

The Presentation of Mallory-Weiss Syndrome Secondary to Underlying Pathologies

Azhar Hussain^{1,2*}, Jasdeep Kaler², Elsa Tabrez³, Neha Ali⁴, Sheharyar Hussain⁵ and Shams Tabrez⁶

¹Doctoral Candidate of HealthCare Administration, Franklin University, Ohio, USA

²Medical Student, Xavier University School of Medicine, Aruba

³Medical Student, American University of Integrative Sciences, Barbados

⁴Psychiatry Resident, Nassau University Medical Center, New York, USA

⁵Doctoral Candidate of Clinical Psychology, John Jay College of Criminal Justice, New York, USA

⁶Assistant Professor of Medicine and Board-Certified Gastroenterology and Hepatology at University of Central Florida, Florida, USA

*Corresponding Author: Azhar Hussain, Medical Student, Xavier University School of Medicine, Aruba.

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Abstract

Mallory-Weiss Syndrome (MWS) is one of the common causes of acute upper gastrointestinal (GI) bleeding, characterized by the presence of longitudinal superficial mucosal lacerations. The esophageal lacerations that are seen with MWS stem from forceful retching and vomiting. The increased intraabdominal pressure causes gastric contents to be forced into the esophagus. The force itself has been postulated as being the cause of the Mallory-Weiss tears. The most common precipitating factors are considered vomiting and retching in correlation with a history of excessive drinking or physical findings consistent with chronic alcohol abuse. While chronic alcohol abuse is a well-known precipitating factor, other conditions such as hyperemesis gravidarum, bulimia nervosa, scleroderma, gastrointestinal reflux disease, and chemotherapy-induced hyperemesis can also lead to MWS. The diagnosis of MWS is suggested clinically by a typical history of hematemesis that is known to occur after one or more episodes of non-bloody vomiting. Diagnosis is achieved via upper GI endoscopy visualizing the Mallory-Weiss tears within the esophageal membrane. If the patient is stable, medical intervention is unnecessary. In the event that the amount of blood vomited is extensive, supportive management may be required such as blood transfusion, electrocautery, balloon tamponade.

Keywords: Mallory-Weiss Syndrome; Upper Gastrointestinal Bleed; Hematemesis; Bulimia Nervosa; Hyperemesis Gravidarum; Portal Hypertension; Cirrhosis; Chemotherapy-Induced Hyperemesis; Anorexia Nervosa

Introduction

Mallory-Weiss Syndrome (MWS) is one of the common causes of acute upper gastrointestinal (GI) bleeding, characterized by the presence of longitudinal superficial mucosal lacerations (Mallory-Weiss tears) [1]. Mallory-Weiss Syndrome is the cause of 5% of gastrointestinal (GI) hemorrhage episodes [2]. The most common precipitating factors are vomiting and retching related to a history of excessive drinking or physical findings consistent with chronic alcohol abuse [3]. Although Mallory-Weiss Syndrome was originally thought to be a characteristic complication of chronic alcoholics, research later debunked this as MWS was also visible in any patient who vomits forcefully [2]. This theory led to the consideration of MWS as a medical complication of bulimia nervosa [4]. Bulimia nervosa is a serious, potentially life-threatening eating disorder characterized by a cycle of bingeing and compensatory behaviors, one of which includes self-

induced vomiting [5]. The self-induced, forceful vomiting that is seen as characteristic of bulimia nervosa could lead to the complication of MWS, amongst many others. The association of MWS with hiatal hernia is still a matter of debate; however, a hiatal hernia was found in a considerable number of cases with MWS [6]. Other risk factors include hyperemesis gravidarum and gastroesophageal reflux disease (GERD) [1]. Upper gastrointestinal endoscopy procedures as such have only 0.07% to 0.49% complication rates to develop Mallory-Weiss Syndrome, and hence the risk is low [7].

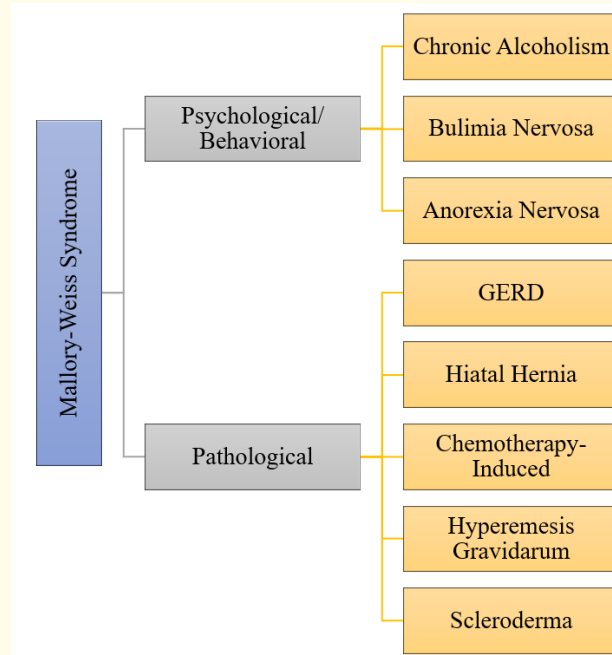


Figure 1: The associations of Mallory-Weiss Syndrome.

Epidemiology

Mallory-Weiss Syndrome was first described in 1929 by Dr. G. Kenneth Mallory and Dr. Soma Wiess who noted hematemesis and esophageal tears after bouts of vomiting and retching in 15 alcoholic patients [9]. It was further noted that because of its association with vomiting and retching, Mallory-Weiss Syndrome is not characteristic of just chronic alcoholism but is present in other conditions, as shown above in Figure 1. Mallory-Weiss Syndrome accounts characteristic of 1 - 15% of all gastrointestinal bleeding episodes; however, it occurs more frequently in individuals with alcoholism [10], specifically upper gastrointestinal bleeds. With the damage being associated with the esophagus, Mallory-Weiss Syndrome can predispose an individual to Boerhaave Syndrome, a spontaneous esophageal perforation. The highest incidence is between 40 and 60 years [8]. Males are 2 to 4 times more likely to develop Mallory-Weiss Syndrome than women [1]. The exact reason as to why men are more susceptible is not fully understood. However, the higher number of MWS diagnoses in male patients compared to female patients could be associated with the fact that the greater percentage of chronic alcoholic patients are male; hence, leading to greater susceptibility within the male gender. Hyperemesis is a frequent etiology for MWS present in young women and as such, pregnancy testing should be considered. In 85% of patients, the presenting symptom of MWS is hematemesis though the amount of blood is variable; ranging from blood-streaked mucus to massive bright bleeding [1,8]. In the more severe cases of MWS, other symptoms such as melena, dizziness, or syncope can be manifested [1]. This manuscript aims to explain the different risk factors leading to Mallory-Weiss Syndrome, the differentiating symptoms amongst the different risk factors, along with the treatment and management.

Discussion

Figure 1 presents with a visual representation of the various risk factors that increase susceptibility to Mallory-Weiss Syndrome. These risk factors, though all causing MWS, vary in manifestation and pathophysiology. The key similarity in these conditions is the involvement of the esophagus, regurgitation of gastric contents into the esophagus, and an increase in esophagus lumen pressure. The diagnosis of MWS tears is achieved via upper GI endoscopy by visualizing longitudinal tears within the esophageal mucosa. A history of hematemesis occurring after one or more episodes of non-bloody vomiting is typically clinical of MWS. The episodes of bleeding can be minimal in cases in which the patient is stable, but there could also be cases of severe bleeding in which significant intervention would be necessary. Since MWS is mostly self-limited and recurrence is uncommon, the initial management aims at stabilizing the general condition of the patient, and a conservative approach would be appropriate in most patients [1]. Sengstaken-Blakemore tube compression is the last resort in the treatment of a bleeding Mallory-Weiss tear in debilitated patients [1,10].

It is important to distinguish between Mallory-Weiss Syndrome and Boerhaave Syndrome, as both present with damage to the esophagus. While Mallory-Weiss Syndrome is a non-transmural esophageal tear, Boerhaave Syndrome is a transmural perforation of the esophagus [11]. The esophageal rupture in Boerhaave Syndrome is postulated to be the result of a sudden rise in intraluminal pressure produced during vomiting, caused by neuromuscular incoordination leading to failure of the cricopharyngeus muscle to relax [12]. Although the exact mechanism of Mallory-Weiss Syndrome is unknown, it has been postulated that when the intraabdominal pressure suddenly and severely increases, the gastric contents rush proximally under pressure into the esophagus [2]. It is this excess pressure from the gastric contents that results in longitudinal mucosal tears which may reach deep into the submucosal arteries and veins resulting in an upper gastrointestinal bleed [2,10]. Hiatal hernia, hyperemesis gravidarum, and bulimia nervosa all cause MWS via the theory of increased intraabdominal pressure. In chronic alcoholism and gastroesophageal reflux (GERD), causes of MWS tends to differ.

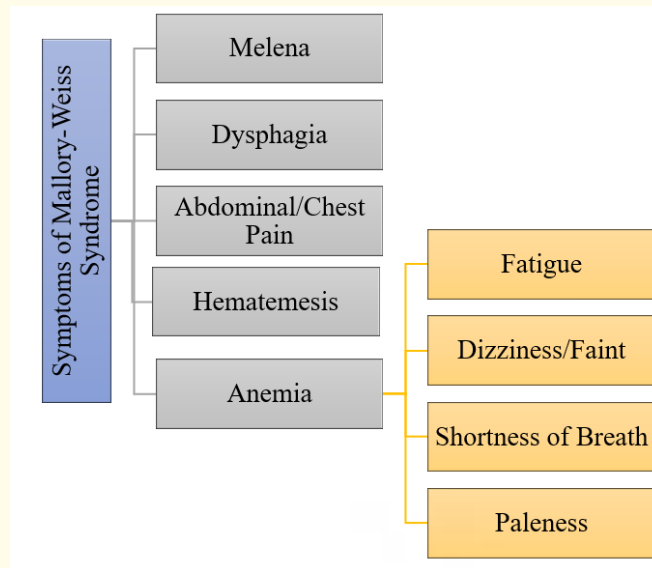


Figure 2: Symptoms associated with Mallory-Weiss syndrome.

Melena is a darker stool resulting from the presence of partly digested blood originating from the Mallory-Weiss tears. As the lacerations bleed, the blood enters the stomach, becomes decomposed, and as a result of this decomposition, gives the stool its black, tar-like

hue. Melena is a symptom that is characteristic of upper gastrointestinal bleeds such as, bleeds in the esophagus, as seen with in Mallory-Weiss Syndrome. The paleness can be an associative symptom of anemia. Mallory-Weiss tear bleeds can stop spontaneously and recur. Because of the recurrent nature of the bleeds, patients can present with anemia. Patients with MWS can present with secondary characteristics associated with anemia such as fatigue, shortness of breath, and others mentioned in Figure 2. In patients with Mallory-Weiss Syndrome, the hue of the blood in the vomit ranges from bright to dark. If the blood is fresh, it will bright red. More commonly, patients with Mallory-Weiss Syndrome will present vomit that is dark, clotted, and resembles the appearance of coffee grounds. The typical patient with Mallory-Weiss Syndrome will present with forceful retching that is followed by an episode of hematemesis. The hematemesis can be an insignificant amount, such as a tablespoon but can also be significant and may present with symptoms of hemodynamic instability. The abdominal/chest pain that can be seen with MWS is in relation to the forceful retching.

Psychological/behavioral risk factors

Chronic alcoholism

Alcoholism is highly prevalent and can cause advanced-alcoholic-liver-disease from alcoholic hepatitis or cirrhosis [13]. Globally, alcoholism affects 240 million people, mostly in Europe and the Americas [14]. Chronic alcoholism leads to excessive vomiting, leading to lacerations in the esophagus that are referred to as Mallory-Weiss tears. Heavy alcohol ingestion is considered to be one of the most important predisposing factors as about 50% to 70% of patients diagnosed with Mallory-Weiss Syndrome have a history of the same [15]. Bubrik, *et al.* noted that in the 59 patients in which Mallory-Weiss gastroesophageal lacerations were described, a history of chronic alcoholism was present in 69.5% of the individuals, and an episode of recent binge drinking present in 52.5% of the patients [16]. Pacha, *et al.* introduced a 51-year-old male with a past medical history of alcohol dependence had presented to the emergency room (ER) with hematemesis; an emergent endoscopy was performed, and a large mid-esophageal Mallory-Weiss tear was identified [17]. Though the exact association between chronic alcoholism and Mallory-Weiss tears requires more research, several case reports have been able to make the correlation. Patients with alcohol dependency or chronic alcohol use are much more likely to present to the ER with hematemesis. These Mallory-Weiss tears are noted during the endoscopic procedure that is done to locate the source of the bleed. In such extensive cases, medical intervention is required in order to contain the bleed and ensure the esophageal laceration is repaired.

Anorexia nervosa and bulimia nervosa

The differentiation between bulimia nervosa and anorexia nervosa is imperative when it comes to distinguishing between the two eating disorders. Individuals suffering from anorexia nervosa tend to present with a lower than normal body mass index (BMI) relative to their body type and height. This is a key difference between bulimia nervosa and anorexia nervosa as individuals with bulimia nervosa tend to present with a relatively normal BMI [18]. Anorexia nervosa can be characterized into two subcategories: binge/purge type and restrictive [19]. Similar to bulimia nervosa, patients with the binge/purge subtype of anorexia nervosa will self-induce vomiting to alleviate the fear of gaining weight. Furthermore, purgatory behavior can be seen as a method, for these patients, to alleviate some guilt that may be associated with indulging in ‘forbidden’ foods. Other purgatory behaviors besides self-induced vomiting may be the abusing laxatives, or excessive exercise. The restrictive type of anorexia nervosa encircles the notion of holding immense self-discipline. Patients with the restrictive subtype will significantly reduce their caloric intake to an extent that can be equivalent to self-starvation. Anorexia nervosa binge/purge type bears resemblance to bulimia nervosa and thus, may present with an association to Mallory-Weiss Syndrome. Bulimia nervosa is defined as an intense preoccupation with body weight and shape, with regular episodes of uncontrolled overeating (binge eating) associated with extreme measures to counteract the feared effects of overeating [20]. Due to the extremely secretive nature of binge eating and purgative behavior, bulimia nervosa may actually be quite difficult to identify.

DSM-V Criteria for Bulimia Nervosa	
•	Recurrent episodes of binge eating. An episode of binge eating is characterized by BOTH of the following: <ul style="list-style-type: none"> • Eating in a discrete amount of time (ex. within a 2-hour period) an amount of food that is definitely larger than what most individuals would eat in a similar period of time under similar circumstances. • Sense of lack of control overeating during an episode (ex., a feeling that one cannot stop eating or control what or how much one is eating).
•	Recurrent inappropriate compensatory behavior in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise.
•	The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for 3 months.
•	Self-evaluation is unduly influenced by body shape and weight.
•	The disturbance does not occur exclusively during episodes of anorexia nervosa.

Table 1: DSM-5 criteria for diagnosis of bulimia nervosa.

Table 1 presents the DSM-5 criteria for the diagnosis of bulimia nervosa. An essential feature that is used in the diagnosis is the recurrent use of inappropriate compensatory behaviors to prevent weight gain. Vomiting is the most common compensatory behavior seen in bulimia nervosa [21]. This can provide relief from physical discomfort and reduce the fear of gaining weight. This can lead to many medical complications including skin and dental erosion, electrolyte abnormalities, cardiovascular arrhythmias, esophageal pathologies, endocrine abnormalities, and in some cases, death. As this becomes a chronic condition, most that suffer will be able to induce vomiting without any aids. Those with eating disorders should be screened with a complete blood count, serum electrolytes, blood urea nitrogen, creatinine, and serum glucose [22]. An electrocardiogram is also preferred. Depending on what symptoms are presented, muscle enzyme values, lipid levels, and magnesium and zinc concentrations, use of electromyography, chest roentgenogram, and abdominal flat plate and endoscopic evaluation may be warranted [23]. The association of bulimia nervosa with Mallory-Weiss Syndrome is due to the purgatory behavior that is associated with the eating disorder. The purging behavior that is seen with bulimia nervosa can predispose an individual to Mallory-Weiss Syndrome. The forceful retching and vomiting can cause Mallory-Weiss tears as the self-induced vomiting can cause an increase in intraabdominal pressure. The increase in pressure will force the gastric contents from the stomach and into the esophagus. Purgatory behavior is the risk factor in patients with bulimia nervosa. Treatment would focus on treating the underlying eating disorder. With the management of bulimia nervosa, the purgatory behaviors decrease and the so does the feared complication of Mallory-Weiss Syndrome. Treatment of bulimia nervosa focuses on increasing control overeating, eliminating food avoidance, and changing maladaptive attitudes [24].

Pathological risk factors

Gastroesophageal reflux disease

Gastroesophageal reflux disease (GERD) is a condition that develops when there is a retrograde flow of stomach contents causing symptoms or complications [25]. GERD is sometimes also referred to as heartburn due to the retrosternal burning discomfort that is located in the epigastric area, radiating up towards the neck, and typically occurs in the postprandial period [25,26]. Some patients may report that postural changes, such as bending forward or laying supine can worsen the symptoms [25,27]. GERD is a chronic digestive disorder that affects the lower esophageal sphincter (LES), a muscular ring adjoining the esophagus and stomach [28]. GERD is extremely common, with a prevalence of approximately 20% of adults in the western culture [25]. Although there is no significant difference in prevalence among males and females, males tend to have a higher rate of complications with the rate of esophagitis 2:1 in males compared to females [25,26]. The pathophysiology of GERD has been described as one that is multifactorial in the sense that it involves esophageal alterations, disruption of the gastroesophageal junction, gastric factors, and visceral hypersensitivity [27]. The typical manifestation of GERD is heartburn, regurgitation, dysphagia while other symptoms can also include globus (lump in the throat) sensation, odynophagia, and nausea [28].

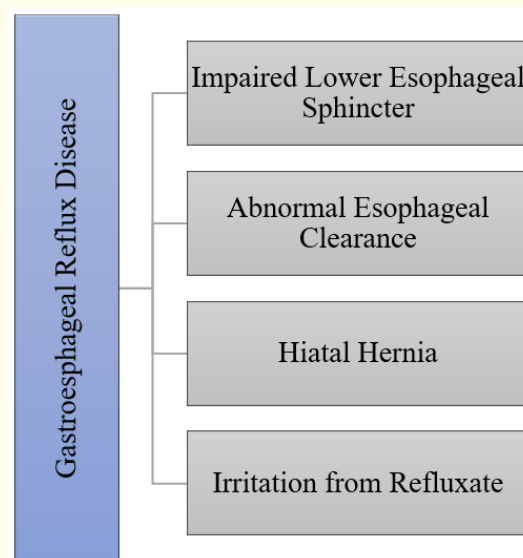


Figure 3: Proposed pathophysiology of GERD.

Figure 3 describes the various components of the pathophysiology of GERD that have been postulated. The lower esophageal sphincter (LES) acts as an anti-reflux barrier at the gastroesophageal junction, preventing acid from the stomach from entering the esophagus [25]. In normal individuals, a certain amount of gastroesophageal reflux will occur due to the transient relaxation of the LES that allows for the passage of a meal into the stomach. During that transient relaxation, gas from the stomach also escapes into the esophagus. In patients with GERD, increased relaxation of the LES is noted due to the association with a reduction in the pressures of the sphincter [25,26]. It should be noted that there are multiple known risk factors for decreased LES pressure such as pregnancy, diabetes, scleroderma, obesity, and some medications such as cholinergic antagonists, oral contraceptives, nicotine from smoking, and calcium channel blockers [25]. Hiatal hernias, on the other hand, common and usually do not present with symptoms. That being said, in patients with GERD, hiatal hernias are associated with higher amounts of acid reflux and delayed esophageal acid clearance [25,26]. Larger hiatal hernias are also known contributors to a decreased LES tone. Figure 3 also states irritation from refluxate as a mechanism of GERD. The pH of the gastric acid is less than 4, and, is extremely caustic [25]. Prolonged exposure of gastric contents to the esophageal mucosa can predispose an individual to develop esophagitis; the inflammation of the esophagus. Patients with GERD may also present with abnormal esophageal clearance. Under normal circumstances, the acid that reaches the esophagus from the stomach is cleared and neutralized by esophageal peristalsis and salivary bicarbonate [25,27]. During sleep, peristalsis is infrequent, prolonging acid exposure to the esophageal mucosa, and this can prove to be an explanation as to why the heartburn associated with GERD is more debilitating symptoms [25]. Due to the regurgitation of gastric contents into the esophagus, GERD is noted as a risk factor for Mallory-Weiss Syndrome [1].

Hiatal hernia

Hiatal hernia is defined as the protrusion of an organ, usually the upper part of the stomach into the chest cavity through the esophageal hiatal orifice of the diaphragm [1]. The esophageal hiatal orifice is an opening in the diaphragm through which the esophagus departs the mediastinum and attaches to the stomach. Under normal circumstances, the esophagus is anchored to the diaphragm such that the stomach cannot be displaced through the hiatus into the mediastinum [29]. Protrusion through the esophageal hiatal orifice becomes possible as the hiatal orifice is usually a little larger than the circumference of the esophagus. The slightly larger size of the hiatal orifice is to accommodate for the esophagus' change in circumference as food passes down through peristaltic waves. Because the esophageal orifice is slightly larger than that of the esophagus, protrusion into the mediastinum becomes possible.

The most common type of hernia is type 1 - sliding hiatal hernia. In a sliding hiatal hernia, there is a widening of the muscular hiatal tunnel and circumferential laxity of the phrenoesophageal membrane, allowing a portion of the gastric cardia to herniate upward [29,30]. The major significance of type I hernias is in their association with reflux disease [29]. Types II, III, and IV are the less common varieties and are collectively referred to as paraesophageal hernias. These paraesophageal hernias result from a localized defect in the phrenoesophageal membrane [30]. When it comes to sliding hernias, they are most commonly identified in two high pressure zones; the lower esophageal sphincter and the crural diaphragm [29,30]. Though there is no clear relationship between hiatal hernia and MWS, hiatal hernias have been found in a considerable number of cases with MWS [1]. It has been postulated that retching increases the potential for mucosal laceration by creating a higher-pressure gradient in the hiatus hernia as compared to the rest of the stomach [31]. It can be proposed that patients with a hiatal hernia are predisposed to a greater increase in the pressure of gastric contents entering the esophagus and in doing so, the pressure creates the longitudinal tears referred to as Mallory Weiss tears.

Figure 4 is a diagrammatic representation of how hiatal hernias could lead to the presentation of Mallory-Weiss syndrome. Hiatal hernias become a risk factor in the sense that, even with the slightest retching, a condition of increased pressure can be created, causing Mallory Weiss tears. It should be noted that despite hiatal hernias being seen as a co-finding in patients with Mallory-Weiss syndrome, the exact correlation is yet to be established. Symptoms and presentation of Mallory-Weiss Syndrome is similar to those depicted above in fig-

ure 2. The presentation of hiatal hernia, sliding or paraesophageal, is very similar to that of MWS. Due to the similarities in the symptoms, it can be postulated that as the presence of the hiatal hernia persists, symptoms cause the esophageal lining to weaken in a way that could lead to the presentation of Mallory-Weiss tears. Due to the dysphagia seen in hiatal hernia and the presence of possible of regurgitation of food content, a patient may retch or begin to vomit stomach food contents. The retching from regurgitation, along with dysphagia, could lead to the presentation of Mallory-Weiss tears. It should be noted that Figure 4 presents with a theoretical understanding of the mechanism of action of why a hiatal hernia may act as a risk factor for Mallory-Weiss Syndrome. Furthermore, the widening of the hiatal tunnel that can lead to a hiatal hernia can also be caused by a rise in pressure in the lower abdomen as seen in pregnancy, coughing, or straining. Regularly occurring regurgitation of the acidic stomach contents into the esophagus may cause damage to the esophagus and may even cause bleeding to occur as the submucosal arteries are disrupted.

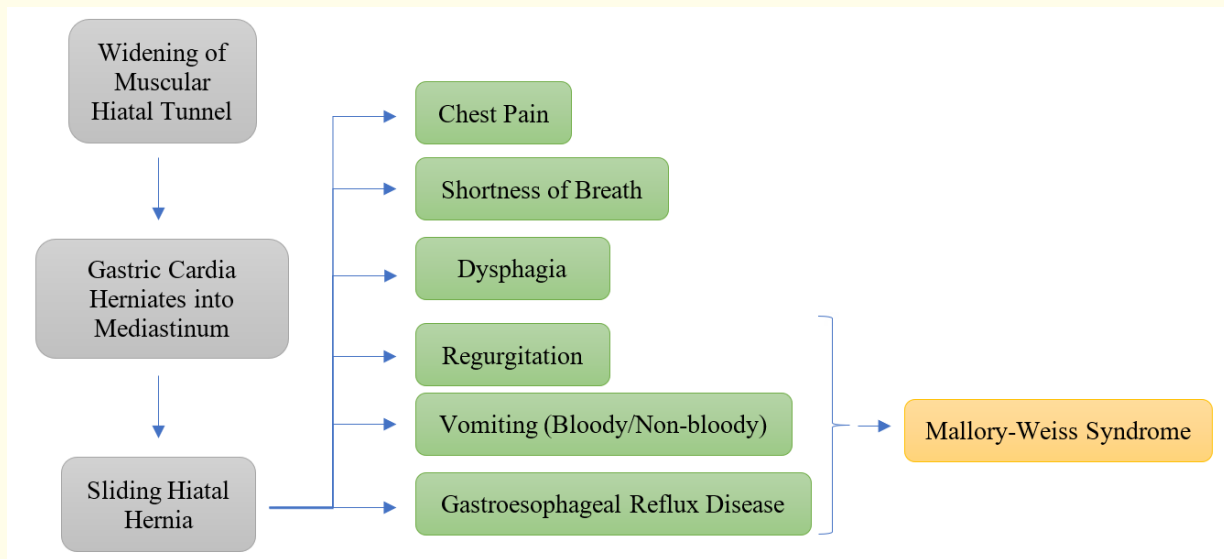


Figure 4: Proposed association of hiatal hernia causing Mallory Weiss syndrome.

A hiatal hernia is most commonly diagnosed when doctors conduct an endoscopy to investigate reflux, or when a barium x-ray has been performed. While an endoscope is most commonly used, it does not make a definitive diagnosis; it is suggestive. The hiatal hernia can show up as a bulge that is positioned between the esophagus and stomach. In most cases, hiatal hernias can be asymptomatic; however, symptoms can be seen in larger hernias. Treatment of a hiatal hernia is focused on the management of symptoms, such as the gastroesophageal reflux through the administration of medication. Furthermore, lifestyle changes may be recommended such as ensuring minimal straining or lifting heavy objects to avoid the chest pain that may be present. Hiatal hernias are only surgically corrected in the event that medication is not able to cause symptomatic relief. Early intervention in patients with a hiatal hernia could potentially lead to a decreased risk of development of MWS; however, the exact prevalence of such an event occurring is unknown.

Chemotherapy-Induced Vomiting

Studies conducted in laboratory animals provide evidence of the importance of two primary sources of afferent input to the key hindbrain areas that can initiate the emetic reflex after exposure to chemotherapy [32]. The abdominal vagal afferents appear to have the greatest relevance for chemotherapy-induced nausea and vomiting [32,33]. A postulated theory has been identified by Borison and colleagues as they researched the area postrema, a circumventricular structure located at the caudal end of the fourth ventricle [32,34].

Studies in animal models have demonstrated that opioids and dopaminergic agonists can induce emesis when they bind to the area postrema, which is also referred to as the ‘chemoreceptor trigger zone’ [34]. It is conceivable that gut-derived peptides and metabolites of chemotherapeutic agents also induce emesis in part through binding to this site at the chemoreceptor trigger zone, however, such potential mechanisms remain to be investigated in detail [32,34]. Okauchi, *et al.* reported a 68-year-old woman who developed Mallory-Weiss syndrome within a day after cytotoxic chemotherapy [35]. Vomiting and retching are the characteristic symptoms preceding Mallory-Weiss tears. The actions of vomiting and retching itself consequently increases intraluminal pressure within the esophagus, leading to the tears. Hence, Mallory-Weiss tears must be considered a potential differential diagnosis in patients with hematemesis and epigastric pain after chemotherapy-induced vomiting [36].

Hyperemesis Gravidarum

Hyperemesis gravidarum (HG) is a condition causing severe nausea and vomiting in early pregnancy often resulting in hospital admission [37]. Up to 80% of all pregnant women experience some form of nausea and vomiting during their pregnancy [38]. The International Statistical Classification of Disease and Related Health Problems, Tenth Revision, defines hyperemesis gravidarum as persistent and excessive vomiting starting before the end of the 22nd week of gestation and further subdivides the condition into mild and severe [39]. HG is a condition of intractable vomiting during pregnancy, leading to fluid, electrolyte and acid-base imbalance, nutrient deficiency, and weight loss often severe enough to require hospital admission [37]. Patients with hyperemesis are more likely to be younger, non-smokers, and non-Caucasians [40]. Other risk factors include increased placental mass in the setting of a molar pregnancy or multiple gestations has been associated with a higher risk of hyperemesis gravidarum [41]. HG is most prevalent during, but not limited to, the first trimester of pregnancy when both the placenta and corpus luteum are producing hormones and the body is adapting to the pregnant state [37]. In a review of 15 published prospective studies (1990-2004) investigating the relationship between human chorionic gonadotropin (hCG), 11 reported that there were significantly higher levels of serum hCG in hyperemesis patients than in controls [40]. The exact mechanism in which hCG causes hyperemesis remains unclear, but proposed mechanisms include a stimulating effect on the secretory process in the upper gastrointestinal tract (GIT) [37]. Alternatively, hCG is structurally similar to thyroid-stimulating hormone (TSH) and possibly causes hyperemesis by stimulation of the TSH receptor [40].

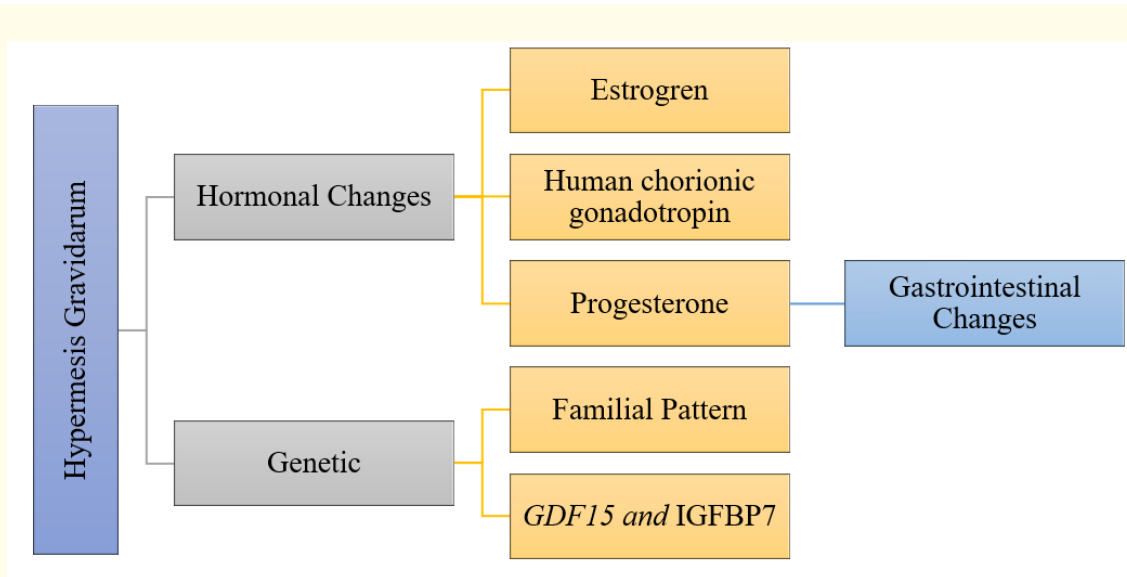


Figure 5: The various proposed theories of hyperemesis gravidarum.

Figure 5 presents a diagrammatic representation of the different theories of hyperemesis gravidarum. As mentioned earlier, hCG levels peak during the first trimester, corresponding to the typical onset of hyperemesis symptoms, however, this data has not been consistent [42]. Estrogen is also known to cause nausea and vomiting in pregnancy. The levels of estradiol are noted to increase early in pregnancy and decrease later, mirroring the typical course of hyperemesis in pregnancy [41]. Furthermore, nausea and vomiting are known side effects of estrogen-containing medications. As the level of estrogen increases, so does the incidence of vomiting [43]. Changes in the gastrointestinal system encircle the laxity of the lower sphincter during pregnancy that has been noted to be due the elevation of both pregnancy and progesterone [41]. The laxity of the lower sphincter also leads to the predisposition to gastroesophageal reflux disease (GERD). Though the exact mechanism is still being researched, it can be postulated that due to the laxity of the lower sphincter, vomiting and nausea increases. The increased predisposition to vomiting and nausea can be seen in hyperemesis gravidarum and this increase in vomiting can lead to the occurrence of Mallory-Weiss tears in the esophagus, leading to the feared complication of Mallory-Weiss Syndrome. As Figure 5 shows, there is also an increased risk of hyperemesis gravidarum has been demonstrated among women with family members who also experienced hyperemesis gravidarum. The familial pattern of hyperemesis allows for the ability to practice primary prevention and thus, reduce the complication of Mallory-Weiss Syndrome from occurring, which is seen with chronic vomiting. Two genes, *GDF15* and *IGFBP7*, have been potentially linked to the development of hyperemesis gravidarum, however, this association is still being researched [44].

Scleroderma/CREST syndrome

While a majority of the cases of Mallory-Weiss tears are either isolated cases or have a direct correlation with chronic alcohol abuse, certain underlying pathologies can predispose individuals to develop these tears [1]. Since the mechanism behind the tears stems from the increase in esophageal luminal pressure causing rupturing of the mucosa, any situation that causes an increase in intraluminal or intraabdominal pressure can result in the tears. CREST syndrome, an autoimmune localized subtype of scleroderma, is a condition in which individuals could be more susceptible to Mallory-Weiss tears. Localized scleroderma is characterized by calcinosis, Raynaud's phenomenon, esophageal dysmotility, syndactyly, and telangiectasias; hence, CREST syndrome [45]. The esophageal dysmotility seen in CREST syndrome is attributed to fibrosis and smooth muscle atrophy in the distal portion of the esophagus [46]. The decrease in peristaltic contractions within the distal two-thirds of the esophagus leads to excessive reflux and regurgitation from the lower esophageal sphincter. The increase in volume within the lumen as a result of the reflux, significantly increases the pressure to produce the characteristic longitudinal Mallory-Weiss tears. Furthermore, the acidic quality of the reflux has a potential to irritate the esophageal mucosa leading to erosive esophagitis [47], which significantly increases the chances of a tear. Cho., *et al.* reported a 24-year-old pregnant female with scleroderma who developed severe gastrointestinal hemorrhage secondary to Mallory-Weiss tears [48]. The overall fragility of the esophagus combined with the vomiting and retching attributed to the patient's pregnancy, paves the way for increased susceptibility to Mallory-Weiss tears.

Treatment of Mallory Weiss

Management of Mallory-Weiss syndrome is based on the amount of hematemesis. If the amount of blood is minimal and the patient is stable, there may be no need for any interventions, as it is considered to be self-limited in this situation [1]. The decision on whether or not any type of intervention needs to be introduced differs from patient to patient. There are different methods of interventions that may be utilized in patients with active bleeds, however, there is still research being done in the realm of the most effective approach [50].

The decision to treat or not treat Mallory-Weiss tears is dependent on the situation of whether there is an active bleed. In about 80% to 90% of cases, the bleeding in Mallory-Weiss Syndrome will stop on its own [49]. In patients who present with active bleeds or in the event that the bleedings will not stop, there are several methods of management that can be looked into, as shown in Figure 6. Some of the common endoscopic procedures include injection therapy, sclerotherapy, and coagulation therapy. Injection therapy, also known as an epinephrine injection, is known to reduce or stop bleeding via a mechanism of vasoconstriction and tamponade [49]. An epinephrine injection therapy is an approach that is more commonly used in conjunction with other treatments, such as an approach referred to as

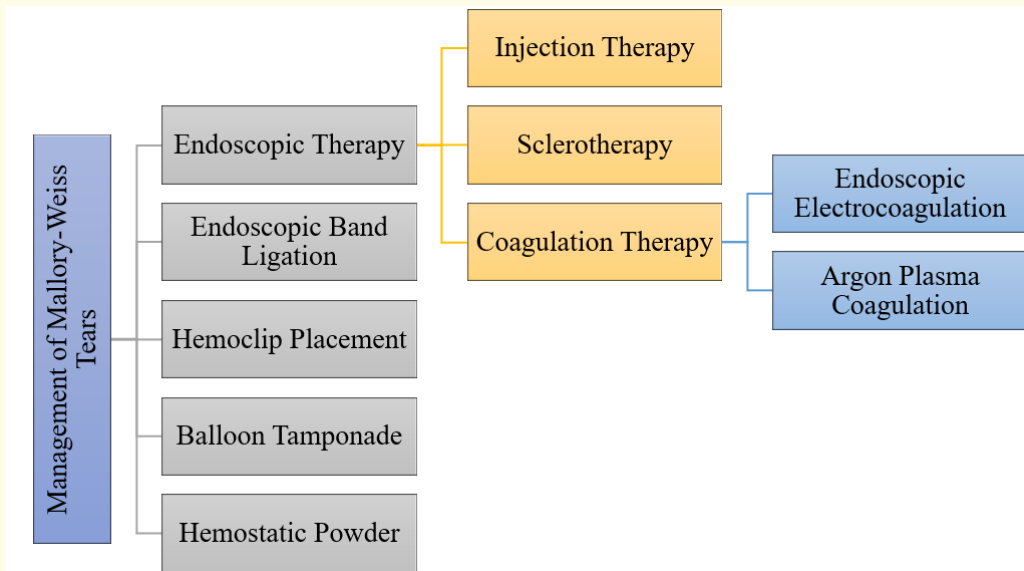


Figure 6: Methods of management of Mallory-Weiss tears.

contact thermal treatment, also referred to as coagulation therapy. Epinephrine injury therapy improves outcomes in terms of recurrent bleeding, hospital stay, and transfusion requirement compared with supportive measures alone [50]. The administration of an epinephrine injection must be very meticulously monitored as submucosal esophageal injection of epinephrine may enter the systemic circulation and under such circumstances, it may cause ventricular tachycardia [49,50]. Because of this risk, epinephrine injection therapy is an approach that must be avoided in patients with previous cardiovascular conditions. The exact hemostatic effect of epinephrine therapy, on its own, in a bleeding Mallory-Weiss is controversial; a study conducted by Peng, *et al.* (2001) noted that primary hemostasis from an epinephrine injection therapy was 100%, however, the rebleeding rate was 5.8% to 44% [51]. Epinephrine therapy may also be insufficient for patients with a large and/or long plexus of vessels [50]. For such reasons, epinephrine therapy is considered to be most effective when it is used in combination with other therapies [49,50]. In addition to the injection of epinephrine, the injection of sclerosants has also been reported [49]. Injection of sclerosants, such as alcohol, or polidocanol have been reported, however, this not recommended due to its potent tissue-damaging effects, risk of deep tissue necrosis, and potential perforation [49,52]. Battalar, *et al.* (1994) suggests safer alternatives in contrast to sclerotherapy [52].

Coagulation therapy is another type of endoscopic procedure that is utilized in the treatment of Mallory-Weiss tears. Coagulation therapy is the simultaneous application of both heat and pressure to the bleeding lesion by electrocoagulation [50]. While multipolar electrocoagulation has improved hemostasis, repetitive coagulation brings the risk of a potential transmural injury [50,53]. Another complication could be perforation because of the relatively thin esophageal wall and lack of serosa at the tear site [50]. Another type of coagulation therapy available is argon plasma coagulation in which a probe is placed at a distance from the bleeding site, and high-frequency electrical current, with a relatively low argon gas flow rate (1L/min), results in coagulation of the bleeding lesion [49-50]. The lack of contact between the catheter and the tissue results in a superficial burn, reducing unwanted tissue damage and perforation [50].

Band ligation is considered to be particularly useful for bleeding Mallory-Weiss tears that are associated with portal hypertension and gastroesophageal varices [49]. The main advantage of endoscopic band ligation is its technical ease in comparison to the other hemostatic

procedures currently available [50]. A French study conducted by Lecleire, *et al.* (2009) found there to be significantly less recurrent bleeding occurred in patients with band ligation in comparison with hemoclip placements with epinephrine injection [54]. In a small, prospective, randomized study of 34 patients with actively bleeding lesions, no difference was noticed in the efficacy of band ligation versus epinephrine injection [49]. Endoscopic hemoclip placement is an easy-to-use procedure for treating bleeding lesions in nonfibrotic tissue, specifically with Mallory-Weiss patients [50]. For the placement of a hemoclip, the margins of the tear are approximated, starting at the distal end of the tear and applying successive clip-ins in a manner towards the head of the tear [49]. Cho, *et al.* (2008) compared the efficacy of band ligation and hemoclip placement in Mallory-Weiss patients and concluded that both the procedures were equal in efficacy for equivalent hemostasis (100%) and rebleeding rate (6% vs. 10%, respectively) [55]. A balloon tamponade has been mentioned as a treatment for Mallory-Weiss tears, however, it is not beneficial and should be avoided as it recreates the force that may further widen the tear [49].

Hemostatic powder has deemed to be safe and is associated with a high rate of initial hemostasis, whether it is utilized as a primary therapy or rescue therapy [56]. Hemostatic powder is an inorganic powder that only attaches to the active bleeding areas [57]. It is a granular, mineral, nonabsorbable powder that becomes cohesive and adhesive when it comes into contact with the moisture in the esophagus [58,59]. The adhesive nature of hemostatic powder allows for it to create a mechanical barrier over the tear and thus, aiding in hemostasis. The nature of the powder does not allow for it to be metabolized or absorbed by the mucosal tissue and therefore, there is no risk of systemic toxicity [58].

Conclusion

With the various risk factors leading to Mallory-Weiss Syndrome, the primary objective is to focus on prevention. In order to prevent the occurrence of the tears, identification, and treatment of the underlying pathology is of greatest importance. It is imperative to understand that there are multiple pathologies that can lead to the presentation of Mallory-Weiss syndrome, secondary to the underlying pathology. Understanding the underlying pathophysiology of the primary condition is what allows for physicians to ensure patients do not become predisposed to the development of Mallory-Weiss tears. Retching and vomiting are considered to be the greatest risk factors for Mallory-Weiss tears. Portal hypertension can cause esophageal varices and the rupture of these varices may also lead to a tear that presents as a Mallory-Weiss tear. Understanding the differences between the rupture of esophageal varices and a Mallory-Weiss tear may be crucial for treatment options and methods of intervention. Diagnosis of MWS is usually achieved via upper GI endoscopy in which longitudinal tears can be seen in the lower two-thirds of the esophageal mucosa. While a majority of Mallory-Weiss tears are self-limited and require no treatment, in certain cases either pharmacological or surgical interventions may be required. Determining which type of intervention is applied ultimately depends on the underlying pathology. Understanding the underlying pathophysiology may also allow physicians to eliminate risk factors that may cause the future of presentation of Mallory-Weiss tears.

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