Research Article

Analysis of factors affecting mortality outcome in ischemic bowel disease- a study of 50 cases

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Abstract

Introduction: Ischemic bowel disease is the outcome of inadequate supply of oxygen to the intestine leading to ischemia having a plethora of symptoms and signs which are often inconspicuous leading to delayed diagnosis exacerbating already poor patient outcomes. There is a definite need to classify patients into high and low risk categories, so that intensive monitoring and care can be delivered to improve mortality outcome. **Methods:** We have done a prospective study of 50 adult cases of ischemic bowel disease confirmed on radiology, intra-operative findings and histopathology and compared the mortality and severity of disease with various patient parameters and analyzed significant correlations if any. **Results:** Majority of patients were adult males above age of 50 years with acute presentation. Hypertension and diabetes were commonly seen. Clinically, tenderness and tachycardia were common. ECG was abnormal in 72% patients. On imaging, thrombotic SMA involvement was present in majority of patients. Therapeutically, 90% patients were explored with a high mortality rate (71%) commonly the cause being sepsis (47%). Overall mortality was 64%. Small bowel was commonly affected. Majority of patients suffered from sepsis requiring ionotropic and ventilatory support. All patients with SMV thrombosis survived. Raised serum creatinine and altered pH were strongly associated with mortality. Also patients with ischemic bowel segment more than 80cm were at a high risk of death. **Conclusion:** The need for a scoring system based on parameters discussed has to be addressed, to stratify patients who will require critical and specialized intensive care and improve mortality outcomes.

Keywords: Bowel ischemia, Bowel necrosis, Acute abdomen, Metabolic acidosis, Deranged serum creatinine.

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Introduction

Ischemic bowel disease is the outcome of inadequate supply of oxygen to the intestine leading to ischemia. It comprises of a plethora of symptoms and signs which are often inconspicuous leading to delayed diagnosis exacerbating already poor patient outcomes. Spectrum of bowel injury ranges from complete reversible alteration of bowel function to transmural haemorrhagic necrosis of intestinal wall. Ischemia or hypoxic injury to the bowel occurs with sudden or varying degrees of gradual occlusion of mesenteric arterial or venous circulation. It is a relatively modern age disease brought on by changing diet and unhealthy lifestyles. Incidence of Acute Mesenteric Ischemia (AMI) is 0.1 % of all admission [1].

Incidence of diagnosis is also on the rise due to readily available technology and higher rates of suspicion amongst the medical faculty. Surgical treatment of arterial embolism has improved outcome. However the mortality rates following surgery for arterial thrombosis and non-occlusive ischemia remains poor [2].

Early diagnosis based on a high degree of clinical suspicion and confirmed by radiological investigations can improve outcomes in embolism. Still, there is a dearth of curable treatment modalities mainly unhinged by late diagnosis adding to the mortality of this disease.

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There are multiple modalities which can be used to great effect, if used at the precise time in the progression of disease. Various studies have shown that the renal insufficiency, leucocytosis, age more than 70, small bowel involvement greater than 100cm predicted poor outcomes. [3, 4] Biochemistry of patients showing raised urea, alkaline phosphatase, amylase, gamma-glutamyltransferase were also associated with poor mortality outcomes [5].

In our prospective study, we enrolled 50 cases of ischemic bowel disease to study and compare the mortality and severity of disease with various patient parameters and analyze significant correlations if any.

Aims

The aim of our study was to assess epidemiological factors, comorbid conditions whether controlled and uncontrolled and relation to arterio-venous diseases in cases of ischemic bowel disease.

Further a detailed correlation of the disease process and outcomes in terms of mortality and morbidity were to be performed with a multivariate analysis of patients case history, clinical, investigations and postoperative findings.

Methodology

A total of 50 indoor patients above 18 years of age in the surgical wards of a major government hospital with definitive evidence of ischemic bowel disease based on preoperative radiological investigations or intra-operative evidence of bowel ischemia and patients with histopathological findings of ischemic bowel in resected specimens were enrolled into a prospective study ranging over a period of one year. Cases of bowel strangulation in hernia, volvulus, intussusception, adhesive obstruction and ischemic bowel disease diagnosed in post mortem reports were excluded. Data was collected from patient's history, linical examination findings, blood investigations including complete hemogram, renal function tests, liver function tests, lipid profile and arterial blood gases, radiological investigations like chest x-ray**,** abdominal x-ray**,** ultrasonography of the abdomen with or without doppler and a contrast enhanced CT scan. Also intra operative findings encompassing grade of peritonitis, presence of perforated bowel, pre-ischemic changes, gangrenous bowel segment length and histopathological reports of resected specimens were evaluated. The morbidities (if any) developed during hospital stay, condition at discharge or mortality figures were included in the data collection.

Results

On analysis of epidemiological factors and symptomatology, it was found that majority of the patients were males above the age of 50 years, with symptom duaration of less than 5 days and presenting with tachycardia and acute abdomen. Further on blood and radiological investigations, leucocytosis, altered pH, deranged serum creatinine, abnormal ECG and thrombotic / embolic phenomenon of superior mesenteric artery were observed. No major co-morbidities were seen except hypertension which was seen in 44% and diabetes in 26% of patients. The only drawback was that I-FABP, CABA and D-lactate could not be performed since facilities were not available. Almost 90% of the patients underwent a surgical procedure, of which resection and primary anastomosis were done in 40% and a stoma in 50% (Table 1).

Table-1: Percentage distribution of epidemiology, clinical presentation and diagnostic investigations in 50 patients of ischemic bowel disease.

Parameter	Percentage (of all 50 cases)
Age (>50yrs)	64%
Males	54%
Duration of symptoms (<5 days)	72%
Tachycardia	82%
Acute abdomen presentation	96%
Abnormal ECG	72%
Thrombotic SMA involvement	48%
Leucocytosis	66%
Deranged Sr creatinine	33%
Altered pH	42%
Underwent surgery / Stoma	90% / 50%

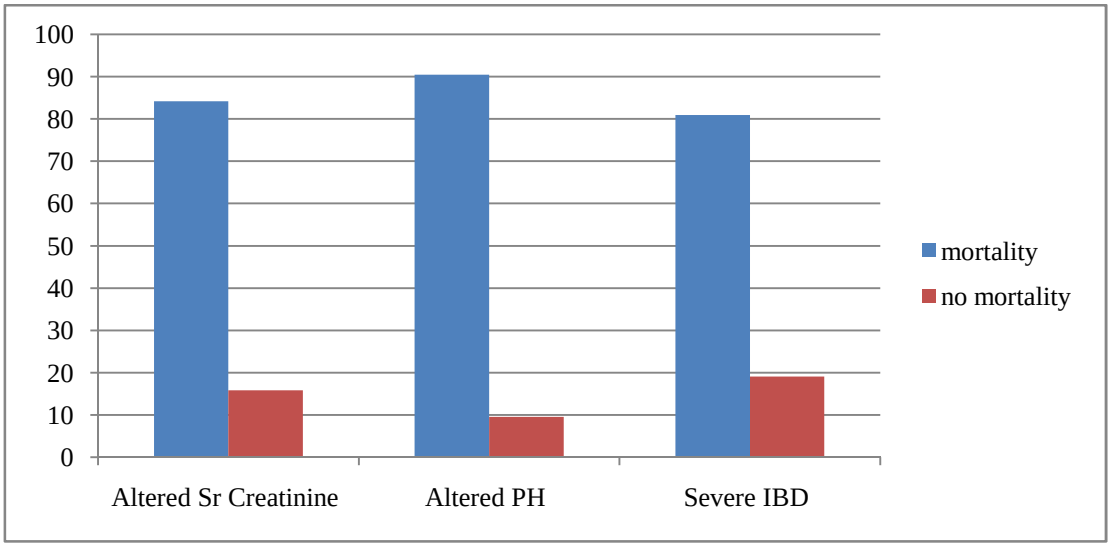
Table-2: Percentage distribution of the post-operative events in 45 cases.

Parameter	Percentage
Small bowel invovlement	99%
Ionotropic supports	56%
Post op intubation	42.2%
Sepsis	57.7%
Re-exploration	22.2%
Wound infection	77.7%
Mortality	71%

Table-3: Percentage association of significant factors affecting mortality in the total 50 patients.

Parameter	Percentage mortality
Age (>50yrs)	64%
Males	54%
Presented late (>5days)	85.7%
Stoma group / primary anastomosis	46% / 28%
SMA thrombosis	64%
Sepsis	88.4%
Deranged Serum creatinine	84.2%
Length of bowel (>80cm)	66.6%

Table-4: Stastically significant factors affecting mortality in IBD patients.



Of the total 45 patients who were explored, small bowel was most commonly affected and the mean length of gangrene was 66.5 + 39.57 cm with an overall mortality rate of 71%. Post-operative course was monitored and it was found that sepsis (57.7%) and wound infection (77.7%) were commonly observed. (Table 2). Of the total 50 patients, 32 died and 18 were discharged irrespective of being operated or conserved. Of those who succumbed, 64% had SMA thrombosis, 46% had stoma as a procedure and 54% had primary anastomosis. All patients with SMV thrombosis survived (18%). The most common cause of death was sepsis (47%) followed by myocardial infarction (25%) suggesting that postoperative sepsis was an important reason for mortality. Renal failure was found to be the cause in 15.6% of deaths as a result of sepsis, hypotension, renal vascular compromise. A minority of patients (6.25%) died due to ARDS. (Table 3)

On evaluation of association of mortality with laboratory and clinical parameters we found 64% of patients were above the age of 50 years, 54% were males and mortality was equally distributed. Twelve of the 14 patients who presented late

(> 5 days symptoms) died. Raised serum creatinine levels had a statistically significant association with mortality with P value of 0.0067 by Fischers exact test and positive predictive value of 0.4063 and negative predictive value of 0.1667. Altered pH (metabolic acidosis) was also associated strongly with mortality with a P value of 0.001, sensitivity of 0.9048 and specificity of 0.5517. Based on statistical analysis between successive increase in segment of ischemic bowel with mortality, the length of less than 80cm had a weak association and greater than 80cm had significant association with mortality. It was observed that the trend towards primary bowel anastomosis after resection of bowel segment less than 80 cms had a good prognosis with statistical significance having a P value of 0.0029 and odds ratio of 0.1176. (Table 4)

Discussion

Ischemic bowel disease is an enigmatic disease which shows an iceberg phenomenon and therefore can present as a diagnostic dilemna. Incidence of Acute Mesenteric Ischemia (AMI) is 0.1% of all admission in tertiary institutes[6]. Intestinal ischemia is an abdominal emergency that accounts for approximately 2% of gastrointestinal illnesses [7].

In our study, no significant association of advancing age with mortality was proved. Wadman M et al reported advanced age as a strong risk factor for death after operation for ischaemic bowel disease [8]. Elderly patients and those with a prolonged duration of symptoms had worse outcomes following surgical intervention for acute mesenteric ischemia in some series [9, 10].

In our study, there was a male preponderence in view of sex distribution of disease (54%) which correlates with world wide data. In our study, history of pain was elicited in 88% and distenstion in 52% of patients, which roughly averages to world literature. Vomiting was present in 48% of patients, the most common cause being ileus. In a study by Pecoraro F et al, vomiting and diarrhoea were in seen in 60-70% of patients [11]. In a study by Park WM et al, vomiting and diarrhoea were present in 35% each [12]. Our study findings were similar to results in western literature as well. History of fever was seen in 18%, however fever as a predictor has not been used on review of the literature. Park WM et al reported 21% patients had fever on presentation, but no correlation to the disease process could be found [12]. In our study, prolonged duration of symptoms (>5 days) was seen in 28% patients and was associated with 37.5% mortality whereas the mortality was 62.5% in patients having duration of symptoms less than 5 days. In a study by Rhee R et al, 75% patients had symptoms longer than 5 days, which was associated with increased mortality [13]. Kougias P et al reported that prolonged duration of symptoms were associated with higher mortality [9].

Comorbid conditions play an important role towards being predictors of disease outcomes. In our study, hypertension was seen in 44% and diabetes in 28% of patients. Across multiple studies, previous cardiac illness was shown to have a negative effect as independent risk factor of mortality of acute mesenteric ischemia and was corroborated by Acosta MA et al [14]. Diabetes mellitus was found to be negative predictor of the perioperative mortality in a study by Alhan E et al [15]. In study by Dahlke MH et al, in 83 operated IBD patients, hypertension (68%) and diabetes (64%) were the most common risk factor [16]. In our study there were no patients with DVT. DVT was not compared as risk factor in literature. In our study, 2 patients had hypercoagulable disorder. In a study by Rhee R et al, hypercoagulable states were the most prevalent associated conditions with IBD [13].

In our study, 82% had tachycardia, 28% had hypotensive shock, 96% had tenderness in the abdomen and 48% had abdominal guarding. In a study by Sitges-serra et al based on clinical parameters, tachycardia was found in 60%, hypotensive shock in 34% and 57% showed evidence of peritonitis [17]. Thus most patients of IBD do not present with hypotensive shock. In a study by Park KS et al, abdominal pain and tenderness were the main complaints in approximately 90% of patients [18]. In our series, absent bowel sounds was present in 18% of patients suggestive of ileus due to bowel wall edema secondary to ischemia. But Radonak J et al reported a predominant clinical picture of ileus in 35.9% of patients [19]. Therefore presentation of tachycardia, vomiting, acute abdomen without hypotension and clinical ileus may be a pointer towards IBD and should raise the level of suspicion and warrant investigations to prove or disprove the same.

In our study, higher incidence of abnormal ECG was seen in 72% which was suggestive of a risk factor in such patients. In a study by Kougias P et al, 28% of patients had arrythmias on ECG [9]. In our study, 58% of patients had normal abdominal radiograph,18% showed evidence of complications of IBD such as pneumoperitoneum and multiple air fluid levels,

whereas ileus was seen in 24% of the patients. In a study by Bottger T et al , x-ray of the abdomen showed signs of ileus in more than half of the patients, whereas Kougias et al reported ileus pattern in 68% of their series [9, 20].

Ultrasonography results were inconclusive and inconsistent in our study since mesenteric vasculature was not delineated due to excessive bowel gas and therefore not used as a diagnostic aid. In literature, ultrasonography has proven to be successful in 42.3% of cases of mesenteric ischemia, more so in chronic cases [17]. Doppler ultrasonography has been used to detect a significant stenosis (more than 50% block) in the mesenteric vessels in patients with chronic mesenteric arterial occlusive disease, but its role in AMI seems limited [21].

In our series, CECT Abdomen was suggestive of SMA involvement in 68% of people and SMV in 18% of which 48% had SMA thrombosis and 20% had SMA embolic phenomenon. It is considered to be gold standard investigation. CT is a very sensitive and specific tool to diagnose IBD as suggested by a meta-analysis from 1999-2006 which showed a pooled sensitivity of 93.3% and specificity of 95.9% [22]. Conventional angiography was not available at our facility.

Leucocytosis and leucopenia was seen in 66% of our patients with similar trends in previous series by Paladino NC et al and Oldenburg WA et al [10, 21]. In our study deranged serum creatinine was observed in 38% of patients. In a study by Bilgic IC et al, urea and creatinine, were significantly higher in non survivors, when compared to that of survivors [5]. In our study, Acidotic PH was seen in 42% of patients. In similar studies by Huang HH et al and Oldenburg WA et al, metabolic acidosis was commonly noted especially in elderly patients with deranged BUN and creatinine leading to poor prognosis [21, 23]. Metabolic acidosis as the most common biochemical derangement in approximately 70% of patients was reported by Sitges-Serra A et al thus corroborating with findings in our series [17]. In our study, 10% patients had a deranged LFT. In the study by Huang HH et al, increased AST were seen commonly in patients of IBD and were associated with poor prognosis [23]. We didn't find similar data on this kind of association in our review of literature.

Diagnosis was based on radiological, intraoperative findings and histopathology reports of resected segments of bowel. In our study, SMA involvment was common (92%), SMV was involved in only 8% of cases and we didn't have a single case of NOMI or focal segmental ischemia. Across studies, it has been shown that SMV involvement is seen in only 5-15% of patients whereas SMA occlusion was observed in more than 50% of cases. NOMI has an incidence of 0.3 – 8.5 % among critical ICU patients. [21] In our series, 5 out of 9 patients who had SMV involvement were operated on and all were discharged without any mortality. Out of 41 patients having SMA thrombosis/embolism 32 patients died and 9 were discharged. Arterial involvement was an adverse predictor for mortality.

None of our patients underwent endovascular management since the facility was not available. In our study, 90% of patients were operated on the basis of clinical judgment and imaging results. In a study by Park WM et al, 18% of patients were operated and bowel resection done. [12] Our data suggests that majority of patient were operated owing to the fact that they presented late to us or there was delay in diagnosis. Of the 9 cases with SMV involvement, 5 were operated and the rest were managed conservatively. Treatment of MVT is somewhat controversial and depends on the extent of intestinal ischemia. Patients without evidence of bowel infarction often recover spontaneously without operative intervention, and many are treated with anticoagulation alone [21]. The presence of peritoneal signs necessitates emergency laparotomy.

In our study, resection was performed in 90% of patients, with primary anastomosis in 40% and a stoma in 50%, in view of poor preoperative state of patients. Bowel resection was necessary in 31% patients as reported by Kougias P et al whereas Park WM et al had a resection rate of 34% in their series. [12, 9] The skewing of data towards bowel resection might be attributed to late presentation of patients in the course of disease, with non viable bowel and lack of vascular surgery facilities.

Post operatively, patients were monitored and incidence of complications if any were charted. Five patients had an uneventful course in the wards and were discharged. In our series, 42% were intubated who failed extubation trial post operatively. With similar trends, Radonak J et al noted a 23% intubation rate whereas Park WM et al reported respiratory insufficiency as one of the most frequent post- operative complication requiring intubation in 36% of patients. [12, 19] Wound

infections were found in 77% of our patients of Southampton grading 4-5. Meta-analysis of 1197 patients showed that 50% of operated IBD cases developed wound infection and sometimes burst abdomen. [8] Of the total explored patients, 22.2% were rexplored. Bile leak was present 24% of our patients, necesitating rexploration and stoma creation. In the study by Kougias P et al, second-look operation was performed in 53% patients for review of new onset ischemia / biliary peritonitis. [9] Park WM et al reported a re-exploration rate of 40% in their series. [12] In our series, 55% of patients were on ionotropic supports post operatively due to persistent hypotension following sepsis and 57% of these eventually succumbed.

In a study by Park WM et al, sepsis was a common post operative morbidity (31%) whereas Kougias P et al reported a sepsis rate of 10% in postoperative patients. [9, 12] In our study, we had a mortality rate of 64%, which corroborates with western literature ranging from 50 -75%. [6] Acute mesenteric ischemia (AMI) is a potentially fatal vascular emergency with overall mortality of 60% to 80%. [17, 24] In a study by Sitges-Serra A et al, the overall mortality rate was 71 per cent [17] All our 32 deaths had SMA involvement and undergone surgery, with 28% having primary anastomosis and stoma in 72%. A meta-analysis of 1197 patients having IBD showed that the operative mortality rate for mesenteric ischemia was 47%. [3]

In our study, 55.5% of deaths were due to sepsis which remains the leading cause of mortality, followed by renal failure (15.6%) and ARDS (9.5%). In our study, 32.5 % of deaths occurred in individuals with prolonged duration of symptoms. Survival is approximately 50% when diagnosis occurs within 24 hours after onset of symptoms, but it drops sharply to 30% or less when diagnosis is delayed but was statistically not significant. [21] In our study, acidotic PH and deranged serum creatinine was statistically significant with occurrence of mortality thus having prognostic value in prioritising patients who need intensive care and urgent management.

In our study, age (>50yrs), sex (M>F) and prolonged duration of symptoms (>5 days) were equally distibuted with mortality and statistically not significant. In a study by Kougias P et al, renal insufficiency ($P < 0.02$), age >70 ($P < 0.001$), metabolic acidosis ($P < 0.02$), symptom duration ($P < 0.005$), and bowel resection in second-look operations ($P < 0.01$) were associated with mortality. [9] In a study by Ozturk G et al, postoperative morbidity and mortality were determined to be associated with previous acidosis, septic shock, acute renal failure, extent of the ischemia and extent of resection, second look operations, previous cardiac events, and the kind of affected bowel (colon involvement). [25] As per Cudnik MT et al, age, time delay to surgery, shock, and acidosis significantly increase the risk of mortality due to IBD, whereas intestinal resection has a protective effect. [3] Thus as compared to previous studies only pH and serumr creatinine were significant in predicting mortality whereas the rest were equivocal.

In literature, there is no classification for severity of IBD in post operative patients and such comparison with patient parameters has not been done. The need of such a comparison is to identify high risk post operative patients who would succumb to death if no timely intervention is done following intensive monitoring of patient paratmeters.

In our study, we have used the length of necrosed bowel (80cm) as a benchmark around which parameters of the patient were analysed to find correlation and trends similar to a study by Akilidiz HY et al, where the length of the necrosis and renal insufficiency were the primary factors that resulted in poor outcomes in IBD patients. [4]

The methodology for assumption is based on statistical analysis between successive increase in segment of ischemic bowel with mortality, where we found that 80cm had a weak association with mortality outcomes and hence ischemic bowel =>80cm was considered as severe IBD.

After analysis, we found that age, tenderness, tachycardia, hypotension, absent bowel sounds, deranged WBC counts, deranged PH, deranged INR, bile leak were equally distributed among severe and non-severe IBD, showing no trends towards statistical significance. Deranged serum creatinine was statistically significant with severe IBD, whereas abnormal ECG and post operative intubation had trends towards significance suggesting cardiac comorbidities and assisted ventilation had a role to play in the outcome of such patients. The main drawbacks of the study were the sample size and duration, wherein a longer duration of study may help achieve more conclusive parameters. None of our patients had ischemic colitis, celiac axis thrombosis, NOMI and

focal segmental ischemia. Endovascular treatment of high risk patients and on table revascularisation procedures were not performed in our patients due to lack of facilities and skilled abdominal vascular surgeons.

Conclusion

Acidotic PH and deranged serum creatinine are statistically significant with occurrence of mortality and thus have prognostic value in patients of ischemic bowel disease. Arterial involvement (SMA) is an adverse predictor for mortality. More than 80cm necrosed bowel (severe IBD) has a strong association with mortality outcomes. Sepsis remains a leading cause of death.

The need for a scoring system encompassing parameters discussed has to be addressed to stratify patients who will require critical and specialized intensive care and improve mortality outcomes. Record keeping of this rare but high mortality disease will give us more robust data for analysis and more conclusive results.

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