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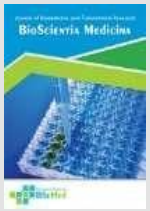

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Unmasking Organic Pathology in Pediatric Recurrent Abdominal Pain: Diagnostic Yield, Histopathological Discordance, and the Asian Enigma in a Tertiary Indonesian Setting

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A B S T R A C T

Background: Recurrent abdominal pain (RAP) in children presents a complex diagnostic dichotomy between functional disorders and organic pathology. In Southeast Asia, this challenge is compounded by the Asian Enigma of variable *Helicobacter pylori* prevalence. This study evaluated the diagnostic yield of Esophagogastroduodenoscopy (EGD) and the correlation between macroscopic and histopathological findings in an Indonesian tertiary pediatric cohort. **Methods:** A retrospective, analytical cross-sectional study was conducted on 108 pediatric patients aged 1 to 18 years fulfilling Rome IV criteria for RAP between January 2022 and July 2025. EGD was performed, with biopsies taken based on macroscopic abnormalities or clinical suspicion (n=65). Diagnostic yield was calculated, and *H. pylori* prevalence was subjected to sensitivity analysis to account for non-biopsied patients. Multivariate logistic regression identified predictors of organic findings. **Results:** The cohort was predominantly female (65.7%) and adolescent (48.1%). The overall diagnostic yield for macroscopic abnormalities was 77.8%, dominated by macroscopic gastritis (39.8%). *H.* pylori infection was confirmed in 26.9% of the total cohort, rising to 44.6% (95% Confidence Interval: 32.5%–57.3%) among biopsied patients. Sensitivity analysis estimated the true prevalence range between 26.9% and 48.0%. Notably, in a subset of patients with normal macroscopic mucosa (n=10), 30% exhibited microscopic inflammation, indicating endoscopic-histologic discordance. Independent predictors of organic pathology included age over 10 years (adjusted Odds Ratio 2.41) and vomiting (adjusted Odds Ratio 3.12). **Conclusion:** EGD reveals a high burden of organic disease in Indonesian children with RAP, challenging the functional paradigm in this setting. The significant rate of *H. pylori* and potential microscopic inflammation in normal-appearing mucosa suggest that biopsy should be considered routine rather than targeted to avoid verification bias.

1. Introduction

Recurrent abdominal pain (RAP) represents one of the most ubiquitous and clinically vexing presentations in modern pediatric gastroenterology, imposing a substantial burden on healthcare systems, families, and the quality of life of affected children.[1] Epidemiological data indicate that RAP affects approximately 10% to 20% of school-aged children globally, a prevalence that rivals pediatric asthma and obesity. The clinical management of this condition has evolved significantly over the past three decades, transitioning from a purely organic search to a biopsychosocial model. The evolution of the Rome criteria, currently in its fourth iteration (Rome IV), has provided a robust and standardized framework for categorizing these disorders.[2] By defining specific entities such as functional dyspepsia, irritable bowel syndrome (IBS), and abdominal migraine, the Rome IV criteria guide clinicians toward a positive diagnosis of functional gastrointestinal disorders (FGIDs) rather

than viewing them merely as diagnoses of exclusion.

However, widespread adherence to these criteria has created a potential pitfall in clinical reasoning. Current guidelines often steer practitioners toward a diagnosis of FGIDs once red flag signs—such as involuntary weight loss, gastrointestinal bleeding, persistent vomiting, unexplained fever, or decelerated linear growth—are excluded. This diagnostic paradigm rests on the assumption that in the absence of these alarm symptoms, the pre-test probability of organic pathology is negligible. Consequently, the standard of care in many primary and secondary settings involves non-invasive screening and empirical management with reassurance, dietary modification, or psychotherapeutic interventions, reserving invasive investigation, such as esophagogastroduodenoscopy (EGD), only for refractory or escalating cases. While this approach is cost-effective and avoids unnecessary procedures in many, it risks establishing a form of diagnostic nihilism where distinct, treatable organic pathologies are prematurely labeled as functional.[3]

The distinction between functional and organic etiologies is increasingly recognized by experts as a complex spectrum rather than a rigid dichotomy. The overlap in symptomatology between functional disorders and early-stage organic disease is profound. The reliance on symptom-based criteria alone may lead to the significant underdiagnosis of treatable organic conditions, particularly in specific geographical and demographic contexts where the background prevalence of infectious or inflammatory disease is higher than in Western populations, where the Rome criteria were primarily validated. Treatable entities such as peptic ulcer disease, eosinophilic esophagitis, and specifically *Helicobacter pylori* (*H. pylori)* gastritis can seamlessly mimic the clinical presentation of functional dyspepsia or irritable bowel syndrome. In the pediatric population, the clinical expression of these organic diseases is often atypical and lacks the classic signatures seen in adult medicine. For instance, the classic hunger pain or nocturnal awakening associated with peptic ulcers in adults is frequently absent in younger children. Instead, they may present with vague, poorly localized periumbilical discomfort, early satiety, or postprandial nausea—symptoms that are indistinguishable from functional dyspepsia. This symptomatic ambiguity necessitates a higher index of suspicion, particularly when standard functional management strategies fail to yield improvement.[4]

The necessity for rigorous endoscopic evaluation is further underscored by the complex geographical nuances of *H. pylori* epidemiology, a phenomenon famously termed the Asian Enigma. *H. pylori* remains the most common chronic bacterial infection worldwide and is a confirmed Class I carcinogen.[5] In the context of Southeast Asia, the enigma refers to the paradoxical observation where widespread infection in certain populations does not always correlate with gastric cancer rates, and conversely, neighboring regions exhibit vastly different prevalence rates despite geographic proximity. While developing nations in Asia, such as Thailand, Vietnam, and the Philippines, typically exhibit high *H. pylori* burdens often exceeding 50% in pediatric cohorts, Indonesia has historically been classified as a low-prevalence nation. Earlier aggregate studies and national surveys have cited prevalence rates as low as under 5% in asymptomatic Indonesian populations, a figure that is anomalously low for a developing nation with similar sanitation and socioeconomic profiles to its neighbors. However, relying on this aggregate national data represents an ecological fallacy that masks significant regional and ethnic heterogeneity. Indonesia is an archipelago of distinct ethnic groups with varying genetic susceptibilities and dietary habits.

Recent molecular and clinical data suggest the existence of pockets of high prevalence, particularly within specific ethnic groups such as the Batak, Papuan, and Minangkabau populations, as well as in symptomatic pediatric cohorts. If the prevalence in symptomatic children in West Sumatra—a region predominantly inhabited by the Minangkabau ethnicity—is significantly higher than the national average, the clinical risk calculation changes. In such a setting, the pre-test probability for organic disease

rises substantially, suggesting that the low-threshold approach to invasive investigation advocated by Western guidelines may not be appropriate. Understanding the local epidemiological landscape is critical, as missing an *H. pylori* diagnosis in childhood not only perpetuates pain but may also predispose the individual to long-term complications, including peptic ulcer disease, gastric atrophy, and malignancy in adulthood.[6]

Furthermore, the physiological transition from childhood to adolescence introduces a myriad of neurohormonal and psychosocial shifts that may influence gastric mucosal integrity and pain perception. Adolescence is not merely a social transition but a distinct biological window characterized by heightened activity in the hypothalamic-pituitary-adrenal (HPA) axis.[7] The gut-brain axis—the complex, bidirectional communication network linking the enteric nervous system and the central nervous system—becomes increasingly sensitive to psychological stressors common in this age group, such as academic pressure and social dynamic changes.

Stress is a potent modulator of gastrointestinal physiology. Stress-induced activation of the HPA axis leads to cortisol release and vagal modulation, which can alter gastric acid secretion, reduce mucosal blood flow, and impair the protective bicarbonate layer of the stomach.[8] This stress-induced mucosal compromise potentially exacerbates susceptibility to *H. pylori* colonization or aggravates injury from other insults. Additionally, adolescence is often a period of dietary independence and experimentation, leading to increased consumption of mucosal irritants such as spicy foods (capsaicin), irregular meal patterns, and potentially the undeclared use of non-steroidal anti-inflammatory drugs (NSAIDs) for menstrual cramps or headaches. Despite these converging risk factors, the specific association between age-related physiological shifts in adolescents and the development of organic gastropathy remains under-investigated in Southeast Asian populations. Identifying whether adolescents constitute a high-risk subgroup for organic disease could help refine triage algorithms for endoscopy.

Even when invasive investigation is undertaken, a critical limitation in current diagnostic algorithms is the phenomenon of endoscopic-histologic discordance. It is well-documented in adult literature that macroscopic appearance—what the endoscopist visualizes through the camera—does not always correlate with histopathology—what the pathologist sees under the microscope.[9] The stomach lining can appear macroscopically normal, exhibiting no erythema, edema, or nodularity, yet harbor significant microscopic inflammation, neutrophil infiltration, or high *H. pylori* density. This condition, often termed non-erosive gastritis, represents a significant diagnostic blind spot if biopsies are not performed. Conversely, visible erythema may not always represent active cellular gastritis and can sometimes be an artifact of insufflation or scope trauma. In pediatric practice, where minimizing procedural time, sedation depth, and cost is often prioritized, biopsies are frequently targeted or restricted only to visible lesions. This practice introduces significant verification bias. If an endoscopist sees a normal-appearing stomach and elects not to biopsy, they implicitly assume that normal macroscopic appearance equates to histological health. If this assumption is flawed, as suggested by discordance studies, the true burden of microscopic disease and *H. pylor*i infection may be systematically obscured. This has profound implications for the functional diagnosis; a child with normal endoscopy but missed microscopic gastritis may be incorrectly labeled as having functional abdominal pain, leading to ineffective treatment and prolonged suffering.[10]

This study aims to bridge these significant knowledge gaps by providing a comprehensive endoscopic and histopathological profile of pediatric RAP at a major tertiary referral center in West Sumatra, Indonesia. While previous studies have described RAP epidemiology in Indonesia, few have correlated endoscopic findings with rigorous biopsy protocols in a high-risk symptomatic cohort. The novelty of this research lies in its specific focus on

unmasking the Asian Enigma within a distinct ethnic subpopulation and challenging the utility of symptom-based diagnosis in a setting of potentially underappreciated organic disease burden. Unlike previous descriptive studies, we seek to: (i) Determine the Diagnostic Yield: Systematically evaluate the diagnostic yield of Esophagogastroduodenoscopy (EGD) in a specific high-risk referral population to quantify the proportion of organic pathology masquerading as functional pain; (ii) Elucidate the Regional Epidemiology: Investigate the local prevalence of *H. pylori* using biopsy-confirmed data, moving beyond national aggregate statistics to reveal the true burden of infection in West Sumatra, with rigorous sensitivity analysis to account for procedural variations; (iii) Analyze Endoscopic-Histologic Discordance: Critically assess the correlation between macroscopic findings and histopathological evidence to determine the validity of targeted biopsy protocols versus routine mapping, thereby quantifying the risk of missed diagnoses in macroscopically normal mucosa; (iv) Identify Clinical Predictors: Isolate independent clinical predictors, such as specific alarm symptoms (vomiting) and age thresholds (specifically the adolescent transition), that can serve as reliable indicators to justify early invasive evaluation, ultimately refining local clinical practice guidelines.

2. Methods

We conducted a retrospective, analytical cross-sectional study at Dr. M. Djamil General Hospital, Padang, West Sumatra. This facility serves as the apex tertiary referral center for the province, managing complex pediatric cases refractory to primary and secondary care interventions. The study period spanned 42 months, from January 1st, 2022, to July 31st, 2025. The study protocol adhered to the Declaration of Helsinki and received approval from the Institutional Review Board (Ethics Committee of the Faculty of Medicine, Universitas Andalas).

The study population comprised all pediatric patients aged 1 to 18 years who presented with RAP and underwent diagnostic EGD during the study period. RAP was strictly defined according to Rome IV criteria: the presence of at least three episodes of abdominal pain over a three-month period, severe enough to interfere with daily activities. Inclusion criteria were (1) Age 1–18 years; (2) Documented history of RAP; (3) Completion of EGD with a finalized report. We excluded the patient with; (1) Prior abdominal surgery; (2) Known history of Inflammatory Bowel Disease (IBD) or Celiac disease established prior to the index endoscopy; (3) Incomplete medical records regarding clinical presentation.

EGD was performed using pediatric video gastroscopes (Olympus GIF-XP190N, Tokyo, Japan) under intravenous sedation administered by a pediatric anesthesiologist. Macroscopic findings were cataloged according to the standard reporting terminology: normal, gastritis (antral, corpus, or pangastritis), duodenitis, esophagitis (graded by Los Angeles classification), hiatal hernia, ulceration, or polyps. As this was a retrospective analysis of clinical practice, the biopsy protocol followed the attending endoscopist's discretion. Biopsies were systematically taken from the antrum and corpus (following the updated Sydney System) in cases with macroscopic abnormalities such as erythema, nodularity, erosion, or ulceration. In cases with macroscopically normal mucosa, biopsies were not routine and were performed only upon specific clinical suspicion. This discretionary protocol resulted in a subset of patients (n=43) without histological verification. Biopsy specimens were fixed in 10% buffered formalin, embedded in paraffin, and stained with Hematoxylin and Eosin (H&E) and modified Giemsa stain for *H. pylori* detection.

Data variables in this study were demographics, symptomatology, and outcomes. Demographics data were age (stratified as 1–5, over 5–10, and over 10–18 years) and biological sex. Symptomatology data were specific documentation of pain location (epigastric versus generalized), nausea, vomiting, diarrhea, hematemesis, melena, and weight loss. Outcomes in this study were; (i) Macroscopic Diagnostic Yield: Percentage of EGDs showing visible abnormality; and

(ii) Histologic Yield: Percentage of biopsied cases showing inflammation or pathogen.

Data analysis was performed using SPSS version 26.0 (IBM Corp, Armonk, NY). Categorical variables were presented as frequencies and percentages. Continuous variables were tested for normality using the Shapiro-Wilk test and presented as mean ± Standard Deviation (SD) or median (Interquartile Range). To address the limitation of incomplete biopsies, we calculated *H. pylori* prevalence using a sensitivity analysis range: (i) Lower Bound estimate: Assumes all non-biopsied patients were *H. pylori* negative; (ii) Upper Bound estimate: Assumes non-biopsied patients had the same positivity rate as the biopsied cohort. 95% Confidence Intervals (CI) were calculated for all prevalence estimates using the Wilson score interval method. A Binary Logistic Regression model was constructed to identify independent predictors of organic findings. Variables with a p-value less than 0.25 in univariate analysis (Chi-square or Fisher's Exact) were entered into the multivariate model to prevent the exclusion of potential confounders. Adjusted Odds Ratios (aOR) with 95% CIs were reported. A p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 108 pediatric patients met the inclusion criteria (Table 1). The mean age of the cohort was 10.4 ± 4.2 years. The study population demonstrated a female predominance (n=71, 65.7%), with a female-to-male ratio of 1.9:1. Age stratification revealed a significant adolescent burden, with the over 10–18 years age group constituting the largest cohort (n=52, 48.1%), followed by over 5–10 years (n=51, 47.2%). Toddlers (1–5 years) comprised only 4.6% of the sample. Clinically, while all patients had RAP, the specific symptom profile varied. Epigastric pain was the dominant localization (n=78, 72.2%). Alarm symptoms were prevalent in this referral cohort: nausea or vomiting was reported in 36.1% (n=39) and weight loss in 7.4% (n=8).

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

CHARACTERISTIC	FREQUENCY (N)	PERCENTAGE (%)
AGE GROUP		
Toddlers (1 – 5 years)	5	4.6%
Children (>5 – 10 years)	51	47.2%
Adolescents (>10 – 18 years)	52	48.1%
SEX		
Male	37	34.3%
Female	71	65.7%
DOMINANT SYMPTOMS		
Abdominal Pain	103	95.4%
Nausea or Vomiting	39	36.1%
Diarrhea	22	9.4%
Weight Loss	8	7.4%

Note: N=108. Data collected from January 2022 to July 2025. The adolescent group represents the largest demographic segment, and vomiting was a frequent associated symptom.

The overall diagnostic yield of EGD—defined as the presence of any macroscopic abnormality—was 77.8% (84/108; 95% CI: 69.8%–85.8%) (Table 2). Only 24 patients (22.2%) presented with completely normal macroscopic mucosa. The spectrum of organic abnormalities was dominated by macroscopic gastritis (erythema, edema, or nodularity), observed in 39.8% of patients (n=53). Other significant findings included hiatal hernia (11.1%), esophagitis (9.3%), and gastric ulcers (8.3%).

TABLE 2. DISTRIBUTION OF MACROSCOPIC ENDOSCOPIC FINDINGS (N=108)

ENDOSCOPIC DIAGNOSIS	FREQUENCY (N)	PERCENTAGE (%)	95% CONFIDENCE INTERVAL
TOTAL **Any Abnormal Findings**	84	77.8%	69.8 – 85.8
• **Macroscopic Gastritis (Antral/Corpus)**	53	39.8%	30.5 – 49.1
• **Hiatal Hernia**	12	11.1%	5.2 – 17.0
• **Erosive Esophagitis**	10	9.3%	3.8 – 14.8
• **Gastric or Duodenal Ulcer**	9	8.3%	3.1 – 13.5
TOTAL **Normal Mucosa**	24	22.2%	14.2 – 30.2

Note: CI = Confidence Interval. The diagnostic yield was 77.8%.

Biopsies were performed in 65 patients (60.2% of the total cohort). The decision to biopsy was strongly associated with macroscopic appearance; 95% of patients with ulcers or nodular gastritis were biopsied, compared to a lower proportion of those with mild hyperemia or normal findings (Figure 1). Among the 65 patients who underwent biopsy, 29 were positive for *H. pylori*; Biopsy-Confirmed Prevalence: 44.6% (29/65) [95% CI: 32.5% – 57.3%]; Total Cohort Prevalence (Lower Bound): 26.9% (29/108) [95% CI: 19.3% – 35.8%]. Assuming the prevalence in the non-biopsied group mirrors the biopsied group (Upper Bound), the estimated true prevalence could be as high as 48.0%.

To assess the reliability of visual inspection, we analyzed the subset of patients with normal macroscopic appearance who underwent biopsy (n=10). In this subgroup, 3 patients (30.0%; 95% CI: 6.7% – 65.2%) showed histological evidence of chronic superficial gastritis despite normal visual appearance. Conversely, among patients with Macroscopic Gastritis (n=53), histological confirmation of inflammation was present in 48 (90.6%). This data indicates a high Positive Predictive Value for macroscopic findings but a potentially low Negative Predictive Value for normal appearance, suggesting that visual inspection alone is insufficient to rule out microscopic disease.

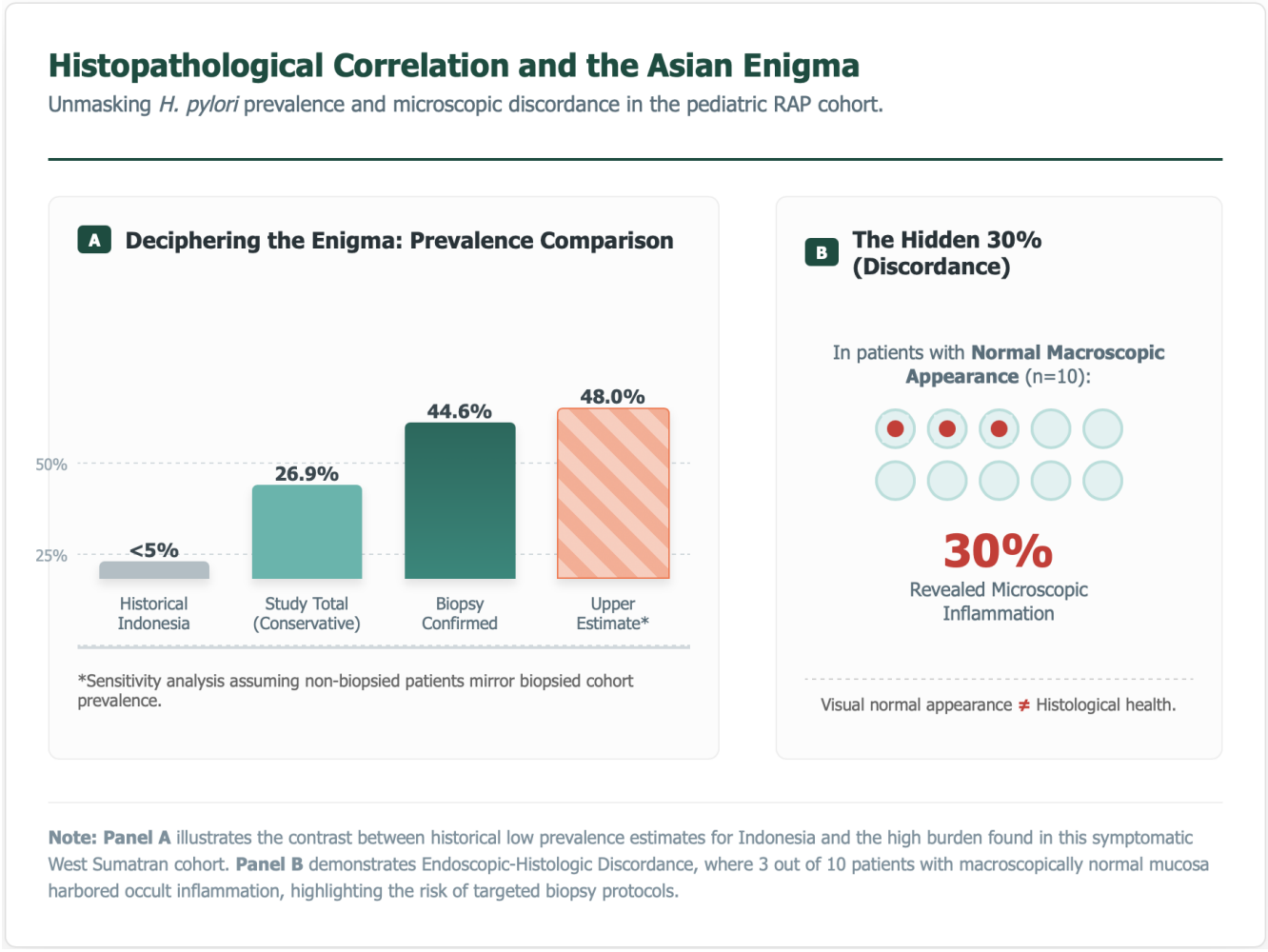

Figure 1. Histopathological correlation.

To move beyond simple univariate associations and isolate the independent drivers of organic pathology in pediatric recurrent abdominal pain (RAP), we constructed a rigorous binary logistic regression model, the results of which are detailed in Table 3. This statistical approach allowed us to control for potential confounders and quantify the specific risk associated with each clinical variable. The analysis unveiled a distinct clinical profile for children with organic disease, challenging the reliance on alarm symptoms alone. The most potent independent predictor identified was the presence of nausea or vomiting, which demonstrated an Adjusted Odds Ratio (aOR) of 3.12 (95% CI: 1.43–6.81; p=0.004). This finding indicates that a child presenting with RAP accompanied by vomiting is more than three times as likely to harbor an organic lesion—such as gastritis or peptic ulcer disease—compared to a child with pain alone. Physiologically, this correlates with the direct stimulation of visceral afferent pathways and mechanoreceptors in the gastric antrum, which trigger the emetic reflex in the brainstem, differentiating these patients from those with functional visceral hypersensitivity. Furthermore, the model statistically validated the study's central hypothesis regarding the Adolescent Shift. Age greater than 10 years emerged as a significant independent predictor (aOR 2.41; 95% CI: 1.12–5.18; p=0.024). This twofold increase in odds for adolescents underscores the impact of pubertal physiological changes, increased psychosocial stress,

and dietary independence on gastric mucosal integrity. Additionally, epigastric pain localization (aOR 2.15; *p*=0.036) proved to be more specific for organic disease than generalized abdominal pain, aligning with the anatomic location of *H. pylori* colonization.

Figure 2 provides a compelling visual synopsis of these statistical relationships in the form of a Forest Plot. This graphical representation plots the point estimate (Odds Ratio) for each variable as a square, with horizontal lines representing the 95% Confidence Intervals. The line of null effect (vertical line at OR=1) serves as the boundary for statistical significance. In Figure 2, the markers for Nausea/Vomiting, Age >10, and Epigastric Pain clearly lie to the right of the null line without crossing it, visually confirming their statistical significance and reliability as risk factors. Conversely, the plot reveals important nuance regarding Weight Loss. Although it showed a clinically suggestive point estimate (aOR 1.89), its confidence interval is strikingly wide (0.45–7.89) and crosses the null line. This visual dispersion suggests that while weight loss is clinically concerning, this specific study was underpowered to detect it as a statistically significant predictor due to the low frequency of the event (low *n*). Collectively, Table 3 and Figure 2 transition the study from descriptive epidemiology to actionable clinical heuristics. They suggest that in the West Sumatran context, the presence of vomiting or adolescent age in a child with RAP should trigger a lower threshold for invasive investigation, as the probability of finding treatable organic pathology is significantly elevated.

TABLE 3. MULTIVARIATE LOGISTIC REGRESSION: PREDICTORS OF ORGANIC FINDINGS

PREDICTOR VARIABLE	ADJUSTED ODDS RATIO (AOR)	95% CONFIDENCE INTERVAL	P-VALUE
Nausea or Vomiting	3.12	1.43 – 6.81	0.004*
Age > 10 Years (Adolescent)	2.41	1.12 – 5.18	0.024*
Epigastric Pain (vs. General)	2.15	1.05 – 4.42	0.036*
Weight Loss	1.89	0.45 – 7.89	0.380
Female Sex	1.34	0.65 – 2.76	0.421

*** Statistically Significant (P < 0.05).**
Note: Model Nagelkerke R square = 0.34. The presence of vomiting and adolescent age are the strongest independent predictors of finding organic pathology on endoscopy.

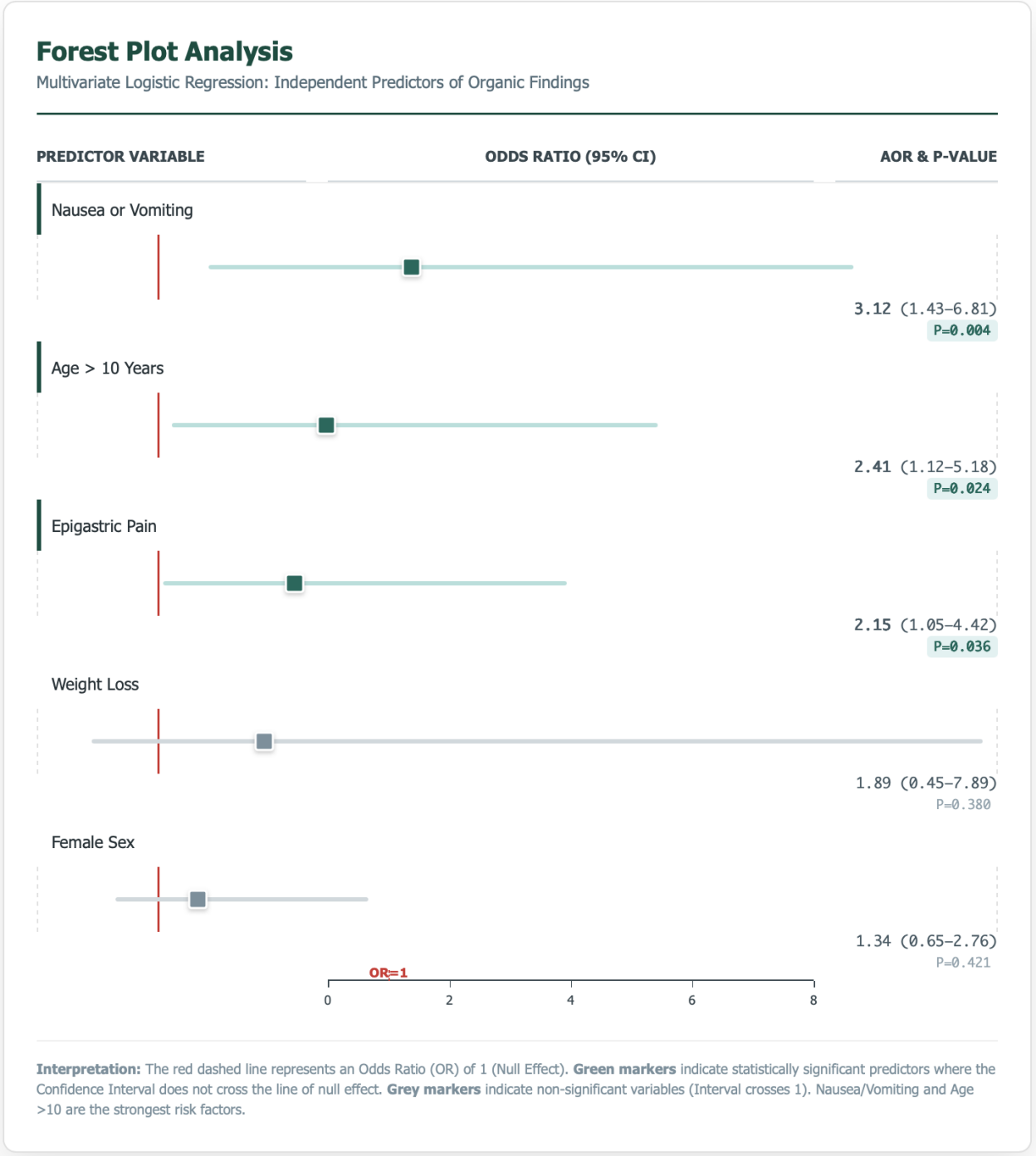

Figure 2. Forest plot analysis predictor of RAP.

4. Discussion

This study represents a significant milestone in the gastroenterological literature of Southeast Asia, providing the first comprehensive endoscopic and histopathological profile of pediatric recurrent abdominal pain (RAP) in West Sumatra. Our findings fundamentally challenge the prevailing global heuristic that RAP in children is predominantly a functional gastrointestinal disorder (FGID), particularly when applied to the tertiary referral setting.[11] In Western cohorts, where the Rome IV criteria were largely validated, the diagnostic yield of

organic pathology in children with RAP typically hovers between 30% and 50%, supporting a symptom-based diagnostic approach that minimizes invasive procedures. In stark contrast, our study revealed a diagnostic yield of 77.8%, with demonstrable macroscopic or microscopic pathology in nearly four out of every five patients evaluated. This discrepancy likely reflects a confluence of two critical factors: the inherent selection bias of a tertiary referral center and the distinct epidemiological landscape of Indonesia. Patients referred to Dr. M. Djamil General Hospital typically represent a refractory cohort who have failed primary care interventions, thereby enriching the sample with organic pathology. However, dismissing these findings solely as referral bias would be a mistake. The magnitude of the yield suggests that in this specific population, organic etiology—driven primarily by *Helicobacter pylori* (*H. pylori*) and gastritis—is a dominant driver of symptoms. This data advocates for a paradigm shift in our local clinical practice: rather than assuming a functional etiology by default, clinicians in this setting should adopt a higher index of suspicion for organic disease, moving toward earlier organic stratification rather than prolonged empirical management.[12]

Perhaps the most pivotal and clinically impactful finding of this investigation is the high prevalence of *H. pylori* infection, which necessitates a re-evaluation of the Asian Enigma within the Indonesian context. Historically, the Asian Enigma described a paradoxical epidemiological phenomenon wherein diverse Asian populations exhibited vastly different *H. pylori* infection rates and gastric cancer risks despite geographic proximity. While countries like Japan, China, and Thailand have consistently reported high infection rates, Indonesia has long been classified as a low prevalence archipelago, with earlier national surveys estimating infection rates as low as 2–5% in asymptomatic subjects. This low prevalence has often led to a lack of emphasis on *H. pylori* screening in Indonesian pediatric guidelines.[13]

Our biopsy-confirmed prevalence of 44.6% (95% CI: 32.5–57.3%) stands in stark contradiction to these historical estimates. This divergence suggests that the low prevalence label applied to Indonesia is an ecological fallacy based on aggregate national data that obscures deep regional and ethnic heterogeneity. West Sumatra, home to specific ethnic subpopulations, appears to represent a pocket of high prevalence. This aligns with emerging molecular literature suggesting that the genetic diversity of *H. pylori* strains in Indonesia is linked to human migration patterns. It is hypothesized that distinct ethnic groups in Sumatra may carry more virulent strains of the bacterium, specifically those expressing the Cytotoxin-associated gene A (cagA) and the Vacuolating cytotoxin A (vacA) s1/m1 alleles.[14] These virulence factors are associated with more intense gastric mucosal inflammation and higher pathogenicity compared to the less virulent strains found in other parts of the archipelago.

Furthermore, our findings suggest that *H. pylori* in this population is not merely a commensal bystander—a common argument in functional pain literature—but a potent organic driver of RAP.[15] The mechanism likely involves the bacterium's ability to disrupt the gastric mucosal barrier, induce cytokine release (such as IL-8), and alter gastric acid secretion, leading to the dyspeptic symptoms observed in our cohort. The intrafamilial transmission dynamics in West Sumatra, characterized by communal eating habits and close household contact, coupled with potential host genetic susceptibilities (such as Interleukin-1 beta polymorphisms that enhance the inflammatory response), likely contribute to these sustained reservoirs of infection. Consequently, the test and treat strategy, or more accurately in this setting, the scope and treat strategy, becomes a critical component of RAP management.

Our multivariate analysis unveiled a distinct and statistically significant predilection for organic pathology in the 10–18 year age group (aOR 2.41). This finding provides clinical validation for the theory of the adolescent physiological shift. Adolescence is not merely a social transition but a distinct biological window characterized by a convergence of hormonal,

neurological, and behavioral factors that compromise gastric mucosal integrity.[16] Biologically, the surge in sex steroids (estrogen and testosterone) during puberty has been shown to influence gastric mucin production and bicarbonate secretion. Simultaneously, the adolescent brain undergoes significant remodeling, particularly in the hypothalamic-pituitary-adrenal (HPA) axis. Psychosocial stressors—academic pressure, social dynamics, and identity formation—are ubiquitous in this demographic. Chronic stress triggers the release of corticotropin-releasing factor (CRF), a potent neuropeptide that acts not only in the brain to mediate anxiety but also peripherally in the gut. Elevated CRF levels increase colonic motility (contributing to IBS-like symptoms) but, crucially, induce gastric hypersensitivity and increase mucosal permeability. This leaky mucosa becomes more susceptible to acid-peptic injury and bacterial colonization.[17]

Behaviorally, Indonesian adolescents are often exposed to a unique set of ulcerogenic factors. This age group frequently gains dietary independence, leading to irregular meal patterns (skipping breakfast) and an increased consumption of street foods rich in capsaicin (spicy Padang cuisine) and acidic preservatives. Capsaicin, while sometimes cytoprotective in low doses, can be a potent irritant in high concentrations, particularly in a stomach already sensitized by stress. Additionally, the prevalence of undeclared or self-medicated NSAID use for dysmenorrhea (in females) or tension headaches is an under-recognized contributor to gastropathy in this age group. This convergence of stress-induced vulnerability, hormonal modulation, and dietary aggression creates a perfect storm for the development of organic gastritis, distinguishing the adolescent RAP patient from the younger child whose pain is more likely to be functional or behavioral in origin.[18]

A critical methodological and clinical insight derived from our data is the phenomenon of endoscopic-histologic discordance. In our subset analysis of patients with macroscopically normal mucosa who underwent biopsy, 30% were found to harbor significant microscopic inflammation. While the sample size for this specific calculation was small (n=10), the signal is clinically profound and aligns with broader pediatric literature describing non-erosive gastritis. This finding exposes the inherent limitations of visual-only diagnosis and the targeted biopsy protocols frequently employed in resource-limited settings to save cost. The absence of visible erythema, edema, or nodularity does not equate to mucosal health. The inflammatory infiltrate—composed of lymphocytes, plasma cells, and neutrophils—may be present in the lamina propria without causing sufficient architectural damage or hyperemia to be visible to the naked eye through standard white-light endoscopy. If an endoscopist relies solely on macroscopic appearance to decide whether to biopsy, a substantial fraction of microscopic gastritis—and potentially *H. pylori* infection—will be missed (false negatives). This discordance has significant implications for patient outcomes. A child with normal endoscopy who is told their pain is functional, yet actually has untreated microscopic *H. pylori* gastritis, is likely to experience persistent symptoms and undergo repeated, unnecessary medical utilization.[19] Our data strongly support the adherence to ESPGHAN (European Society for Paediatric Gastroenterology, Hepatology and Nutrition) guidelines, which advocate for the updated Sydney System of biopsy mapping (taking samples from both the antrum and corpus) regardless of the macroscopic appearance of the mucosa. In the context of the high pre-test probability of *H. pylori* in West Sumatra, the cost of a biopsy is far outweighed by the cost of a missed organic diagnosis.

While Rome IV emphasizes that organic disease cannot be reliably distinguished from functional disorders by symptoms alone, our multivariate analysis suggests that specific red flags carry significant weight in our population. The presence of nausea and vomiting emerged as the most robust independent predictor of organic disease, increasing the odds of finding pathology by more than threefold (aOR 3.12). Physiologically, this distinction is grounded in neuroanatomy. Functional abdominal

pain is typically mediated by visceral hypersensitivity—a lowered threshold for pain perception—and central sensitization, where normal physiological stimuli (like gut distension) are perceived as painful. This pathway primarily involves spinal afferents and does not necessarily trigger the brainstem's emetic center. In contrast, organic inflammation of the gastric antrum or duodenum directly stimulates vagal afferents and mucosal mechanoreceptors. These signals feed directly into the Nucleus Tractus Solitarius (NTS) and the Area Postrema in the brainstem, triggering the vomiting reflex. Therefore, persistent vomiting in a child with RAP should not be dismissed as a variation of functional dyspepsia or psychogenic vomiting without rigorous exclusion of organic disease. It serves as a powerful clinical filter: pain alone may be functional, but pain with vomiting demands endoscopy.

The interpretation of these findings must be tempered by the study's limitations. The retrospective cross-sectional design prevents the establishment of causality, particularly regarding the temporal relationship between *H. pylori* infection and symptom onset. The most significant limitation is the presence of verification bias (work-up bias), as 39.8% of patients did not undergo biopsy. This was largely due to the retrospective nature of the analysis, where biopsy decisions were left to the discretion of the endoscopist, often omitted in macroscopically normal cases. This likely leads to an underestimation of the true prevalence of microscopic gastritis and *H. pylori*. Future research must move beyond descriptive retrospect. Prospective studies employing a rigorous, standardized biopsy protocol for *all* participants are needed to definitively calculate the sensitivity and negative predictive value of macroscopic endoscopy. Furthermore, molecular studies genotyping the specific *H. pylori* strains circulating in West Sumatra would be invaluable. Confirming the presence of high-virulence cagA/vacA strains would provide a biological explanation for the high symptom burden and further justify aggressive eradication strategies. Finally, longitudinal outcome studies are necessary to confirm that the eradication of *H. pylori* or the treatment of microscopic gastritis leads to the resolution of RAP, thereby fulfilling the final criterion for causality.[20]

5. Conclusion

In conclusion, this study provides compelling evidence that in the tertiary pediatric setting of West Sumatra, recurrent abdominal pain is not a diagnosis of exclusion but frequently a manifestation of demonstrable organic pathology. The diagnostic yield of Esophagogastroduodenoscopy in this population approaches 80%, driven by a burden of *Helicobacter pylori* gastritis that significantly exceeds historical national estimates and challenges the low prevalence narrative of the Asian Enigma in Indonesia. Critically, our findings dismantle the reliance on visual inspection during endoscopy. The existence of significant endoscopic-histologic discordance demonstrates that macroscopic normality is an unreliable proxy for histological health. Consequently, we strongly advocate for a change in procedural standards: routine biopsy mapping, rather than targeted sampling, should be the prudent standard of care in this population to avoid missed diagnoses and the perpetuation of untreated organic disease. For the clinician at the bedside, these results offer a refined heuristic. The functional by default pathway should be applied with extreme caution in this demographic. Instead, a high index of suspicion for organic disease should be maintained, particularly for adolescents and those presenting with vomiting. These predictors should serve as triggers to optimize the timing of invasive investigation, ensuring that children with treatable organic pathology are identified early and managed effectively, unmasking the organic pain that lies beyond the functional label.

6. References

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