

## Prevalence, Pattern of Presentation, Risk Factors and Outcome of Acute Mesenteric Venous Thrombosis in Taif Province, Saudi Arabia, A Single Center Study

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### Abstract

**Background and aim of the study:** Mesenteric venous thrombosis has a global incidence of 10-15% of all cases of mesenteric ischemia; however reports from high altitude provinces of Saudi Arabia as Taif and Aseer recorded an incidence above 60%. The aim of this study is to record the incidence, pattern of presentation, risk factors; diagnostic tools and outcome of treatment in a single center (King Abdul Aziz Specialist Hospital) Taif, Saudi Arabia.

**Material and method:** In this retrospective chart review study, we reviewed the records and data of all patients presented to King Abdul Aziz Specialist Hospital, Taif, Saudi Arabia from January 2009 to January 2013 and their final diagnosis were proved to be acute mesenteric venous thrombosis. Traumatic, postoperative and non occlusive cases were excluded from the study.

**Results:** Sixteen patients with final diagnosis of acute mesenteric venous thrombosis were included in this study, out of 26 patients (61.5%) presented and diagnosed as acute occlusive mesenteric ischemia. Males were more affected than females. The mean age of the patients was  $55 \pm 13.4$  years. The mean duration of symptoms was  $4.9 \pm 1.4$  days. The most common presenting symptoms were; abdominal pain followed by nausea, vomiting, anorexia, bloody diarrhea and fever. The most prevalent physical findings was tachycardia followed by ileus, 5 patients presented by marked peritoneal signs 3 of them were shocked. Multiple risk factors were detected in all patients. Laboratory findings were not conclusive and diagnosis was established by CT angiography in most of the patients. During operation, all patients were found to have a segment of infarction of the small intestine and in one of them the cecum was involved. Resection of the gangrenous parts was done for all patients. Second look operation was performed in 25% of patients. The total mortality was 18.75%.

**Conclusion:** Acute mesenteric venous thrombosis is the most common cause of acute occlusive mesenteric ischemia in Taif province and this may be related to multiple risk factors. Being familiar with this disease is essential in making the correct diagnosis to be followed by prompt resuscitation with heparinization to be continued postoperatively to prevent recurrent thrombosis. Laparotomy should be performed as soon as metabolic and hemodynamic correction is done with resection of any infarcted segment. A second look operation may be required. If these steps are followed strictly and without delay, the prognosis of mesenteric venous thrombosis is often favorable.

**Keywords:** Mesenteric, venous thrombosis, Taif, Saudi Arabia.

### Introduction

Acute mesenteric venous thrombosis (AMVT) is defined as new-onset symptomatic thrombosis with presenting symptoms of less than 4 weeks duration (1). The disease accounts for approximately 10-15% of all cases of acute mesenteric ischemia (AMI), however, reports from high altitude regions of Saudi Arabia recorded a very high incidence of this disease approximating 60% of AMI or even more (2, 3). The risk of acute mesenteric venous thrombosis increases in patients with hypercoagulable states (4). Taif, Saudi Arabia is located in the western region at 1,879 meters (6,165 feet) above sea level.

As the altitude increases, atmospheric pressure decreases, with reduction of the partial pressure of oxygen and starts to affect humans at altitudes above 1,500 meters (4,900 ft) (3, 5). As a consequence of the hypobaric hypoxic environments, human residents at high altitudes develop numerous physiologic responses, especially on coagulation system and in particular, increased factor VIIa activity, in addition to dehydration, polycythemia and vascular spasms which may lead a higher liability for thrombo-embolic disorders (2- 6). Smoking, diabetes, pancreatitis, perforated viscus with

intra-abdominal sepsis, malignancy, portal hypertension and congestive heart failure are also common risk factors for acute mesenteric venous thrombosis (4). Blunt abdominal trauma and postoperative conditions especially after splenectomy, colectomy, and Roux-en-Y gastric bypass increase the risk of subsequent portal venous thrombosis, which rarely results in bowel infarction (7, 8). The most common presenting symptoms include diffuse, intermittent abdominal pain, this disproportionate pain has a slow progression and usually accompanied by low-grade symptoms for at least 48 hours (1). However, typical signs and symptoms of acute bowel ischemia are usually found and the surgeon must put in mind the aphorism of Warren and Eberhard (9), as they said; not everyone is aware that violent abdominal pain, ileus, and collapse may mean mesenteric vascular occlusion. Although abdominal distention is the most frequently presenting sign of acute mesenteric ischemia, it is not universally present (10). Other findings include; nausea, vomiting, and constipation, however, bloody diarrhea is also common (1, 10). The disease is now diagnosed at an earlier stage, largely because of the advent of readily available, highly sensitive, and specific diagnostic imaging modalities in addition, the proportion of cases in which the cause remains unexplained has decreased as accurate testing for hypercoagulable conditions has become more routine (1, 10, 11). Patients with acute MVT would have a fairly good prognosis if rapid diagnosis is reached and appropriate surgical therapy is done and long-term outcomes are good if patients receive long-term anticoagulant therapy (1, 12, 13). The aim of this retrospective chart review study is to record the incidence, pattern of presentation, risk factors; diagnostic tools and outcome of treatment in a single center (King Abdul Aziz Specialist Hospital) Taif, Saudi Arabia.

#### Patients and method

In this retrospective chart review study, we reviewed the records and data of all patients presented to King Abdul Aziz Specialist Hospital, Taif, Saudi Arabia from January 2009 to January 2013 after approval of the ethical committee and written consents were taken from the patients or the relatives of dead patients to use the data in their hospital records. The Inclusion criteria included; the

patients who had symptomatic thrombosis of duration less than 4 weeks and their diagnosis were proved to be acute mesenteric venous thrombosis. Exclusion criteria included; traumatic, postoperative and non occlusive cases. We reviewed age, gender, pattern of presentation, associated risk factors, laboratory, radiological and Intraoperative findings in addition to results of treatment and follow up data if available, in the 16 patients included in the study. Results were expressed as mean  $\pm$  standard deviation using SPSS program, version 15.

**Results:** Sixteen patients with final diagnosis of acute mesenteric venous thrombosis were included in this study, out of 26 patients (61.5%) presented and diagnosed as acute occlusive mesenteric ischemia. Male : female ratio was 3.2:1 other demographic data are shown in table 1. The mean duration of symptoms was  $4.9 \pm 1.4$  days. Figure 1 shows that the most common presenting symptoms were; abdominal pain (100%), nausea (85.7%), vomiting (68.75%), anorexia (56.25%), bloody diarrhea (25%) and fever in (25%). Figure 2 shows the physical findings showing that tachycardia were found in all patients (100%), however; shock is detected only 18.75% of patients, distension and ileus was the second most common finding (56.25%). Tenderness was found in all patients but marked peritoneal signs (rebound tenderness and rigidity) were detected in 31.25% of the patients only. Table 2 shows the associated risk factors. Laboratory findings; leucocytic count and D-Dimer level was high in all patients (100%). Secondary polycythemia was seen in 7/16 patients (43.75%). Diagnosis was established by CT angiography in 11/16 patients (68.75%) while in the 5 patients (31.25%) with marked peritoneal signs; diagnosis was established after exploratory laparotomy. Preoperative resuscitation was done for all patients with intravenous antibiotics and heparin was administered immediately intravenously once diagnosis was established, either preoperatively after CT angiography or intraoperatively after exploration. Operative findings are shown in table 3 and figure 3; during operation, all patients were found to have a segment of infarction of the small intestine with obvious thrombosis of the mesenteric veins but with patent mesenteric arteries; the ileum was the most commonly

affected followed by the jejunum; however in one patient (6.25%), the infarction extended from ileum to the Cecum. The mean length of the infarcted intestine was  $144\pm 98$  cm. resections with primary anastomosis were done of the affected intestinal segments and right hemicolectomy was performed for the patient with cecal involvement. Exploration revealed association of perforated acute appendicitis in 2 cases and appendectomies were done. Second look operation was performed in 4 cases and further resection was required in 3 (75% of the second look operations).

The total mortality was 3/16 patients (18.75%); one patient died intraoperatively from cardiac arrest and the other 2 patients died in the early postoperative period from the sequelae of sepsis. The dead patients presented in shock status, with marked peritoneal signs and during operation; the infarcted segment was  $>2m$  in all of them.

### Discussion:

Acute mesenteric ischemia was first described by Elliot in 1895 (14), as a cause of intestinal infarction, however; mesenteric venous thrombosis was first recognized and differentiated from mesenteric arterial occlusion by Warren and Eberhard in 1935 (9), and in the same year, Donaldson and Stout (15), performed experiments in dogs showing that AMVT might not lead to gangrene, may allow spontaneous recovery, and was probably related to the same factors causing venous thrombosis in other parts of the body. The proportion of cases of AMVT as a cause of acute mesenteric ischemia has varied widely in the literature but generally has decreased since its initial description where Warren and Eberhard's (9), meta-analysis yielded a rate of 35% to decrease in the recent reports in various studies to 5-15% (1, 4, 7, 10). In our study mesenteric venous thrombosis represented 61.5% of all cases of acute mesenteric ischemia. Similar results were recorded in Taif and Aseer (2 & 3). However the number of cases in this study and the other 2 studies is too small and larger studies are needed to validate this high incidence and its correlation to different risk factors.

The mean age of patients at presentation of acute mesenteric venous thrombosis is reported to be between 45 and 60 years, with

a slight male to female gender predominance (1). In the present series the mean age of the patients was  $55\pm 13.4$  years and male: female ratio was 3.2:1 which is similar to other studies (4, 13, 16).

The clinical features of AMVT are determined by the location and timing of thrombus formation within the mesenteric veins (1, 4, 10). The duration of symptoms before presentation in patients with MVT ranges from 5–14 days, and in over 75% of patients, the least reported duration were 2 days (10, 12, 13). The most common presentation is severe colicky, mid-abdominal pain that lasts for at least a few hours and which, early on, is out of proportion to the abdominal physical signs, however; non-specific symptoms are often reported as the presenting complaints so, a high index of suspicion is necessary for early diagnosis (1-4, 7). In our study the abdominal pain with mean duration of  $4.9\pm 1.4$  days was the most common presenting symptom (100% of patients) other symptoms included; nausea (85.7%), vomiting (68.75%), anorexia (56.25%), bloody diarrhea (25%), fever (25%) and tenderness was found in all patients but marked peritoneal signs (rebound tenderness and rigidity) were detected in 31.25%. Our results were in accordance to that recorded in other studies; in a series of 31 patients, Abu-Daff, et al. (13), recorded abdominal pain in 100% of patients with mean duration of 11.7 days, nausea or vomiting in 77% of patients, diarrhea in 16% of patients and peritoneal signs in 58.1% of patients, in the study of Acosta-Merida, et al. (4), which involved 21 patients; pain was found in 95.2% with peritoneal signs in 71.4% of patients, and in the study involved 53 patients, Rhee et al (16), reported that; pain was found in 83% of patients, bloody diarrhea in 51%, anorexia in 53%, nausea or vomiting in 42% and peritoneal signs in 36% of patients.

The risk of acute mesenteric venous thrombosis increases in patients with hypercoagulable states (thrombophilia) as polycythemia, protein C and S deficiencies, malignancy (may cause thrombosis because of thrombophilia or by direct extension of the tumor), portal hypertension, perforated viscus with intra-abdominal sepsis, blunt abdominal trauma, previous abdominal surgery (open or laparoscopic), pancreatitis, smokers, oral

contraceptives are also at increased risk of venous thrombosis (4, 7, 8). Orr *et al.* (17), in his study revealed that, two or more concomitant risk factors, whether inherited, acquired, local or systemic have been identified in some patients supporting the concept of a 'two-hit' hypothesis for MVT. In the present study all patients had at least 2 risk factors or more supporting the previous hypothesis where all of them were living in altitude or high altitude environment (Taif province and related districts) with the known effect of hypobaric hypoxia on coagulation system with increased factor VIIa activity, in addition to dehydration, polycythemia and vascular spasms which may lead to a higher liability for thrombosis (2, 3, 5, 6). Moreover, secondary polycythemia was seen in 43.75% of our patients and in 31.25% a history of DVT was found, which is coincident with that reported in the literature (2-6, 15). Gupta and Ashraf (6), in their study found that venous stasis, hypercoagulability, and vessel-wall injury which represent the three leading factors of Virchow triad, appear to be present at altitude and high altitude areas inducing thromboembolic disorders, however; they concluded that, these factors may not exist, and further investigations are needed to understand the possible underlying mechanisms of increased risk of thromboembolism in such conditions.

Other possible risk factors which were detected in our patients were, 62.5% of patients were smokers, 62.5% were diabetics, 18.75% had congestive heart failure, in 18.75% there was liver cirrhosis with portal hypertension, in 12.5% there was a history of biliary pancreatitis and during exploration; concomitant perforated acute appendicitis were found in 2 cases (12.5%). It has to be noted that postoperative and traumatic causes were excluded from the study.

The lack of adequate sensitivity or specificity of the laboratory testing and plain films of the abdomen decrease their reliability to exclude or confirm the presence of MVT (1, 10, 11). In our study, leucocytic count and D-Dimer level was high in all patients (100%) and secondary polycythemia was seen in 43.75%. These data are non specific and were not related to the mortality. However; several studies have shown that D-Dimer level would have a high negative predictive value, and D-Dimer testing may be useful for the exclusion

of patients with suspected acute MVT (18). Abdominal x rays which were performed in our patients had no specific findings.

Abdominal CT with adequate portal venous phase contrast is the most reliable modality to diagnose AMVT with high sensitivity and specificity and the findings include; sharply defined enhancing venous wall representing the contrast in the vasa vasora with central attenuation that represents the thrombus (11). In the present study; CT angiography was helpful in preoperative diagnosis of all patients who underwent the procedure (68.75% of our cases), however, in the patients presented with marked peritoneal signs (31.25%); diagnosis was established after exploratory laparotomy, saving the time required for CT.

In this retrospective series of patients; preoperative resuscitation was done for all patients in addition to intravenous antibiotics and heparin was administered by intravenous route immediately after establishing the diagnosis, either preoperatively by CT angiography or intraoperatively after exploration. Early intervention and immediate heparinization upon diagnosis in addition to appropriate resuscitation with prompt correction of the hemodynamic and metabolic derangement are the most effective approach to save the patient (1, 4, 12, 13, 19). Naitove and Weisman (20), in their retrospective meta-analysis of anticoagulant use in 33 patients with MVT, showed that mortality was 50% for patients who did not receive heparin compared with 0% for those who received postoperative anticoagulation, these results have been reported in other studies (16, 21). Heparin prevents propagation of the thrombus and allows collateral vessels to develop, thereby improving survival, in addition it has been shown to prevent recurrence of thrombosis after intestinal resection and to be associated with lower mortality when recurrence does occur (12, 22). It is recommended that patients with acute MVT and a temporary risk factor to receive 3–6 months of anticoagulation with warfarin and lifelong therapy if persistent thrombophilia is expected (12, 23). In anticoagulated patients most thrombosed veins (> 80%) had been recanalized within 6–12 months compared with < 10% of non-anticoagulated patients (23).

The rapidity of thrombus formation in addition to its location and extent determine the severity of intestinal injury, however; gradual occlusion of the vein allows the development of collateral venous drainage without ischemic damage (1, 4, 10). Operative findings in this study showed that all patients were found to have a segment of infarction of the small intestine, the jejunum was involved in 43.7% and the ileum alone in 50% and in one patient (6.25%), the infarction involved the ileum and the Cecum. In agreement of our findings, other studies revealed that the ileum and the jejunum are the most common sites to be involved in acute MVT and the least is the colon and duodenum, the colon is less affected than other parts of the GIT because of its collateralization into the systemic circulation via the left renal vein, splenic vein and inferior hemiazygous system (13, 16, 24).

Non surgical interventions are still investigatory, however, recent studies have shown that angiography and vasodilator or thrombolytic agent injection before appearance of peritoneal signs or hemodynamic derangements, might have good results and may replace surgical intervention in a large number of those patients (11, 25).

Once intestinal infarction is suspected immediate exploration of the abdomen by laparotomy or laparoscopy has to be done with resection of short non-viable segments of intestine and it has been found that the use of intra-arterial papaverine will reverse associated arterial spasm and to avoid resection of potentially viable long ischemic segments (1, 4, 6). Moreover, infusion of thrombolytic agents via operatively placed catheters will help with heparin to prevent extension of infarction (26). In the present study, resections with primary anastomosis were done of the affected intestinal segments and right hemicolectomy was performed for the patient with cecal involvement. The mean length of the infarcted intestine was  $144 \pm 98$  cm, however; the infarcted segment was  $>2$  m in all the patients who died which was in accordance with many studies which correlated the mortality to the length of gangrenous lesion rather than the part affected (1, 13, 24).

In this study second look operation was performed in 4 cases and further resection was required in 75% of the second look

operations. Similar results were obtained by other investigators (10, 27, 28). Harnik and Brandt (1), declared in their study that; planned second-look operation during the first 12–48 postoperative hours is recommended by many authors to assess any questionable viability of intestinal segments limiting the extent of the initial resection.

The total early postoperative mortality in this series was 18.75% and mortality was significantly related to presentation in advanced stage and the length of the gangrenous lesion. The 3 patients who died in this study presented with shock and marked peritoneal signs which reflect a significant relation between mortality and presentation in advanced stage, a finding which was in accordance with other studies (1-4, 7, 13). Warren and Eberhard (9) reported an early postoperative mortality of 34%, Rhee et al, reported 30 day mortality of 27% (16). However there is overall decrease in mortality rates over the past four decades to reach 10–20%, which is similar to the results of our retrospective series (29). In conclusion; being familiar with acute mesenteric venous thrombosis is essential in making the correct diagnosis as it is the most common cause of acute occlusive mesenteric ischemia in Taif province and its related districts. This may be explained by the presence of certain risk factors which include; the altitude and high altitude environment with a higher liability for thrombosis in addition to the high incidence of smoking, diabetes, cardiac diseases and liver cirrhosis. Prompt resuscitation with effective antibiotics should be started immediately and intravenous heparin should be administered after establishing the diagnosis and continued postoperatively to prevent recurrent thrombosis and other possible thrombotic complications. Laparotomy should be performed as soon as metabolic and hemodynamic correction is done with resection of any infarcted segment, however some patients may require a second look operation for re-evaluation of the viability of the intestine. If these steps are followed strictly and without delay, the prognosis of mesenteric venous thrombosis is often favorable.

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**Table (1): Demographic parameters of the patients**

Total number of patients	16
Gender: Male	11(68.75%)
Female	5 (31.25%)
Age (years)	
Mean $\pm$ SD	55 $\pm$ 13.4
Residence:	
Altitude district > 1500m	16 (100%)

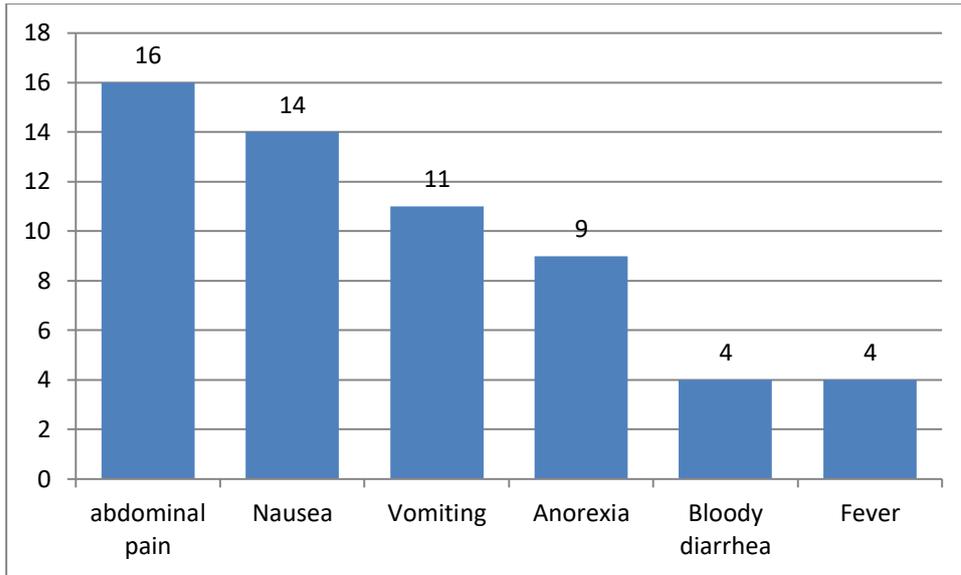
**Table (2): Associated risk factors**

Associated Factors	No (%)
Smoking	10 (62.5%)
D.M.	10 (62.5%)
Hypertension	9 (65.25%)
History of Cardiac problem	6 (37.5%)
History of C.H.F.	3 (18.75%)
History of D.V.T.	5 (31.25%)
History of liver cirrhosis	3 (18.75%)
History of biliary Pancreatitis	2 (12.5%)
Perforated acute appendicitis; (intraoperative)	2 (12.5%)

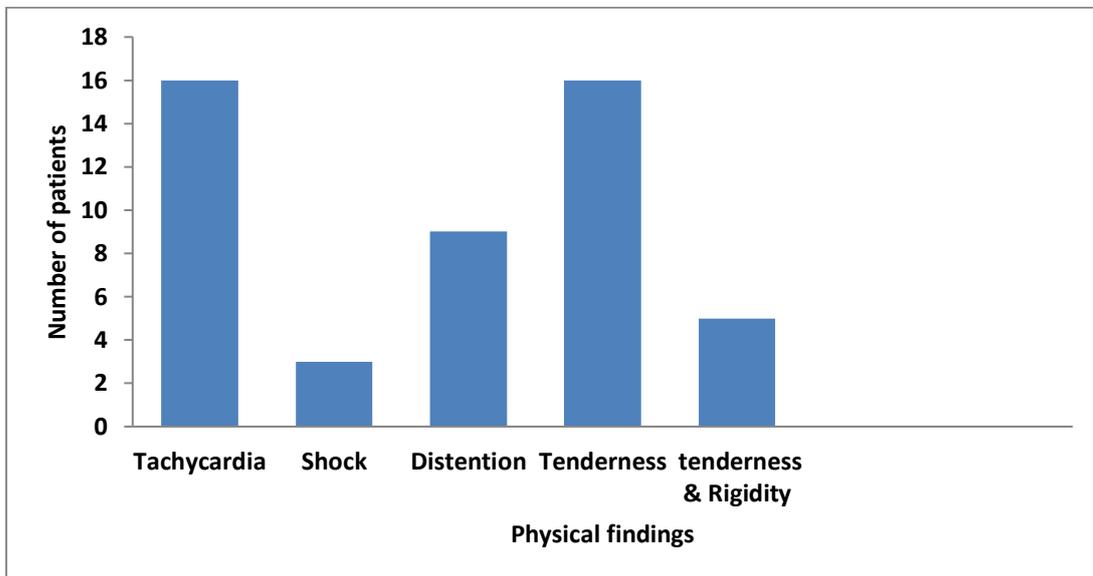
**Table (3): Operative findings**

<b>During operation</b>	<b>Infarction of the small intestine;</b> involvement of the jejunum:	43.75%
	involvement of the ileum alone	50%
	involvement of the ileum and cecum	6.25%
<b>2<sup>nd</sup> look operation;</b>	<b>2<sup>nd</sup> look operation;</b>	4 (25%)
	Further resection:	3 (75%)

**Figure (1): Symptoms in patients with acute mesenteric venous thrombosis**



**Figure (2): Physical finding in patients with acute mesenteric venous thrombosis**



**Figure 3:** operative findings after resection and anastomosis of the gangrenous part of the terminal ileum.

