PPI) was also commenced. With commencement of therapy, vomiting reduced significantly in frequency and volume, he

began to tolerate feeds by mouth and was discharged home within two weeks of commencement of treatment. Weight on the 10th day after commencement of treatment, was 2.35kg, length was 47cm and head circumference was 32.5cm. Patient continued to show sustained improvement with good weight gain, no longer vomiting and tolerating feeds. His weight at 16 weeks, 17 weeks and 20 weeks of life were 2.75kg, 2.95kg and 3.6kg respectively. At 20 weeks of life, symptoms had completely resolved. PPI was discontinued after eight weeks of treatment

Case two: A 15-year-old female adolescent presented to the Paediatric Gastroenterology clinic with history of recurrent chest pain of two-years and recurrent abdominal pain of one-year duration. She had positive history of heart burn and several regurgitations daily. Abdominal pain was worse with intake of spicy food, radiates to the centre of the back and wakes patient up at night. Father had similar symptoms of recurrent upper abdominal pain. She was occasionally given non-steroidal anti-inflammatory drugs for the pain. On examination, she was not in painful distress, not clinically pale, had marked epigastric tenderness. Her weight was 86kg with a height of 1.68m; her BMI was 30.7kg/m², which was between +2 and +3 z score. Other examination findings were normal.

Investigations done included Electrocardiography (ECG), Echocardiography (ECHO), upper GI endoscopy and faecal antigen test for *Helicobacter pylori* (*H. pylori*). Findings of the ECG, ECHO were normal and Upper GI endoscopy showed no evidence of reflux oesophagitis. Faecal antigen for *H. pylori* was positive. She was commenced on protein pump inhibitor and antibiotics. Patient was also advised to reduce the intake of spicy food and to reduce weight. A repeat of faecal antigen test for *H. pylori* was negative after treatment. She was followed-up for three years and symptoms of GERD had subsided.

DISCUSSION

Gastroesophageal reflux disease (GERD) in children and adolescents have varied clinical symptoms and presentations.^{7,8,12} GERD over the years have been shown to cause failure to thrive (FTT) in preterms with associated apnoea and in older children, they could present with non-cardiac chest pain.^{8,13} The prevalence of GERD in Africa is believed to be increasing possibly due to demographic and epidemiologic transition.¹⁻⁴ GERD can occur at any age in children from the neonatal period to the adolescent period as seen in the two case

reports where one occurred in the neonatal period and the other in the adolescent age group. The non-specific clinical manifestations, outcome, and specific diagnostic tests, result in confusion regarding the diagnostic dilemma and treatment of GERD in children,¹¹ therefore a high index of suspicion in making a diagnosis especially in the neonatal period is highly required.¹² This was evident in the first case report where the neonate developed apnoea and vomiting which could occur in other clinical conditions presenting in the same age group. Dhillon et al⁸ in their study noted a higher prevalence of GER in the preterm age group with most of their diagnosis being clinical and others had their diagnosis confirmed with investigations. In the same study,⁸ vomiting and apnoea were the common features seen as was observed in our first case report. Investigations requested in their study was based on high index of suspicion for the disease.

In the second case report, patient only presented to the Paediatric Gastroenterology clinic after two years as a result of non-specificity of the symptom of chest pain which could mimick cardiovascular or respiratory clinical conditions. The request for Echocardiogram and electrocardiogram was still based on the suspicion of cardiovascular origin. Nwokediuko et. al¹³ corroborated this in their study where they found an overlap of symptoms of GERD with chest pain.

Abdominal pain, though non-specific is a common feature seen in children with GERD as in the second case report. Nelson et al⁶ in their study, found abdominal pain was a more common presenting complaint in children aged 10-17 years which corroborates the finding in the second case report and chest pain was noted more in children aged 3-9 years of age. Diagnosis of GERD in children is based on both clinical and laboratory investigations.¹⁻⁴ Clinical studies have shown the usefulness of multichannel intraluminal impedance by confirming that non-acid volume reflux is a common cause of persistent reflux symptoms in patients receiving treatment for acid suppression³. Also, combining pH, pH of oropharyngeal mucous secretions, multichannel intraluminal impedance, and manometry has also been shown to be useful in extra-oesophageal reflux disease such as to detect cough.¹⁴⁻¹⁶ This technique documents when acid or non-acid reflux triggers cough and identifies patients who would be missed or wrongly diagnosed by standard pH studies. Continuous intra-oesophageal pHmetry

is currently the most reliable method of demonstrating and quantifying acid reflux.^{8,14-16} Sensitivity and specificity of prolonged pHmetry in the diagnosis of GERD greater than 90%.⁸ Extended (24-h) pHmetry has also been proven to be the most reliable method to identify infants and children with acid GER. Piesman et. al¹⁷ in their study emphasized the importance of pH monitoring in determining the extent of the reflux. These investigations could not be done in our patients due to their unavailability in our clime. This poses a challenge in diagnosis and follow up of patient with GERD.

pH manometry was requested for but could not be done due to unavailability of the equipment in our clime. Our facility is one of the few in Nigeria that offers Paediatric endoscopy services which started recently in Nigeria¹⁸ however, lack of a neonatal scope limited the neonate from benefiting from this procedure. This procedure is useful for evaluation and monitoring of structural changes of the oesophagus in suspected cases of GERD, especially in patients with increased severity of reflux symptoms where patient could present with reflux oesophagitis. Upper GI endoscopy was however, carried out in the second patient and findings were normal which is in keeping with other studies whereby GERD could be associated with either normal or abnormal findings.^{1,2}

Helicobacter pylori (*H. pylori*) infection has been implicated as a known causative trigger of GERD.³ The second patient had a positive test result to *H. pylori* using the faecal antigen test method. A repeat test after treatment with PPIs and antibiotics was negative. A systematic review have shown that eradication of *H. pylori* reduces the symptoms of GERD.³

In the first case report, following the diagnosis which was made clinically, feeds were reduced but symptoms of apnoea persisted until the PPIs were introduced. In some studies, supine posture has been associated with worsening symptoms.^{19,20} Unfortunately, in the preterm infants, avoidance of a supine posture is near impossible and this may have contributed to worsening clinical features seen in the neonate.

Lifestyle and behavioural modification is key in the management of GERD. In the second case report, the adolescent was overweight and weight reduction was advised. Ness-jensen et. al²¹ corroborated this in their study where resolution of symptoms of GERD was associated

with lifestyle modification such as weight reduction, avoidance of late night meals and other modifications.

Hoda et al¹⁹ associated obesity with GERD in children when compared with children who were not obese. Hegar et al⁵ in their study of infants over a one year period noted that partially breastfed infants were more prone to GER than their breastfed counterparts. Though the infant in the first case report was given breastmilk and symptoms persisted, other factors may have played a role. Prone or left-lateral positioning especially in neonates and infants has been found useful in the reduction of GER.^{15,20} However, there are concerns about the increased risk of sudden infant death syndrome (SIDS) with both the prone and lateral positions.²² This position was therefore not used in the preterm infant despite its usefulness.

In the treatment of GERD in infants, thickening of feeds alleviate symptoms as shown in the study by Vandeplasse et. al²³ but this was not employed in the management of the preterm as breastmilk was preferred based on its accrued benefits but this posed a challenge thus medications had to be introduced. H₂ -receptor blockers have been proven efficacious in reducing gastric acid secretion and increasing intra-gastric pH,^{23,24} although, its role in neonates with GER is still controversial. Proton-pump inhibitors (PPIs) have been proven to improve clinical symptoms though use of PPIs in infants have met with varied views as regards its efficacy in alleviating symptoms of GERD.²⁵ It was found to be useful in the management of the two cases reported in this study.

Despite that both cases had resolution of symptoms, management was challenging due to unavailability of proper diagnostic equipment, late recognition of the non-specific symptoms in the preterm neonates and the adolescent, out of pocket payment for medical services and financial constraints.

CONCLUSION

These case reports show that GERD occurs in Nigerian children including pre-term neonates and they could present with non-specific symptoms including apnoea, vomiting and failure to thrive. Though this medical condition can be successfully managed in Nigeria, challenges of late presentation also due to late recognition of the non-specific symptoms, lack of appropriate investigative equipment, financial constraints due to out of pocket

payment for medical services pose challenges to management of GERD in children. Increased awareness of the disease, and access to Paediatric gastroenterologists is therefore advocated for.

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AUTHORS CONTRIBUTION

Jl – Conceptualized the study and wrote up the manuscript, KU and OA -contributed to the manuscript writing, OI and FA - had an overview of the manuscript, EE critically reviewed the final manuscript.

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