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Research Article

Paediatric Gastrointestinal Endoscopies: Correlation between Macroscopic and Histological Findings

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Abstract

Introduction: Paediatric gastrointestinal (GI) endoscopies are frequently performed to assist with the diagnosis of abdominal symptoms. In children, routine biopsies are taken during the endoscopy which may exert extra cost pressure on the National Health Service (NHS). These procedures also produce much single use waste and have a negative impact on the environment. We aimed to explore whether diagnoses can be made based on macroscopic findings only or if routine biopsies are required for histological confirmation.

Methods: A retrospective cohort study was carried out, comparing macroscopic and histological findings during GI endoscopy in children. Multiple statistics were produced to assess how well the findings correlated.

Results: Data was collected on 125 procedures including 98 oesophagogastrodoudenoscopies (OGD) and 27 colonoscopies on 100 children aged 3-18 years with the mean age of12 years. Correlation percentage for OGD, colonoscopy and combined OGD+Colonoscopy was 72.45%, 96.30% and 77.6% respectively. Cohen's kappa for OGD, colonoscopy and combined OGD + Colonoscopy was 0.3, 0.924 and 0.497 respectively. Sensitivity + Specificity for OGD, colonoscopy and combined OGD + Colonoscopy were 1.262, 1.917 and 1.462 respectively.

Discussion: The correlation noted between macroscopic and histological findings is slightly below that recommended for a test to be considered reliable and accurate, so routine biopsies during paediatric GI endoscopies should still be recommended. Although, high correlation in colonoscopy could indicate that routine biopsies may not be required during the procedure, precise histological diagnosis of conditions like inflammatory bowel disease is of paramount importance from management perspective.

Keywords: Oesophagogastrodoudenoscopy; Colonoscopy; Correlation; Children; Histology; Macroscopy

Introduction

Paediatric gastrointestinal (GI) endoscopy has been available since the 1970s [1]. The procedure is mostly used for diagnostic purposes but may also be carried out for therapeutic indications, such as foreign body removal or polypectomy [1]. There are many indications for diagnostic GI endoscopy, such as persistent abdominal pain, suspected gastro-oesophageal reflux disease, recurrent vomiting, blood loss from the rectum, confirming/ruling out coeliac disease, inflammatory bowel disease, helicobacter pylori gastritis/duodenitis and eosinophilic esophagitis [2,3].

When an adult undergoes an endoscopy, a biopsy is usually only taken is an abnormality is observed. On the other hand, in paediatric GI world, it's a common practice to take tissue samples for histology during oesophagogastroduodenoscopy (OGD) and colonoscopy [4]. Combination of macroscopic findings during the procedure and histology results are utilised to confirm or refute a diagnosis. During OGD, samples are taken from oesophagus, stomach and duodenum. A complete ileo-colonoscopy can be difficult to achieve in 100% of the cases with young age, poor bowel preparation, and florid colitis increasing the risk of perforation and loop formation being a few contributory factors [5].

It is important to recognise whether taking a biopsy from visually normal mucosa can be justified as it increases the risk of complications in addition to increasing the cost [6]. On the other hand, not taking biopsies will reduce the risk of complications as well as procedure time. Therefore, consideration should be made before performing a GI endoscopy in children, and the benefits should always outweigh the associated risks [7]. Although paediatric GI endoscopies have been available for at least 50 years, the procedure is relatively expensive as it requires highly trained endoscopy staff and costly equipment. Moreover, in the developed world, paediatric GI endoscopists prefer performing the procedure in paediatric theatres in the presence of paediatric anaesthetist under general anaesthesia [2,7].

GI endoscopy is a highly resource intensive procedure which makes significant contribution to greenhouse gas emissions and waste generation [8]. Endoscopy is the second highest waste producing department per clinical procedure due to high volume of patients requiring the procedure, use of single-use items, resource-heavy decontamination and water consumption in addition to patient/staff travel [8]. Being able to reduce the number of endoscopies being performed would therefore reduce the impact on environment pollution. While considering ways to decrease the number of endoscopies being performed, it cannot be forgotten that an endoscopy that yields no diagnosis can help put the patient and family at ease and may halt further unnecessary procedures and appointments [8]. A high number of referrals for endoscopy

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increases the wait list and has high-cost implication which puts further pressure on already strained National Health Service (NHS) finances.

Exploring the correlation between its macroscopic and histological findings during paediatric GI endoscopy is useful. If there is a high correlation then it can negate the need for routine biopsies when the macroscopic findings are normal. This would save time, reduce the costs, and patient anxiety that can be caused by taking routine biopsies from normal GI mucosa. On the other hand, if there is a poor correlation between macroscopic and histological findings, it would justify the collection of routine biopsies even when there are no macroscopic abnormalities4. The objective of this study was to evaluate the correlation between macroscopic and histological findings during paediatric GI endoscopies carried out in a large District General Hospital setting in the United Kingdom (UK).

Methods

This retrospective cohort study was carried out at the University Hospitals of Derby and Burton NHS Foundation Trust (UHDB NHS FT) in the UK. All patients under 18 years of age at the time of the procedure (OGD and/or colonoscopy) between February 2021 and December 2022, and having had at least one biopsy taken were included in the study. A total of 119 paediatric patients were identified. However, complete electronic records could not be accessed for 19 patients. Hence, anonymised data was collected for 100 patients undergoing paediatric GI endoscopy by accessing Lorenzo, the electronic patient record system used at the UHDB NHS FT.

In addition to demographic statistics, indications for the procedure were noted. Macroscopic and histological findings were recorded, and their correlation was ascertained. Impact of final diagnosis on patient management was determined using subsequent clinic consultation or correspondence with the family.

All statistical analysis was carried out on Microsoft Excel and GraphPad Prism, and all graphs were produced using GraphPad Prism. Descriptive statistics were produced to describe the population characteristics. The statistics used to assist with looking at correlation were sensitivity, specificity, positive predictive value (PPV) and negative predicative value (NPV) [9,10]. The following definitions were used to calculate the statistics:

- True Positive (TP) - when there was positive macroscopic finding during the endoscopy with abnormal histology.
- True Negative (TN) - when there was normal GI mucosa during the endoscopy with normal histology.
- False Positive (FP) - when there was positive macroscopic finding during the endoscopy but normal histology.
- False Negative (FN) - when there was normal GI mucosa during the endoscopy but abnormal histology.

Cohen's kappa, a measure of concordance and agreement, is a robust measure of correlation as it considers the possibility of the agreement occurring by chance [11]. It was calculated from the online calculator using the following formula [12].

Probability of agreement - Probability of random agreement

1 - probability of random agreement

It is recommended, and widely accepted, that correlation percentage should be above 80% for a diagnostic test to be acceptable [13]. Another statistic to look at is Sensitivity + Specificity. If it is above 1.5 then the test can be considered useful [14]. For Cohen's kappa, there are many ways to interpret it but the most common one is the scale below [15].

- Kappa < 0: No agreement
- Kappa between 0.00 and 0.20: Slight agreement
- Kappa between 0.21 and 0.40: Fair agreement
- Kappa between 0.41 and 0.60: Moderate agreement
- Kappa between 0.61 and 0.80: Substantial agreement
- Kappa between 0.81 and 1.00: Almost perfect agreement

It is becoming widely accepted that to place confidence in a test, it should have a kappa value over 0.613.

Results

A total of 125 procedures were performed in 100 patients between February 2021 and December 2022 with 98 (78%) OGDs and 27 (22%) colonoscopies. 25 (20%) patients underwent both the procedures. The mean age of patients was 12 (±3.6) years, with the mode being 15 years. The youngest patient was 3 years old and the oldest was 18 years of age (Table 1). Table 2 outlines indications for GI endoscopy with possible coeliac disease as the most common reason for the procedure. Many of these patients had multiple reasons for undergoing the procedure.

Table 1: Demographic details (N = 100).

Demographic Details	% of total (N = 100)
Sex	
Female	0.58
Male	0.42
Age	
0-8 years	0.19
9-12 years	0.25
13-14 years	0.25
15-18 years	0.31

Table 2: Reason for GI endoscopy (N = 100).

Reason for GI endoscopy	% of total (N = 100)
Raised tTG antibodies	0.29
Abdominal pain	0.19
Other	0.1
Rectal bleeding	0.08
Nausea	0.06
Reflux	0.05
Rumination	0.05
Epigastric pain	0.05
Diarrhoea	0.04
Dysphagia	0.03
Vomiting	0.03
Dyspepsia	0.03

The overall rate of positive macroscopic findings was 25% and the overall rate of positive histological findings was 39% (Table 3). Relatively poor correlation during OGD is likely to reflect many patients undergoing the procedure for the confirmation of coeliac disease where macroscopic findings are likely to be normal as opposite to histology and the presence of mild, non-

specific gastropathy in biopsies from gastric antrum with normal macroscopy at the time of procedure. On the other hand, there was a good correlation between macroscopic and histological findings during colonoscopy.

Table 3: Positive macroscopic and histological findings in OGD, Colonoscopy, and GI endoscopy (combined OGD and Colonoscopy).

	OGD	Colonoscopy	GI endoscopy
Macroscopic	0.1531	0.5926	0.248
Histological	0.3469	0.5556	0.392

Correlation, sensitivity, specificity, PPV, NPV and Cohen's kappa for all patients who had OGD, colonoscopy and GI endoscopy (combined OGD and Colonoscopy) is shown in Table 4, Figure 1A and B. The overall correlation for positive and normal findings for GI endoscopy (combined OGD and Colonoscopy) was 77.60% with a Cohen's kappa value of 0.497 which shows moderate agreement. Correlation was slightly lower for OGD at 72.45% with a Cohen's kappa value of 0.300 which shows fair agreement. In contrast, colonoscopy had a very high correlation at 96.30% and a Cohen's kappa of 0.924 which depicts almost perfect agreement.

Table 4: Correlation, sensitivity, specificity, PPV, NPV and Cohen's kappa for all patients that received OGD, colonoscopy and GI endoscopy.

	OGD	Colonoscopy	GI endoscopy
Correlation	0.7245	0.963	0.776
Sensitivity	0.324	1	0.531
Specificity	0.938	0.917	0.934
PPV	0.733	0.938	0.839
NPV	0.723	1	0.755
Cohen's kappa	0.3	0.924	0.497

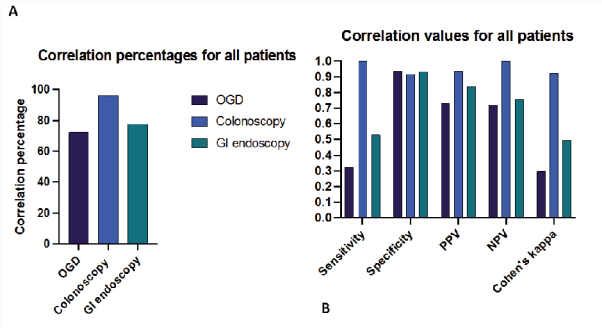

Figure 1: A) Correlation percentages for all patients who underwent OGD, colonoscopy or GI endoscopy. B) Sensitivity, specificity, PPV, NPV and Cohen's kappa values for all patients who underwent OGD, colonoscopy or GI endoscopy.

Sub-analysis was performed on different characteristics based on age and sex for patients undergoing OGD, colonoscopy, and GI endoscopy (OGD and Colonoscopy combined) as outlined in Table 5-7 respectively.

Another important statistics to look at when deciding if a clinical test is useful is the value of "sensitivity + specificity" (Table 8). Colonoscopy produced consistently high sensitivity + specificity values when compared with OGD and combined GI endoscopy.

Discussion

The results of this study indicate correlation discrepancy between macroscopic and histological findings in paediatric GI endoscopies. Overall, the correlation was 77.60%, sensitivity + specificity was 1.462, and Cohen's kappa was 0.497. While these are all below the recommended values for a test to be considered reliable, correlation and sensitivity + specificity are very close to the recommended values of 80% and 1.5 respectively. However, when rounded to one decimal place, sensitivity + specificity hits the recommended value of 1.5. A larger sample size could help bring up the value of these statistics and reduce the effect of anomalies.

A study by Dahshan and Rabah has quoted a correlation value of 63.8% [16]. A large study looking at duodenal biopsies with sample size of 1793 patients found correlation of 55.6% [16] while another study looking at 1000 patients mentioned final correlation value of 69.9% when looking at biopsies from all locations [4]. Figure 2 visually represents comparative results between this study and two large studies by Sheiko et al. and Ali et al. [4,17].

When compared to Sheiko et al., our results are very similar in most categories apart from sensitivity and specificity. Our study has a significantly lower sensitivity but higher specificity. There may be a discrepancy in sensitivity and specificity as stand-alone values but when looking at sensitivity + specificity, both studies again produce similar values. Sensitivity + specificity for Sheiko et al. are 1.352 which is close to our finding of 1.262 during OGDs. In contrast, comparison with a study conducted in Egypt by Ali et al revealed significant difference in NPV and correlation percentage.

A number of studies with small sample size and methodological limitations have quoted much lower values of correlation between macroscopic findings during OGDs and histology [18-22]. Research is sparse in paediatric patients when looking at colonoscopy correlation. Kovach et al. looked at the initial colonoscopy of patients with presumed ulcerative colitis and observed more severe changes confirmed on histology when compared to macroscopic assessment made by the endoscopist with correlation being described as weak [23]. Other studies also depict relatively poor correlation in patients with ulcerative colitis, necessitating the need to continue with the practice of routine biopsy collection [24-25].

The correlation percentage seen in our study is higher than previously published research. A number of previous studies have mostly looked at OGD correlation or have only looked at one biopsy region or a specific diagnosis. Some of these studies have very small sample size or have been carried out over 30 years ago which makes the results less reliable. Higher correlation in our study is likely to reflect an improvement in the endoscopy equipment. As a result, endoscopists have the ability to see more clearly into the GI tract during the procedure. It could also demonstrate an impact of longer waiting times during COVID-19 pandemic causing diseases to become more advanced and therefore more likely to be visible macroscopically rather than merely on histology. A study by Ahmed et al. looked at the correlation between predicted and documented findings in paediatric GI endoscopy. It found that in 84% of cases, the predicted findings by the clinicians were similar to what was documented macroscopically during the procedure [7]. This demonstrates that many clinicians can predict what the results of an endoscopy will be before it is performed. This implies a possible overuse of GI endoscopy as a procedure when the predicted outcome is normal, therefore putting unnecessary pressure on endoscopic services.

In our study, OGDs have a lower correlation, sensitivity

Table 5: Correlation, sensitivity, specificity, PPV, NPV and Cohen's kappa values for patients who had OGD.

OGD	Correlation	Sensitivity	Specificity	PPV	NPV	Cohen's
All patients	0.7245	0.324	0.938	0.733	0.723	0.3
Female	0.7759	0.421	0.949	0.8	0.771	0.421
Male	0.65	0.2	0.92	0.6	0.657	0.138
0-8 years	0.6316	0.125	1	1	0.611	0.142
9-12 years	0.72	0.286	0.889	0.5	0.762	0.201
13-14 years	0.7917	0.5	1	1	0.737	0.538
15-18 years	0.7333	0.333	0.905	0.6	0.76	0.273

Table 6: Correlation, sensitivity, specificity, PPV, NPV and Cohen's kappa values for patients who had colonoscopy.

Colonoscopy	Correlation	Sensitivity	Specificity	PPV	NPV	Cohen's
All patients	0.963	1	0.917	0.938	1	0.924
Female	1	1	1	1	1	1
Male	0.9333	1	0.75	0.917	1	0.815
0-8 years						
9-12 years	1	1	1	1	1	1
13-14 years	1	1	1	1	1	1
15-18 years	0.8889	1	0.833	0.75	1	0.769

Table 7: Correlation, sensitivity, specificity, PPV, NPV and Cohen's kappa values for patients who had GI endoscopy.

GI endoscopy	Correlation	Sensitivity	Specificity	PPV	NPV	Cohen's
All patients	0.776	0.531	0.934	0.839	0.755	0.497
Female	0.8143	0.522	0.957	0.857	0.804	0.532
Male	0.7273	0.538	0.897	0.824	0.682	0.443
0-8 years	0.6316	0.125	1	1	0.611	0.142
9-12 years	0.7742	0.5	0.905	0.714	0.792	0.439
13-14 years	0.8611	0.737	1	1	0.773	0.726
15-18 years	0.7692	0.5	0.885	0.667	0.793	0.412

Table 8: Sensitivity + Specificity values for OGD, Colonoscopy and combined GI Endoscopy.

Out of the 100 patients, 48 had final diagnosis confirmed after the procedure and histology results with coeliac disease (22) being the most common diagnosis (Table 9).

Sensitivity + Specificity	OGD	Colonoscopy	GI Endoscopy
All patients	1.262	1.917	1.462
Female	1.37	2	1.479
Male	1.12	1.75	1.435
0-8 years	1.125		1.125
9-12 years	1.175	2	1.405
13-14 years	1.5	2	1.737
15-18 years	1.238	1.833	1.385

Table 9: Final diagnoses for 48 patients.

Final diagnosis	Number (N = 48)	% of total (N = 48)
Coeliac Disease	22	0.458
Ulcerative Colitis	8	0.167
Crohn's Disease	7	0.146
Gastro-oesophageal Reflux Disease	4	0.083
Gluten Intolerance (non-Coeliac)	3	0.062
Eosinophilic Esophagitis	2	0.042
Helicobacter PyloriGastritis	1	0.021
Achalasia	1	0.021

+ specificity and Cohen's kappa at 72.45%, 1.262 and 0.300 respectively. In contrast, colonoscopies performed much better with 96.30%, 1.917 and 0.924 respectively. Combined GI endoscopy consistently performed better than OGD, throughout all categories. This is due to the addition of the near perfect correlation results from colonoscopy. For OGDs and GI endoscopies, specificity is a lot higher than sensitivity. This shows that both tests are better at identifying patients without a disease than identifying patients with a disease. The high specificities throughout the study are testament to the low FP results during paediatric GI endoscopies.

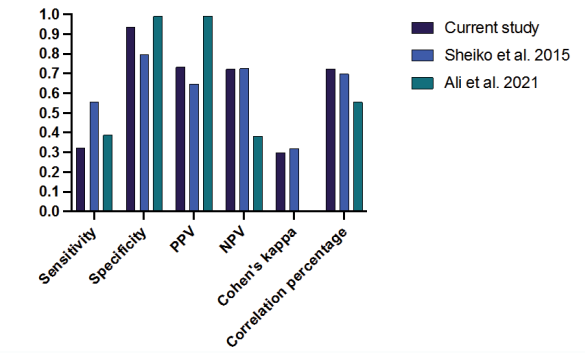

Figure 2: Comparison of the correlation statistics produced in this study with those of Sheiko et al. and Ali et al.

Only 27 patients underwent colonoscopy in our study, leading to very small sample size when data was split down into different categories. As a result, this data (Table 4 and Table 6), is less reliable than OGD and combined GI endoscopy and cannot be extrapolated to the whole population. Out of 27 colonoscopies, only one procedure that did not correlate, leading to sensitivity and NPV values of 1. It also led to little variation when comparing different categories.

The strength of our study is evaluation of OGD and colonoscopies separately as well as combined GI endoscopy along with analysing different population characteristics i.e. age and sex. Our study provides a range of data for comparison with future studies in paediatric population. Our study has reasonable overall sample size (125) although we accept that relatively small sample size for colonoscopy is a limitation of this study.

Out of the 100 patients included in this study, 48 were given a final diagnosis after their GI endoscopy (Table 9). Coeliac disease was, by far, the most common diagnosis in this cohort of patients. A reason for this is the need for a duodenal biopsy for the confirmation of coeliac disease in children with tissue transglutaminase (TTG) antibodies less than ten times the upper limit of normal as per European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines [26-27]. Children with slightly raised TTG antibodies above normal are more likely to have normal macroscopic finding during OGD when compared to children with significantly high TTG antibodies who do not undergo OGD anymore as per current ESPGHAN guideline. When looking at the correlation for our patients with final diagnosis of coeliac disease, the percentage is very low (18.18%) for the reasons outlined above. This percentage is similar to other studies [2]. This low correlation percentage could be a contributory factor to over OGD correlation being much lower than colonoscopy in our study. Our findings confirm that when diagnosis of coeliac disease is suspected, duodenal biopsies should always be taken even when upper GI mucosa looks normal macroscopically.

GI endoscopy can be a procedure that causes a lot of emotional stress, especially for young children and their parents1. Hence, the outcome must have a positive impact on patient management and care to justify the procedure. In 48% of patients in our study, the procedure provided a positive outcome which altered/confirmed a clinical diagnosis. Remaining 52% patients could have been disappointed with the lack of diagnosis and explanation for their symptoms. As a result, the impact may have been negative, especially if they had a bad experience during the procedure. However, as noted by Ahmed et al, normal GI endoscopy can also put the patient/family at ease and reassure them by refuting sinister diagnoses, therefore indirectly eliciting a positive overall outcome even when macroscopic and histological findings are normal [7].

Conclusion

This study shows a good correlation between macroscopic and histological findings in paediatric GI endoscopies. OGD has lower correlation than GI endoscopy so not high enough to be considered a useful and reliable test without taking biopsies for histology. Colonoscopy, however, shows near perfect correlation but only with a small sample size. Hence, these results support the current practice of continuation of the collection of routine biopsies during OGD. Although, high correlation in colonoscopy could indicate that routine biopsies may not be required during the procedure, precise histological diagnosis of conditions like inflammatory bowel disease is of paramount importance from management and counselling perspective. Further research with larger sample size and in diverse settings is required to compare with our results and substantiate the evidence provided in this study.

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