

**ORIGINAL STUDY**

**GASTRO-ESOPHAGEAL REFLUX SYNDROME IN ALCOHOLICS**

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**ABSTRACT**

*The chronic and acute consumption of alcohol has effects upon the mucosa as well as upon the muscular tunic of the esophagus. Thus, the alcohol increases the permeability of the esophageal mucosa at the inferior level for the H<sup>+</sup> ions, increasing the susceptibility for acid-peptic aggression. Our study wants to emphasize the etiological, clinical and evolutionary particularities of the reflux syndrome GERS in the case of the abusive alcohol consumers.*

**KEYWORDS:** *esophagus, acid-peptic aggression, alcohol*

**1. Introduction**

The chronic and acute consumption of alcohol has effects upon the mucosa as well as upon the muscular tunic of the esophagus. Thus, the alcohol increases the permeability of the esophageal mucosa at the inferior level for the H<sup>+</sup> ions, increasing the susceptibility for acid-peptic aggression [1]. Regarding the esophageal muscles, the alcohol has a dual action: on one side it inhibits its motility, thus decreasing the esophageal clearance, and on the other side it modifies the pressure of the inferior esophageal sphincter [2]. Clinically, the alteration of the esophageal physiology can be asymptomatic, or on the contrary can manifest itself very loud by the gastro-esophageal reflux syndrome (GERS), dysphagia, nausea and vomiting, retrosternal pains or aspiration syndrome.

GERS was defined by the presence of pyrosis and/or acid regurgitations as the predominant or frequent clinical element (over one episode/week), and the chronic character given by the persistence of this symptoms for over 4 weeks during one year [3].

Our study wants to emphasize the etiological, clinical and evolutionary particularities of the reflux syndrome GERS in the case of the abusive alcohol consumers.

**2. Material and methods**

The current study was made on a number of 633 patients enlisted from 2005 in the study made in the Internal Medicine Clinic II from the “Sfântul Apostol Andrei” Emergency Hospital from Galați regarding the medical pathology in the case of alcoholic patients. The criteria for their participation were: over 18 years old; alcoholic drinks

consumption for at least 5 years; the possibility to confirm the consumption of alcohol by at least one person from the close circle of friends of the indexed subject; the acceptance in writing regarding the participation to the study after being correctly informed about the purpose and the conditions of this study; the absence of previous chronic diagnosis in connection or not with the consumption of alcohol.

The alcohol consumption was evaluated by self-reporting with the help of a questionnaire with 12 items specifically designed and managed using the "face to face" method in the moment the patients were included in the study. It was confirmed by the discussion with a close relative of the patient (parent, brother/sister, husband/wife, child) and afterwards by a second questionnaire, built using "the last 7 days" principle. In order to facilitate the quantification and to allow for comparison, the alcohol consumption was expressed in grams of pure alcohol, using the following equivalents: 0,5 l of beer 5° = 20g alcohol; 1 l of wine 12° = 120 g alcohol; 50 ml liquors 20° = 10 g alcohol; 50 ml distilled drinks 40° = 20 g alcohol.

In this manner the patients were grouped according to the recommendations of WHO (4) into 4 risk categories (table I): low risk (LR), medium risk (MR), high risk (HR) and very high risk (VHR).

**Table I.** Risk categories according to the consumption level of alcoholic drinks expressed in grams of pure alcohol [4].

Risk category	Daily pure alcohol consumption (g)	
	Men	Women
Low risk	≤ 40	≤ 20
Medium risk	41 – 60	21 – 40
High risk	61 – 100	41 – 60
Very high risk	> 100	> 60

The patients that have shown during the clinical examination pyrosis and/or acid regurgitations as a predominant digestive symptom or frequent digestive symptom (more than one

episode/week) or chronic (more than 4 weeks per year) have been diagnosed with GERS and represent the persons included within our study. The severity of GERS was appreciated using another multidimensional questionnaire Glasgow Dyspepsia Severity Score, GDSS, made up and validated by El-Omar and col [5]. All the patients were endoscopic investigated. Esophageal mucosa biopsies were made where there were observed macroscopic esophagitis lesions and gastric mucosa present in the lesion areas, or in the case the endoscopic aspect was normal from the antral area, 2 cm from the pylorus, for the quick urease test (Pronto Dry, Medical Instruments Corp, France) and a histo-pathological examination. The severity of the esophagitis was appreciated according to the Los Angeles classification [6]. The gastritis was described histological and endoscopic according to the recommendation of the Sydney system [7]. After the diagnosis all the patients were informed upon the significance of the disease and of the possible relation with alcohol and they received a treatment with omeprazol (2 x 20 mg /day). The patients infected with *H. pylori* have received additionally treatment with amoxicillin (2 x 1000 mg/day) and clarithromycin (2 x 500 mg/day) for 7 days. The patients were called back for a medical examination 4 weeks after the treatment, but the actual medical examination was made after a medium time interval of 6,27 weeks (CI95% 5,39-7,15 weeks). The evolution was clinically evaluated by administrating a global Likert scale with seven points, which validation is internationally recognized [8].

The data are presented as an average with the confidence (trust) interval 95% (CI 95%). The analysis of the data was made with the help of S-Plus 2000 Professional Edition for Windows (TIBCO Software Inc, Palo Alto, California). The averages were compared using the t student test for unequal variations. The accepted significance was the one of 5%.

### 3. Results and discussions

#### The GERS occurrence

The GERS was shown in the case of 139 subjects, representing 21.96% of the study group. The occurrence is higher than the one reported in the European population (9,8-18 %, 3), but it is in accordance with the regional and ethnical differences reputed [9], and our group was selected on the basis of a precise criteria, the one of alcohol consumption.

The occurrence of the disease based upon the sex was similar, GERS being diagnosed in 22.05% from the total men and 21,85% from the total women from the group.

The average age in the moment of the diagnosis was 45.01 years (CI95% 42,78-47,24 years), without significant differences between sexes or between risk groups. The occurrence based upon age groups was shown in Figure 1. Unlike the data extracted from the database of the British family doctors which show an increase of the GERS occurrence in the persons up to 69 years, when the tendency reverses [10], our data do not emphasize a precise correlation, but show an increases frequency of GERS for the groups aged between 50-59 years (27,01%) and over 60 years (26,88%) in comparison with the younger groups (20,51% in the case of the persons below 30 years), 21,32% in the case of the persons between 30-39 years and 17,86% in the case of the subjects between 40-49 years).

A particularity is probably due to the eating behavior differences, if the urban population represented 62.09% from the group total, a higher proportion of (71.94%) from the GERS cases was coming from the urban environment.

Regarding the occurrence of GERS according to the alcohol consumption, the allocation of the cases within the risk groups is given by Table II. From the data presented below we can notice that the smallest number of cases, overall and according to

sex was recorded in the MR group. This "protective" effect of the moderate alcohol consumption is more obvious in the case of men, but remains difficult to explain in the condition in which the esophageal pH-metric and manometer examination were not available. One of the hypotheses is that in moderate quantities, the alcohol has antiseptic effects due to the fact that in all the MR group GERS cases the *H. pylori* were absent.

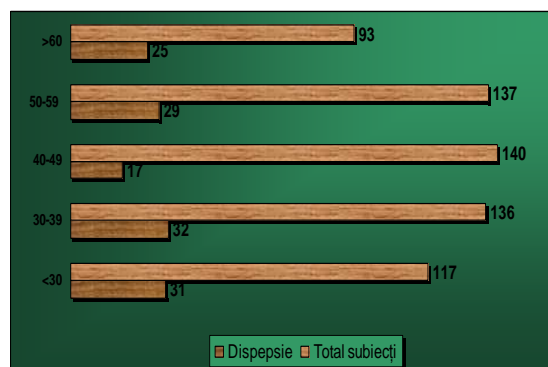


Figure 1. GERS occurrence based on age groups.

Table II. GERS occurrence according to the consumption of alcohol.

	Total group	Men	Women
LR	42 (21,88%)	26(23,64%)	16 (19,51%)
MR	23 (14,56%)	11(13,25%)	12 (16%)
HR	42 (26,25%)	20(27,78%)	22 (25%)
VHR	32 (26,02%)	1 (24,24%)	16(28,07%)

If we sum up the GERS cases recorded within the LR and MR groups and we compare these social drinkers with the heavy drinkers from the groups HR and VHR we reach the conclusion that the exaggerated alcohol consumption increases the risk of developing GERS to the limit of the statistical significance (RR=1,64, CI95% 1,05-1,89). In the specialty literature there are two epidemiological studies (cited by 9) that identify the significant association between the consumption of alcohol and the GERS diagnosis (in the first study RR=1,8 with CI95% 1,4-2,4, in the other study RR=1,9 with CI95%=1,1-1,3), but the investigated limiting

quantities were much smaller than the ones from our study.

The GERS occurrence was not influenced neither by the duration of the alcohol consumption neither by the preferred type of alcohol drink.

*The clinical picture*

The symptoms shown by the GERS patients are summed up in Table III. We can see that together with pyrosis and acid regurgitations, the other symptoms defining the GERS, the patients from our study group accumulate on the background, but with a significant frequency, symptoms characteristic to the dyspeptic syndrome (epigastric pains that define the dyspeptic ulcer-like syndrome, precarious satiety and epigastric plenitude post-meal characteristic to the dysmotility dyspeptic syndrome), as well as intestinal transit disorders.

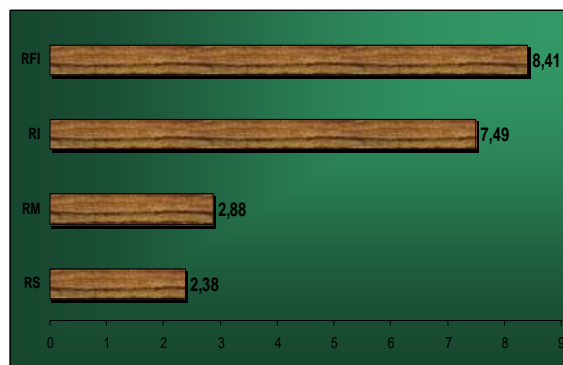
**Table III.** *The symptoms of GERS patients.*

Symptom	Occurrence
Pyrosis	139 (100%)
Acid regurgitations	113 (81,29%)
Epigastric pains	77 (55,40%)
Precautious satiety	65 (46,76%)
Post-meal epigastric plenitude	57 (41,01%)
Diarrhea	32 (23,02%)
Constipation	14 (10,07%)
Retrosternal pains	8 (5,76%)
Dysphagia	5 (3,60%)

Remarkable is also the fact that only 26 cases (18.71% from the total number of patients with GERS) were mono-symptomatic. Our patients accused an average of 3,64 (CI95% 3,30-3,98) symptoms, 81.29% of them having at least two symptoms, and 46.76% of them had five or more symptoms.

Comparing the two groups of social drinkers (LR and MR) with the other two groups (HR and VHR), the alcoholic persons have usually poly-symptoms (figure 2). Thus, the average number of symptoms in the cases of the social drinkers was 2.34

(CI95% 1,94-2,74), and in the cases of the alcoholics was 4.89 (CI95% 4,53-5,25 p<0,001).



**Figure 2.** *The extent of the symptoms of GERS according to the consumption of alcohol expressed by the average number of symptoms/patient*

Regarding the GERS symptoms, some of them had a higher occurrence rate in the case of alcoholics than in the case of the social drinker: acid regurgitations (ratio of 68/45), epigastric pain (60/16), precarious satiety (53/12), post-meal epigastric plenitude (45/12) and diarrhea (31/1). Although it is accepted the fact that the *per se* gastritis does not produce dyspepsia, the fact the 55 out of the 60 heavy drinkers with GERS which also presented epigastric pains had endoscopic lesions (histological confirmed) of gastritis, and these pains diminished in the cases of the persons that adequately treated their gastritis (*vide infra*) suggests a weak causal relationship. On the other hand, the high frequency of the dysmotility symptoms can also result from confusing those symptoms with the diminishing of the appetite which is characteristic for an alcoholic. The association of diarrhea with GERS results from intestinal motility disorders and the malabsorbtion induced by the alcohol.

The duration of the GERS evolution until the diagnosis was also higher in the cases of the heavy drinkers (7,11 months, CI95% 4,83-9,39 months in the HR group and 8,23 months, CI95% 5,77-10,69 months in the VHR group) in comparison with the *social* drinkers (3,83 months, CI95% 2,81-4,85

months in the LR group and 3,53 months, CI95% 2,42-4,64 months in the MR group).

*The severity of GERS*

The severity of GERS appreciated using DGSS is presented in Table 4. GERS was lighter in the MR group (6,74, CI95% 5,43-8,05), although it was not statistically significant in comparison with the LR group (8,45, CI95% 6,07-10,83), again suggesting a "protective" effect of alcohol consumed in moderate quantities (see Figure 6). The severity of GERS in the case of the *social* drinkers (7,85, IC95% 5,86-9,84) was significantly smaller than the one recorded in the case of the heavy drinkers (15,82, CI95% 11,96-19,68, p<0,001).

Accepting the limit score of 15 in order to define severe GERS, the alcoholic has a higher risk to develop severe GERS forms than the *social* drinker (RR=16,98, CI95% 9,87-24,79).

**Table IV.** *The severity of GERS according to the consumption of alcohol. GDSS= Glasgow Dyspepsia Severity Score. CI95% in brackets.*

Risk group	GDSS score
<b>LR</b>	
Total	8,45 (6,07-10,83)
Men	8,42 (6,21-10,63)
Women	8,50 (5,40-10,83)
<b>MR</b>	
Total	6,74 (5,43-8,05)
Men	7,09 (5,98-8,05)
Women	6,42 (4,60-8,24)
<b>HR</b>	
Total	15,40 (11,39-19,41)
Men	15,35 (11,21-19,49)
Women	15,45 (11,57-19,33)
<b>VHR</b>	
Total	16,38 (13,21-19,55)
Men	16,31 (13,08-19,54)
Women	16,43 (13,32-19,54)

*The GERS etiology*

The endoscopic examination was negative in the case of 77 patients (55.40% from the group), in which case the final diagnosis remained functional GERS. The percentage of normal endoscopies was of 69.05% in the LR group, 82.61% in the MR group, 45.24% in the HR group and 31.25 in the VHR group. Overall, the social drinkers had normal

endoscopies in 73.85% of the cases, and the heavy drinkers only in 39.19% of the cases (p<0,001). Therefore the probability that an alcoholic person with GERS to have an esophagus-gastro-duodenal mucosa with pathologic endoscopic aspect is significantly increased (RR=2,33, CI95% 1,56-3,10).

The distribution of the esophagus-gastro-duodenal endoscopic lesions according to the alcohol consumption is given in Table V. The most frequently endoscopic diagnosed lesions were esophagitis (26.15% in the case of the LR and MR patients and 60.81% in the case of the HR and VHR patients), followed by gastritis (in 10.77% from the social drinkers and in 58.11 % from the heavy drinkers).

**Table V.** *The endoscopic lesions found in the case of 139 patients with GERS, according to the alcohol consumption. The sex distribution in brackets (Men/Women).*

	RS	RM	RI	RFI
<b>Esophagitis</b>	13	4 (1/3)	23 (10/13)	22 (9/13)
Class A	(12/1)	3 (1/2)	11 (6/5)	7 (3/4)
Class B	4/0	1 (0/1)	11 (3/8)	11 (5/6)
Class C	9 (8/1)	0	1 (0/1)	4 (1/3)
	0			
<b>Gastritis</b>	5 (4/1)	2 (1/1)	23(10/13)	20 (8/12)
Antral	5 (4/1)	2 (1/1)	20 (8/12)	16 (6/10)
Pangastritis	0	0	3 (2/1)	4 (2/2)
<b>Gastric ulcer</b>	1 (1/0)	0	0	1 (1/0)
<b>Duodenitis</b>	3 (2/1)	0	0	0
<b>Duodenal ulcer</b>	1 (1/0)	0	1 (0/1)	0

In the case of the social drinkers from the LR and MR groups, out of the 17 cases of esophagitis, 7 of them (41.18%) were grade A and 10 of them (58.82%) were grade B. In the case of alcoholics, out of the 45 diagnosed cases, esophagitis was considered grade A in 18 cases (40.00%), B grade in 22 cases (48.89%) and C grade in 5 cases (11.11%).

All the 50 diagnosed cases of gastritis found in the patients with GERS have been confirmed histopathologically and were frame in the 2<sup>nd</sup> degree (light superficial gastritis) or the 3<sup>rd</sup> degree (superficial gastritis), without any difference related

to the alcohol consumption. All the 7 cases of diagnosed chronic gastritis in the patients from the LR and MR groups were erythematous exudative gastritis.

Out of the 43 diagnosed cases found in alcoholics, 31 (72.09%) were antral erythematous exudative gastritis, 5 (11.63%) were antral superficial gastritis and 7 (16.28%) were erythematous exudative pangastritis.

In the case of the social drinkers *H. pylori* were identified in 4 cases (2 cases of antral gastritis, 1 case of gastric ulcer and 1 case of duodenitis), and in the case of the heavy drinkers in 6 cases (2 cases each of antral erythematous exudative gastritis and antral superficial gastritis and pangastritis).

From the above mentioned data it results that the alcoholics with GERS have a significantly larger risk to develop esophagitis endoscopic lesions (RR=2,33, CI95% 1,49-3,64), and the one identified with esophagitis have a significantly larger risk to have also gastritis lesions (RR=2,95, CI95% 1,39-6,21), usually light and limited to the antral region. In exchange, the chronic abuse of alcohol does not increase the risk of gastric or duodenal ulcer and neither the one of *H. Pylori* infection.

#### *The GERS evolution*

The functional GERS was diagnosed in 77 cases (41 men and 36 women, vide supra). At the post-therapeutic control, 47 of the patients (61.04%) proved to be asymptomatic, 29 of them (37.66%) have recognized the improvement of the initial symptomatology and only one (1.30%) has considered the clinic table as stable. By analysing the incidence of the remissions according to the alcohol consumption, this was of 65.52% in the LR group, 84.21% in the MR group, 36.84% in the HR group and 50% in the VHR group. Overall, 72.92% from the social drinkers and only 41.38% from the heavy drinkers with functional GERS have become asymptomatic ( $p < 0,001$ ).

The patients that remained symptomatic after 4 weeks of treatment have required the continuation of omeprazol treatment for 22.47 days (CI95% 19,36-25,58 days) in the case of the social drinkers and 47.22 days (CI95% 38,58-55,86 days) in the case of the heavy drinkers ( $p < 0,001$ ).

We have not recorded significant differences between the two sexes, neither regarding the resistance of GERS to the treatment and neither regarding the duration of the therapy with proton pump inhibitor.

An organic etiology of GERS was endoscopically identified in 62 cases (44.60% of the patients with GERS), 32 men and 30 women (see Table 5). At the post-therapy control, 41 of these patients (66.13%) have become asymptomatic, 18 of them (29.03%) were improved and 3 of them (4.84%) remained clinically stable.

There were no significant differences between the clinic evolution on the short term of organic GERS and that of functional GERS. Linking the evolution of organic GERS with the alcohol consumption, the clinic healing after 4 weeks of treatment with omeprazol was of 100% in the LR and MR groups, and of 56.52% in the HR group and of 50% in the VHR group (53.33 % from the total of the heavy drinkers). From the comparative data between the functional GERS and the organic GERS (mentioned in Table VI) we can state that the post-therapy risk like the initial symptomatology to persist is significantly larger in the case of functional GERS than in the case of the organic GERS (RR = 1,80, CI95% 1,57-2,09), no matter if we are talking about social drinkers (Peto RR = 1,85 CI95% 1,54-2,16) or alcoholics (RR = 1,84, CI95% 1,57-2,11,  $p > 0,05$ ). In other words, the efficiency of omeprazol in the first case treatment of GERS is not dictated by the exaggerate consumption of alcohol but it is dictated by the etiology.

**Table VI.** The post-therapy evolution of functional (F) GERS compared with the organic (O) GERS according to the alcohol consumption. N = number of cases. In brackets, the percentage values. AS = asymptomatic; IM = improved; S = stable

	RS (N=42)		RM (N=23)		RI (N=42)		RFI (N=32)	
	F (N=29)	O (N=13)	F (N=19)	O (N=4)	F (N=19)	O (N=23)	F (N=10)	O (N=22)
AS	19 (65,52)	13 (100)	16 (84,21)	4 (100)	7 (36,85)	13 (56,52)	5 (50,00)	11 (50,00)
IM	10 (34,48)	-	3 (15,79)	-	11 (57,89)	8 (34,78)	5 (50,00)	10 (45,45)
S	-	-	-	-	1 (5,26)	2 (8,70)	-	1 (4,55)

The patients that remained symptomatic continued their treatment with omeprazol. Its duration was significantly smaller in the cases of the social drinkers (20.25 days with CI95% 14,62-25,88) compared with the one in the case of alcoholics (49.44 days, with CI95% 41,66-57,27 days,  $p < 0,001$ ), the same as in the case of the functional GERS, towards which there were not registered significant differences ( $p > 0,05$ ).

Therefore, if the answer to the standard treatment depends to the functional or organic etiology of GERS, the duration of the extra treatment necessary for the clinical remission depends upon the alcohol consumption. From the total of 74 alcoholics with GERS (with functional or organic etiology), 70 of them required extra treatment over 25 days, while 58 out of the 65 social drinkers with GERS have responded to the treatment within this time interval. It results that the probability that the alcoholic with GERS will require proton pump inhibitor treatment of over 25 days is much larger than the one of social drinkers: RR = 7,84 (3,90-15,73).

#### 4. Conclusions

The excessive alcohol consumption has increased the risk of developing GERS at the limit of the statistical significance (RR=1,64, CI95% 1,05-1,89). The alcoholics have shown a higher risk to develop severe forms of GERS (GDSS >15) than the

social drinkers (RR=16,98, CI95% 9,87-24,79), with a more complex clinic picture, poly-symptomatic, in which there are frequently associated also dyspeptic accuses with intestinal transit disorders. The GERS etiology in alcoholics is often organic (RR=2,33, CI95% 1,56-3,10). Although the efficiency of omeprazol in the first treatment of GERS is not dictated by the exaggerate consumption of alcohol but by the etiology of the condition, the probability that the alcoholic with GERS will require proton pump inhibitor treatment of over 25 days is significantly larger than the one in the case of social drinkers (RR = 7,84, CI95% 3,90-15,73). Thus, by its dragged evolution, the GERS contributes to the increase of the medical costs of the alcohol abuse and addiction.

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