

Study to evaluate the etiology of iron deficiency anemia at a teaching hospital in northeastern part of India

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ABSTRACT

Introduction: The causes of iron deficiency may be either due to excessive loss or, less frequently, decrease absorption. Data related to etiology are not available from this part of the country. **Objective:** A study to evaluate the etiology of iron-deficiency anemia at a teaching hospital in the northeastern part of India. **Materials and Methods:** In this cross-sectional study, cases of iron-deficiency anemia were selected from the OPD and indoor, after taking proper written consent. Iron-deficiency anemia was diagnosed by sending the complete hematological investigations. Other specific investigations including imaging were done in selected patients as per indications. **Results:** A total of 102 patients of iron-deficiency anemia were included in the study. The age of the selected population was between 18 and 80 years. 37.3% were male and 62.7% were female patients. Upper gastrointestinal endoscopy was done in 56, out of these, 9.7% had antral gastritis and 2.9% had a duodenal ulcer. Lower gastrointestinal endoscopy was done in 30 patients and out of these seven patients had hemorrhoids, one patient had multiple ulcers in the colon, one had ulcers in the sigmoid colon, and one had ulceroproliferative mass in the transverse colon. Biopsy through the upper gastrointestinal endoscopy showed chronic duodenitis in three patients (2.9%), carcinoma stomach in one (0.98%), and periampullary carcinoma in one (0.98%). Biopsy after lower gastrointestinal endoscopy showed one case each of carcinoma colon, ulcerative colitis, nonspecific colitis, and nonspecific enteritis. **Conclusion:** Diagnosis of iron-deficiency anemia is not sufficient without the diagnosis of underlying etiology. Special concern will be taken to gastrointestinal malignancies like colorectal cancers in which iron-deficiency anemia may be the only manifestation and diagnosis that can be missed if we do not investigate properly.

Keywords: GI bleed, iron-deficiency anemia

Introduction

Anemia is a global health problem affecting people of various ages, especially children; adolescents, elderly people, and females of reproductive age group. Iron deficiency is defined as the decrease in the total amount of iron in the body. Iron deficiency anemia (IDA) occurs when iron deficiency is sufficiently severe

to reduce the production of hemoglobin. IDA affects more than 1.2 billion individuals globally, and iron deficiency without anemia is even more common.^[1-5] The condition has an alarming prevalence rate among pregnant women that is 88% and 74% in nonpregnant.^[6] IDA occurs in 2–5% population of adult male and postmenopausal women in most of the developed world.^[7,8] In India, as per the National Family Health Survey-4 survey, which was conducted in 2015–16, more than 50% of pregnant women were diagnosed with IDA.^[9] One study on IDA conducted on adolescent girls at tertiary care hospital in India showed 50% of the adolescent girls were anemic and out of this 43.3% were mildly anemic, 3.3% was moderately anemic, and 3.3% were

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severely anemic.^[10] The causes of iron deficiency may be either due to excessive loss or, less frequently, decrease absorption. Various studies were done on anemia at various parts of India including Tamil Nadu, Maharashtra, Gujarat, Uttar Pradesh, but they focused on the prevalence of IDA, not on etiologies. In this study, we evaluate the etiology of IDA in OPD and admitted patients at Sir Sunderlal Hospital, Institute of Medical Sciences Banaras Hindu University, Varanasi.

Objectives

Study to evaluate the etiology of IDA at a teaching hospital in the northeastern part of India

Materials and Methods

This is a cross-sectional study conducted at the department of medicine at a tertiary care hospital from June 2018 to June 2019. Cases of IDA were selected both from the OPD and indoor, after taking proper written consent. Inclusion criteria: age >18 years, a patient of IDA with hemoglobin <11 g/dL. Exclusion criteria: age <18 years, a patient who did not give consent, microcytic hypochromic anemia other than IDA. Complete history and physical examination were done and patients were evaluated for etiologies of IDA. IDA was diagnosed by sending the complete hematological investigations including complete blood count, reticulocyte count, peripheral blood smears, serum iron, total iron-binding capacity (TIBC), ferritin, lactate dehydrogenase, stool for occult blood and ova, cysts, liver and renal function. Proctoscopy, anti-tissue transglutaminase/anti-gliadin antibody, serum hepcidin, upper gastrointestinal (GI) endoscopy, lower GI endoscopy, bone marrow examination including iron staining, X-ray, ultrasonography of the abdomen, computed tomography scans of the abdomen were done in selected patients as per indications.

Statistical analysis

Data were extracted and analyzed using SPSS version 16.0. The data were presented as mean \pm standard deviation for continuous variables and frequency with their respective percentages for categorical variables. Patient characteristics were described in terms of the median. For categorical data, the Chi-square test and Fischer's exact test were used and for continuous data student's *t*-test was used.

Results

A total of 102 patients of IDA were included in the study. The age of the selected population was between 18 and 80 years. Out of these 102, the majority of the patients (25.5%) belonged to the age group 21–30 years. 37.3% were male and 62.7% were female patients. The majority of females belonged to the age group 21–30 years. The main presenting complaint was weakness and easy fatigability which was present in 91% of patients, the next one was hemorrhoid in 31.4%. Menorrhagia was present in 23.6% of total female patients. 62.70% of patients were vegetarian and 37.3% were consuming a mixed diet. Four (3.9%) had a

history of pica and 2.9% had nonsteroidal anti-inflammatory drugs (NSAIDs) intake for a long period. The mean hemoglobin in male patients was 5.4 ± 1.4 and in female patients was 5.99 ± 2.01 . Digital rectal examination and proctoscopy were done in 62 patients, among them 34 patients (33.3%) had hemorrhoid (includes grade I, II, II with one or more than one columns), 25.5% had no abnormal findings and 0.98% had an anal fissure. Stool for occult blood was done in the majority of patients (95.1%) and before documenting it negative three samples of stool were sent. If 1st sample of stool comes positive then the 2nd and 3rd samples were not sent. 2nd and 3rd stool samples were sent of only those patients who had 1st stool sample negative for occult blood. Stool for occult blood was positive in 33.3% of patients in the 1st sample, 2.9% in the 2nd sample, and 1.96% in the 3rd sample. Ova and cyst were present in 16 of the total samples sent. Out of these, 10.8% had hookworm and 4.9% had *Ascaris lumbricoides*. Upper GI endoscopy was done in 56 patients who had either stool for occult blood positive or suspicious of upper GI bleeding. Out of 56 patients, 27 had normal upper GI endoscopy. 9.7% had antral gastritis, 2.9% had duodenal ulcer [Table 1]. Lower GI endoscopy was done in 30 patients and out of these 19 had no significant findings. Four patients (3.9%) had grade I internal hemorrhoid, two (1.96%) had grade II internal hemorrhoid, one (0.98%) had grade IV internal hemorrhoid, one had multiple ulcers in the colon, one had caecal diverticulitis, one had ulcers in the sigmoid colon, and one had ulceroproliferative mass in the transverse colon [Table 2]. Upper GI endoscopy with biopsy was done in selected patients and findings of the biopsy showed chronic duodenitis in three patients (2.9%), *Helicobacter pylori* gastritis in two patients (1.96%), carcinoma stomach in one (0.98%), periampullary carcinoma in one (0.98%), celiac disease in one (0.98%), and one (0.98%) had chronic inflammatory changes in the fundus.

Biopsy, after lower GI endoscopy, findings showed one case each of carcinoma colon, Ulcerative colitis, nonspecific colitis, and

Table 1: Upper gastrointestinal endoscopy (UGIE) findings

UGIE	Frequency	Percent
Not done	46	45.1
Normal	27	26.5
Antral gastritis	10	9.7
D1 and D2 ulcer	3	2.9
Sliding hiatus hernia with fundal erosion	3	2.9
Erythema and edema of D1 mucosa (duodenitis)	2	1.96
Gastritis with live worms in duodenum	2	1.96
Ulceroproliferative growth at GEJ and fundus	1	0.98
Periampullary mass with active bleeding	1	0.98
Decreased mucosal fold	1	0.98
Esophageal polyp with active bleeding	1	0.98
Gastric nodule	1	0.98
Isolated fundal varix	1	0.98
Pangastritis with D1 erosion	1	0.98
Scalloping of D2 segment	1	0.98
Severe PHG, nodularity of mucosa	1	0.98

nonspecific enteritis [Table 3]. Lower GI bleeding was the leading cause of IDA present in 39.2% of patients followed by upper GI bleeding (in 26.4%), menorrhagia (23.4% of total female), unclassified (20.5%), infectious including hookworm in 10.7% and *A. lumbricoides* in 4.9% of patients, celiac disease in 0.98%. In upper GI lesion/pathology group, maximum patients were in the age group of 61–70 (6.8%) followed by 51–60 (4.9%), 41–50 (4.9%), 21–30 (3.9%), and then 1.96% each of group 18–20, 31–40, and 71–80 years. In the lower GI lesion group, maximum patients belonged to group 51–60 year (10.7%) followed by 61–70 year (8.8%), 41–50 year (7.8%), 31–40 year (5.8%), 21–30 year (3.9%), and 1.96% in 18–20 year age group. In menorrhagia group, maximum female patients were in the age group 21–30 years (14%) followed by 31–40 years (6.2%), 18–20 years (1.56%), and 41–50 years (1.56%) [Table 4]. Some patients in this study group had multiple etiologies. One patient of 71–80 year age group had upper GI lesions with hookworm infestation, 1 patient in same age group had upper GI lesion with *Ascaris* infestation. 6 (5.9%) Patients had both upper and lower GI lesion and they belong to two patients from 61–70-year group and one each from 18–20, 21–30, 31–40, 51–60 years. Four patients had lower GI lesions with hookworm infestation and they belong to two from 61–70 years, one from 51–60 and one from 41–50 years. One patient of 31–40 year age group had lower GI lesions with an *Ascaris* worm infestation. One patient of 18–20 year age group had both upper and lower GI lesions with

menorrhagia and in one patient with both upper and lower GI lesions with hookworm infestation. Out of total 38 male patients, 14 (36.8%) had upper GI lesion, 19 (50%) had lower GI lesion, three (7.8%) had hookworm infestation, three (7.8%) had *Ascaris* infestation, one (2.6%) had celiac disease, and five (13.1%) were the unclassified group in which cause could not identify. Out of 64 female patients, 13 (20.3%) had upper GI lesions, 21 (32.8%) had lower GI lesions, 15 (23.4%) had menorrhagia, 8 (12.5%) had hookworm infestation, 2 (3.1%) had *Ascaris* infestation, and 16 (25%) were unclassified in which etiology not found. The etiologies of upper GI lesions include antral gastritis which is seen in 10 patients (9.8%) and out of these 10 patients 3 were (7.89%) and 7 (10.94%) were female. Next include chronic duodenitis which was seen in one male (2.63%) and two female (3.02%) patients, a total of three patients (2.94%). *H. pylori* gastritis was seen in two patients (2.94%), in one male (2.63% of total male) and one female (1.56%). Hiatus hernia was seen in a total of two patients (1.96%) and both were male. One male patient had NSAIDS-induced gastritis (0.98% of total). Pan gastritis is seen in one male patient (0.98% of total patients). The esophageal polyp was seen in one male patient (0.98% of total), fundal varix in a patient of chronic liver disease was seen in one patient (0.98% of total). Carcinoma of the stomach was seen in one female patient (0.98% of total), periampullary carcinoma was seen in one male patient (0.98% of total), and one patient of hemophilia had the feature of upper GI bleed. Other than these, on upper GI endoscopy two patients had live worms in the duodenum. One male patient had features of celiac disease. In lower GI pathology, hemorrhoid was the most common cause in both male (44.7% of male) and female (29.6% of female) population. The majority of patients having hemorrhoid belongs to mid to elderly age population. Only 7 out of 35 patients with hemorrhoids were below 40 years of age. Other pathology of lower GI tract includes ulcerative colitis in a 19-year-old female (0.98% of total) which also had features of duodenitis; nonspecific colitis was seen in one female patient (0.98% of total), nonspecific enteritis was seen in one male patient (0.98% of total), and one male patient (0.98% of total) had carcinoma of the colon. Total 15 female patients had menorrhagia, out of these one (6.67%) had fibroid uterus, one (6.67%) had an endometrial polyp, one (6.67%) patient had idiopathic thrombocytopenic purpura which responded after treatment, and one (6.67%) had hypothyroidism, and in other 11 patients (73.3% of menorrhagic female) there was no obvious etiology for menorrhagia and they put into dysfunctional uterine bleeding (unclassified group).

Table 2: Lower gastrointestinal endoscopy findings

LGIE	Frequency	Percent
Not done	72	70.6
Normal	19	18.6
Grade I internal hemorrhoid	4	3.9
Grade II internal hemorrhoid	2	1.96
Grade IV internal hemorrhoid	1	0.98
Multiple ulcers in colon	1	0.98
Small caecal diverticulitis, multiple small ulcers in ileum	1	0.98
Ulcer in sigmoid colon	1	0.98
Ulceroproliferative mass in transverse colon	1	0.98

Table 3: Upper gastrointestinal tract biopsy/lower gastrointestinal biopsy findings

	Frequency	Percent
Upper gastrointestinal tract biopsy findings		
Chronic duodenitis	3	2.9
<i>H. pylori</i> chronic gastritis	2	1.96
CA stomach	1	0.98
Periampullary carcinoma	1	0.98
Celiac disease	1	0.98
Chronic inflammation of fundus	1	0.98
Lower gastrointestinal biopsy findings		
CA colon	1	0.98
Feature of ulcerative colitis	1	0.98
Nonspecific colitis	1	0.98
Nonspecific enteritis	1	0.98

Discussion

This study was carried out at a tertiary care hospital between June 2018 and June 2019 and it gives us a fair idea of the etiologies of IDA in the eastern part of India. IDA is not a disease itself but a manifestation of an underlying disease, therefore, searching for the underlying disease is more important than replacing iron stores. Blood loss is a major cause of IDA, however, the commonest cause of IDA in developing countries is still nutritional deficiency.^[11,12] Upper and lower GI tract

Table 4: Age group-wise etiological classification

Age	18-20	21-30	31-40	41-50	51-60	61-70	71-80	Total
Etiology major classification								
Upper GI lesion								
<i>n</i>	2	4	2	5	5	7	2	27
%	1.96	3.92	1.96	4.90	4.90	6.86	1.96	26.47
Lower GI lesion								
<i>n</i>	2	4	6	8	11	9		40
%	1.96	3.92	5.88	7.84	10.78	8.82		39.22
Menorrhagia								
<i>n</i>	1	9	4	1				15
%	1.56	14.06	6.25	1.56				23.44
Infectious								
Hookworm								
<i>n</i>	3	1	1	2	1	2	1	11
%	2.94	0.98	0.98	1.96	0.98	1.96	0.98	10.78
Ascaris								
<i>n</i>		2	1				2	5
%		1.96	0.98				1.96	4.9
Celiac disease								
<i>n</i>		1						1
%		0.98						0.98
Unclassified								
<i>n</i>	2	6	2	1	5	4	1	21
%	1.96	5.86	1.96	0.98	4.90	3.92	0.98	20.5

evaluation is necessary to detect the cause of IDA, particularly in men >50 and in postmenopausal women, in whom iron deficiency is suspected to occur from a bleeding lesion. The majority of studied patients belonged to the reproductive age group and the elderly population. Females in the reproductive age group require more iron and also prone to develop IDA due to loss of blood during menstruation. In the elderly age group, the incidence of IDA was more because of the lesser intake of iron and losses of blood from the GI tract (hemorrhoids, malignancies). This study shows a preponderance of female patients (64 out of 102 patients) and females were predominant in all age groups. WHO also says that 30% of nonpregnant and 42% of the pregnant female have anemia and a majority of them belongs to IDA. As per the National Family Health Survey 2015–2016, 53% of all women in India were anemic.^[9] Among the occupation of the cases, the maximum belonged to the housewife group (48 out of 102) and next was the student group (19 out of 102 cases). In our study, IDA was more commonly seen in patients who were vegetarian by diet as compared to mix diet. 3.9% of our studied patients had a history of pica. On further investigation, all of these patients have worm infestation also. 2.9% of patients have a history of NSAIDs for a long time and one of them had features of NSAIDs-induced gastritis. Bleeding lesions in the GI tract were identified in about 50% of patients with IDA.^[13] IDA is considered an alarm sign for the presence of possible GI malignancies, and inadequate evaluation of patients with IDA may delay the diagnosis of GI malignancies especially colorectal cancer.^[14] Most of the studies shown that substantial GI lesions, particularly those of the upper GI tract are more common in patients with IDA. Cook *et al.* and

Kepczyk *et al.* showed 40% and 55% of patients had upper GI tract lesions, respectively.^[15,16] In our study, 26.4% (27 out of 102 patients) had upper GI lesions. The lesions seen in upper GI endoscopy were antral gastritis in 9.8%, chronic duodenitis in 2.9%, duodenal ulcer in 2.9%, *H. pylori* gastritis in 1.9%, hiatus hernia in 1.9%, and 0.98% each of pangastritis, esophageal polyp; NSAIDs-induced gastritis, carcinoma stomach, periampullary carcinoma, and celiac disease [Table 5]. Another study was done by Serefhanoglu *et al.* (2011) on 91 patients of IDA, in which upper and lower GI endoscopy was done and they found that 52 (57%) patients had upper GI tract conditions. The common abnormalities in the upper GI tract were esophagitis, gastritis, or duodenitis, gastric ulcer or duodenal ulcer and gastric cancer. The most common abnormalities included were antral gastritis (26.7%), *H. pylori* gastritis (20%), duodenitis (13.9%), and pangastritis (10.7%).^[17] These data showed that the incidence of antral gastritis, duodenitis, *H. pylori* gastritis were more in the above study than in our study. In our study, endoscopy was only done in selected patients, so this may be the reason for the lower incidence of the above findings. Two patients had a gastric ulcer, two had a duodenal ulcer, and one patient had gastric cancer which was also seen in our study. In a few studies, the rate of lower GI tract abnormality in IDA patients was 13.5–30%. In these studies, the most common lower GI lesion was found to be hemorrhoid (28.7%).^[13,17] In our study, the hemorrhoid was also the most common lower GI lesion found in 35.3% of IDA patients which was slightly more as compared to the abovementioned studies [Table 6]. Other lower GI lesions found in the present study were nonspecific colitis (0.98%), nonspecific enteritis (0.98%), carcinoma colon (0.98%), and

Table 5: Etiology of upper GI pathology/bleed

Etiology	Male		Female		Total	
	n	%	n	%	n	%
Antral gastritis	3	7.89	7	10.94	10	9.8
Chronic duodenitis	1	2.63	2	3.02	3	2.94
Duodenal ulcer	2	5.26	1	1.56	3	2.94
<i>H. pylori</i> gastritis	1	2.63	1	1.56	2	1.96
Hiatus hernia	2	5.26	0	0.0	2	1.96
NSAIDS-induced gastritis	1	2.63	0	0.0	1	0.98
Pangastritis	1	2.63	0	0.0	1	0.98
Esophageal polyp	1	2.63	0	0.0	1	0.98
Fundal varix	0	0.0	1	1.56	1	0.98
Carcinoma stomach	0	0.0	1	1.56	1	0.98
Periampullary carcinoma	1	2.63	0	0.0	1	0.98
Hemophilia	1	2.63	0	0.0	1	0.98

Table 6: Etiology of lower GI pathology/bleed

Etiology	Male		Female		Total	
	n	%	n	%	n	%
Hemorrhoid	17	44.74	19	29.69	36	35.3
Ulcerative colitis	0	0.0	1	1.56	1	0.98
Nonspecific enteritis	1	2.63	0	0.0	1	0.98
Carcinoma colon	1	2.63	0	0.0	1	0.98
Nonspecific colitis	0	0.0	1	1.56	1	0.98

ulcerative colitis (0.98%) which was also shown in a study, which had chronic colitis in 3%, inflammatory bowel disease (3%), and carcinoma colon in 1.5% of patients.^[17] Another major group in our study was the unclassified group in which we could not find the etiology of IDA. Since the majority of our studied patients were vegans, they had more chances of nutritional deficiency anemia as studied in the literature.^[11] In the female of reproductive age group, menorrhagia was also a leading cause of IDA.^[18] As observed in our study, total 15 (14.8% of total patients and 23.4% of the total female patients) out of 64 female patients had menorrhagia (causes identified were one each of fibroid uterus, endometrial polyp, idiopathic thrombocytopenic purpura, and hypothyroidism other 11 patients had no identifiable cause) so it is one of the major causes of IDA. Worm infestation was also one of the major causes of IDA. Among worm infestation, hookworm infestation is most common worldwide and it is a common cause of occult GI bleeding and anemia.^[19,20] Each worm can suck about 0.1–0.4 mL blood/day which may reach to >250 mL/day in cases of heavy worm infestation and leads to IDA as seen in our study that out of 102 patients 16 (15.7%) had worm infestation (2 patients had live worms detected in upper GI endoscopy). In our study, 11 patients (10.8%) had hookworm infestation and five patients (4.89%) had *A. lumbricoides* infestation.

Limitations of our study were that we could not go for capsule endoscopy because it is not available at our institute so we could not find the lesion between the duodenum and terminal ileum. One another limitation in our study was that we did not advice upper and lower GI endoscopy in all patients and studies show

that even in patients who have stool occult blood negative they may have GI lesions so we can miss these GI lesions.

Conclusion

Although the nutritional deficiency is the most common cause of IDA worldwide, the diagnosis of IDA alone without the diagnosis of underlying etiology is insufficient. Special concern will be taken to GI malignancies such as colorectal cancers in which IDA may be the only manifestation and diagnosis that can be missed if we do not investigate properly. Management of underlying pathology after replenishment of iron store is also very important in some specific groups like adolescents, reproductive age group, pregnancy, elderly populations, and patients with comorbidities like coronary artery disease to avoid frequent hospitalization and repeated blood transfusion.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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