

## WINE INTOLERANCE IN ITALY: A PILOT STUDY

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### ABSTRACT

Intolerance to wine has been investigated under different aspects. In our study, we explored intolerance/allergy reactions in Italy by means of a survey including 901 questionnaires.

Prevalence of wine or beer intolerance was 6%, of which 11 reported that was verified by a doctor. Odds ratio for wine intolerance with another declared allergy/intolerance is 1.6.

In conclusion, we observed a high prevalence of intolerance to wine in Italy, highlighting that some sections of the population (young people and women) may be more exposed to these phenomena.

*Keywords:* alcoholic drinks, allergy, intolerance, Italy, survey, wine

## 1. INTRODUCTION

Over the last few years, consumers have become increasingly interested not only in safety of food and beverages, but also in their healthiness. At the same time, the cultural conception of the consumed products has gained importance in relation to shared cultural and social significance and practice in a given environment or geographical area. When dealing with wine, the cultural connotation is well defined: in Mediterranean culture, the emotional and cultural aspects of wine have always been strongly connected. Moreover, in western culture, wine is often associated with festive and/or convivial moments. The effects of wine consumption have been extensively studied and a moderate alcohol consumption was proven to have positive healthy effects (RONKSLEY *et al.*, 2011); however, as for other food, allergic reactions and intolerances were also reported for wine (NIESTIJL JANSEN *et al.*, 1994; VALLY *et al.*, 1999; ARMENTIA, 2008; BÖHN *et al.*, 2013; JAECKELS *et al.*, 2015; BANSAL *et al.*, 2017; WÜTHRICH, 2018). A recent study reported prevalence of 74% for upper airway symptoms and 51% for lower respiratory symptoms after alcohol ingestion in patients with aspirin-exacerbated respiratory disease (CARDET *et al.*, 2014). Additional risk factors include female sex, history of allergic rhinitis, chronic obstructive pulmonary disease, and asthma (NIHLEN *et al.*, 2005).

The etiology of this reaction is still unclear, because wine is a complex beverage, with several potential allergens. Potential allergens include proteins from grape, molds, yeasts, as well as proteins from insects that have contaminated the mash. Milk derivatives as caseine and potassium caseinate, and other animal-derived products as isinglass and gelatin are used in the fining process to remove phenolic and tannin compounds from white wine, and egg white (albumin) is used to remove tannin compounds from red wine. Non-grape-derived tannins such as those from the bark and galls of trees are also used. These fining agents are added to the wine and the precipitates removed (ROLLAND *et al.*, 2006). Allergic reactions have been described also for components like ethanol, acetaldehyde, acetic acid and sulfites. Ethanol, acetaldehyde and acetic acid, flavonoids (anthocyanins and chatechines), sulfites, histamine and other biogenic amines are the main causative agents of intolerance reactions (pseudoallergic reactions) to wine (VALLY *et al.*, 1999; WÜTHRICH, 2018).

Actually, the presence of histamine in red wine as a source of intolerance has been controversial. Several studies observed a clear correlation between the red wine consumption (more rich in histamine than white wine) and the insurgence of the typical symptoms for food intolerance, such as sneezing, flush, headache, diarrhea, skin itch, and shortness of breath (JARISCH and WANTKE, 1996; WANTKE, HEMMER, HAGLMÜLLER, *et al.*, 1996; WANTKE, HEMMER, HAGLMULLER, *et al.*, 1996). Moreover, well trained wine assessors were able to identify elevated histamine concentrations in wine (ROHN *et al.*, 2005). Nevertheless, other studies did not observe such correlation between wine intolerance and histamine content of wine (KANNY *et al.*, 2001). In either cases, sample size was very low, and this may be the reason for this contradiction. Similar challenges were conducted to investigate the role of sulfites on the pathogenesis of wine-induced asthma, with no clear correlation, but more likely, this phenomenon appears to be a complex phenomenon, involving several different mechanisms (VALLY *et al.*, 1999).

In asthmatics, alcoholic drinks trigger asthma symptoms in more than one third of these patients (AYRES and CLARK, 1983; VALLY *et al.*, 2000). With regard to the prevalence of wine intolerance/allergy in general population, two surveys were conducted in Germany and Denmark (LINNEBERG *et al.*, 2008; WIGAND *et al.*, 2012). The German study was

localized in Mainz, the capital of Rhineland-Palatinate, a wine-producing region of Germany, and was conducted by means of a questionnaire survey (WIGAND *et al.*, 2012). The intolerance to wine was reported to be 3.2%, but only two persons reported that a wine allergy was verified by a physician. A cross-sectional study by means of postal questionnaire was conducted in Copenhagen, Denmark, in 2006, involving over 4,000 respondents out of 6,000 invited people (LINNEBERG *et al.*, 2008). The survey investigated the hypersensitivity reactions following consumption of alcoholic beverages divided by symptoms from the nose, lower airways, and the skin, with a prevalence of 7.6%, 3.2%, and 7.2%, respectively, and a cumulative prevalence of 13.9%. This study investigated all types of alcoholic beverages, including beer, red wine, white wine, dessert wine, and spirits.

To the best of our knowledge, no data are available about the prevalence of intolerance/allergy symptoms induced by wine in the Mediterranean countries, like Italy, that have a strong tradition in wine consumption. According to a 2014 FAO report, Italy is at the first place in the world ranking of wine producing countries, followed by Spain and France.

Aim of the study was to explore whether intolerance/allergy reactions are also present in the general population of a wine-producing country, such as Italy, and to estimate the prevalence by means of a questionnaire survey.

## 2. MATERIALS AND METHODS

The questionnaire about wine consumption and intolerance developed by Wigand and colleagues (WIGAND *et al.*, 2012) was translated in Italian, slightly modified and transferred to Google Surveys (<https://surveys.google.com>). Questionnaires were submitted either by face-to-face interview or self-submission after receiving the link to the Google form. For face-to-face interview, the answers were either recorded on a printed survey and then added later on the Google form by our personnel, or directly entered on the online survey from a portable device.

Subjects were included in the study with a convenience sampling, enrolling for the face-to-face interview 170 people attending to two events held in September 2017 in Piedmont (Cheese 2017: <http://cheese.slowfood.it/en/> and European Researchers' Night 2017: <http://nottedeiricercatori.piemontevalledaosta.it>). Snowball sampling starting from researchers involved in the study was used to enroll additional 731 people, using the online form.

As described by Wigand and colleagues, the questionnaire, in addition to standard questions on age and sex, included questions on whether allergy-like symptoms had occurred after wine consumption: participants had to choose among a list of symptoms (Table 1) experienced after the consumption of red, white and rosé wine. The intensity and the time of occurrence of each symptom was also assessed by the participants (intensity: none, weak, moderate, strong, very strong; time: <15 minutes, 15 minutes to 1 hour, 1 to 2 hours, >2 hours). In addition, participants were asked about intolerance to various known allergens, listed in Table 2. For each reported intolerance, participants had to declare if it was medically diagnosed. According to Wigand and colleagues (WIGAND *et al.*, 2012), all reported symptoms, except for headache, were considered as symptoms of intolerance and a score was given (Table 1). Each subject scoring more than 10 was defined as "intolerant to wine".

**Table 1.** Symptoms of wine intolerance, their score and prevalence with CI 95%.

Symptoms	Score	Number of participants	Prevalence	CI 95%
Circulatory collapse	10	2	0.2	0-0.8
Shortness of breath/asthma	8	25	2.9	1.9-4.2
Tachycardia	7	50	5.9	4.4-7.7
Itching	6	48	5.6	4.2-7.4
Flushed skin	5	160	21.6	18.7-24.7
Low blood pressure	5	51	6	4.5-7.8
Rhinorrea	4	30	3.4	2.3-4.9
Burning sensation in lips, palate, neck	4	47	5.5	4.1-7.3
Stomach or intestinal cramps	3	99	12.3	10.1-14.8
Diarrhea	3	48	5.6	4.2-7.4
Vomiting	3	33	3.8	2.6-5.3
Skin rash, hives, oedema	-	23	2.6	1.7-3.9
Headache	-	353	64.4	60.2-68.4
Other symptoms	-	48	5.6	4.2-7.4

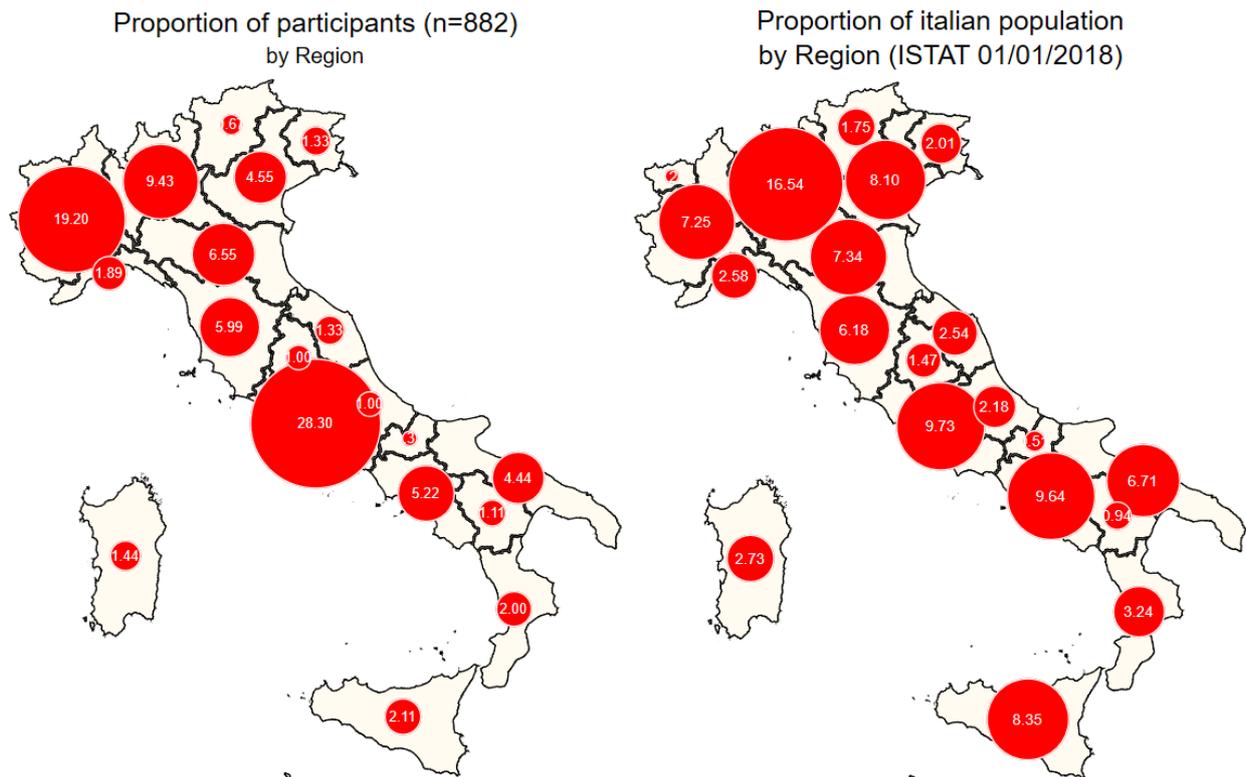
Once ended the survey, we performed a descriptive analysis of the characteristics of participants, of the frequency and of the preferences in alcohol consumption. Then, we calculated the prevalence and the 95% confidence interval (95% CI) of each symptom, and the prevalence of people intolerant to wine. Odds ratio (OR) and their 95% CI were calculated applying a logistic regression model to verify if there was some gender or age difference among people classified as intolerant to wine. The presence of allergies among participants was described and gender or age differences were assessed by calculating OR and their 95% CI. Finally, OR and their 95% CI were calculated to describe the relationship between intolerance to wine and the presence of allergies. All the statistical analyses were carried out using the software STATA 15.1 (StataCorp LLC, College station TX77845, Texas, USA, [www.stata.com](http://www.stata.com)).

### 3. RESULTS

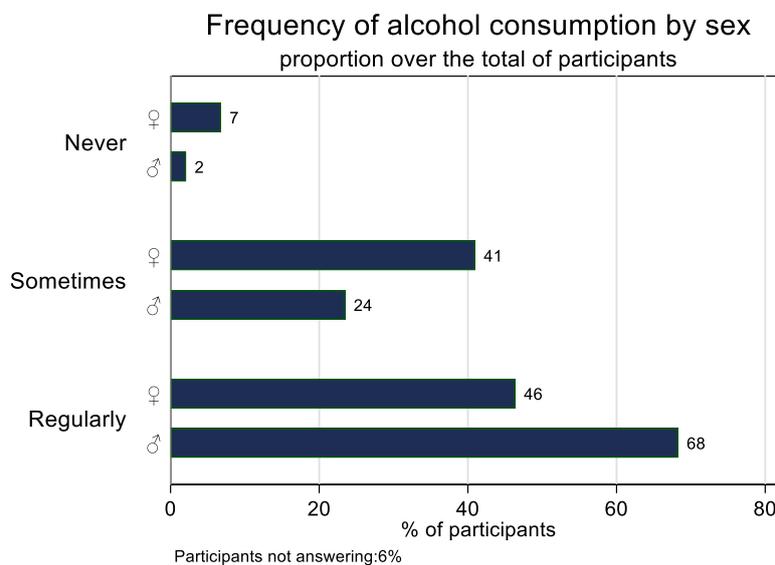
A total of 901 questionnaires were included in the study, and sex was equally distributed with 52% (n=486) of females and 48% (n=429) males. The geographical proportion and the proportion for age among participants do not reflect the proportion in the general population, as reported in Fig. 1, with an overrepresentation of people under 55 years of age.

As shown in Fig. 2, most of participants affirmed to drink wine more than once a month, and only a minority declared to have never drunk wine. Generally, men drank more than women (OR 2.78, 95% CI 2.09-3.70)

In our survey, 54 (6%) participants declared to have an intolerance to wine or beer, most of which were females; 11 of them reported that the allergy was verified by a doctor. The 36% of participants reported at least one symptom of intolerance after drinking wine. The prevalence of each symptom consequent to drinking wine, reported by participants is summarized in Table 1.



**Figure 1.** Comparison between the geographical distribution of the Italian general population at Jan, the 1-2018 (right), and people enrolled in the study (left).



**Figure 2.** Alcohol consumption: proportion of alcohol consumption by sex among people enrolled in the study. *Never*: never drunk wine; *Sometimes*: once a month; *Regularly*: more than once a month.

Having achieved a wine intolerance score of at least 10, a total of 138 subjects were classified as intolerant to wine (18%, 95% CI 15-21%), with an increased risk of intolerance to wine in females (OR 1.89, 95%CI 1.29-2.75), without differences in the age classes considered or in the type of wine. The 61% of participants declared to have at least one allergy/intolerance, with a risk of reporting at least one allergy/intolerance increased in females (OR 1.96, CI95% 1.49-2.58), without differences in the age classes considered or in the type of wine. The prevalence of each allergy/intolerance self-declared by participants is reported in Table 2.

**Table 2.** Prevalence of each allergy/intolerance self-declared by participants and declared as medically diagnosed.

Allergens	Self-declared		Medically diagnosed	
	Prevalence	CI 95%	Prevalence	CI 95%
Alcohol	4	2.8-5.6	1.2	0.6-2.2
Banana	2.2	1.3-3.3	1.5	0.8-2.5
Beer	3.8	2.6-5.3	1.3	0.7-2.3
Carrots	1.6	0.9-2.6	1.3	0.7-2.3
Celery	1.2	0.6-2.2	1.1	0.5-2.1
Cherries	2.3	1.4-3.5	1.5	0.8-2.5
Crustaceans	3.8	2.6-5.3	1.9	1.1-3.1
Eggs	2.5	1.6-3.8	1.6	0.9-2.6
Fish	1.7	1-2.8	1.3	0.7-2.3
Gluten	5.3	3.9-7	1.9	1.1-3.1
Grapes	1.6	0.9-2.6	1.2	0.6-2.2
House dust	36.1	32.4-39.9	16.9	14.3-19.7
Kiwi	5.1	3.8-6.8	1.8	1-2.9
Latex	4.8	3.4-6.4	1.7	1-2.8
Lupines	1.5	0.8-2.5	1.1	0.5-2.1
Medications	13.6	11.3-16.2	9.2	7.3-11.4
Milk and derivates	15.5	13-18.2	4.2	2.9-5.7
Mustard	1.8	1-2.9	1.1	0.5-2.1
Nickel	13.3	11-15.9	5.3	3.9-7
Nuts	6.9	5.3-8.8	3.3	2.2-4.7
Peaches	4	2.8-5.6	1.9	1.1-3.1
Peanut	3.3	2.2-4.7	1.9	1.1-3.1
Pears	2.2	1.3-3.3	1.5	0.8-2.5
Peppers	4	2.8-5.6	1.5	0.8-2.5
Plums	1.5	0.8-2.5	1.2	0.6-2.2
Pollen	39.7	35.9-43.6	21.4	18.5-24.6
Seafood	4.9	3.5-6.6	2.3	1.4-3.5
Sesame	1.6	0.9-2.6	1	0.5-1.9
Soya	1.8	1-2.9	1	0.5-1.9
Strawberries	4	2.8-5.6	2.3	1.4-3.5
Sulphites	11.9	9.8-14.4	1.6	0.9-2.6
Tomatoes	4.9	3.5-6.6	1.8	1-2.9
Wine	4.5	3.2-6.1	1.2	0.6-2.2

Participants classified as intolerant to wine showed an increased risk to have a medically-diagnosed allergy/intolerance (Table 3).

The OR of being intolerant to wine when declaring one medically diagnosed allergy/intolerance is 1.6 (CI95% 1.1-2.3). Table 3 reports the OR of being intolerant to wine for each medically diagnosed allergy/intolerance.

**Table 3.** Odds ratio and their 95% confidence interval of having a medically diagnosed allergy/intolerance when classified as intolerant to wine.

Allergens	Wine intolerants only	
	Odds ratio	CI95%
Banana	33	7-307.4
Carrots	29.7	6.2-280.3
Celery	53.2	7.2-2332.6
Cherries	33	7-307.4
Crustaceans	14.4	4.6-53
Eggs	14.8	4.2-65.4
Fish	29.7	6.2-280.3
Gluten	10.9	3.6-36.5
Grapes	59.5	8.3-2586.2
House dust	2.2	1.3-3.4
Kiwi	26.3	7.1-145.3
Latex	16.4	4.8-71.5
Medications	2.7	1.5-4.6
Milk and derivates	5.5	2.6-11.5
Nickel	3.7	1.8-7.2
Nuts	5.6	2.4-12.8
Peaches	8.4	2.8-26.5
Peanut	10.9	3.6-36.5
Pears	33	7-307.4
Peppers	33	7-307.4
Plums	59.5	8.3-2586.2
Pollen	1.5	0.9-2.4
Seafood	11.2	4.1-33.8
Strawberries	11.2	4.1-33.8
Sulphites	21.9	5.7-123.4
Tomatoes	18.1	5.3-77.7

#### 4. CONCLUSIONS

Wine is one of the oldest beverages, whose production can be traced back to 5,000 BC and it is nowadays often associated with convivial moments.

Intolerance to wine has been investigated under different aspects, albeit the unclear etiology. The prevalence of such intolerance was investigated in Nordic countries like Germany and Denmark, but no information about Mediterranean countries has been

published. Our survey aimed to fill this lack and showed that wine intolerance is present also in Italy. The prevalence of intolerants to wine (6%) is higher than the prevalence reported in Germany (3.2%), but lower than the one reported in Denmark (13%). This high percentage may be explained by the inclusion of all the alcoholic drinks in the Danish study without differentiation, although the Authors reported that red wine was listed as the main cause for hypersensitivity symptoms, as well as spirits (LINNEBERG *et al.*, 2008). Both the previous studies reported that symptoms of intolerance were more frequent after drinking red wine rather than white wine, while we found no differences among the type of wine. WÜTHRICH (2018) reported that the most frequent reactions are intolerance reactions to sulfites, which occur particularly after the ingestion of white wine and in asthma patients, and to histamine and other biogenic amines, mainly after ingestion of red wine. Particularly in white wine, allergy-like intolerance reactions are caused by sulfite (VALLY *et al.*, 2000; VALLY *et al.*, 2001). Asthma patients are especially sensitive.

In agreement with the previous studies, we also found an increased risk of being classified as intolerant to wine in females than in males. In line with what reported in the literature (NIHLEN *et al.*, 2005; CARDET *et al.*, 2014), our study highlighted a greater risk of being intolerant to wine in people who claim to have allergies or intolerances diagnosed by the doctor. On the other side, participants classified as intolerant to wine showed an increased risk to have a medically-diagnosed allergy/intolerance. Specifically, the highest associated risks (OR>50) were detected for celery, plums, and (as predictable) grapes.

Even in this case, however, it must be borne in mind that the analyzed data were reported by participants and were not investigated through the execution of clinical tests, therefore they might be subject to distortions.

Furthermore, the selection of a sample of convenience could cause a loss of external validity of the study, therefore the quantitative results of this study must be interpreted with caution.

The wine also contains molecules (biogenic amines like histamine and putrescine, and sulphites), which can cause phenomena mimicking allergies, making it difficult to distinguish between false allergy phenomena (for example histamine reactions) and real allergies. In fact, allergy/intolerance to sulfites had a significant OR (21.9) in those persons classified as intolerant to wine.

In conclusion, although with some limitations, our study indicates a high prevalence of the phenomenon of intolerance to wine, highlighting that some sections of the population (young people and women) may be more exposed to these phenomena. However, the relationship between the presence in the wine of molecules that can cause false allergy phenomena must be further investigated.

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