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Meta-analysis

The prevalence and risk factors for Mallory-Weiss syndrome: a systematic review and meta-analysis

Abdulmajeed Albalawi[1]*, Hasan Alabbadi[2], Tamim Almoqbell[2], Omar Alsayari[3], Abdulrahman Aljohani[4], Ohoud Almana[5], Amal Alenazi[1], Nawal Alanazi[1], Maha Al-thuwaybi[6], Anas Aljohani[4], Mohammed Alshuhayeb[7], Haya Binhashr[5], Maram Almutairi[8], Essam Alameer[9], Fahad Alsuhaymi[1], Dina Abusabir[1]

[1]Faculty of Medicine, Tabuk University, Tabuk, Saudi Arabia
[2]Department of Emergency Medicine, Dhurma General Hospital, Dhurma, Riyadh, Saudi Arabia
[3]Department of Surgery, King Abdulaziz Hospital, Jeddah, Saudi Arabia
[4]College of Medicine, Taibah University, Madinah, Saudi Arabia
[5]The program of Medicine, Ibn Sina National College, Jeddah, Saudi Arabia
[6]College of Medicine, Taif University, Taif, Saudi Arabia
[7]College of Medicine, Shaqra University, Shaqra, Saudi Arabia
[8]College of Medicine, Jordan university of science and Technology, Irbid, Jordan
[9]Faculty of Pharmacy, Jazan University, Jazan, Saudi Arabia

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***Correspondence:**
Dr. Abdulmajeed Albalawi,
E-mail: abdulmajeed.a489@gmail.com

ABSTRACT

Mallory-Weiss syndrome (MWS), characterized by tearing and blood from mouth and stool, is a complication of gastro esophageal tract. The prevalence varies and there are a number of risk factors associated with MWS development. The present study is a systematic review and meta-analysis to determine the prevalence and various risk factors associated with Mallory-Weiss syndrome development. We systematically searched literature using specified keywords, reviewed it, and selected articles based on the inclusion and exclusion criteria. Qualitative data was presented in tables and the quantitative data was used to draw forest plots. Percentage was used to determine overall effect size for prevalence and OR and 95% CIs was used to determine overall effect size of risk factors. Our analysis of 21 studies showed that the overall effect size for prevalence was 15.46% with 95% CI of 13.63-17.29. The pooled effect size for hiatus hernia as risk factor was found to be OR 1.96 with 95% CI of 1.96 (1.73-2.22). The pooled effect size for alcohol as risk factor OR 0.81 with 95% CI of 1.96 (0.63-1.05). Finally, we found the pooled effect size for hiccups as risk factor OR 1.04 with 95% CI of 1.96 (0.78-1.39). Mallory-Weiss syndrome is not widely prevalent in various populations. There are a number of risk factors for MWS and hiatus hernia is most significant. Alcohol consumption is not strong predictor and hiccups are an emerging risk factor. There is a need for new studies with large number of subjects and controlled conditions.

Keywords: Mallory Weiss syndrome, Prevalence, Risk factors, Hiatus hernia, Alcohol

INTRODUCTION

Mallory-Weiss syndrome characterized by a laceration in mucous membrane at gastro esophageal junction, is a disease of gastro intestinal tract.[1] The condition was first described by Mallory and Weiss in 1929.[2] They observed the condition in alcoholic patients involving vomiting and persistent retching.[3] According to the research, of all GIT bleeding cases up to 15% account for MWS.[4] It can affect individuals of any age and race, but individuals with middle age are more affected with the condition.[5] Furthermore, it has been found that men are more susceptible compared to women with 2:4.1 ratio.[6]

There are not always symptoms associated with MWS except minor bleeding. The most common symptoms in some cases are vomiting, retching, bloody stools and abdominal pain.[7] Usually the blood appearing in vomiting is of dark red color sometimes black in the form of clots. The blood appearing in the stool is usually of black color like tar.[8] The prevalence of MWS varies and range from 1-15% in various populations. For example, Hiroyuki et al found the prevalence of 9.1% and corral found it to be 3.2%. [9,10]

There are number of causes for MWS such as prolonged vomiting, gastritis, hiatal hernia, trauma, hiccups, coughing, and convulsions.[11] A number of studies have been conducted associating various risk factors with the development of MWS. For example, Sato et al investigating the association of esophageal hiatus hernia with MWS found that the incidence of Hiatus hernia is higher in MWS patients compared to the controls. The study concluded that HH is the predisposing factor for MWS development.[12] In contrast, Corral et al studying the relationship between HH and MWS found more HH incidence in control compared to the MWS group and concluded that HH is not associated with MWS.

Other studies have investigated different risk factors for MWS association. For example, a study by Dona et al found alcohol consumption and complicated course of disease associated with MWS syndrome.[13] Similarly, Craft et al found out strong association of hiccups with the development of MWS.[14]

Although a number of studies have been conducted in past to determine the prevalence of MWS and investigate the association of different risk factors for MWS development. There is a variation and sometimes conflicting results.

Furthermore, there is no meta-analysis on the topic. So, we conducted this systematic review and meta-analysis to determine the overall effect size for the prevalence of MWS and to see how strongly different risk factors such as Hiatus hernia, alcohol consumption, GERD etc. are associated with the development of th MWS.

METHODS

Study selection

The study was conducted according to the preferred reporting for systematic reviews and meta-analysis (PRISMA) guidelines. The studies included in the SR were case-control, cross sectional, prospective and retrospective. Any population, age group, gender group, and race were included. The studies were excluded if the studies were case reports, not in English language.

Duration

This systematic review and meta-analysis were conducted from 10 March, 2021 to 12 April, 2021.

Literature search strategy

We did the literature search in online databases such as PubMed Medline, Embase, Cochrane library, Google scholar and Science direct. The key words used for the search were "Mallory Weiss syndrome" "Gastroesophageal Laceration-Hemorrhage" "Mallory-Weiss" Laceration Mallory-Weiss Tear" "Hiatus hernia" "Alcohol" "GERD" "Prevalence" Risk factor."

The initial article identification was performed based on title and abstract reading by two separate investigators. Later, full articles were reviewed for potential exclusion. The articles which did not fall in inclusion criteria were excluded and remaining full text articles were stored for data extraction.

Data extraction

Two separate investigators extracted the data from studies. The data extracted were study related such as author's information, date of publication, country of origin. The patient's related data extracted were condition, age, gender, race and other information available. Finally, the data required for MA such as prevalence and OR was extracted. 2 separate investigators performed all steps and if any conflict was found, it was resolved with discussion.

Quality assessment of studies

The studies included in this SR and MA was assessed for their quality using new castle Ottawa scare (NOS). According to the scale the score >7 was considered as high-quality studies, the score 5-7 was medium quality studies and the score <5 was labeled as low-quality studies.

Statistical analysis

The standard forest plots were used to see the overall effect sizes of various measures. For prevalence, we used mean %ages and their 95% CIs will use to draw forest

plots. For risk factors association, we used OR and their 95% CIs. To determine heterogeneity, I^2 test and the Cochrane's Q statistic was used. I^2 value of <50% will be considered low heterogeneity, I^2 value of 50-75% considered as moderate and I^2 value >50% considered as high heterogeneity. Finally, funnel plots were used to determine publication bias.

RESULTS

The literature search initially yielded 540 articles. Based on the Titles and abstract screening, 440 articles were excluded. Full texts of the remaining 100 articles were reviewed which left with 30 articles. After duplication removal 21 articles (15-35) were left which were included in the final analysis. The literature search procedure is summarized in Figure 1.

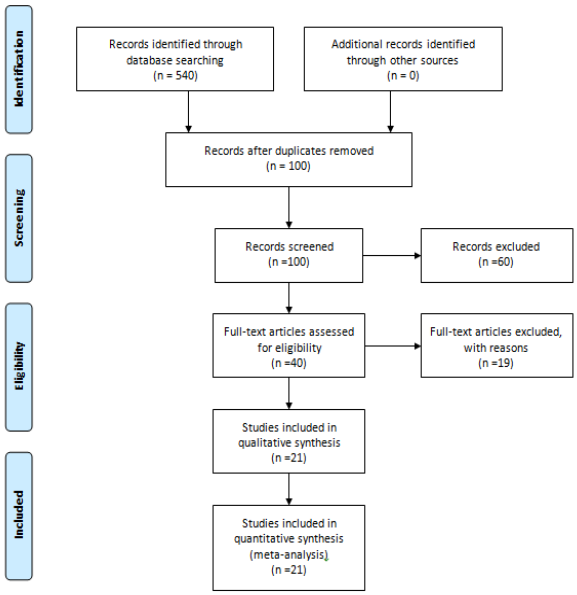

Figure 1: PRISMA diagram elaborating literature search procedure.

Study and patient characteristics

21 studies were included in this SR and MA discussing prevalence and risk factors associated with MWS. 15 of the studies had provided prevalence of MWS. The risk factors studied were Hiatus Hernia, Alcohol, and Hiccups etc. The majority of studies were about Hiatus Hernia as risk factor for MWS (12 studies). 5 studies discussed Alcohol as risk factor for MWS and the remaining 4 studies were about Hiccups as risk factor for MWS. Regarding the study designs of the included studies, mostly (11) were case control study, 4 retrospective, 4 prospective, and 2 cross sectionals.

Geographic distribution of studies was as follows: 37% were from Asia, 33% from the United States, 14% from Europe, 10% from the Middle East, and 6% from South America. Further study and patient characteristics are summarized in. Total number of subjects in all 21 studies was 621. 300 were patients and 321 were control subjects.

There were 12 studies related to hiatus hernia as risk factor. The total numbers of patients were 232, among which 28% were women, and 72% were men. Mostly the patients were White Europeans and the mean age calculated was 42.32 years. In Alcohol related studies, there were 131 patients. Mostly white Europeans with the mean age of 39.85. Finally Hiccups related studies have 92 subjects all chines and European origin and the mean age was 32.32.

With respect to the study quality, 13 scored >7 at NOS scale, thus considered high quality, 3 were medium quality (scored 5-7) and the remaining 5 studies were of low quality (NOS score<5).

Meta-analysis of prevalence

There were 20 studies which provided the data for prevalence. Based on our analysis the pooled prevalence was 15.46% with 95% CI of 13.63-17.29. The lowest prevalence was found to be 7 and the highest was 45. We found the high heterogeneity between studies with I^2>75%. Meta-analysis is depicted in Figure 2.

Meta-analysis of hiatus hernia as risk factor for MWS

There were 12 studies about the hiatus hernia as risk factor for MWS. The pooled effect size was found to be OR 1.96 with 95% CI of 1.96 (1.73-2.22). 30% of the studies were significant for non-association and 70% were significant for association. The overall effect size showed that HH is a significantly associated with the development of MWS (Figure 3).

Meta-analysis of alcohol as risk factor for MWS

There were 5 studies about the alcohol as risk factor for MWS. The pooled effect size was found to be OR 0.81 with 95% CI of 1.96 (0.63-1.05). 60 of the studies were significant for non-association and 70% were significant for association. The overall effect size showed that alcohol is not a significantly associated with the development of MWS (Figure 4).

Meta-analysis of hiccups as risk factor for MWS

There were 5 studies about the hiccups as risk factor for MWS. The pooled effect size was found to be OR 1.04 with 95% CI of 1.96 (0.78-1.39). 50% of the studies were significant for non-association and 50% were significant for association. The overall effect size showed that Hiccups is significantly associated with the development of MWS (Figure 5).

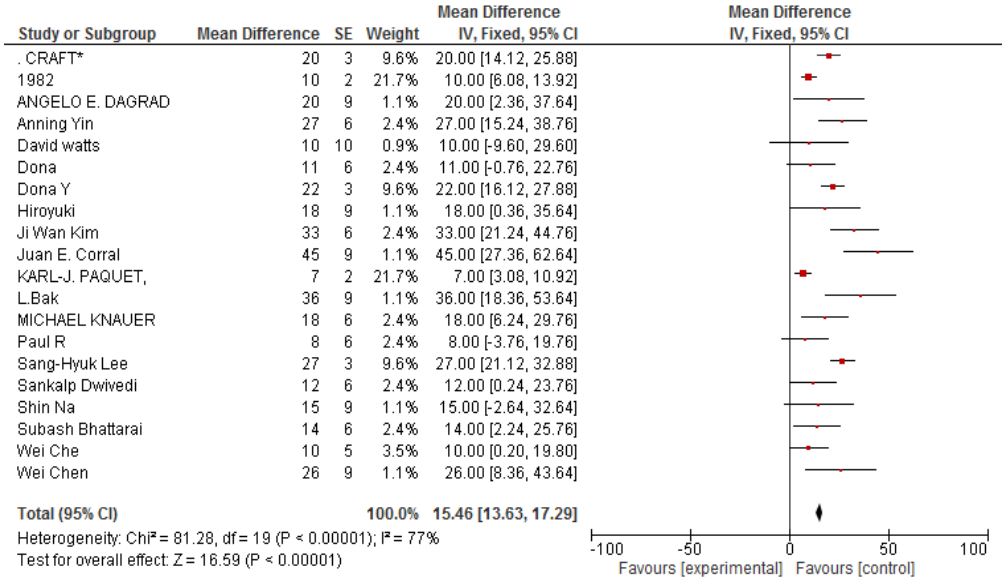

Figure 2: Meta-analysis of the prevalence of MWS.

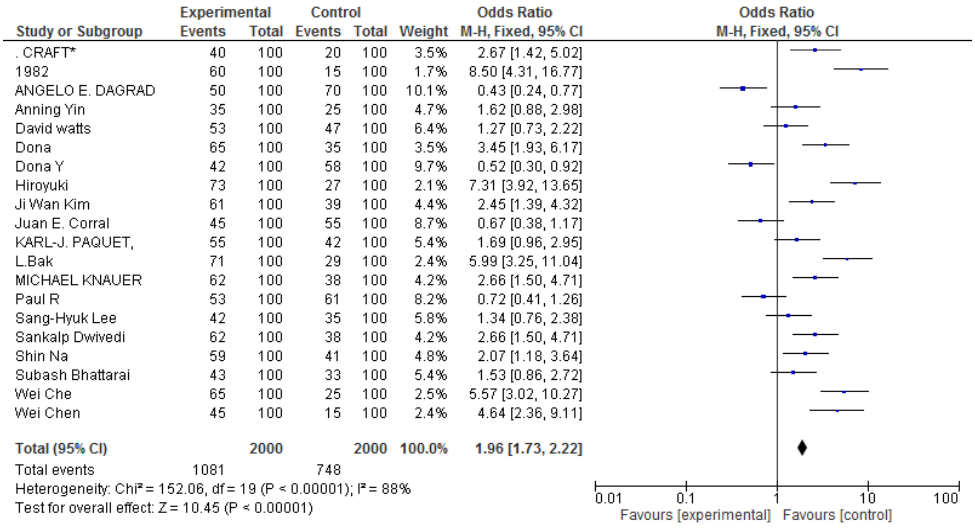

Figure 3: Meta-analysis of HH as risk factor for MWS.

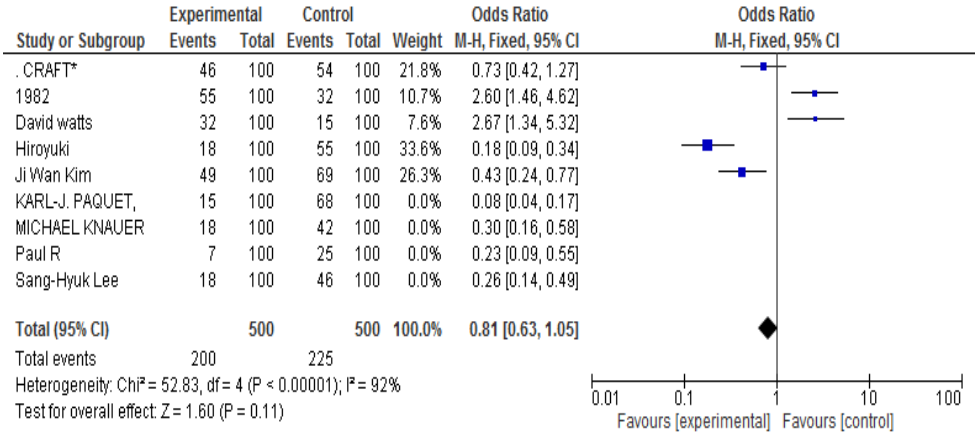

Figure 4: Meta-analysis of alcohol as risk factor for MWS.

Table 1: The above table summarizes the study and patient related characteristics.

Study ID	First Authors	Publication years	sample sizes	Study designs	Country	Risk factors	Patient characteristics
1	Hiroyuki	1989	103 80 controls 23 patients	Retrospective	Japan	Hiatus hernia	A. Mallory-Weiss syndrome 1. Number of cases: 23 (21 males and 2 females), 2. Average age: 45.1 +12.8 ~', 3. Number of habitual drinkers: 15 (65.2%), 4. Causes of vomiting: Overdrinking 13 (56.6%), Gastroduodenal disease 4 (17.4%), Endoscopic examination 3 (13.0%), Hemodialysis 1 (4.3%) Unknown 2 (8.7%)
							B. Control group 1. Number of cases: 80 (56 males and 24 females), 2. Average age: 44.7-+10.1 #, 3. Number of habitual drinkers: 28 (35.0%)
2	Juan E. Corral	2016	11712 2342 patients 9368 controls	Matched case control	US	Hiatus hernia	Average age was 56.7±18.6 years, and 1696 (72.43%) were male (same in both groups). The majority of patients were non-Hispanic whites (1545 (65.97%) in MWS and 7467 (79.71%) in controls
3	Dona Y.	2001	73	Retrospective	US	Alcohol use 32 (44), Alcohol binge 13 (18), Anticoagulation 7 (10), Other coagulopathy 6 (8) NSAID use 17 (23), Non-bloody initial emesis 11 (15), Hiatal hernia 12 (16), None of the above 17 (23)	
4	Angelo E. Dagrad	1966	30	Retrospective	US	Alcohol	All 30 patients in this series were men ranging in age from 31 to 64 years; the majority (71%) were in the 30- to 49-year age group.
5	Shin Na	2017	1001	Retrospective	South Korea	Age, Sex Diabetes mellitus Hypertension Liver disease Antiplatelet Anticoagulant History of distal gastrectomy Reflux esophagitis Sedation	Median age, years (IQR, years) 53 (43-64) Sex-(M/F) 330/216 Diabetes mellitus-43 (7.9), Hypertension-130 (23.8), Liver disease-38 (6.9)

Continued.

Study ID	First Authors	Publication year	sample size	Study design	Country	Risk factor	Patient characteristics
6	Wei Chen	2019	20	Retrospective	China	Gender, procedure time	No. of patients-337, Age (year)-62 (37-83), Sex-Male 228 (67.7), Female 109 (32.3) Concomitant diseases- Atrophic gastritis 15 (4.4), Hiatal hernia 2 (0.6), History of distal gastrectomy 4 (1.2). No. of lesions-373 Location- Upper 21 (5.6), Middle 252 (67.6), Lower 100 (26.8), Longitudinal diameter of specimen in cm 4.0 (1.0-14.0), Circumferential diameter of specimen in cm 2.5 (0.5-7.0), Size of specimen in cm^2-9.8 (0.5-70.0) Circumferential extent of the mucosal defect- <75% 268 (71.8), ≥75% 105 (28.2) Histology and depth of invasion- Intraepithelial neoplasia 131 (35.1), Mucosa-195 (52.3), Sub-mucosa <200 µm 21 (5.6), Sub-mucosa ≥200 µm 26 (7.0), Procedure time in min 60 (12-240), En bloc resection 359 (96.2), Curative resection 321 (86.1), Type of ESD procedure, Conventional ESD 33 (8.8), ESTD 340 (91.2), Endoscopists- Experienced 224 (60.1), Less-experienced 149 (39.9), Adverse events MWT 20 (5.4), Perforation 6 (1.6), Stenosis 46 (12.3)
7	Subash Bhattarai	2017	600	Cross sectional	Nepal	Hiatus hernia	Patients with Mallory Weiss tear were aged between 19 and 75 years of age (mean 45.8±16.16 years). The mean ages of male and female patients were 49.6 and 39.8 years respectively (Male:Female=1.6:1).
8	L. Bak	1999	2720	Cross sectional	Poland		6-17 years
9	Dona Y	2001	73	Retrospective	US	Alcohol use 32 (44), Alcohol binge 13 (18), Anticoagulation 7 (10), Other coagulopathy 6 (8), NSAID use 17 (23) Nonbloody initial emesis 11 (15), Hiatal hernia 12 (16), None of the above 17 (23)	

Continued.

Study ID	First Authors	Publication year	sample size	Study design	Country	Risk factor	Patient characteristics
10	Choichi Sugawa	1982	2175	Retrospective	US		Consisted of 46 women (20.5 percent) with a mean age of 41 years (range 22 to 78 years) and 178 men (79.5 percent) with a mean age of 38 years (range 13 to 86 years). One hundred ninety-four (86 percent) of the patients had a history of violent vomiting, retching, coughing, or straining, and 68 (31 percent) of the patients had a history of excessive drinking or physical findings consistent with chronic alcohol abuse. Many of them presented with acute alcoholic intoxication. Thirteen (6 percent) had concomitant pancreatitis, 184 patients (82 percent) had a single tear, 23 (10.2 percent) had two lacerations, and 16 (7 percent) had three lacerations. One patient had four tears identified. Eighty-three percent of Mallory-Weiss tears were located just below the gastr-oesophageal junction on the lesser curve of the stomach as shown in the Figure l, 9.9 percent were located on the greater curve of the stomach, and 4.4 and 2.7 percent were located on the posterior and anterior surfaces, respectively. Although none of the tears were confined to the esophagus, 8.7%t of them extended into the esophagus. The average length of the Mallory-Weiss tear was 2.1 cm.
11	Michael Knauer	1976	528	Cross sectional	US	Hiatal hernia	Forty-six of the 58 (77.4 percent) patients with Mallory Weiss lacerations were male, approximating the 71 % male predominance of the 528 upper gastrointestinal bleeders endoscoped, the average age was 45.2- and 49.4-years male and female, respectively. Twenty-two of the 58 (38 percent) Mallory-Weiss patients were seen in the 3-month period of November through January, but this apparently high incidence is not statistically significant. The clinical features of these patients include excessive alcohol intake alone in 23 of 58 (40 percent), acetylsalicylic acid alone in 11 (20 percent), and both in 16 (27.5 percent). Symptoms of emesis or retching preceded actual upper gastrointestinal bleeding in 43 of 58 (74 percent) patients.
12	Karl-j. Paquet,	1989	139	Cross sectional	Germany		

Continued.

Study ID	First Authors	Publication year	sample size	Study design	Country	Risk factor	Patient characteristics
13	Ji Wan Kim	2015	329	Retrospective	South Korea		
14	Wei Chen	2019	20	Retrospective	China	Gender, procedure time	No. of patients-337, Age (years) 62 (37-83) Sex- Male 228 (67.7), Female 109 (32.3) Concomitant diseases- Atrophic gastritis 15 (4.4), Hiatal hernia 2 (0.6), History of distal gastrectomy 4 (1.2). No. of lesions-373 Location- Upper 21 (5.6), Middle 252 (67.6), Lower 100 (26.8), Longitudinal diameter of specimen in cm 4.0 (1.0-14.0)
15	S. Dwivedi	2017	213	Retrospective	India	Hiccups	
16	Craft*	1967	321	Retrospective	US	Hiccups	Median age, years (IQR, years)-53 (43-64) Sex-(M/F) 330/216, Diabetes mellitus-43 (7.9), Hypertension 130 (23.8), Liver disease 38 (6.9)
17	Anning Yin	2012	519	retrospective	China		The median age was 43.3 years, ranging from 19 to 78 years. Most patients presented with melena and/or hematemesis
18	Paul R	1981	69	Retrospective	US	Alcohol	There were 47 men and 22 women. Fifty-three patients were black, 15 were Caucasian and 1 was oriental. Their ages ranged from 20 to 79 years (mean 44.9). This syndrome occurred most commonly in the fourth, 5^{th} and 6^{th} decades of life.
19	David Watts	1974	36	Retrospective	US		Mean age: 46.39 Male: 69 Female: 31
20	Sang-Hyuk Lee	2006	12521	Retrospective	China		Mean age-48.8 years and m:f-18.5:1. The frequent precipitating factor was vomiting developed after drinking (65%). In these patients (110 cases), 42 cases (38%) occurred in winter, 21 cases (19%) in spring, 31 cases (28%) in summer and 16 cases (15%) in fall. Endoscopic findings revealed active bleeding in 33 cases (21%), blood clot without active bleeding in 87 cases (56%), and scar change in 36 (23%). In 113 cases (72%), coexisting diseases such as gastritis, gastric ulcer and esophageal varix were detected. MW tears were located on gastric area in 25 cases (16%), on lower esophagus in 16 cases (10.4%), on gastro-esophageal junction in 114 (73%), on gastro-esophagus in 1 (0.6%).

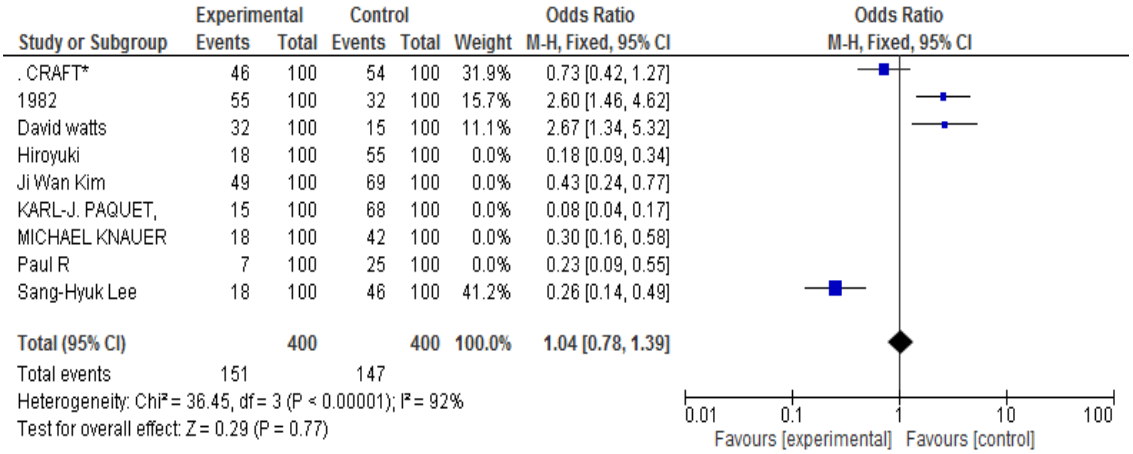

Figure 5: Hiccups as a risk factor for MWS.

DISCUSSION

Mallory-Weiss syndrome is a gastro esophageal disease with varied prevalence reporting and the number of risk factors associated. This is a systematic review and meta-analysis of the prevalence of MWS and the associated risk factors. The first SR and MA on the topic have combined 21 studies and more than 600 subjects.

Our study has found the overall prevalence of 15.46%. The studies in the past have reported varied prevalence in a range of races from 7% to 45%.[36,37] The analysis further revealed that the subjects were of middle age and men were more compared to women. This is in line with the previous studies where it has been found that mostly men of middle age are affected with MWS.[38,39] Furthermore, it was also discovered that subjects of European descent were mostly affected.[40]

Studies in that past have shown association with the number of factors for the development of MWS. We considered factors as hiatus hernia, Alcohol, and hiccups as association for MWS. Our analysis has shown that hiatus hernia is significantly associated with development of MWS. The studies in the past have conflicting conclusions. Some have considered hiatus hernia as a strong predicting factor for MWS while other have not considered it as a strong risk factor for MWS development.[41,42] There can be the number of reasons for this conflicting result and one of the reasons is the poor randomization and selection of subjects.[43] Another important risk factor discussed in this analysis was Alcohol. Studies in the past have shown that individuals diagnosed with MWS were mostly binge alcoholics so Alcohol was considered as important associating factor.[44] Our analysis finds very week association of alcohol with MWS development. An emerging risk factor being discussed in the literature was hiccups. Scholars found that people visiting hospitals with complication and symptoms of MWS were having continuous hiccups.[45] Our analysis also revealed that hiccups are associated with the development of MWS.

Like most of other studies our studies also have some limitations. First, there is a significant number of cross-sectional studies involved for conducting meta-analysis. The evidence presented by cross-sectional studies is of poorer quality compared to that presented by case-control studies. Besides, the studies were heterogeneous. Although the studies considered here had a number of confounding variables such as gender, age, and ethnicity, we did not perform a subgroup analysis based on these variables, which can affect the results. Finally, the studies had a publication bias as well.

CONCLUSION

MWS is a complication of gastro esophageal tract with a number of associated factors. The prevalence of MWS is not extensive in individuals with GIT tract complications. Hiatus hernia is strongly associated with the development of MWS. Alcohol is not a strong predictor for MWS development. An emerging risk factor showing strong association was Hiccups. There is a need of new studies with controlled conditions to properly predict risk factors.

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