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Quantification of eosinophil densities in the oesophagus, stomach and small bowel of adults: A review of endoscopic and surgical specimens with normal histology, Free State Province, South Africa

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Summary. Aim. Studies defining eosinophil densities in the gastrointestinal tract (GIT) are limited. To assess whether eosinophils are pathologically infiltrating the GIT, it is important to evaluate eosinophil densities for specific populations.

Methods. A retrospective, quantitative, comparative study was conducted to determine the number of eosinophils in the oesophagus, stomach and small bowel of patients in central South Africa and to investigate whether a statistically significant difference occurred between ethnic and gender groups.

Results. In total, 309 histological sections from the oesophagus, gastric corpus, gastric antrum and small intestine were sampled from male and female, African and Caucasian patients. Histology reports and review of the slides confirmed the absence of histological abnormality. The number of eosinophils in the epithelium and lamina propria were manually quantified. The eosinophil values across gender, ethnicity and location were 0-2.0/mm^2 for the oesophagus, 0-53.0/mm^2 for the gastric corpus and 7.1-115.3/mm^2 for the small intestine. Regarding the gastric antrum, African and Caucasian females had eosinophil values of 1.0-35.7/mm^2 and 0-22.4/mm^2, respectively. Males had an eosinophil density of 0-31.6/mm^2 in the gastric antrum. The eosinophil values in the oesophagus, gastric corpus and small bowel were not significantly different between genders and ethnic groups. The only site where ethnicity influenced the number of eosinophils was the gastric antrum, a discrepancy that cannot be explained.

Conclusion. To the authors' knowledge, this is the first report on the eosinophil densities in the oesophagus, stomach and small bowel of adults in South Africa.

Key words: Eosinophils, Eosinophil density, Oesophagus, Gastric antrum, Gastric corpus, Small intestine

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Introduction

The term "eosinophilic gastroenteritis" was first used by Kaijser (1937). Since then, there have been many nomenclature changes for eosinophilic disorders affecting the gastrointestinal tract and this term is no longer preferred when describing eosinophilic disorders of the GIT (Dellon et al., 2022). Dellon et al. (2022) recently defined eosinophilic gastrointestinal disorders (EGIDs) as an all-encompassing term for diseases of the gastrointestinal tract with eosinophilic inflammation in the absence of secondary causes (Dellon et al., 2022). EGIDs refer to abnormal eosinophilic infiltrates of the oesophagus, stomach, small bowel or colon with resulting clinical symptoms (Gonsalves, 2007). Currently, EGIDs are separated into eosinophilic oesophagitis (EoE), eosinophilic gastritis (EoG), eosinophilic enteritis (EoN) and eosinophilic colitis (EoC) (Dellon et al., 2022).

Abbreviations. CEGIR, Consortium of Eosinophilic Gastrointestinal Disease Researchers; EGID, Eosinophilic gastrointestinal disease; Eos/HPF, Eosinophils per high power field; Eos/mm^2, Eosinophils per square millimeter; GERD, Gastro-oesophageal reflux disease; GIT, Gastrointestinal tract; H&E, Haematoxylin and eosin; HPF, High-power field (1 HPF=0.27 mm^2); HSREC, Health Sciences Research Ethics Committee; IQR, Interquartile range; NHLS, National Health Laboratory Service; SNOMED, Systematized Nomenclature of Medicine; UFS, University of the Free State

Many patients with EGIDs have a history of atopy, and symptoms depend on the severity of the infiltrate and the layers of the gastrointestinal tract that are involved (McCarthy and Sheahan, 2018). Historically, three criteria were used to diagnose EGIDs, namely gastrointestinal symptoms, histological documentation of increased eosinophils and exclusion of other causes of secondary gastrointestinal eosinophilia, such as medication, parasites and inflammatory bowel disease (Talley et al., 1990; Conner and Kirsch, 2017). Currently, well-defined criteria for the diagnosis of EGIDs, except EoE, are still lacking (Yang, 2023). The definition of increased eosinophils is also still debated (Conner and Kirsch, 2017).

The incidence of EGIDs is increasing (Lamousé-Smith and Futura, 2006; McCarthy and Sheahan, 2018). Nevertheless, few studies defining the reference range of eosinophils in the gastrointestinal tract (GIT) have been conducted, of which the majority have been in children (DeBrosse et al., 2006; Saad, 2011; Matsushita et al., 2015; Chernetsova et al., 2016; Silva et al., 2018; Koutri et al., 2020; Hoofien et al., 2022). It is important to recognise that eosinophils normally occur in the GIT, and their mere presence does not necessarily indicate pathology (DeBrosse et al., 2006). In addition, eosinophil densities should also be determined for specific populations, as a variety of environmental factors can influence eosinophil counts (Silva et al., 2018). These factors include environmental hygiene and sanitation (Matsushita et al., 2015) that can affect the parasitic burden and, consequently, the eosinophil count.

A thorough literature search yielded no previous South African studies measuring the eosinophil values in the GIT. Therefore, the aim of this study was to quantify the eosinophil density in the oesophagus, stomach and small bowel in adults with no apparent GIT disease in our local population.

Materials and methods

Study design, setting and sampling

A retrospective, quantitative, comparative study was undertaken. A Systematized Nomenclature of Medicine (SNOMED) search was performed on the National Health Laboratory Service (NHLS) laboratory information system for oesophageal, stomach and small bowel specimens received by the Department of Anatomical Pathology (affiliated with the NHLS and the University of the Free State [UFS]) between 1 January 2014 and 31 December 2019. The department provides histology services to all public sector healthcare facilities in the Free State Province of South Africa, with a mixed urban and rural population.

After consultation with the Department of Biostatistics, UFS, and taking into account the availability of specimens, it was decided to include 60 specimens from African (30 male and 30 female) and 60 samples from Caucasian patients (30 males and 30 males) obtained from the oesophagus, gastric corpus, gastric antrum and small bowel, respectively.

Patients were excluded if they were under 18 years of age, had a clinical history of atopy or evidence of a parasitic infection, *Helicobacter pylori* (*H. pylori*) infection or EGID. Information pertaining to the patient's age, sex, race, medical history and clinical indication for biopsy was obtained from the histology reports.

Laboratory investigation and data collection

After the specimens were identified, the slides were retrieved from the departmental archives. Before inclusion in the study, the slides were reviewed to confirm that there was no evidence of a condition that could have caused abnormally elevated eosinophils. The cases included were then analysed using an Olympus light microscope (model CX41; Olympus Corporation; Tokyo, Japan). Haematoxylin and eosin (H&E) stained tissue cut at 3 µm thickness was used in this study.

Method for eosinophil counting

Four high power fields (HPFs) x400 (0.245 mm^2) were visualised for each specimen and the number of eosinophils in the crypts and lamina propria were counted manually. The number was expressed as Eos/mm^2, and the conversion factor used to convert Eos/0.98 mm^2 to Eos/mm^2 was 1.02. For example, if 10 eosinophils were counted in 4 x 400 fields of 0.245 mm^2 each, 10 was multiplied by 1.02, giving 10.2 Eos/mm^2. Eosinophil counts were rounded to 1 decimal place.

Eosinophil exclusion criteria

Eosinophils were not counted if they were less than one HPF from the Peyer's patches in the small bowel or other lymphoid aggregates, if they were within blood vessels or degranulated. Only whole eosinophils were included in the eosinophil counts. Figure 1 shows photographs of eosinophils present in the various locations in the GIT.

Excluding H. pylori

All gastric biopsy specimens received at the NHLS, Universitas, undergo routine histochemical methylene blue staining to assess for *H. pylori*. If the suspicion for *H. pylori* infection is high on H&E evaluation, and no organisms are identified on methylene blue histochemical stains, an immunohistochemical stain for *H. pylori* is performed. Methylene blue histochemical stains are not performed on specimens received from the oesophagus or small bowel. Only gastric biopsies that were negative for *H. pylori* were included in this study.

Pilot study

A pilot study of 10 cases was performed and these cases were included in the final study.

Data analysis

Statistical analysis was performed by the Department of Biostatistics, University of the Free State (UFS), using SAS Version 9.4 (SAS Inc.; Cary, NC, USA). Results were summarised by frequencies and percentages (categorical variables) and means, standard deviations or percentiles (numerical variables). Subgroups were compared using non-parametric Mann-Whitney tests. Due to the skew distribution of the data, 95% ranges were calculated non-parametrically.

Ethical considerations

Approval to conduct the study was obtained from the Health Sciences Research Ethics Committee (HSREC) of the UFS (ethics reference number: UFS-HSD2019/0318/2603). Permission from the NHLS was obtained prior to this study. Due to the retrospective nature of the study and the use of archived laboratory specimens, informed consent from patients was not required.

Results

Biopsies from 309 patients who had histological specimens taken between 2014 and 2019 were evaluated. A total of 333 histological sections were reviewed, as some patients had more than one anatomical site biopsied. In all the specimens analysed, gastrointestinal

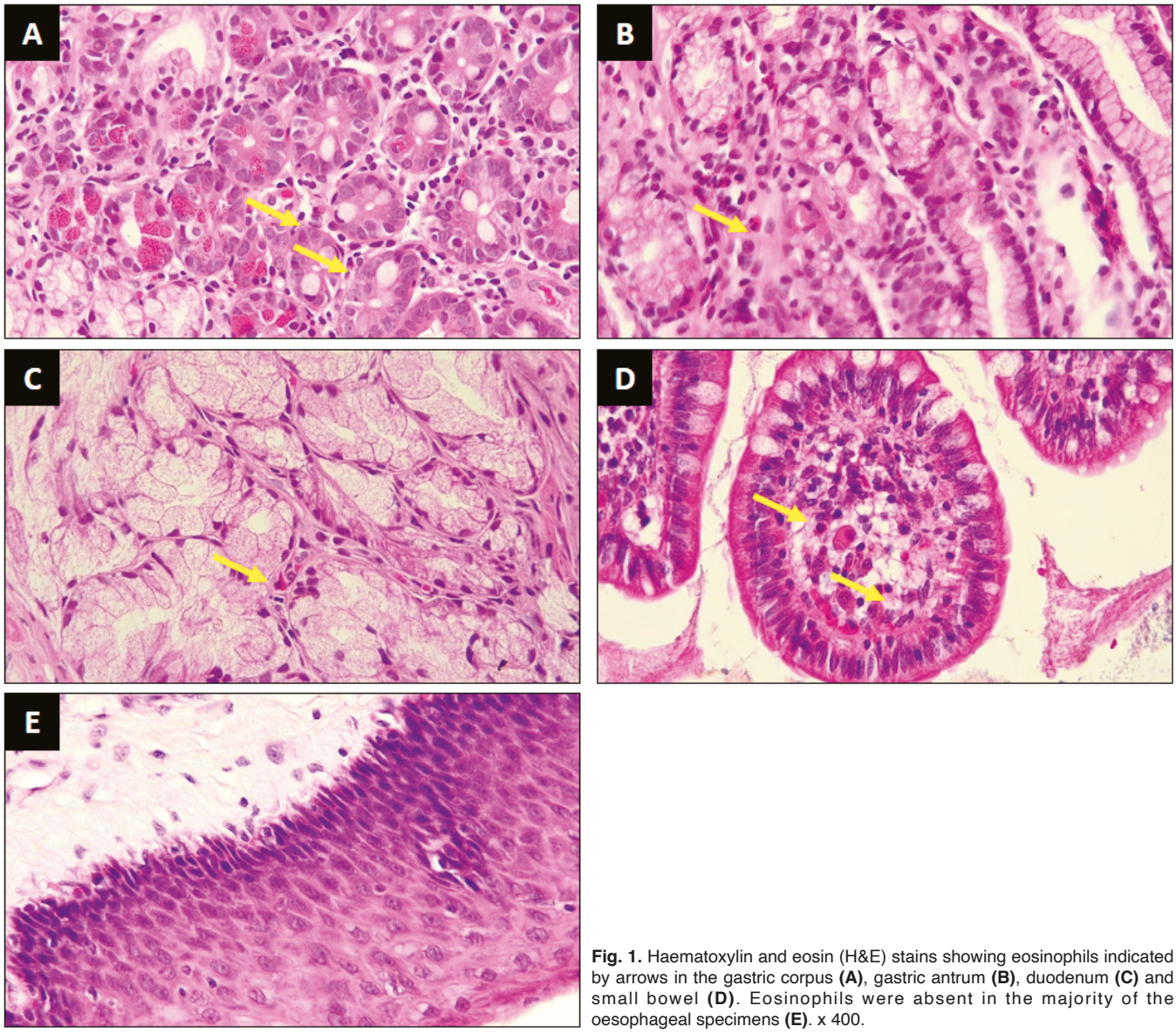

Fig. 1. Haematoxylin and eosin (H&E) stains showing eosinophils indicated by arrows in the gastric corpus **(A)**, gastric antrum **(B)**, duodenum **(C)** and small bowel **(D)**. Eosinophils were absent in the majority of the oesophageal specimens **(E)**. x 400.

pathology was excluded on histology. In Table 1, the demographic information of the study population is summarised per section of the GIT investigated. The only significant difference in age between Caucasian and African patients was found in small intestine specimens of males ($p<0.01$). Gender differences regarding age were found in gastric corpus specimens of Caucasians ($p=0.03$) and small intestine specimens of African patients ($p=0.01$). The indications for biopsies of the GIT are shown in Table 2.

Table 3 provides a summary of the eosinophil values in the GIT according to anatomical site (Eos/mm^2). The only significant difference, per biopsy site, was found in the gastric antrum of females, where the ethnic groups differed significantly regarding eosinophils observed in the lamina propria and epithelium ($p<0.03$ in both cases). Fewer eosinophils were observed in the epithelium *versus* the lamina propria, as indicated in Table 3.

The eosinophil densities in the GIT of adults are given in Table 4 and Table 5. Table 4 takes into consideration the race and gender of patients and highlights the distribution of eosinophils within the tissue. Table 5 gives the most appropriate eosinophil densities to use for comparison when analysing samples from the GIT. For the oesophagus, gastric corpus and small bowel, it is permissible to use the overall eosinophil densities, as no statistically significant differences considering gender or ethnicity were observed. Due to the racial differences between females regarding the gastric antrum values, eosinophil densities should be considered separately for females of different races. The eosinophil densities for Caucasian females were 0-22.4 Eos/mm^2 and 1.0-35.7 Eos/mm^2 for African females. The eosinophil densities in the antrum in males of both ethnic groups were 0-31.6 Eos/mm^2. The results in this study are reported as Eos/mm^2 for comparison with other studies in adults. To convert the values from Eos/mm^2 into Eos/HPF (1 HPF=0.27mm^2), the value in Eos/mm^2 should be multiplied by 0.27.

Table 1. Demographic profile of adults whose gastrointestinal tract (GIT) specimens were included in the study.

Section of the GIT	Frequency	Mean age (range) (years)
Oesophagus		
African female	16	63 (44-79)
African male	19	56 (23-79)
Caucasian female	12	56 (37-80)
Caucasian male	13	60 (22-89)
Gastric corpus		
African female	9	55 (35-79)
African male	21	52 (22-80)
Caucasian female	19	50 (25-70)
Caucasian male	23	59 (31-79)
Gastric antrum		
African female	22	51 (27-78)
African male	15	53 (29-79)
Caucasian female	28	57 (28-83)
Caucasian male	14	61 (42-79)
Small intestine		
African female	30	53 (24-86)
African male	30	41 (20-89)
Caucasian female	31	59 (32-88)
Caucasian male	31	58 (34-86)

Discussion

Eosinophils naturally reside in the GIT and are found in greater quantities in the GIT mucosa than in other tissues (DeBrosse et al., 2006). Eosinophils in the GIT can have variable morphology and distribution depending on disease processes occurring in the GIT (Yantiss, 2015). Aggregates of eosinophils and extensively degranulated eosinophils are always a pathological finding and can indicate underlying GIT pathology. Hypersensitivity reactions, parasitic infections and several GIT conditions can cause eosinophilia, and include gastro-oesophageal reflux

Table 2. Indications for biopsy of the gastrointestinal tract (GIT) per anatomical site.

Oesophagus	1.	Surveillance for oesophageal malignancy (n=19)
	2.	Dysphagia (n=9)
	3.	Strictures (n=5)
	4.	Oesophagectomy for oesophageal carcinoma (n=6)
	5.	Surveillance for Barrett oesophagus (n=4)
	6.	Other* (n=17)
Stomach	1.	Vitamin B12 deficiency (n=35)
	2.	Peptic ulcer disease (n=16)
	3.	Iron deficiency anaemia (n=15)
	4.	Tumour resections** (n=13)
	5.	Gastric outlet obstruction (n=10)
	6.	Other*** (n=62)
Small bowel	1.	Bowel obstruction (n=26)
	2.	Acute abdomen (n=13) and traumatic bowel injury (n=13)
	3.	Strangulated hernia (n=8) and vitamin B12 deficiency (n=8)
	4.	Small bowel masses not otherwise specified (n=6)
	5.	Other**** (n=48)

*Other indications for oesophageal biopsies included oesophageal stenosis, vitamin B12 deficiency, gastrectomy for gastric carcinoma, gastritis not otherwise specified, anaemia not otherwise specified, dyspepsia, GERD, caustic injury, upper gastrointestinal bleeding, hiatus hernia, Zenker diverticulum, polyps not otherwise specified, malaena stools, and miscellaneous indications (n=between 3 and 1). **Reasons for tumour resections included Whipple pancreatoduodenectomy, gastric adenocarcinoma and gastric tumours not otherwise classified. ***Other indications for stomach biopsies included gastritis not otherwise specified, epigastric pain, upper gastrointestinal bleeding, gastric polyps, dyspepsia, dysphagia, Barrett oesophagus, hiatus hernia, abdominal pain not otherwise specified, previous caustic ingestion, wheat intolerance, portal hypertension, chronic nonsteroidal anti-inflammatory drugs (NSAIDs) usage, and miscellaneous indications (n=between 9 and 1). ****Other indications for small bowel biopsies included caecal tumours not otherwise specified, hernias, gastric outlet obstruction, intussusception, intra-abdominal adhesions, iron deficiency anaemia, obstructive jaundice, right iliac fossa masses not otherwise specified, spontaneous small bowel perforation, stoma closure, upper gastrointestinal bleeds, Whipple pancreatoduodenectomy, epigastric pain, chronic constipation, and miscellaneous indications (n=between 5 and 1).

disease (GERD), *H. pylori* infection, autoimmune gastritis, infections, drug reactions, inflammatory bowel disease, radiation enteritis and collagen vascular disease (Yantiss, 2015).

Eosinophils are commonly found in the lamina propria and, to a lesser extent, in the epithelium (DeBrosse et al., 2006; Yantiss, 2015; Silva et al., 2018). According to previous studies, eosinophils are consistently absent from the mucosa of healthy oesophageal tissue (Matsushita et al., 2015; Silva et al., 2018). Research also confirms that the highest number of eosinophils in the stomach are located in the antrum, with a mean of 7.8±12.4 Eos/mm^2 (Silva et al., 2018). Although results from previous studies correlated regarding eosinophil numeration in the oesophagus and stomach, there was a discrepancy between results for the small bowel. McCarthy and Sheahan (2018) found that the normal number of eosinophils in the small intestine can be up to 30 Eos/HPF (x400). However, the minimum eosinophil count for a pathological diagnosis of EGID ranges between 20 and 50 Eos/HPF. According to Silva et al. (2018), this confirms that a "one-fits-all" number may not be the best option for defining the limits of normality. It is, therefore, important to establish eosinophil densities for specific population groups.

The specimens evaluated in this study were not exclusively received from biopsies performed during endoscopy. For example, some specimens were from patients who underwent surgical interventions for gastrointestinal tumours but had histologically normal appearing oesophageal, gastric or small bowel mucosa. Biopsies from the small bowel were primarily from the ileum and jejunum. Only 27 biopsies from the duodenum were included in this study. The biopsies from the ileum and jejunum were not specified separately and all sites, including the duodenum, were included under the umbrella term "small bowel".

Oesophagus

Eosinophil densities in the oesophagus of patients in this study population were 0-2.0 Eos/mm^2, similar to the range of 0-2.5 Eos/mm^2 reported by Matsushita et al. (2015). There appears to be consensus amongst other studies that eosinophils are rarely detected in the oesophagus (DeBrosse et al., 2006; Silva et al., 2018). DeBrosse et al. (2006) noted that eosinophils were only found in the epithelium. However, Silva et al. (2018) reported that eosinophils were only found in the lamina propria. Our findings are in keeping with the observations by Silva et al. (2018). Eosinophils were absent from the epithelium of the samples we evaluated and were scanty in the lamina propria of the oesophagus.

Gastric corpus

In this study, eosinophil densities in the gastric corpus were 0-53.0 Eos/mm^2. Although Silva et al. (2018) used the ambiguous terms "superficial" and "deep" to describe the location of eosinophils within the gastric corpus, their values were markedly smaller than the lowest mean values in this study. They identified only 0.2±0.6 Eos/mm^2 in the superficial lamina propria of the gastric corpus and 1.1±3.9 Eos/mm^2 in the deep

Table 3. Summary values of eosinophils present in the gastrointestinal tract (GIT) of adults in the Free State Province, South Africa.

	Total (Eos/mm^2)		Epithelium (Eos/mm^2)		Lamina propria (Eos/mm^2)	
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)
Oesophagus						
African female	0.3±0.6	0 (0; 0.5)	0±0	0 (0; 0)	0.3±0.6	0 (0; 0.5)
African male	0.3±0.8	0 (0; 0)	0±0	0 (0; 0)	0.3±0.8	0 (0; 0)
Caucasian female	0.4±0.7	0 (0; 1.0)	0±0	0 (0; 0)	0.4±0.7	0 (0; 1.0)
Caucasian male	0.1±0.3	0 (0; 0)	0±0	0 (0; 0)	0.1±0.3	0 (0; 0)
Gastric corpus						
African female	5.6±4.0	6.1 (2.0; 7.1)	0±0	0 (0; 0)	5.6±7.1	6.1 (2.0; 7.1)
African male	10.0±9.5	7.1 (5.1; 11.2)	0±0	0 (0; 0)	10.0±9.5	7.1 (5.1; 11.2)
Caucasian female	6.1±5.3	5.1 (3.1; 9.2)	0.1±0	0 (0; 0)	6.0±9.2	5.1 (2.0; 9.2)
Caucasian male	11.1±15.7	7.1 (2.0; 11.2)	0.2±0	0 (0; 0)	11.0±11.2	6.1 (2.0; 11.2)
Gastric antrum						
African female	10.1±8.8	7.1 (3.1; 13.3)	0±0	0 (0; 0)	10.1±13.3	7.1 (3.1; 13.3)
African male	7.2±8.5	6.1 (1.0; 10.2)	0±0	0 (0; 0)	7.2±10.2	6.1 (1.0; 10.2)
Caucasian female	6.0±6.4	4.0 (1.5; 8.2)	0±0	0 (0; 0)	6.0±8.2	4.1 (1.5; 8.2)
Caucasian male	5.6±6.8	2.0 (1.0; 9.2)	0.1±0	0 (0; 0)	5.5±8.2	2.0 (1.0; 8.2)
Small intestine						
African female	42.8±31.2	38.3 (23.5; 54.1)	2.5±4.1	1.0 (1.0; 4.1)	40.3±47.9	35.7 (17.3; 47.9)
African male	40.3±22.0	35.7 (25.5; 53.0)	2.0±3.1	1.0 (0; 3.1)	38.3±47.9	34.7 (24.5; 47.9)
Caucasian female	43.4±42.7	31.6 (21.4; 42.8)	2.5±3.1	1.0 (0; 3.1)	41.0±40.8	30.6 (20.4; 40.8)
Caucasian male	37.7±21.0	35.7 (20.4; 51.0)	1.7±3.1	1.0 (0; 3.1)	36.0±51.0	32.6 (18.4; 51.0)

Eos/mm^2: eosinophils per square millimeter; SD: standard deviation; IQR: interquartile range.

lamina propria of the gastric corpus (Silva et al., 2018). This also confirms that geographic location affects eosinophil counts.

Our study showed that African females had the lowest mean number of Eos/mm^2 (mean 5.6±7.1 Eos/mm^2) in the gastric corpus, and Caucasian males had the highest number of Eos/mm^2 (mean 11.0±11.2 Eos/mm^2). Silva et al. (2018) also described an eosinophil density that was substantially lower than the density measured in this study. The reference range of eosinophils in the superficial lamina propria of the gastric corpus in the study by Silva et al. (2018) was 0-2 Eos/mm^2 in the superficial gastric mucosa and 0-14 Eos/mm^2 in the deep gastric corpus mucosa, which was notably different to our eosinophil density of 0-53.0 Eos/mm^2. This finding highlights that our population had a higher average number of eosinophils in the gastric corpus than reported by Silva et al. (2018) and re-affirms that eosinophil ranges cannot be regarded as "one-fits-all".

Gastric antrum

The gastric antrum is the only site identified in this study where a statistically significant (p=0.03) difference was found in eosinophil values between patients of different ethnicity. African females were noted to have a higher total number of eosinophils in the gastric antrum, with values between 1.0-35.7 Eos/mm^2, in comparison to Caucasian females, who had eosinophil values between 0-22.4 Eos/mm^2. Based on our data, it is therefore acceptable for African females to have a higher number of eosinophils in the gastric antrum, without the eosinophils being considered pathologic.

According to Silva et al. (2018), the mean eosinophilic density in their study was significantly higher in the antrum (p=0.021) in comparison to other gastric sites. When evaluating the eosinophil densities in the gastric antrum in our study, the values appeared to be lower than those in the gastric corpus.

Small bowel

As noted in specimens from the oesophagus and the stomach, more eosinophils were identified in the lamina propria of the small bowel in comparison to the epithelium. The eosinophil densities in the small bowel in this study was 7.1-115.3 Eos/mm^2. It was challenging to compare findings from our study with results of other studies, as no standardised method of reporting eosinophils in the small intestine of adults has been published before. Only studies focussed on eosinophil densities in children have been reported, using a standardised method (Papadopoulou et al., 2023).

African versus Caucasian eosinophil values

Although studies comparing the number of eosinophils in Japanese and Caucasian ethnic groups have been conducted (Matsushita et al., 2015), no studies comparing African and Caucasian eosinophil numbers could be located in the literature. Matsushita et al. (2015) suggested that ethnicity only had a slight effect on the eosinophil concentration in their study comparing Japanese, Japanese Caucasian and Japanese American patients' specimens (Matsushita et al., 2015).

In this study, a statistically significant difference (p=0.03) was encountered only in the number of eosinophils between African and Caucasian specimens from the gastric antrum. This indicates that, when evaluating specimens from the gastric antrum histologically, it is important to note the ethnicity of the patient in order to determine whether the number of eosinophils observed is within normal limits.

The explanation behind the differences between these subgroups was not investigated in this study, however, possible reasons include varying parasite burdens between urban and rural-dwelling patients (Talley et al., 1990; Conner and Kirsch, 2017). Other factors that can be investigated include access to health

Table 4. Eosinophil densities (Eos/mm^2) in the gastrointestinal tract (GIT) of adults in the Free State Province, South Africa.

Anatomical site/Location	Female		Male	
	African	Caucasian	African	Caucasian
Oesophagus				
Epithelium	0-0	0-0	0-0	0-0
Lamina propria	0-2.0	0-2.0	0-3.1	0-1.0
TOTAL	0-2.0	0-2.0	0-3.1	0-1.0
Gastric corpus				
Epithelium	0-0	0-1.0	0-0	0-3.1
Lamina propria	1.0-12.2	0-22.4	0-40.8	0-59.2
TOTAL	1.0-12.2	0-22.4	0-40.8	0-60.2
Gastric antrum				
Epithelium	0-0	0-0	0-0	0-1.0
Lamina propria	1.0-35.7	0-22.4	0-31.6	0-21.4
TOTAL	1.0-35.7	0-22.4	0-31.6	0-21.4
Small intestine				
Epithelium	0-10.2	0-15.3	0-13.3	0-6.1
Lamina propria	6.1-155.0	6.1-221.3	2.0-91.8	4.1-82.6
TOTAL	7.1-156.1	6.1-226.4	2.0-91.8	5.1-84.7

Eos/mm^2: eosinophils per square millimeter.

Table 5. Eosinophil densities per anatomical site of the gastrointestinal tract (GIT) of adults in the Free State Province, South Africa.

Anatomical site	Eosinophil densities (Eos/mm^2)
Oesophagus	0-2.0
Gastric antrum in African females	1.0-35.7
Gastric antrum in Caucasian females	0-22.4
Gastric antrum in males	0-31.6
Gastric corpus	0-53.0
Small intestine	7.1-115.3

Eos/mm^2: eosinophils per square millimeter.

care and medication between population groups. This could possibly be due to historical inequalities, however, further investigation into these discrepancies should be undertaken in future studies.

Male versus female eosinophil values

According to the literature, gender does not affect eosinophil counts in the GIT (DeBrosse et al., 2006; Lwin et al., 2011; Saad, 2011; Chernetsova et al., 2016). Our results support these previous findings. After analysing our data, we concurred that no statistically significant difference was observed between the number of eosinophils present in GIT samples from male and female patients.

However, due to the racial differences affecting eosinophil densities in females in the gastric antrum, separate eosinophil densities should be considered when evaluating samples from the gastric antrum. Eosinophil numbers in the gastric antrum of African and Caucasian males can be considered together, i.e., as one predominant value, whereas the concentration of eosinophils in females needs to be considered separately for the two races. No statistically significant difference was noted between specimens of male and female patients from the oesophagus, gastric corpus or small bowel.

Obstacles encountered

It proved challenging to compare our findings to previous studies due to the lack of standardisation when reporting the number of eosinophils found in tissue regarding location within the tissue and anatomical site. Koutri et al. (2020) reported similarities with our observations and also recognised that in previous literature reports, eosinophils were not indicated in standard units (Koutri et al., 2020). In addition, the size of the HPF being used in previous studies is often not specified. This lack of standardisation impedes the comparison of results. The results in this study have been reported per mm^2 to allow for comparison with other studies in adults. It is reassuring to note that recently, the CEGIR has recommended a standardised HPF of 0.27 mm^2 when measuring eosinophils. This standardised HPF is already being reported in the latest literature and will allow for better comparison of results in future publications (Papadopoulou et al., 2023).

The majority of studies quantifying eosinophils in the GIT are focussed on children and adolescents (Koutri et al., 2020; Hoofien et al., 2022; Papadopoulou et al., 2023), which also resulted in challenges comparing our data with other studies.

Although a target of at least 30 males and 30 females were sought from each site, this number was not obtained for all sites examined. In our study, only the small intestine had the required number of samples. Attaining normal histological sections from the oesophagus, gastric antrum and gastric corpus proved challenging. This was likely due to strict criteria required to fulfil before a patient is offered endoscopy. Only 27 duodenal biopsies were included in this study, and were considered as part of the broad category of small intestine. Healthy patients with no suspicion of disease are generally not eligible for endoscopy. Normal specimens from the small bowel were easier to acquire, as the small bowel is usually removed in large sections, resulting in a greater chance of histologically normal tissue being present in these specimens. The study sample was too small to stratify results according to age. In comparison to other studies, however, our sample groups were considerably larger at all anatomical segments of the GIT.

Specimen request forms for histopathological specimens are notoriously poorly completed by clinicians. In the Free State Province public health sector, specimen request forms are completed manually, often not by the most senior clinician. As a result, endoscopy findings, patients' comorbidities and medication history, as well as relevant clinical history, are often inadequately detailed. This, however, is not a problem that is limited to our setting, as similar obstacles have been encountered in other studies (Koutri et al., 2020). Endoscopy reports are not provided with specimens submitted for histopathological evaluation. This was a limiting factor in our study, as it is important to take into consideration these factors when numerating eosinophils in the GIT. It is also unknown whether any of the patients included in this study developed GIT disease or other disease associated with elevated GIT eosinophils following this study.

Conclusion

In light of the increasing incidence of EGIDs, it is important to quantify eosinophil densities within the GIT in adults in the Free State Province, South Africa because of our unique environment and demographic representation. This study provides a baseline evaluation of the densities of eosinophils present in histologically normal samples obtained from adults and aims to contribute to a wider understanding of eosinophils in the GIT.

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