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Research Article
Clinical Utility of Paediatric Endoscopy and Correlation between Endoscopic and Histological Findings

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Background. The number of gastrointestinal endoscopies in children is rapidly increasing without evidence of a parallel increase in disease burden. The positive yield of paediatric endoscopies outside certain conditions is small but the impact of normal "negative" results on clinical management is poorly studied. Routine mucosal biopsy in all paediatric endoscopies is common practice. We aimed to assess the impact of normal endoscopy on patient care, defined by symptom improvement and discharge from hospital follow-up, and calculate the correlation between endoscopic and histological findings. *Methods.* Retrospective analysis of the first diagnostic endoscopy in children (2015–2019) from Evelina London Children' Hospital, in London, UK. Endoscopy and histology findings were recorded. Symptoms and follow-up were reviewed up to six months after the endoscopy. *Results.* 362 children were included; 46.7% were female. Mean age 10.5 (±4.1) years, 66.3% underwent OGDs, and 33.7% underwent combined OGD and colonoscopies. 72.9% of endoscopies and 57.2% of all biopsies were normal. There was a strong positive correlation between endoscopic findings and biopsy results (phi 0.68 $p < .001$). 31.2% of children reported symptom improvement and were discharged from further follow-up after undergoing endoscopy after 1.9 (±1.5) clinics, phi 0.2 $p < 0.001$ between normal endoscopy and discharge. *Conclusion.* Negative endoscopy appears to influence clinical management and discharge from hospital follow-up in about a third of children undergoing endoscopy. The practice of routine biopsies in all paediatric endoscopies should be considered due to a strong positive correlation between normal endoscopies and normal biopsies.

1. Introduction

Paediatric endoscopies, first described in the 1960s, are often used as a diagnostic tool for children with gastrointestinal complaints [1]. The number of endoscopies performed in children is increasing but there is no epidemiological evidence of a parallel increase in disease burden [2, 3]. Many factors can explain this rise; paediatric gastroenterology is a well-established specialty with structured training pathway producing a steady increase in endoscopy competent paediatricians [4]; increased procedure safety and reduced incidence of serious complications coupled with improved management of complications may have changed both medical practitioners and the wider population' attitude towards the "invasiveness" of endoscopy [5, 6]. It can also be difficult

to localise children's symptoms to the gastrointestinal (GI) tract, and they may present with nonspecific symptoms such as anorexia and failure to thrive [7].

It is a routine practice to perform tissue biopsies during paediatric endoscopies even in the absence of gross abnormalities to minimise the risks of repeated procedures and anaesthetics [6]. However, processing and reporting biopsies can contribute to overall financial cost of the procedures considering that more than half of the patients that undergo endoscopy are reported to have no endoscopic or histological abnormalities. [7] [8–10].

Colonoscopies are considered more invasive than oesophagogastroduodenoscopies (OGDs); they require bowel preparation and longer anaesthetic time; they are performed less frequent than OGDs in most paediatric centres with the

aim to investigate specific disorders, but a large proportion of paediatric colonoscopies were also reported as normal [11].

The impact of normal "negative" endoscopy on patient's management is unclear and poorly studied. Negative investigations can prove valuable either by leading to a change in management by preventing unnecessary investigations where the disease is nonorganic or by excluding suspected disorders and offering reassurance [12].

The European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) have produced joint guidelines regarding the indications for diagnostic OGDs and colonoscopies based on expert consensus and low quality evidence [13], but there remains a wide variation in the number of endoscopies performed and their indications in paediatric clinical practice.

In this study, we aimed to assess the yield of the first diagnostic endoscopies (OGDs/colonoscopies) in children and their impact on clinical outcome defined by symptom improvement and discharge from hospital follow-up. We also assessed the correlation between endoscopic and histological findings and their impact on the defined clinical outcomes.

2. Methods

Retrospective data was collected from endoscopy and clinical databases of children below the age of 18 years from June 2015 to July 2019 at Evelina London Children' Hospital, a tertiary paediatric hospital in London, UK. We included first diagnostic endoscopies (OGD and colonoscopies). Subsequent endoscopies, therapeutic procedures, and children with incomplete medical records were excluded. Demographic data, clinical indications, endoscopy and histology findings, number of clinic attendance, and clinical outcomes up to six months postendoscopies were recorded to determine if the child symptoms have improved and/or they were discharged from hospital follow-up. Endoscopic and microscopic abnormalities were identified, localised, and recorded; minor isolated histological changes (such as mild basal cell hyperplasia or mild dilatation of intracellular space in the absence of clinical symptoms) were disregarded. Biopsies were obtained from all included children and were taken based on the anatomic locations in the gastrointestinal tract.

The project was registered with our institution clinical governance board as an audit review of clinical practice, and an ethical review was not required.

Descriptive statistics were used, frequencies for categorical and mean and/or median with standard deviation (±SD) and/or inter quartile range (±IQR) for continuous values. Chi-squared tests were used to investigate potential associations and the phi; Pearson's correlation coefficient was calculated (as appropriate) to quantify the strength of associations. 95% confidence interval (CI) was used where applicable, and $p < 0.05$ was regarded as statistically significant. Statistical analysis was performed using the IBM© SPSS software package version 27.

TABLE 1: Background and demographic data.

Parameter	Results
Number of children included	362
Female (%)	46.7%
Median age (IQR) years	11.5 (7-14)
Procedures (%)	
OGDs	66.3%
OGDs and colonoscopies	33.7%
Symptoms (N) (%)	
Abdominal pain	195 (34.3)
Diarrhoea	80 (14.1)
Rectal bleeding	56 (9.8)
Constipation	57 (10)
Suspected coeliac	48 (8.4)
Gastroesophageal reflux	45 (7.9)
Vomiting	88 (15.5)
Number of visits to discharge, mean (±SD)	1.9 (±1.5)
Number of visits prior to endoscopy (±SD)	1.3 (±.9)

3. Results

A total of 362 children were included; 46.7% were female. Median age 11.5 (interquartile range 7-14) years, 66.3% children underwent OGDs, and 33.7% underwent combined OGD and colonoscopies. The main presenting complaints and demographic profile are detailed in Table 1. All children had the procedure as day case attendance, and we did not record any complications during endoscopy or after taking biopsies. 72.9% of endoscopies were normal, and 57.2% of all biopsies were reported as histologically normal ($p < 0.001$).

Phi correlation coefficient between endoscopy and biopsy results was 0.68, $p < .001$, suggesting a strong positive correlation between endoscopic findings and biopsy results. The relative risk of normal biopsies was 37.37 (95% CI 9.47-147.52) while the relative risk of abnormal histology after a normal endoscopy was 0.23 (95% CI 0.18-0.29). The calculated sensitivity of endoscopy when comparing to biopsy results was 62%, and specificity was 99% leading to a positive predictive value of 98% and a negative predictive value of 78%.

On average, children attended 1.9 (±1.5) clinics prior to being scheduled for endoscopy in both groups (OGDs and OGD/colonoscopies) (Figure 1). 31.2% of children reported symptom improvement in their subsequent clinic visits and were discharged from further follow-up within 6 months after undergoing endoscopy. Percentage of children discharged based on their main presenting symptoms and the odd ratio of discharge is summarized in Table 2. When discharged, 75.5% of children were discharged after two clinic visits postendoscopy and 87.3% after three clinic visits. There was a weak positive (phi 0.2, $p < 0.001$) correlation between endoscopy and discharge at 6 months (odds ratio 3.0, 95% CI 1.7-5.4). There was also a weak (phi 0.29, $p < 0.001$) correlation between histology results and discharge at 6 months (odds ratio 4.1, 95% CI 2.46-6.89). The
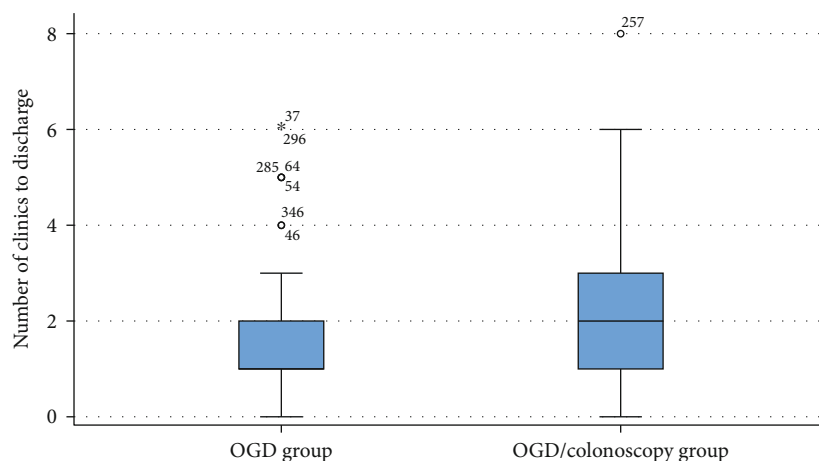
FIGURE 1: Number of clinic visits prior to discharge in the two groups (OGDs and OGD/colonoscopies).

TABLE 2: Discharge percentage based on main presenting complaints and the odds ratio.

Symptom	Percent at discharge	Odds ratio (95% CI)	p value
Abdominal pain	41.4%	1.5 (1-2.4)	0.08
Diarrhoea	31.6%	0.74 (0.4-1.3)	0.29
Rectal bleeding	33.3%	0.83 (0.4-1.6)	0.64
GORD	34.9%	0.9 (0.5-1.8)	0.87
Constipation	40%	1.2 (0.7-2.1)	0.65
Vomiting	36.9%	1.0 (0.6-1.7)	1.0

percentage of children discharged after normal endoscopy and after normal histology is shown in Figures 2 and 3. In terms of safety, there were no complications reported in any of the OGDs or colonoscopies, and all were performed under general anaesthesia as day cases.

4. Discussion

Many studies have documented variable yields of endoscopies (OGDs and colonoscopies) in children, most focusing on positive outcomes that lead to change of clinical management [10, 14, 15]. In the absence of evidence-based indications for paediatric endoscopies, gastroenterologists are often left to their own device to select children who may benefit from endoscopies. The increased referrals to paediatric gastroenterology and the overall increase in burden of gastrointestinal disorders in children can strain the diagnostic pathways [16]. Many paediatric investigations are frequently used to reassure families that a suspected diagnosis is ruled out as a cause for their children's symptoms. Endoscopies are frequently considered both to rule in and rule out specific disorders.

Similar to previous studies, our findings showed more OGDs were performed than combined OGD/colonoscopies, and the indications for the procedures in our institution were in line with international guidance and similar to previously published paediatric studies [8, 17, 18]. In our practice, we did not perform endoscopies in children with

symptoms suggestive of functional disorders as defined by the Rome criteria [19, 20].

27.1% of endoscopies in this study were abnormal, and 42.8% of all biopsies were histologically abnormal; this is higher than previous reports and may reflect strict patient selection in our institution. As per recognised paediatric practice, biopsies are routinely obtained in paediatric endoscopies due to documented discrepancies between endoscopic and histological findings and also to minimise the risks of repeating procedures that are commonly involve sedation and/or general anesthetics [6]. Biopsies can also identify histological abnormalities not visible endoscopically. However, taking biopsies can be time consuming and the subsequent preparation and assessment will add to the overall cost of an already expensive procedure [21–23].

In our cohort, there was a strong positive correlation between endoscopic and histological finding, phi 0.68, $p <$ .001, with relative risk of normal biopsies of 37.37 (95% CI 9.47-147.52) while the relative risk of abnormal histology after a normal endoscopy was 0.23 (95% CI 0.18-0.29). The positive predictive value of 98% suggests the chance of normal histology after a normal endoscopy is very high, while the negative predictive value of 78% suggests the chance of abnormal histology after a normal endoscopy is considerably small.

Outside inflammatory bowel disease and eosinophilic oesophagitis, the commonest histological abnormalities in OGDs are related to GORD [7, 24], which has a poor association between symptoms and histology in paediatric patients [25]. This, together with our findings, should raise the question of whether routine biopsies during paediatric endoscopies are necessary or required. If paediatric endoscopy is to become a routine investigation tool, all efforts should be made to reduce cost and minimise burden to healthcare systems.

The yield of diagnostic procedures should translate to change in management with the aim to improve treatment efficacy [26]. The outcomes of positive endoscopies in patient' care is well documented in children and adults but the outcomes of negative endoscopies are poorly scrutinised. The values of negative endoscopy can be summarised into
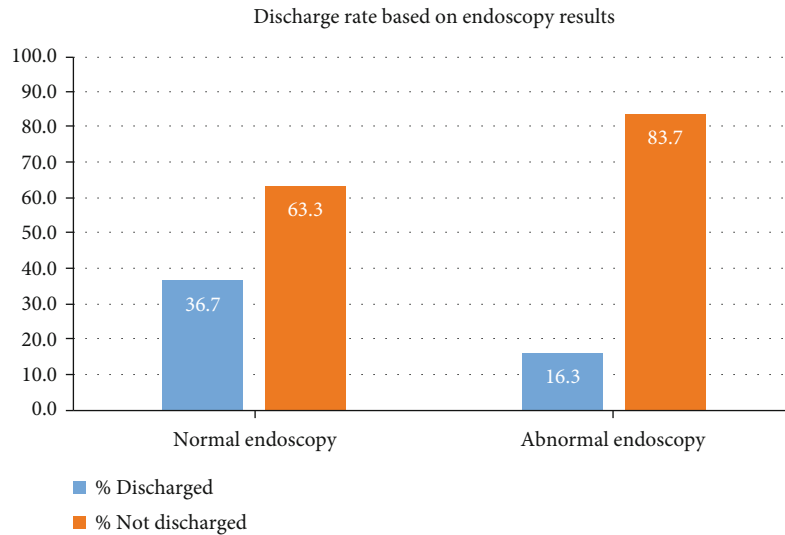
Discharge rate based on endoscopy results

FIGURE 2: Discharge rate and endoscopy results.
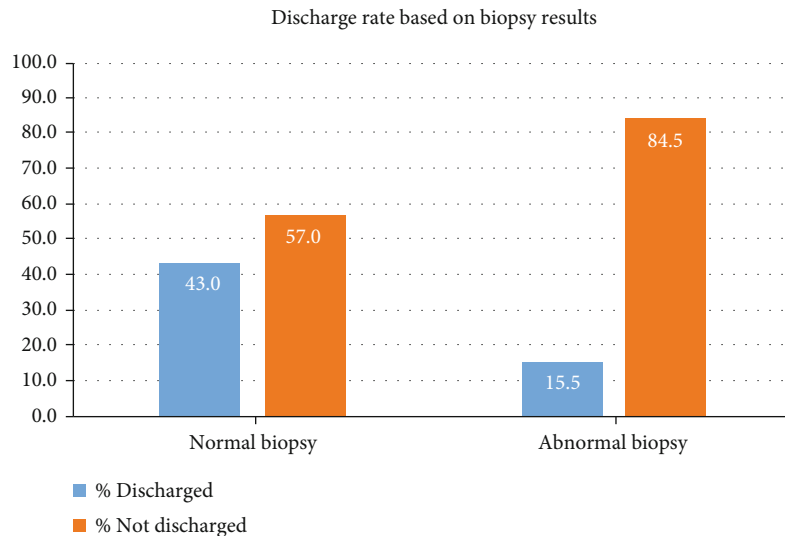
Discharge rate based on biopsy results

FIGURE 3: Discharge rate and histology results.

three main themes; first, it can rule out conditions to help establish disorders that can only be diagnosed by exclusion. Second, it may provide reassurance, hence improve patient quality of life and reduce the overall consumerism of resources. Finally, the wider uptake of endoscopy will invariably detect conditions that otherwise could be missed. Negative endoscopies can thus be considered cost-effective in population terms [27, 28].

From our results, 36.7% of children who have had negative endoscopy reported symptom improvement and were discharged from hospital follow-up within 6 months after the procedure odds ratio 2.29 (95% CI 1.35–3.89). Relative risk for discharge after a normal endoscopy was 1.2 (95% CI 1.09–1.4), and relative risk for ongoing follow-up was 0.54 (95% CI 0.36–0.81). 75.5% of children were discharged after 2 clinic visits following the endoscopy, and most of the children who were discharged underwent endoscopy after

one clinic visit. Normal endoscopies can be a factor to influence discharge from hospital follow-up by providing reassurance to some families. It can also provide an indirect cost saving/benefits by reducing time off work taken by parents/guardians to attend hospital appointments with their children and reduction in time away from school for the child.

The study had several limitations. Children can be discharged from hospital follow-ups for many reasons; there was no nonendoscopy control group to compare the findings but we included all children who underwent endoscopies including the group who require long-term follow-up (such as coeliac and inflammatory bowel disease). This will minimise selection bias and provide a diverse cohort to represent an average gastroenterology service. As a retrospective study, the available data depended on the information available in clinical records. The lack of standardisation with regard to recording data such as the endoscopic appearance of the

mucosa led to inevitable variability amongst physicians which could have affected the comparability of results; hence, we did not grade the degree of inflammation but we reviewed and recorded the results as normal and abnormal. We also did not look at disease-specific clinical outcome measures, but we reviewed clinical records up to 6 months following endoscopies to ensure direct procedural impact on the children's symptoms.

5. Conclusion

This study, to the best of our knowledge, is the only paediatric study to look at the clinical outcomes OGDs and colonoscopies in children in relation to symptom improvement and discharge from hospital follow-up; over half of the patients undergoing first diagnostic endoscopy had normal results. There was strong positive correlation between endoscopic and histological findings. We recommend gastroenterologists to consider the value of routine biopsies from endoscopically normal mucosa. A normal endoscopy result has influenced the discharge from hospital follow-up in the 6 months following the procedure. Among children who were discharged from follow-up, two thirds were discharged after two clinic visits. In this cohort, endoscopies in children were safe, and normal results appeared to offer reassurance and facilitated children discharge from hospital follow-up, potentially reducing the overall burdens to healthcare systems.

Data Availability

Data is available upon reasonable request from corresponding author.

Conflicts of Interest

None of the authors has any conflict of interest to declare.

Acknowledgments

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