Original Article

Health-related Quality of Life of Children with Gastro-oesophageal Reflux Disease after Nissen Fundoplication and Gastrostomy Tube Insertion - A Retrospective Observational Study

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Abstract

Background: Severe gastro-oesophageal reflux disease (GERD) is associated with a poor health-related quality of life (HRQoL). Nissen fundoplication is the most common surgical procedure for patients with GERD. A feeding gastrostomy tube may be inserted at the same time in selected patients where there are unsafe swallowing and/or feeding difficulties. The goals of surgery are to eliminate symptoms, prevent reflux complications and ultimately improve the quality of life. The main objective of this study was to assess the HRQoL of children with GERD after Nissen fundoplication and gastrostomy tube insertion. **Materials and Methods:** This was an observational retrospective cohort study at two private, not-for-profit tertiary hospitals in Nairobi. The study population included children under 18 years of age with GERD who had Nissen fundoplication with or without gastrostomy tube insertion from January 2010 to December 2020. The quality of life was assessed from the caretakers using the Paediatric Quality of Life Inventory applied through a telephone call. Data analysis was done using SPSS version 26. The HRQoL was summarised using mean and standard deviation (SD) with a 95% confidence interval (CI) around the scores. Independent samples *t*-test was conducted to compare the means of HRQoL for gender, complications and comorbidities. Spearman's correlation was done for HRQoL and age. **Results:** Eighty-two children were included in the study. Eighty-four per cent had comorbidities, with almost three-quarters of them having neurological impairment. Majority (91%) had open Nissen fundoplication, while 9% had laparoscopic Nissen fundoplication. One-third of these children reported complications post-procedure. Nissen fundoplication failure rate was 10%. Two-thirds had a concurrent gastrostomy tube insertion. The global mean HRQoL score was 75.8 (SD: 23.5, 95% CI: 70.4–81.2). Gastrostomy tube insertion had no impact on the quality of life. Children with neurological impairment had significantly lower quality of life than those without neurological impairment. **Conclusion:** The global score of the HRQoL following Nissen fundoplication in this cohort of children was 75.8. Further studies to reduce the proportion of children who experience complications postoperatively in this setting are required.

Keywords: Gastro-oesophageal reflux disease, Nissen fundoplication, quality of life

Introduction

Gastro-oesophageal reflux (GER) is the retrograde passage of gastric contents into the oesophagus from the stomach.[1,2] Reflux is considered a normal physiologic process in up to more than half of all infants, children and adults.[1,2] This becomes pathologic GER disease (GERD), when bothersome symptoms, esophagitis, extra-oesophageal complications and poor nutrition develop.[2,3] In children, the common features of GERD include failure to thrive, refusal to feed, hoarseness of the voice, recurrent vomiting, heartburn, chronic cough, irritability, wheezing and Sandifer syndrome.[4] About 2%–7% of parents of older children report that their children experience GER, while 5%–8% of adolescents report such symptoms.[4]

Health-related quality of life (HRQoL) depends on physical symptoms and the impact of a disease on mental, emotional,

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behavioural and school functioning. The HRQoL tool is a multi-dimensional measurement of domains associated with physical, mental, emotional and social functioning. The tool's main focus is on the impact of health status on quality of life.[5] GERD is a long-term illness associated with negative effects on quality of life.[6] A cross-sectional survey of 520 adolescents in Jakarta found that more than 60% had this negative effect due to disruption of their sports activities, inability to enjoy food and sleep disturbance.[7] The negative impact of GERD also extends to the caregivers.[8]

The goal of therapy in GERD is to eliminate symptoms and prevent complications and therefore improve the quality of life.[9] Management of GERD is multipronged and involves conservative, medical and surgical interventions.[3] Surgery is indicated in confirmed GERD when the conservative and medical approaches have been optimised and/or when there is confirmed anatomical disruption of the natural anti-reflux mechanism. The aim of anti-reflux surgery is to control symptom of GERD, prevent further complications and ultimately improve quality of life.[10-12] Nissen fundoplication is the most common procedure done in children with GERD.[10,13]

Evaluation of the impact of medical and surgical interventions aims to provide reliable evidence for better clinical decision-making, formulating recommendations, patient selection and counselling. Measurement of HRQoL and patient satisfaction is a key part of this evaluation. There has not been a much-documented focus on the impact of Nissen fundoplication and gastrostomy tube insertion on the HRQoL of children with GERD in our geo-economic region.

The primary objective of this study was to assess the quality of life of children <18 years of age with GERD who had undergone Nissen fundoplication alone or Nissen fundoplication and gastrostomy tube insertion in two tertiary private not-for-profit referral hospitals between 1 January 2010 and 31 December 2020 using the Paediatric Quality of Life Inventory. The secondary objective was to describe the complications associated with Nissen fundoplication and gastrostomy tube insertion.

Materials and Methods

Ethics

Ethical approval for this study was granted by the research and ethics review boards of the two hospitals and the Kenyan National Commission for Science, Technology and Innovation. Informed consent was obtained from the study participants (parents/caretakers). This was in the form of verbal consent recorded as an audio file via a telephone call. No participants were coerced or induced to participate in the study. Participation was voluntary and the participants were free to withdraw from the study at any point. All personal identifiers were removed from the data entered into Microsoft Excel. Only the researcher had access to the data collected in the questionnaires, data collection forms and audio recordings.

Study design

This was an observational retrospective cohort study on the HRQoL of children with GERD after Nissen fundoplication and gastrostomy tube insertion and the associated complications carried out at two private tertiary hospitals in Nairobi. The study covered a period of 11 years from 1 January 2010 to 31 December 2020. The study population included all children under 18 years of age with GERD who had Nissen fundoplication and gastrostomy tube insertion at the two tertiary hospitals. Exclusion criteria were guardians/caretakers/parents who could not communicate verbally in English. This was because the Paediatric Quality of Life Inventory questionnaire was in English and the study did not aim to translate the questionnaire into any other language. A total of 91 children had Nissen fundoplication in the two hospitals

Table 1: Demographic characteristics of the study participants (*n*=82)

Variable	Statistic
Age at surgery in months	Median 32 (IQR 13-32)
Current age in months	85.5 (IQR 40.0-125.0)
Gender: Males, *n* (%)	39 (47.6)
Gender: Females *n* (%)	43 (52.4)

IQR- Interquartile range

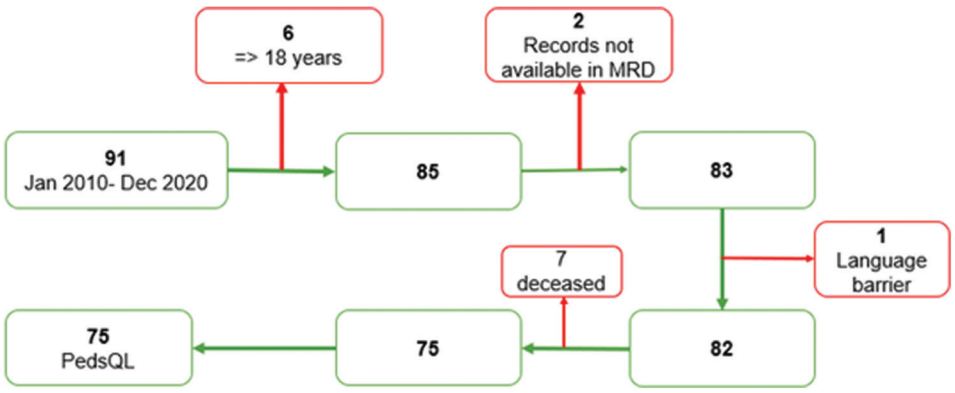


Figure 1: Sampling process

Table 2: Co-morbid conditions by age-groups

Comorbidity	Age-group					Total
	1-24 month	2-4 years	5-7 years	8-12 years	13-17 years	
Total	8 (9.8)	20 (24.4)	12 (14.6)	34 (41.5)	8 (9.8)	82
Neurological impairment						
Yes	4 (6.6)	17 (27.9)	10 (16.4)	25 (41.0)	5 (8.2)	61
No	4 (19.0)	3 (14.3)	2 (9.5)	9 (42.9)	3 (14.3)	21
Hiatal Hernia						
Yes	0 (0.0)	2 (11.8)	2 (11.8)	10 (58.8)	3 (17.6)	17
No	8 (12.3)	18 (27.7)	10 (15.4)	24 (36.9)	5 (7.7)	65

Table 3: Co-morbid conditions by gender

Comorbid condition	Gender		Total
	Male	Female	
Total	39 (47.6)	43 (52.4)	82
Neurological impairment			
Yes	30 (49.2)	31 (50.8)	61
No	9 (42.9)	12 (57.1)	21
Hiatal Hernia			
Yes	10 (58.8)	7 (41.2)	17
No	29 (44.6)	36 (55.4)	65

Table 4: Details of surgery

Open Nissen fundoplication, *n* (%)	75 (91.5)
Laparoscopic Nissen fundoplication, *n* (%)	7 (8.5)
Gastrostomy tube insertion, *n* (%)	56 (68.3)
No tube insertion, *n* (%)	26 (31.7)
Length of hospital stay in days, Median (IQR)	7 (5-12)
Duration of follow-up after surgery in months (*n*=79), Median (IQR)	24 (8-44)

IQR- Interquartile range

between 1 January 2010 and 31 December 2020. Six of these were excluded from the study because they were above 18 years by the time this study was conducted, the medical records of two could not be traced, while one was excluded due to language barrier. A total of 82 children were included in the study. Seven of these children had died by the time this study was being conducted, so the quality of life was assessed for the 75 patients who were alive [Figure 1]. Data collection on demographics, details of surgery and complications was done from the theatre registries and the medical records departments. The family telephone contact retrieved from the medical records was used to contact the parents/caretakers of these children. Informed consent was obtained and recorded as an audio conversation after the investigator had read the consent form to the study participant. Thereafter, the PedsQL™ Generic core questionnaire was administered via the same telephone call and responses were captured on paper.

Statistical analysis

Data analysis was done using SPSS version 26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Age was analysed and presented as median with interquartile ranges (IQRs). Gender was analysed in the form of percentages and frequencies. The overall HRQoL was generated as the total transformed sum of all the Likert items for all the different domains. HRQoL was summarised using mean and standard deviation (SD) with 95% confidence interval (CI) around the scores. HRQoL was also categorised as poor (0–25), medium (26–50), good (51–75) and excellent (76–100) and presented as frequencies and percentages. Complications and comorbidities were analysed as percentages and frequencies. Independent samples *t*-test was conducted to compare the means of HRQoL for gender, complications and comorbidities. Spearman's correlation was done for HRQoL and age.

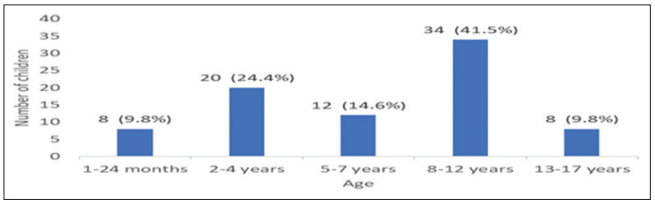


Figure 2: Distribution of participants by age group, $n = 82$

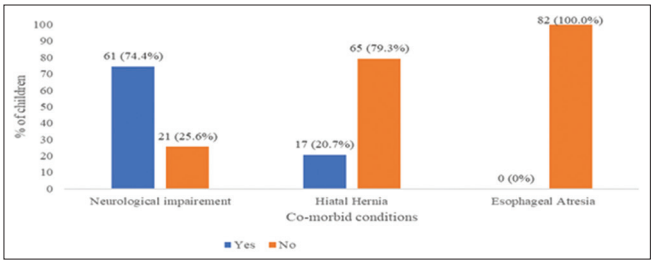


Figure 3: Comorbid conditions

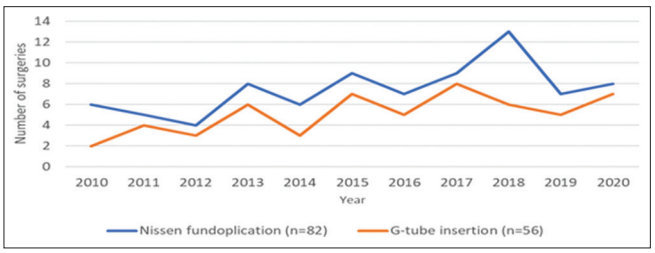


Figure 4: Trend of surgeries (Nissen fundoplication) during the study period

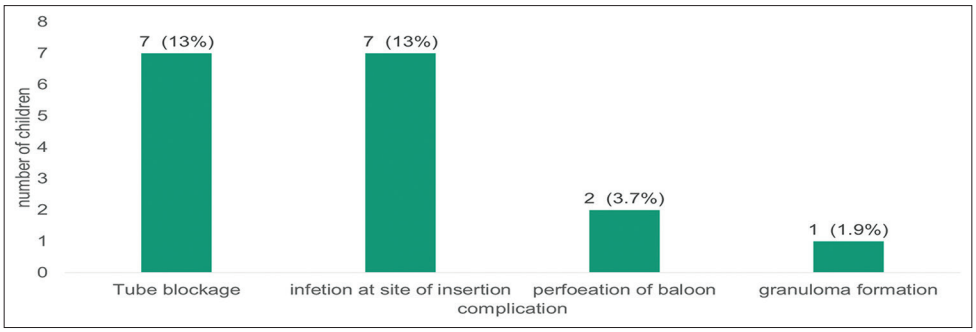


Figure 5: Complications related to gastrostomy tube insertion

Table 5: Health-related Quality of life

Domain	Poor	Medium	Good	Excellent	Mean (SD)	95% CI for the mean
Mean QoL	0 (0.0%)	14 (18.7%)	22 (29.3%)	39 (52.0%)	75.8 (23.5)	70.4-81.2
Physical health summary	15 (20.0%)	11 (14.7%)	11 (14.7%)	38 (50.7%)	68.0 (34.1)	60.1-75.8
Psychosocial health summary	7 (9.3%)	25 (33.3%)	43 (57.3%)	0 (0.0%)	79.6 (20.2)	75-84.3

SD: Standard deviation, CI: Confidence interval, QoL: quality of life

Table 6: Components of HRQoL

Domain	*n*	Mean (SD)
Physical functioning	75	66.8 (34.1)
Emotional functioning	75	92.2 (15.3)
Social functioning	75	73.1 (27.3)
Cognitive functioning	7	89.3 (28.4)
School functioning	53	70.6 (30.9)

Results

Demographic data

A total of 82 children who underwent surgery during the study period were included in the study; 43 (52.4%) of them were female and 39 (47.6%) were male. The estimated median age was 85.5 (IQR: 40.0–125.0) months while the median age at the time of surgery was 32 months (IQR: 13–32) months [Table 1 and Figure 2].

Comorbid conditions

Sixty-nine (84%) patients had one or more comorbidities [Tables 2 and 3; Figure 3]. Seventeen (21%) of the children had hiatal hernia and 61 (74%) had neurological impairment. Other comorbidities included diabetes insipidus, ulcerative esophagitis, oesophageal stricture, tracheo-oesophageal fistula and hypothyroidism. Two patients had congenital heart disease, while one had congenital rubella syndrome with multiple anomalies.

Nissen fundoplication and gastrostomy tube insertion

The highest number (13, 15.85%) of surgeries were conducted in 2018, while the least number (4, 4.88%) were conducted in 2012. Participants who had a concurrent gastrostomy tube insertion were 56 (68.3%). Seventy-five (91%) of the participants underwent open Nissen fundoplication, while 7 (9%) had laparoscopic Nissen fundoplication (LNF) [Table 4 and Figure 4]. The median duration of follow-up after the surgery was 24 (IQR: 8–44) months. The mean length of stay in the hospital was higher for the neurologically impaired patients by 1 day compared to neurologically normal, shorter by 3 days for the laparoscopy approach and the same for those with and without concurrent gastrostomy insertion.

Health-related quality of life

The global mean HRQoL score was 75.8 (SD: 23.5, 95% CI: 70.4–81.2)). The physical health summary score and psychosocial health summary score were 68.0 (SD: 34.1 95% CI: 60.1–75.8) and 79.6 (SD 20.2; 95% CI: 75–84.3), respectively. There was, however, no significant correlation between age and quality of life on Spearman's correlation test (rho: 0.195, $P = 0.94$). An independent-samples *t*-test was conducted to compare the mean quality of life for males and females. There were no significant differences (t [df] = 0.368, 73; $P = 0.714$) in the scores with mean score for males (M = 76.8, SD = 23.7) and females (M = 74.8, SD = 23.6). In comparing the mean quality of life for those with neurological impairment and those without neurological impairment, there were significant differences (t [df] = 10.3, 58.6; $P < 0.001$) in the scores with the mean score for those who were neurologically impaired (M = 67.3, SD = 22.0) lower than those without neurological impairment (M = 98.8, SD = 2.8). There was no significant correlation between the quality of life and duration of follow-up (short-term follow-up <6 months; long-term follow-up >6 months) and whether there was a concurrent g-tube insertion or not [Tables 5-9].

Complications

About 33% (27) of all children who had surgery had one or more complications [Table 10 and Figure 5]. A total of eight patients had fundoplication failure (defined by recurrence of symptoms or need for re-do fundoplication), five had neurological impairment, three had normal neurology and one had a hiatal hernia. Seven had open surgery, while one

Table 7: Health-Related Quality of Life by age-group

	Age-group					Total
	1-24 months	2-4 years	5-7 years	8-12 years	13-17 years	
HRQoL						
Poor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0
Medium	0 (0.0)	7 (50.0)	0 (0.0)	7 (50.0)	0 (0.0)	14
Good	1 (4.5)	4 (18.2)	6 (27.3)	9 (40.9)	2 (15.4)	22
Excellent	4 (10.3)	6 (15.4)	6 (15.4)	17 (43.6)	6 (15.4)	39

SD: Standard deviation

Table 8: Health-Related Quality of Life by gender

	Gender		Total
	Male	Female	
HRQoL			
Poor	0 (0.0)	0 (0.0)	0
Medium	7 (50.0)	7 (50.0)	14
Good	9 (40.9)	13 (59.1)	22
Excellent	20 (51.3)	19 (48.7)	39

Table 9: Independent Samples *t*-test

Variable	*n*	Mean HRQoL	SD	*P*
Neurological status				
Impaired	55	67.45	22.06	<0.001
Normal	20	98.79	2.81	
Gender				
Male	36	76.85	23.68	0.714
Female	39	74.84	23.57	
Duration of follow up				
Short term (< 6 months)	13	76.65	25.99	0.897
Long term (≥ 6 months)	62	75.65	23.99	
Gastrostomy tube insertion				
Yes	50	74.26	22.0	0.424
No	25	78.89	26.3	

Table 10: Complications related to Nissen fundoplication

	Wound infection	Dysphagia	Bloating	Failure	Re-do surgery
Yes	4 (4.9)	13 (15.8)	14 (17.1)	8 (9.8)	4 (4.9)
No	78 (95.1)	69 (84.2)	68 (82.9)	74 (91.2)	78 (95.1)

had laparoscopic surgery. The average time to failure was 32.8 months with a median of 29 months (IQR: 7.0–51.5) and SD of 28.8 months, while the mean, median and SD of age at the time of surgery was 21.8, 18.5 and 20 months, respectively. The numbers were not sufficient for meaningful statistical analysis. 4.9%, 15.8% and 17.1% were complicated with wound infection, dysphagia and bloating, respectively. Fifty-six children had gastrostomy tube insertion, out of which 7 (13.0%) each had tube blockage and infection at the tube insertion site. There was no significant correlation between neurological status and the complications.

Mortality

The overall survival at the time of the study was 91.5%, with a mortality of 8.5% (seven patients). The median time to mortality was estimated to be 5 (IQR: 2–23) months. Three (42%) were male, while 4 (58%) were female. Six (86%) of the seven children had neurological impairment.

Discussion

This study sought to assess the quality of life of children with GERD after Nissen fundoplication and the associated complications. The main findings were a global HRQoL score of 75.8 and a complication rate of 33%, with neurological impairment being the most common comorbidity at 74%.

The number of children who had Nissen fundoplication at the two hospitals during the study period was less compared to studies in other regions. This could be due to low referral rate and surgical uptake within the region, probably due to fewer specialists dealing with the subset of children at risk of GERD. Both hospitals have a combined workforce of five paediatric surgeons. The low numbers could also be from lack of awareness by the caretakers on the availability of these services. A 2005 retrospective cohort study in Atlanta, Georgia, recruited 456 patients over a period of 5 years which is more than four times the size of our study sample.[13] More than half of the children who were included in this study were female. This is in contrast to the Atlanta study, which had more males than females.[13] The mean duration of follow-up for this study (30.5 months) compares well to the duration of follow-up found in the study by Mauritz *et al.* (36.2 months) but less than that in the study by Stellato *et al*.[13,14]

Younger children had Nissen fundoplication in this study compared to other centres. This could be due to the low threshold for doing fundoplication in our study centres as compared to other areas. In a cost–utility analysis of fundoplication versus medical therapy for GERD, laparoscopic fundoplication was shown to have a higher initial cost. However, the long-term analysis showed that LNF was eventually the most cost-effective treatment alternative.[15,16] Mauritz *et al*. reported a mean age of 6 years.[17] The average age at surgery in the study by Stellato *et al*. was 7.3 years.[14] About 84% of all children in this study had a comorbid condition in addition to GERD. These findings are similar to the results of studies from other areas in the world.

In a retrospective review of the outcomes of anti-reflux surgery in the paediatric population, Koivusalo and Pakarinen observed that 72% of the participants had an underlying disorder.[18] These comorbid conditions make the children with reflux more likely to need Nissen fundoplication and compared to the ones who just have pure GERD. Neurological impairment is a common underlying condition in most studies. In this study, more than two-thirds of the children had neurological impairment, mostly cerebral palsy. This is much higher when compared to a prospective review by Stellato *et al*., in which a fifth of the participants had neurological impairment.[14] The number of children who had Nissen fundoplication over the duration of the study (11 years), with an average of 7.4 cases per year is less than reported from other centres around the world. In a hospital in Atlanta, Georgia, the average number of fundoplication that were done over a 5-year period was 91 cases per year.[13] This difference could be because of the differences in the health-seeking behaviour in the populations that are served by these facilities. A majority of the Nissen fundoplication in our study were done by the open method, in contrast to the current trend in the developed world where surgeons have embraced LNF.[13,17] This could be due to the preference of the study centres, but also it could result from the limited access to paediatric laparoscopic surgery.

Gastrostomy tube insertion at the time of fundoplication provides a safe route for feeding. This is usually in patients with clinical evidence of unsafe or inefficient swallowing mechanism. More than two-thirds of the children in this study had a concurrent gastrostomy tube. The review by Pilli *et al*. found 100% tube insertion in one of the studies and 50% in two studies.[19] The number of concurrent gastrostomy tube insertion has progressively increased over the years with increasing evidence of its benefits in selected patients.

This study is amongst the few studies that have used the validated and standardised Paediatric Quality of Life Inventory. The global score of 75.8 after surgery was lower than the findings in a 2017 study by Mauritz *et al*. of 82.5.[17] The physical health and psychosocial health summary scores were about 20 points lower than those from the Mauritz study. This could be a result of the different socio-demographic factors and the rates of comorbidities.[17] Neurologically impaired children have a poorer quality of life than those who are neurologically normal. This finding was replicated in this study. Of all the different domains of HRQoL, emotional functioning had the highest mean score (92.2%), while school functioning had the least mean score (70.6%). The poorer score in school functioning is likely because a majority of these children have cerebral palsy which negatively affects their social and intellectual interactions. The rigid education systems in low-income countries may present a challenge to children who are living with chronic conditions and intellectual deficits. This is further magnified by lack of the human and infrastructure resources in low-income regions.

The rate of complications related to Nissen fundoplication and gastrostomy tube insertion was 33%, which was about five times as high as that reported by Esposito *et al*. (6%) and Rosales *et al*. (6%).[10,20] This rate could have been much higher if there was a standard format/tool of following up these patients and documenting the complications. Most (90.2%) of the participants had an intact Nissen fundoplication with a failure rate of 9.8%. All the failures occurred in open Nissen fundoplication. This rate was high when compared to a 2014 study by Lopez-Fernandez *et al*. in which 2.5% of the respondents had a failed fundoplication.[21] In the Pilli *et al*. study, 12% of the patients required re-operation.[19] Stellato *et al*. reported a failure rate of 39% after 5 years.[14] The differences that were observed in these studies could have occurred as a result of lack of a standardised and universal definition of failure. Patient selection can also account for these differences, with centres that select patients who are likely to have a better outcome after surgery having low failure rates.

Conclusion

The HRQoL of children with GERD post-surgery was excellent for most patients. Younger children had Nissen fundoplication in the two centres during the study period with more females than males. Age and gender did not have a significant effect on the quality of life. Majority of children had a concurrent gastrostomy tube insertion. This did not have a significant influence on the HRQoL. Most patients had comorbidities, with neurological impairment being the most common. Children with neurological impairment had significantly higher rates of mortality and poorer HRQoL. There was a higher rate of complications related to surgery compared to some of the similar studies. The rate of failure of the Nissen fundoplication was low. This being a retrospective study, it was not possible to assess the quality-of-life pre-surgery.

Recommendations

1. A prospective study is recommended to compare the quality of life before and after the Nissen fundoplication and to further understand the challenges faced by this population.

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Conflicts of interest

There are no conflicts of interest.

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