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# A Cross-sectional Study by Esophagogastroduodenoscopy for Occult Bleeding in Chronic Hemodialysis Patients at Tanta in Egypt

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## Abstract

**Background and study aims:** Chronic hemodialysis patients are susceptible to a lot of complications. Gastrointestinal bleeding is one of the most serious and important complications in these patients result from many contributing factors like chronic uremia, stress and drugs. The present study is concerned with assessment the magnitude of occult gastrointestinal bleeding in chronic hemodialysis patients. Moreover we analyzed type and site of lesions accused in this bleeding.

**Patients and methods:** this study was performed in the period from April 2013 to October 2013, included a ninety chronic hemodialysis patients; fifty three males (58.9%) and thirty seven females (41.1%), at the Nephrology and Hemodialysis unit of Tanta university hospital, all patients investigated for occult bleeding by fecal occult blood test and detecting iron deficiency anemia, and those positive occult bleeding patients were the target of this study to be investigated by esophagogastroduodenoscopy (EGD). If EGD was normal; further colonoscopy was performed however it is not the interest of this study.

**Results:** 23/90 (25.6%) chronic hemodialysis patients were diagnosed to be suffering from occult bleeding. Fecal occult blood test, iron deficiency anemia and both of them were positive in 9, 11 and 3 patients respectively. EGD succeeded to detect source of bleeding in 11/14 occult bleeding chronic hemodialysis patients (78.6%). Stomach (61.1%) and erosions (38.8%) were the most common site and cause of occult bleeding in the studied chronic hemodialysis patients respectively.

**Conclusions:** Occult bleeding was not infrequent in this study (25.6%); Moreover, Upper gastrointestinal lesions detected by EGD were common in the studied chronic hemodialysis patients with occult bleeding (78.6%). Stomach and erosions were the most common site and type of lesions respectively.

**Keywords:** Hemodialysis; Occult bleeding; Gastrointestinal endoscopy; Iron deficiency anemia; Fecal occult blood test

## Abbreviations:

CHD: Chronic hemodialysis; GI: Gastrointestinal; GD: Esophagogastroduodenoscopy; FOBT: Fecal occult blood test; IDA: Iron deficiency anemia

## Introduction

Chronic kidney disease (CKD) is emerging to be an important chronic disease globally. One reason is the rapidly increasing worldwide incidence of diabetes and hypertension [1]. The prevalence of end stage renal disease (ESRD) in Egypt increased from 225 per million populations (pmp) in 1996 to 483 pmp in 2004. The main cause of ESRD in Egypt is hypertension followed by diabetes and still unknown causes represent about 15% [2]. There are about 1 million people in the world alive just because they have access to one form or another of renal replacement therapy (RRT). Ninety percent of them live in the developed countries [3].

Despite advances in dialysis and transplantation, the prognosis of kidney failure remains bleak. The United States Renal Data System (USRDS) reported more than 60000 deaths of patients with ESRD, and an annual mortality rate of dialysis patients in excess of 20% [4].

Anemia is a common feature in many patients with chronic kidney disease who do not yet require dialysis, with anemia becoming increasingly common as glomerular filtration rates (GFRs) decline below 60 mL/min per 1.73 $m^2$, particularly among diabetics [5].

Patients with chronic renal failure are commonly anemic from a combination of factors such as uremia, chronic disease, and gastrointestinal (GI) bleeding. Furthermore, therapeutic interventions, such as hemodialysis may be associated with rapid drops in hemoglobin. These may reflect blood loss during priming of extracorporeal circulation, hemodilution, bleeding associated with heparinization, or coincidental gastrointestinal blood loss. Such patients are at particular risk of gastrointestinal blood loss [6].

The World Health Organization defines anemia as a hemoglobin concentration lower than 13.0 g/dl in men and postmenopausal women and lower than 12.0 g/dl in other women. The European Best Practice Guidelines for the management of anemia in patients with chronic kidney disease propose that the lower limit of normal for hemoglobin be 11.5 g/dl in women, 13.5 g/dl in men, aged equal to or under 70 years old, and 12.0 g/dl in men more than 70 years old [7].

Moreover, other physiological mechanisms can be contributed to an increased bleeding tendency in ESRD patients include uremic platelet dysfunction, use of antiplatelet agents, and anticoagulants. A clue to the need for GI evaluation for blood loss is in patients who are not replenishing their iron stores despite adequate iron replacement or who demonstrate sudden decrease in stable hemoglobin [8].

In fact, the most serious source of bleeding in ESRD is GI bleeding. The risk of GI bleeding is increased in patients with chronic renal insufficiency. From 3% to 7% of all deaths among patients with ESRD are attributed to upper gastrointestinal bleeding [9].

GI bleeding has been frequently reported as a complication of advanced chronic renal failure [1-3] and is the cause of mortality in 3-7% of such patients [10].

Occult blood loss is a common finding in chronic renal failure, with patients frequently exhibiting guaiac-positives tools without a drop in hematocrit. The prevalence of fecal occult blood test (FOBT) positive results in patients with CKD is estimated to be 19% and 6.2% in ESRD on maintenance hemodialysis [11].

Occult GI bleeding is the most common form of GI bleeding and generally presents in the two following clinical scenarios: (1) iron deficiency anemia and, (2) fecal occult blood. Both of these forms of bleeding are unrecognized by the patient, and thus are referred to as "occult" bleeding [12].

In those CHD patients, anemia which is caused by hidden GI bleeding will not be corrected except if the source of bleeding is detected and treated. EGD is the procedure which can examine the upper GI tract in such cases.

The aim of this study to assess the prevalence of the GI occult bleeding problem among patients on CHD, as well as to analyze distribution and characteristics of upper GI lesions responsible for occult bleeding in these patients.

## Patients

This study was carried out on a total of 90 ESRD patients on CHD at the Nephrology and Hemodialysis unit of Tanta university hospital in theperiod from April 2013 to October 2013.

### Inclusion criteria

All patients in this study were chronic on hemodialysis; they have been on hemodialysis for at least 6 months. Those patients were 53 males and 37 females.

We detected occult GI bleeding in CHD patients depending on (FOBT) and/or (IDA). The patient was considered suffering from IDA if Transferrin Saturation (TSAT) was less than 20%.

When occult bleeding is suspected, a GI lesion was expected and most of these occult bleeding CHD patients were investigated by EGD.

When EGD failed to detect source of bleeding patients underwent colonoscopy, however, this was not included in this study.

**We divided CHD patients with occult bleeding into 3 groups:**

Group 1: positive FOBT alone=9 patients

Group 2: IDA alone=11 patients

Group 3: positive for both FOBT and IDA=3 patients

**Patients were excluded** if they had Overt GI bleeding either upper or lower (2 patients) or Bleeding from other orifices e.g. epistaxis, vaginal bleeding or piles (1 patient).

We were looking for detecting prevalence of occult bleeding in the studied CHD patients, moreover, detecting upper GI lesions accused in this bleeding and repeat the FOBT and/or TSAT after one month of treatment to evaluate the outcome.

Written consents were taken from all patients included in this study. The protocol was approved from the ethical committee, Faculty of medicine, Tanta University.

## Methods

All ninety patients were tested for both FOBT and IDA by TSAT.

### Measurement of occult blood in stool [13]

One step diagnostic rapid test for occult blood in stool: using POLYMED ACCURATE cassettes.

### Endoscopic examination

EGD was done by (PENTAX VIDEOSCOPE EPK-1000). All procedures were tolerable without any complications.

## Results

In the period from April 2013 to October 2013, a total of 90 ESRD patients on CHD at the Nephrology and Hemodialysis unit of Tanta university hospital underwent investigations to detect occult bleeding either by FOBT and/or IDA (Table 1 and 2). In these patients whom suffered from occult bleeding, a gastrointestinal lesion was expected and most of them were investigated by EGD.

| | | N | % |
|---|---|---|---|
| Age | Range | 19 to 85 years | |
| | Mean+SD | 55.36+7.36 | |
| Sex | Male | 53 | 58.9 |
| | Female | 37 | 41.1 |
| Duration of hemodialysis | Range | 0.5 to 15 years | |

| | | | |
|---|---|---|---|
| | Mean+SD | 2.25+0.25 | |
| Possible cause of renal failure | HTN | 29 | 32.2 |
| | Obstructive uropathy | 16 | 17.7 |
| | Mixed HTN and DM | 9 | 10 |
| | Toxic nephropathy | 6 | 6.6 |
| | Unknown cause | 6 | 6.6 |
| | DM | 5 | 5.5 |
| | Pyelonephritis | 5 | 5.5 |
| | Hereditary | 4 | 4.4 |
| | Polycystic kidney | 3 | 3.3 |
| | Complicated Pregnancy | 2 | 2.2 |
| | Lupus nephritis | 2 | 2.2 |
| | Surgical removal | 2 | 2.2 |
| | Hypovolemia | 1 | 1.1 |

**Table 1:** CHD patients were 53 males (58.9%) and 37 females (41.1%), their age ranged from 19 to 85 years with a mean age 55.36 years, duration of hemodialysis ranged from 6 months to 15 years with a mean 2.25 years. Regarding the possible cause of renal failure in these patients, hypertension was the first cause in 29 cases (32.2%), obstructive uropathy in 16 patients (17.7%).

| Laboratory test | Minimum | Maximum | Mean | SD. Deviation |
|---|---|---|---|---|
| Hb (g/dl) | 4.9 | 15.9 | 10.49 | 2.01 |
| Platelets X 103 (/cmm) | 50 | 393 | 179.8 | 6.9 |
| RBCs (million/cmm) | 1.87 | 5.43 | 3.62 | 0.68 |
| WBCs (/cmm) | 1700 | 16100 | 6168.8 | 2872.1 |
| Urea (mg/dl) | 40 | 221 | 115.02 | 36.7 |
| Creatinine (mg/dl) | 2 | 15.7 | 8.08 | 2.88 |
| Serum Iron (mcg/dL) | 30 | 202 | 96.78 | 42.7 |
| TIBC (mcg/dL) | 234 | 422 | 291.7 | 33.6 |
| TSAT (%) | 7.5 | 78.9 | 34.6 | 17.7 |
| Serum ferritin (ng/ml) | 24 | 2450 | 930.6 | 738.5 |

**Table 2:** Shows the laboratory results of total subjects and reveals that the mean Hb was 10.49 g/dl, mean platelet count was 179,788.8 /cmm, mean serum urea was 115.02 mg/dl, mean serum creatinine was 8.08 mg/dl, mean serum iron was 96.78 mcg/dl, mean TIBC was 291.7 mcg/dl, mean transferring saturation was 34.6% and mean serum ferritin was 930.6 ng/ml.

| Groups | N | % of total patients (90) |
|---|---|---|
| +VE FOBT | 9 | 10 |
| IDA | 11 | 12.2 |
| Both FOBT and IDA | 3 | 3.3 |

**Table 3:** represents number of occult bleeding CHD patients in 3 groups, the first group was CHD patients with positive FOBT alone (9/90), the second group was CHD patients with IDA alone (11/90) and the third group was CHD patients with both positive FOBT and IDA (3/90) patients.

| Groups | No. of patients did endoscopy | EGD with detected lesions | Normal EGD |
|---|---|---|---|
| +VE FOBT | 7 | 6 | 1 |
| IDA | 4 | 2 | 2 |
| Both FOBT and IDA | 3 | 3 | 0 |
| Total | 14 | 11 | 3 |

**Table 4:** Represents results of EGD examination of the studied occult bleeding CHD patients in the 3 groups, EGD was performed in 7/9 patients from the 1st group (6/7) had endoscopic detected lesions and (1/7) patient was normal EGD result. In the 2nd group 4 out of 11 patients only were investigated by EGD, lesions were detected in (2/4). Regarding the 3rd group the all the 3 patients underwent EGD examination revealed presence of lesions.

| Site of lesions | Type of lesions | N. 18 | Cause of bleeding | N. 11 | % |
|---|---|---|---|---|---|

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | (n=18) | | (n=11) | | |
| Esophagus | 3 | 16.70 % | Reflux esophagitis | 2 | Reflux esophagitis | 0 | 0 |
| | | | Sliding hiatal hernia | 1 | Sliding hiatal hernia | 0 | 0 |
| Stomach | 11 | 61.10 % | Erosive gastritis | 6 | Erosive gastritis | 5 | 45.50 % |
| | | | Gastric ulcer | 2 | Gastric ulcer | 1 | 9.10% |
| | | | Angiodysplasia | 3 | Angiodysplasia | 1 | 9.10% |
| Duodenum | 4 | 22.20 % | Hemorrhagic duodenitis | 1 | Hemorrhagic duodenitis | 1 | 9.10% |
| | | | Erosive duodenitis | 1 | Erosive duodenitis | 1 | 9.10% |
| | | | Duodenal ulcer | 2 | Duodenal ulcer | 2 | 18.20 % |

**Table 5:** Shows results of the total EGD performed to 14 occult bleeding CHD patients according to site, type of lesion and cause of bleeding. A total 18 GI endoscopic lesions were found and tabled. According to site of the lesions, the most common site of lesions was stomach 11/18 lesions (61.1%), duodenum 4/18 lesions (22.2%), and esophagus 3/18 lesions (16.7%) respectively. Regarding the cause of bleeding, 11/14 patients (78.6%) had GI lesions explain occult bleeding. The most common cause of bleeding was gastro duodenal erosions 6/11 patients (54.5%), then peptic ulcer in 3/11 patients (27.3%) and one patient (9.1%) for each gastric angiodysplasia and hemorrhagic bulb duodenitis.

| | **Prognosis (repeated FOBT after 1 month of treatment)** | |
|---|---|---|
| | +ve FOBT | -ve FOBT |
| N | 1 | 8 |
| % | 11.1 | 88.9 |

**Table 6:** Shows the outcome of FOBT positive patients.

| | **Prognosis (repeated TSAT after 1 month of treatment)** | |
|---|---|---|
| | TSAT>20 | TSAT<20 |
| N | 4 | 1 |
| % | 80% | 20% |

**Table 7:** Shows the outcome of FOBT positive patients. FOBT repeated after one month of treatment of patients with detected lesions. Nine patients with repeated the FOBT and eight of them had negative test, while 1 patient still have positive test result. It shows also a significant improvement of TSAT of all IDA patients with detected lesions (5 patients) after 1 month of treatment and IV iron administration. 4 patients had TSAT>20 while only one still have IDA. P value is significant (p=0.003).

| | **Sensitivity** | **Specificity** | **Positive predictive value** | **Negative predictive value** |
|---|---|---|---|---|
| FOBT | 81.82% | 66.67% | 90.00% | 50.00% |
| IDA | 45.45% | 33.33% | 71.43% | 14.29% |

**Table 8:** Moreover, sensitivity and specificity and predictive values of FOBT and IDA in detection of upper GI bleeding depending on endoscopic results were performed. Regarding FOBT, sensitivity was 81.82%, specificity was 66.67%, positive predictive value was 90% and negative predictive value was 50%. While for IDA, Sensitivity was 45.45%, specificity was 33.3%, positive predictive value was 71.4% and negative predictive value 14.29%.

## Discussion

The risk of GI bleeding is increased in uremic patients, From 3% to 7% of all deaths among patients with ESRD in the United States are attributed to upper GI bleeding [14], and among patients with ESRD on hemodialysis, mortality due to upper GI bleeding is 3.5% [15] (Table 3 and 4).

Surprisingly, we detected occult bleeding in our CHD patients in 23 out of 90 patients (25.6%), depending on FOBT and/or IDA. Most of these patients underwent EGD examination 14/23 and we achieved diagnosis in 11/14 (78.6%). Bleeding related GI lesions were found in (52.9%) patients in Huang et al. study [16] and were found in (51.2%) patients in old Japanese study [17].

FOBT was positive 12/90 (13.3%) in both group (1) 9/90 (10%) and group (2) 3/90 (3.3%) CHD patients, which is higher than Akmal et al. (6.3%) [11]. Although patients with renal failure have a false-positive rate of FOBT more than non-renal failure patients, however our results after EGD examination of these patients revealed that 6/7 patients whom tested positive for FOBT, have at least one lesion responsible for occult bleeding (85.7%) and only one had normal EGD, that could be explained by severity of bleeding and high mean urea (115.02 mg/dl) and high mean creatinine (8.08 mg/dl) among our studied patients (Table 5 and 6).

Our results are supported by Bini et al. study [18], revealed that predictive value of FOBT in detecting occult GI bleeding increases as the severity of CKD worsens (from 23.9% in stage 1 CKD to 42.6% in stage 5 CKD). This explain why predictive value of FOBT in detecting upper GI bleeding in CHD patients (90%) is much higher than in non dialysis patients as in Chen et al. (42%) [19], Hisamuddin et al. (36%) [20] and Liu et al. (29%) [21].

In group 2, IDA was detected in 11/90 CHD patients represented (12.2%), however, in group 3 both IDA and positive FOBT were detected in 3/90 CHD patients (3.3%) (Table 7 and 8).

In the present study, IDA was found in group 2 and 3 in 14 patients (15.5%) from all 90 CHD patients depending on TSAT results of less than 20%. This was lower than what was reported in Jacobs et al. [22] (31%), Tessitore et al. (40.8%) [23] and Kalantar-Zadeh et al. (40%) [24]. It is well known that TSAT of 20% seems to be relatively good in terms of sensitivity, meaning that few patients are truly iron deficient with a TSAT much higher than 20% [25].

Regarding the 4/11 patients with IDA without positive FOBT who were examined by EGD, Two patients of them had upper GI lesions (50%), while the other remaining two, had not any upper GI lesions.

In case of the three patients with both positive FOBT and IDA, upper GI lesions were detected in all of them (100%).

Depending on EGD findings, Our results clearly shows that detecting occult bleeding is much higher using both FOBT and IDA (100%), while it is still high if FOBT is used alone (85.7%) and detection of IDA alone achieved the lowest results of presence of UGI lesions (50%). This result was supported by Stray and Weberg study [26].

According to our results, stomach was the most common site of lesions by eleven lesions (61.1%), then duodenum by four lesions (22.2%), and three esophageal lesions (16.7%). This was similar to others studies find thatgastric lesions are the most common in CHD patients as in Sotoudehmanesh et al. [27] (56.5%), Moriyama et al. [28] (71.7%) and Nardone et al. [29] (45.5%). While in Akmal et al. [11] the commonest lesion was duodenal involvement (alone or in combination with other lesions) and was found in 61.1% of the subjects.

Further subanalysis of the detected lesions, and regarding to their types, seven gastroduodenal erosions were detected as the most common type of lesions in these CHD patients (38.8%), followed by 4 peptic ulcers (22.2%), three gastric angiodysplasias (16.7%), two reflux esophagitis (11.1%), one hemorrhagic duodenitis (5.5%) and one sliding hiatal hernia (5.5%). Several different studies (Negri et al. [30], Chacaltana et al. [31] and Moriyama et al. [28]) pointed to the occurrence of erosive changes in (52%, 54% and 58% respectively) of patients of the same stage of renal failure as the most common cause of UGI bleeding. The second most common cause of occult bleeding among our cohort was peptic ulcer, we detected 1 gastric and 2 duodenal ulcers represented (22.2%) while Sibinović-Raičević et al. study on 30 ESRD cases, peptic ulcer was detected in only 2 patients (6%) [32].

An Iranian study of Khedmat et al. [33], revealed that duodenal ulcer in the uremic patients (CKD 16.1%, HD, 13.7%) was common, while an old American study by Zuckerman et al. [34] reported that among the 60 patients with CKD, the most common causes of bleeding were gastric ulcer (37%) and duodenal ulcer (23%), however, In a more recent Korean study by Hwang et al. [16] on 104 anemic CKD patients; The upper endoscopic findings considered gastric or duodenal ulcers to be important sources of GI blood loss (22.5%).

Regarding the outcome of occult bleeding CHD patients, nine patients who tested positive FOBT with EGD detected bleeding lesions, were treated either by endoscopic Argon Plasma Coagulation (APC) or medical treatment by Proton Pump Inhibitors (PPIs). FOBT was repeated after one month of treatment, amazingly, eight of them turned negative with treatment success rate of (88.8%), while one patient remained positive FOBT, he was examined by colonoscopy and no bleeding lesion was found, so he was advised to be examined by enteroscopy to detect the source of occult bleeding.

In case of IDA patients with detected lesions, TSAT was repeated after one month of treatment by PPIs and Iron, four of them had TSAT more than 20% with treatment success rate of 80%, while one patient still had IDA. Few studies conclude that TSAT is good clinical marker for iron supplementation therapy and follow-up in IDA patients [35,36].

According to these, FOBT has a high sensitivity (81.82%), specificity (66.67%), positive predictive value for upper GI lesions (90%) and negative predictive value (50%). While for IDA, Sensitivity was (45.45%), specificity (33.3%) positive predictive value was (71.4%) and negative predictive value (14.29%).

## Conclusion

In conclusion, occult bleeding was not infrequent in this study (25.6%); Moreover, Upper GI lesions detected by EGD were common in the studied CHD patients with occult bleeding (78.6%). Stomach and erosions were the most common site and type of lesions respectively.

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