Iron Deficiency Anemia: The Utility of Upper Gastrointestinal Endoscopy and Histopathology

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Abstract

Background: occult blood loss must be considered as a possible cause in every case of iron deficiency anemia.
Objective: to evaluate upper gastrointestinal endoscopy in finding a potential cause for iron deficiency anemia among children in Al-Anbar governorate.
Methods: Twenty five children aged 2-14 years, referred to the gastroenterology unit in Al-Ramadi General Hospital for upper gastrointestinal endoscopy had iron deficiency anemia. Fiberoptic endoscopy was used under general anesthesia and endoscopic tissue biopsies were taken from 22 patients for histopathological examination.
Results: The main presenting signs and symptoms were pallor, abdominal pain, and stunting. The upper gastrointestinal endoscopy showed thinning of duodenal folds & serrated mucosa in 8 (32%), duodenal ulcer in 3 (12%), esophageal varices in 1 (4%), nodular gastritis in 1 (4%), and reflux esophagitis in1 (4%), with a yield rate of 56%.
While tissue biopsies revealed histopathological findings suggestive of celiac disease in 12 (48%), Giardia lamblia in 2 (8%), Helicobacter pylori gastritis in 1 (4%), and esophagitis in 1 (4%). There was a significant association between the endoscopic finding of thinning of duodenal folds and serrated mucosa and the histopathological finding suggestive of celiac disease, $P<0.05$.
Conclusion: Iron deficiency anemia in children 2-14 years of age warrants upper gastrointestinal endoscopy to find potentially treatable causes for the iron deficiency anemia.
Key words: Children; Iron deficiency anemia; Upper gastrointestinal Endoscopy.

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Introduction

Iron deficiency anemia (IDA) is the most common form of anemia worldwide, resulting when the available iron is insufficient to meet body's requirements[1].
IDA may result because of inadequate iron supply when diets contain insufficient amounts of bioavailable iron, or when there is impaired absorption of iron. It also results because of increased iron requirements when there is rapid growth, blood loss, and during pregnancy and lactation[2].Anemia caused solely by inadequate dietary iron is unusual before 4-6 months but becomes common at 9-24 months of age. Thereafter, it is relatively infrequent. Blood loss must be considered a possible cause in every case of iron deficiency anemia, particularly in older children[3].
Careful history and physical examination including nutritional assessment, may uncover the cause of IDA[4]. The diagnosis of IDA is often confirmed by the outcome of a therapeutic trial of iron but the search for the underlying causes must persist despite a positive response[2]. The current practice in adults with IDA is to investigate both the upper and the lower gastrointestinal tract in order to locate gastrointestinal diseases resulting in IDA[5]. Up to our knowledge there are no such guidelines for children. The prevalence of IDA among primary school children (6-12years) during the year 2000 in Ramadi district was 9.36%[6].
This study aims at evaluating the yield rate of upper gastrointestinal endoscopy and histopathology in finding a potential cause for IDA among children in Al-Anbar governorate.

Methods

Among children referred to the gastroenterology unit in Al-Ramadi general hospital for upper gastrointestinal (GI) endoscopic examination, 25 children (2 – 14) years of age with IDA were included in the study during the period from the 1st February 2004 to the end of October 2004.
A questionnaire form was filled by the researchers for each child asking about age, sex, residence, and the presenting symptoms. Complete physical examination was done for every child including weight (wearing lightest possible clothes) to the nearest 0.1kg. using electronic scale supplied by UNICEF and height to the nearest 0.1cm. using standard stadiometer. The cutoff points for low weight for height (wasting) and low height for age (stunting) were -2 Z-scores as compared to NCHS/
Venous blood samples were examined for hemoglobin(Hb) levels using Drabkin method, Hb less than the lower limit of normal(- 2 standard deviations) for age and sex was considered as anemia[8]. For each anemic child blood film, serum iron, total iron binding capacity was done and transferrin saturation less than 16% was regarded as IDA when the blood film was consistent with IDA [2].
After confirming IDA, the parents of all patients consented in writing to upper GI endoscopy under

general anesthesia. Fiberoptic endoscope (Pentax FG-29W, SN-A 11850, Japan) was used. Endoscopic mucosal tissue biopsies were taken in 21 patients. Esophageal, gastric and distal duodenal in 1 patients, gastric and distal duodenal in 11 patients and only distal duodenal in 9 patients. All tissue specimens were examined by an experienced pathologist.

Chi-square and Fisher's exact probability tests were used to examine the association of endoscopic findings and the histopathological findings. P value less than 0.05 was regarded as statistically significant[9].

Results

A total of twenty five patients were enrolled in the study, fifteen males (60%) and 10 females (40%). The main presenting signs and symptoms are shown in **Table-1**.

The endoscopic findings in order of frequency were: normal in 11 (44%), thinning of duodenal folds and serrated mucosa in 8 (32%), duodenal ulcer in 3(12%), esophageal varices in 1 (4%), nodular gastritis in 1 (4%), and reflux esophagitis in 1 (4%), **Table-2**.The yield rate of upper GI endoscopy for a potential cause of IDA was 56%.

The histopathological findings of the tissue biopsies are shown in **Table-3**. There was a statistically significant association of endoscopic finding of loss of duodenal folds and serrated mucosa with histopathological finding suggestive of celiac disease (subtotal villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis), ($P < 0.05$).

The result of histopathological examination in the eleven patients with normal endoscopic findings showed findings suggestive of celiac disease in six patients, while it was normal in the remaining five without statistically significant difference, **Table-3**.

Discussion

Iron deficiency anemia is a common indication for endoscopy[10], with variable yield rates in finding a potential cause for IDA ranging from 28%[11] to 60%[12] depending on the criteria of patients' selection, experience of the endoscopist and the degree of satisfaction of the gastroenterologist by a lesion to be considered as a potential cause for IDA or a coincidental finding[5]. The yield rate of upper GI endoscopy in finding a potential cause for IDA in this study (56%) is on the high range side, probably because the sample didn't contain children less than two years of age where nutritional IDA is more common[3].

Thinning of duodenal folds and serrated mucosa on endoscopy was significantly associated with histopathological findings suggestive of celiac disease (subtotal villous atrophy, crypt hyperplasia and intraepithelial lymphocytosis). Certain appearances of duodenal mucosa on endoscopy such as reduction or absence of folds, serrated or scalloped mucosa and mosaic pattern have been shown to have a high predictive value in diagnosing celiac disease on biopsy[13]. Awareness of these endoscopic features may alert the endoscopist to the presence of celiac disease and the need for duodenal biopsy in patients undergoing endoscopy for symptoms unrelated to the disease as well as those with vague, non specific manifestations[10]. However, normally looking mucosa on endoscopy does not rule out presence of celiac disease, as 6 out of 11 patients with normal endoscopy proved to have histopathological findings suggestive of celiac disease. Kori et al[14] reported that the negative predictive value of a normal appearing mucosa was 81.5% implying that a normal appearing mucosa does not rule out pathology.

The finding that tissue biopsies were suggestive of celiac disease in 12 out of 25 patients (48%) is consistent with earlier reports[15,16]. Celiac disease is increasingly recognized as a cause of IDA, which may be the only manifestation of the disease. In one series of 1026 patients with subclinical celiac disease, IDA was the most common presenting manifestation occurring in 39% overall[15]. Malabsorption of inorganic iron is thought to be the main cause of IDA[17]. Loss of iron because of mucosal sloughing of enterocytes and occult gastrointestinal bleeding may also be cotributary[16].

The other identified potential causes for IDA, namely duodenal ulcers, esophageal varices, gastritis and esophagitis are associated with chronic occult blood loss that might result in IDA[18]. Helicobacter pylori infection when present may also contribute to the increasing demand for iron and its eradication can be associated with the resolution of IDA[19, 20].

All the identified potential causes for IDA in this study are treatable conditions, when treated properly the response of IDA to iron therapy can be enhanced and recurrence prevented. From this study it can be concluded that IDA in children 2-14 years of age Warrants upper GI endoscopic examination to find out potentially treatable causes for IDA.

(Table-1)
The Presenting Signs and Symptoms in the Studied Children

Signs & Symptoms	*no.*	*%*
Pallor	22	88
Abdominal pain	18	72
Stunting	18	72
Anorexia	12	48
Abdominal distention	11	44
Chronic diarrhea	10	40
Vomiting	10	40
Wasting	2	8
Hematamesis	2	8
Melena	1	4
Total	25	100

(Table-2)
The Upper Gastrointestinal Endoscopic Findings

Endoscopic findings	***no.***	***%***
Normal	11	44
Thinning of duodenal folds & serrated mucosa	8	32
Duodenal ulcer	3	12
Esophageal varices	1	4
Nodular gastritis	1	4
Reflux esophagitis	1	4
Total	**25**	**100**

(Table-3)
Histopathological findings in relation to endoscopic Findings Histopathological findings

Endoscopic finding	*no.*	*Normal*	*Subtotal villous atrophy, crypt hyperplasia and intraepithelial lymphocytes*	*Giardia lamblia*	*H. Pylori gastritis*	*Esophagitis*
Normal	11	5	6	-	-	-
Thinning of duodenal folds serrated mucosa	8	-	6	2	-	-
Duodenal * ulcer	3	-	-	-	-	-
Esophageal varices*	1	-	-	-	-	-
Nodular gastritis	1	-	-	-	1	-
Reflux esophagitis	1	-	-	-	-	1
Total (%)	25 (100)	5 (20)	12 (48)	2 (8)	1 (4)	1 (4)
P value			< 0.05			

* Endoscopic biopsies not done.

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