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Ingrid Arteaga [†] , Meritxell Carmona-Cervelló [*,†] , Guillem Pera , Carla Chacón [*] , Galadriel Diez-Fadrique , Irene Ruiz-Rojano , Maria Palau-Antoja , Faranak Nooriankafshgari , Cristina Vedia , Pilar Montero-Alia , M. Carmen Rodríguez-Pérez , Susana Montesinos , Pere Torán-Monserrat

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Ingrid Arteaga [1,2,3,†], Meritxell Carmona Cervelló [1,2,4,*,†], Guillem Pera [1,2], Carla Chacón [1,2,*], Galadriel Diez Fadrique [1], Irene Ruiz Rojano [1,5], Maria Palau Antoja [1], Faranak Nooriankafshgari [1], Cristina Vedia [1,6], Pilar Montero Alía [1,2,7], M. Carmen Rodríguez Pérez [1,8], Susana Montesinos [1,9] and Pere Torán Monserrat [1,2,4,10]

[1] Unitat de Suport a la Recerca (USR) Metropolitana Nord, Fundació Institut Universitari d'Investigació en Atenció Primària Jordi Gol i Gurina (IDIAP Jordi Gol), 08303 Mataró, Spain
[2] Multidisciplinary and Translational Research Group on Health and Society in Primary Health Care (GREMSAS-TranslAP), IDIAP Jordi Gol, USR MN, 08303 Mataró, Spain
[3] Primary Healthcare Center Vall del Tenes, Gerència d'Àmbit d'Atenció Primària Metropolitana Nord, Institut Català de la Salut (ICS), 08186 Lliçà d'Amunt, Spain
[4] Germans Trias i Pujol Research Institute (IGTP), 08916 Badalona, Spain
[5] Primary Healthcare Center Dr. Barraquer, Gerència d'Àmbit d'Atenció Primària i a la Comunitat Barcelonès Nord i Maresme, ICS, 08930 Sant Adrià del Besòs, Spain
[6] Department of Pharmacy, Gerència d'Àmbit d'Atenció Primària i a la Comunitat Barcelonès Nord i Maresme, ICS, 08911 Badalona, Spain
[7] Primary Healthcare Center La Riera, Gerència d'Àmbit d'Atenció Primària i a la Comunitat Barcelonès Nord i Maresme, ICS, 08302 Mataró, Spain
[8] Primary Healthcare Center Martorelles – Sant Fost, Gerència d'Àmbit d'Atenció Primària i a la Comunitat Vallès Occidental i Vallès Oriental, ICS, 08100 Mollet del Vallès, Spain
[9] Primary Healthcare Center Dr. Guillermo Masriera i Guardiola, Gerència d'Àmbit d'Atenció Primària i a la Comunitat Barcelonès Nord i Maresme, ICS, 08340 Vilassar de Mar, Spain
[10] Department of Medical Sciences, Faculty of Medicine, Universitat de Girona, Girona, Spain
* Correspondence: mcarmonace.mn.ics@gencat.cat (M.C.-C.); Tel.: +34937415338; cchaconv.mn.ics@gencat.cat (C.C.); Tel.: +34937415747
† These authors contributed equally to this work.

Abstract

Background/Objectives: Alcohol consumption and medication use have increased among the elderly population, raising the risk of alcohol–drug interactions and adverse outcomes. Sex-related biological differences may further influence these effects. This study aimed to assess sex-related differences among older adults with risky alcohol consumption, considering medication use, comorbidities, and hepatic biomarkers. **Methods:** A cross-sectional, multicenter study was conducted in adults aged ≥65 years. A total of 455 participants with risky alcohol consumption were included. Sociodemographic and clinical characteristics, medication prescriptions, and blood analytical parameters were collected. **Results:** Of the participants, 41% were women, with a mean age of 71 years. The mean weekly alcohol consumption was 8.4 ± 8.3 standard drink units. Overall, 71.2% were taking at least one medication, with antihypertensives being the most commonly prescribed (62%). Significant sex differences were observed ($p \leq 0.01$): men showed higher use of antidiabetic drugs (24%), anticoagulants (8%), and nitrates (4%), whereas women more frequently used anxiolytics (35%), non-steroidal anti-inflammatory drugs (22%), and antidepressants (18%). Significant differences were also observed in hepatic biomarkers, with higher gamma-glutamyl transferase levels in men and a higher AST/ALT ratio in women ($p \leq 0.01$). Although risky alcohol consumption was more prevalent among men, women had a higher overall medication use. **Conclusions:** A high proportion of older adults with risky alcohol consumption are exposed to concurrent pharmacological treatments, increasing the potential for clinically relevant alcohol–drug interactions. The observed sex differences in

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comorbidities, medication use, and hepatic biomarkers underscore the importance of incorporating a sex-based perspective in research and clinical practice.

Keywords: alcohol drinking; aged; prescription drugs; sex differences; primary health care

1. Introduction

Alcohol consumption among the elderly has increased in recent decades [1–3]. It is estimated that around 8% to 20% of adults aged 65 years and over consume alcohol in excess [4–6]. In Spain, one in four older adults consumes alcohol in quantities that exceed the recommended amount [7–9]. Concurrently, there has been an increase in the utilization of medications, and the phenomenon of polypharmacy is becoming increasingly prevalent [10]. In the elderly population, polypharmacy, defined as the use of five or more drugs [11], affects approximately 22% of adults aged 65 and older [12].

This context suggests that a significant percentage of older adults consume alcohol in conjunction with medications. A meta-analysis revealed that between 21% and 35% of older adults consume alcohol concurrently with drugs that may have the potential for interaction [13,14]. In this regard, even moderate alcohol consumption has been associated with a 24% increase in the risk of adverse drug reactions [15]. In addition to these factors, physiological changes associated with aging contribute to an increased vulnerability to interactions with substances. These changes include alterations in the distribution and metabolism of substances, as well as a heightened sensitivity of the central nervous system [16,17].

Interactions between alcohol and medications have the potential to interfere with the effectiveness of drugs, cause adverse side effects, reduce or exacerbate their effects, and consequently worsen health problems [14]. Evidence suggests that even low levels of alcohol consumption, or any alcohol intake at all, may produce harmful effects when combined with certain medications [14]. In this regard, alcohol has been demonstrated to potentiate the sedative effects of antidepressants, barbiturates, benzodiazepines, and opioids, thereby increasing the risk of falls; exacerbate the gastrointestinal and renal adverse effects associated with nonsteroidal anti-inflammatory drugs (NSAIDs) [18]; and augment the risk of hypoglycemia in diabetics undergoing hypoglycemic treatment [19]. However, the existing literature has yet to explore the differences linked to biological sex in a comprehensive manner.

While research has documented variations in alcohol consumption patterns between men and women, studies have also demonstrated that women exhibit a heightened vulnerability to the effects of alcohol [20]. This vulnerability is partly attributable to biological differences [14], including body composition, pharmacokinetic differences in alcohol metabolism, effects on the brain, and the influence of sex hormones [21]. These disparities also influence the pharmacokinetics and pharmacodynamics of medications, modulating their efficacy, safety, and metabolism [22,23]. However, in individuals with excessive alcohol consumption, there is a paucity of research on potential gender disparities in medication utilization patterns and their correlation with clinical and analytical profiles.

In this context, the present study aims to evaluate sex differences in older adults with risky alcohol consumption, considering medication use, comorbidity burden, and liver biomarkers. This approach provides relevant evidence for future clinical strategies for the detection, prevention, and management of alcohol consumption in older adults who use medications.

2. Materials and Methods

2.1. Study Design and Participants

This community-based study utilizes data from a two-phase population study (ALANE cohort). The cohort included individuals registered at 25 Primary Health Care centers (PHC) in the Barcelona

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Nord and Maresme areas (Catalonia, Spain), recruited between 2015 and 2021. The study area covers a population of approximately 700,000 inhabitants, of whom 82,903 are aged ≥65 years.

Participants were randomly selected from the Primary Care Information System (SIAP), which includes all individuals with national healthcare cards and is equivalent to the population census of Catalonia. This database comprises all the individuals assigned to PHCs in the study area, regardless of healthcare utilization. For more details regarding the study design, please refer to the previous publication [24].

The study population included subjects of both sexes who were 65 years of age or older and were assigned to the participating PHCs. Individuals with conditions that could impede data collection or follow-up were excluded from the study. Such conditions included disabling diseases, cognitive impairment, residence in long-stay centers, or a diagnosis of alcohol dependence according to the International Classification of Diseases (ICD-10).

The term "risky drinker" in ALANE cohorts was defined as [24]:

- Males: consumption of more than 1 SDU (equivalent to 10 g of pure alcohol) per day; or more than 7 SDU per week; or more than 2 SDU on one drinking occasion [25]; or any consumption if they have a medical condition that worsens with alcohol consumption or are taking medications that interact with alcohol.
- Females: from 1 SDU (equivalent to 10 g of pure alcohol) per day; or 7 SDU per week; or more than 1 SDU on one drinking occasion [25]; or any consumption if they have a condition that worsens with alcohol consumption or are taking medications that interact with alcohol.

2.2. Variables

The following variables were collected: sociodemographic variables (age, sex, and educational level), clinical variables (comorbidities, medication intake recorded in computerized medical history or self-reported, and body mass index), substance use (alcohol recorded in SDU and tobacco), and laboratory variables (aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT)).

A pair of indices were calculated based on analytical data, with the purpose of determining the presence of liver disease: AST/ALT ratio, also known as the De Ritis index, was calculated as the ratio between AST and ALT values. This index has demonstrated its efficacy in the diagnosis and prognosis of various liver diseases, including alcoholic liver disease [26]. An AST/ALT ratio > 1.5 strongly suggests alcohol-induced liver damage, and a ratio > 2.0 is almost certainly indicative of alcohol-induced liver damage [27].

The FIB-4 index is a non-invasive serological marker used to stratify the risk of advanced liver fibrosis in patients with suspected chronic liver disease, such as those with excessive alcohol consumption [28]. The calculation was derived using the following formula [29]:

$$\text{FIB-4} = [\text{age (years)} \times \text{AST (U/L)}] \,/\, [\text{platelet count} (\times 10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}]$$

In the population over 65 years of age, a value less than 2.0 allows the presence of advanced liver fibrosis to be ruled out [30].

2.3. Data Collection

Participants were selected using random sampling from SIAP, and initial contact was made by telephone.

Participants who provided consent were scheduled for an initial visit at their respective PHCs, with the objective of identifying individuals who exhibited risky drinking behaviors. During the visit, the inclusion and exclusion criteria were verified, the study information sheet was provided, and written informed consent was obtained.

The identification of at-risk drinkers was conducted through the utilization of computerized medical records and a questionnaire designed to assess healthy habits. The questionnaire encompassed the following inquiries: The quantity and regularity of habitual alcohol consumption

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over the course of the previous three months. Those classified as at-risk drinkers underwent a blood test.

2.4. Statistical Analysis

Distributions of continuous variables were assessed using histograms. Variables following a normal distribution are presented as means and standard deviations, whereas non-normally distributed variables are reported as medians and interquartile ranges. Categorical variables are summarized as frequencies and percentages.

For group comparisons, independent samples t-tests were used for normally distributed continuous variables. The Mann-Whitney U test was used when normality assumptions were not met. The Kruskal-Wallis test was applied for comparisons involving more than two groups. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate.

All tests were two-sided, and a p-value < 0.05 was considered statistically significant. Analyses were performed using Stata (v18) and RStudio (v4.4.0).

3. Results

3.1. Characteristics of the Total Sample

The total sample included 931 participants, of whom 513 were women (55%), with a mean age of 71 ± 5 years. Overall, 63% of the participants consumed alcohol, with 78% of these individuals exhibiting risky consumption patterns; among risky drinkers, 59% were men.

The median number of medications consumed per participant was 2, with antihypertensive medications being the most prevalent (51%), followed by analgesics (32%) and anxiolytics, antiepileptics, and hypnotics (23%). The number of medications was significantly lower among participants with non-risk alcohol consumption (p < 0.01). Individuals who did not consume alcohol had a higher prevalence of polypharmacy (5% vs. 2–3%; p < 0.01). The main descriptive characteristics are shown in Table 1.

Table 1. Characteristics of the total sample (n = 931).

	Abstainer (n = 349)	Non-risk drinker (n = 127)	Risk drinker (n = 455)	Total (n = 931)	*p*
Sex					
Male	88 (25.2%)	62 (48.8%)	268 (58.9%)	418 (44.9%)	< 0.01
Female	261 (74.8%)	65 (51.2%)	187 (41.1%)	513 (55.1%)	
Age	70.0 (67.5-75.1)	70.0 (67.8-75.4)	69.8 (67.8-72.8)	70.0 (67.7-74.1)	0.30
Educational level					
No formal education	127 (36.6%)	33 (26.8%)	88 (19.8%)	248 (27.1%)	
Primary education	172 (49.6%)	71 (57.7%)	238 (53.6%)	481 (52.6%)	< 0.01
Secondary or higher education	48 (13.8%)	19 (15.5%)	118 (26.6%)	185 (20.2%)	
Alcohol consumption					
SDU per week	0 (0)	1 (0-3)	7 (2-14)	0 (0-7)	< 0.01
SDU per time	0 (0)	1 (1-1)	2 (1-2)	1 (0-2)	< 0.01
Number of drugs					
0	114 (32.7%)	92 (72.4%)	45 (9.9%)	251 (27.0%)	
1	51 (14.6%)	17 (13.4%)	146 (32.1%)	214 (23.0%)	
2	74 (21.2%)	8 (6.3%)	133 (29.2%)	215 (23.1%)	< 0.01
3	55 (15.8%)	6 (4.7%)	83 (18.2%)	144 (15.5%)	
4	36 (10.3%)	2 (1.6%)	35 (7.7%)	73 (7.8%)	
≥5	19 (5.44%)	2 (1.6%)	13 (2.9%)	34 (3.7%)	
Drugs consumption					

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NSAID	62 (17.8%)	16 (12.6%)	78 (17.1%)	156 (16.8%)	0.39
Analgesics	107 (30.7%)	8 (6.3%)	182 (40.0%)	297 (31.9%)	< 0.01
Nitrates	12 (3.4%)	1 (0.8%)	13 (2.9%)	26 (2.8%)	0.33
Dicoumarinics	19 (5.4%)	1 (0.8%)	26 (5.7%)	46 (4.9%)	0.04
Antidepressants	49 (14.0%)	2 (1.6%)	49 (10.8%)	100 (10.7%)	< 0.01
A3	89 (25.5%)	5 (3.9%)	118 (25.9%)	212 (22.8%)	< 0.01
ANTH	3 (0.9%)	2 (1.6%)	7 (1.5%)	12 (1.3%)	0.66
Antipsychotics	6 (1.7%)	0 (0%)	6 (1.3%)	12 (1.3%)	0.44
Antiparkinsonian	0 (0%)	0 (0%)	3 (0.7%)	3 (0.3%)	0.38
H1	8 (2.3%)	2 (1.6%)	9 (2.0%)	19 (2.0%)	0.95
Opioids	8 (2.3%)	4 (3.2%)	5 (1.1%)	17 (1.8%)	0.20
Methotrexate	1 (0.3%)	1 (0.8%)	0 (0%)	2 (0.2%)	0.12
Antidiabetics	72 (20.6%)	8 (6.3%)	91 (20.0%)	171 (18.4%)	< 0.01
HTA	173 (49.6%)	19 (15.0%)	282 (62.0%)	474 (50.9%)	< 0.01

Note: NSAID, Non-steroidal anti-inflammatory drug; A3, Anxiolytics, antiepileptics and hypnotics; ANTH, Antihistamines antiallergics; H1, Antihistaminics H1 and antiemetics; HTA, Antihypertensive and alpha blockers. Categorical variables are presented as n (%), and continuous variables as mean ± standard deviation (normally distributed variables) or median (interquartile range) (non-normally distributed variables).

3.2. Characteristics of High-Risk Alcohol Consumers

Table 2 shows the characteristics of high-risk consumers (n = 455) according to sex. The female population constituted 41% of the sample. A statistically significant difference was identified in the mean SDU for both weekly and per-occasion consumption, with higher values observed in the male population ($p < 0.01$). Also, the proportion of current and former smokers was notably higher in the male group ($p < 0.01$).

Regarding the presence of comorbidities, the most prevalent were dyslipidemia (65%), hypertension (63%), and diabetes mellitus (25%). The mean total number of comorbidities was marginally higher among males (2.51 ± 1.43 vs. 2.14 ± 1.27, p = 0.02). Significant differences were observed in the prevalence by sex of heart disease (22% vs. 8%, $p < 0.01$), cancer (13% vs. 6%, p = 0.01), and chronic obstructive pulmonary disease (12% vs. 4%, $p < 0.01$).

Table 2. Characteristics of the risk drinkers by sex (n = 455).

	Female (n = 187)	**Male (n = 268)**	**Total (n = 455)**	***p***
Age	69.59 (67.59-72.12)	70.25 (67.83-73.18)	69.84 (67.78-72.80)	0.14
Educational level				
No formal education	45 (24.7%)	43 (16.4%)	88 (19.8%)	
Primary education	97 (53.3%)	141 (53.8%)	238 (53.6%)	0.05
Secondary or higher education	40 (22.0%)	78 (29.8%)	118 (26.6%)	
IMC	29.2 ± 4.5	29.0 ± 3.9	29.1 ± 4.2	0.72
Tabaco				
No smoker	154 (88.0%)	56 (22.6%)	210 (49.7%)	
Ex-smoker	14 (8.0%)	145 (58.5%)	159 (37.6%)	< 0.01
Smoker	7 (4.0%)	47 (19.0%)	54 (12.8%)	
Alcohol consumption				
SDU per week	2 (1-7)	9 (6-16)	7 (2-14)	< 0.01
SDU per time	1 (1-2)	2 (1-3)	2 (1-2)	< 0.01
Number of drugs				
0	8 (4.3%)	37 (13.8%)	45 (9.9%)	
1	65 (34.8%)	81 (30.2%)	146 (32.1%)	
2	56 (30.0%)	77 (28.7%)	133 (29.3%)	0.08

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3	37 (19.8%)	46 (17.2%)	83 (18.2%)	
4	15 (8.0%)	20 (7.5%)	35 (7.7%)	
≥5	6 (3.21%)	7 (2.6%)	13 (2.9%)	
Number of comorbidities	2 (1-3)	2 (2-3)	2 (1-3)	0.02
Comorbidities				
Hypertension	107 (60.1%)	161 (64.4%)	268 (62.6%)	0.37
Diabetes Mellitus	40 (22.5%)	69 (27.6%)	109 (25.5%)	0.23
Dyslipidemia	122 (68.5%)	158 (63.2%)	289 (65.4%)	0.25
Obesity	41 (23.0%)	61 (24.4%)	102 (23.8%)	0.74
Heart disease	15 (8.4%)	54 (21.6%)	69 (16.1%)	< 0.01
Cerebrovascular accident	6 (3.4%)	15 (6.0%)	21 (4.9%)	0.26
Psychiatric disorders	16 (9.0%)	11 (4.4%)	27 (6.3%)	0.05
Peripheral artery disease	1 (0.6%)	9 (3.6%)	10 (2.3%)	0.05
Chronic non-viral liver disease	3 (1.7%)	10 (4.0%)	13 (3.0%)	0.25
Chronic viral liver disease	2 (1.1%)	5 (2.0%)	7 (1.6%)	0.70
Gastroduodenal ulcer	3 (1.7%)	7 (2.8%)	10 (2.3%)	0.53
Bronchial asthma	8 (4.5%)	4 (1.6%)	12 (2.8%)	0.08
COPD	7 (3.9%)	31 (12.4%)	38 (8.9%)	< 0.01
Cancer	10 (5.6%)	32 (12.8%)	42 (9.8%)	0.01

Note: COPD, Chronic Obstructive Pulmonary Disease. Categorical variables are presented as n (%), and continuous variables as mean ± standard deviation (normally distributed variables) or median (interquartile range) (non-normally distributed variables).

Among participants with risky alcohol consumption, 10% were not taking any medication, 65% were taking one or two medications. A total of 62% of high-risk consumers were prescribed antihypertensive medications or alpha blockers, followed by analgesics (40%), with no statistically significant differences observed based on sex. The analysis revealed that women exhibited a similar mean number of drugs consumed (2.02 ± 1.15 vs. 1.83 ± 1.27, $p = 0.08$), with a significant increase in the use of anxiolytics, antiepileptics and hypnotics (35% vs. 19%, $p < 0.01$), anti-inflammatories (22% vs. 14%, $p = 0.02$), and antidepressants (18% vs. 6%, $p < 0.01$). Conversely, a higher proportion of male patients exhibited increased consumption of antidiabetics (24% vs. 15%, $p = 0.03$), anticoagulants (8% vs. 3%, $p = 0.02$), and nitrates (4% vs. 1%, $p = 0.01$) (Figure 1).

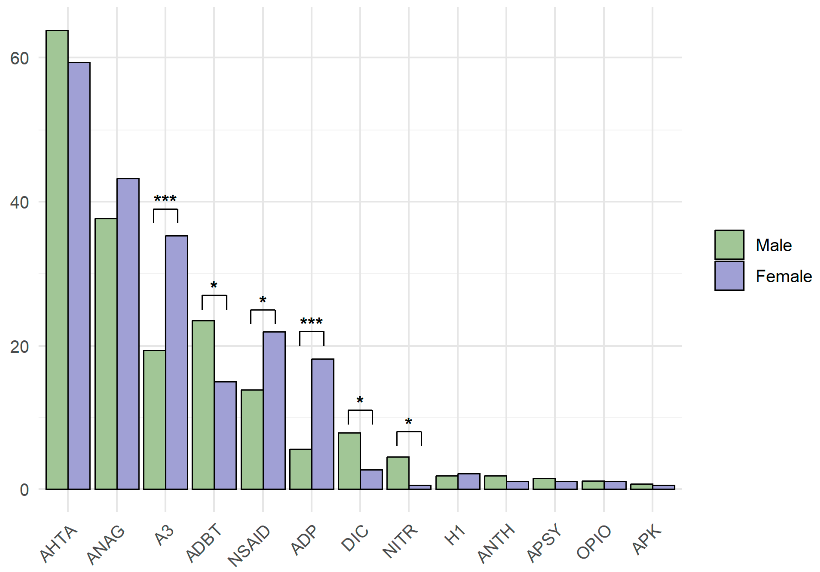

Figure 1. Medication use among the risk drinker by sex (n = 455). Note: Medications not used by any participants (methotrexate and lithium carbonate) were excluded from the graph. *$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. AHTA,

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Antihypertensive and alpha blockers; ANAG, Analgesics; A3, Anxiolytics, antiepileptics and hypnotics; ADBT, Antidiabetics; NSAID, Non-steroidal anti-inflammatory drug; ADP, Antidepressants; DIC, Dicoumarinics; NITR, Nitrates; H1, Antihistaminics H1 and antiemetics; ANTH, Antihistamines antiallergics; APSY, Antipsychotics; OPIO, Morphine and opioids; APK, Antiparkinsonian.

3.3. Blood Biochemistry Parameters of High-Risk Alcohol Consumers

Mean GGT level were significantly higher in men than in women: 41.52 ± 44.31 U/L vs. 21.88 ± 12.57 U/L, respectively ($p < 0.001$). The distribution of GGT values by sex is shown in Figure 2a.

Statistically significant differences were also observed in the De Ritis index or AST/ALT ratio by sex ($p = 0.01$). The mean value for males was 1.10 (0.45–1.91), while for females it was 1.24 (0.48–2.89). These results are shown in Figure 2b.

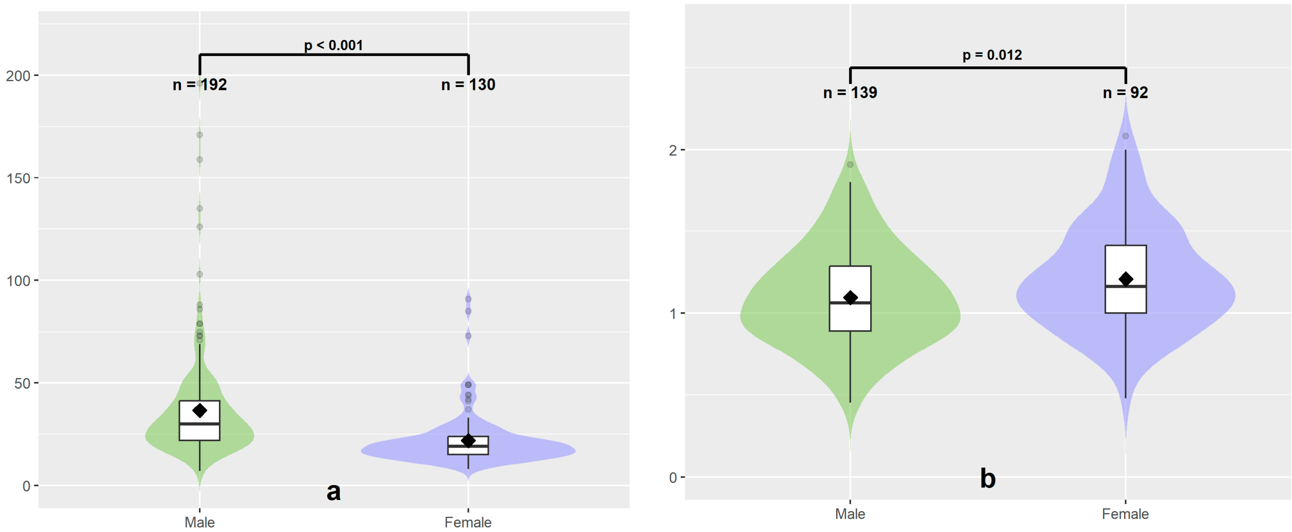

Figure 2. (a) Distribution of Gamma-glutamyl transferase (U/L) by sex. (b) De Ritis ratio by sex.

Twenty-four percent of the participants had FIB-4 scores above 2.0, while 10% had scores above 2.67. After excluding participants with chronic liver disease, these prevalences decreased slightly to 22% and 9%, respectively. A statistically significant difference was identified between male and female subjects ($p < 0.001$). Specifically, 13% of male subjects demonstrated scores above 2.67, while this proportion was 4% among female subjects (Figure 3).

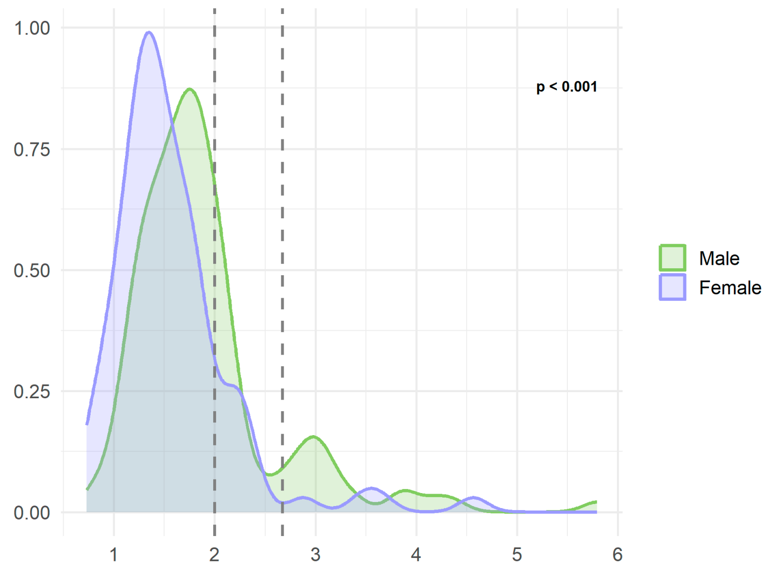

Figure 3. Distribution of FIB-4 by sex (n = 223; male = 131, female = 92). Note: Participants with known chronic liver disease, viral or non-viral, were excluded from this analysis (n = 19).

4. Discussion

The findings of this study indicate a significant proportion of older adults with risky alcohol consumption who are simultaneously receiving pharmacological treatment. This coexistence is clinically relevant, as it may increase the likelihood of alcohol–drug interactions and the occurrence of adverse effects. It has been suggested that even with lower amounts of alcohol use (less than 40g of alcohol per day) may be associated with a higher frequency of adverse drug reactions, with some evidence indicating that this risk could be greater in women; however, sex-specific data remain limited [14,15].

Consistent with previous studies, men reported higher alcohol consumption than women, both weekly and per occasion. However, recent evidence suggests that alcohol consumption among women has increased over time [31–33]. Despite reporting lower levels of consumption, women may be more susceptible to the effects of alcohol due to physiological and metabolic differences. Specifically, women exhibit lower levels of gastric alcohol dehydrogenase activity, a lower proportion of total body water, and a higher percentage of adipose tissue, which contributes to higher blood alcohol concentrations [34–36]. In addition, women appear to be more biologically vulnerable to alcohol-related liver damage than men at comparable levels of alcohol exposure, potentially placing them at increased risk even with moderate alcohol consumption in older age [37,38]. These sex-related differences may be further amplified by ageing, becoming more pronounced in older populations.

Approximately 90% of participants with risky alcohol consumption were taking at least one medication, with antihypertensive drugs and analgesics being the most frequently prescribed. Moreover, almost 60% of the sample were taking two or more medications, and 2.9% fulfilled criteria for polypharmacy (≥5 drugs), highlighting a subgroup at particularly increased risk of alcohol–drug interactions and adverse events.

Although men presented a higher burden of comorbidities, women showed a slightly higher mean number of medications consumed with a higher prevalence of polypharmacy; however, this difference did not reach statistical significance. Distinct medication use patterns were nevertheless observed according to sex. Women more frequently used medications related to pain management and mood disorders, whereas men were more likely to receive treatments aimed at the management and prevention of cardiovascular diseases. These findings are consistent with the distribution of comorbidities observed in our sample and with previous epidemiological evidence [39]. The trend towards a higher pharmacological burden among women, despite a lower comorbidity burden, has also been described previously and may be partially explained by sex differences in healthcare utilization, symptom reporting, and the higher prevalence of affective and somatic conditions among women [40,41].

These differences in disease profiles and prescribing patterns underscore the importance of considering potential sex-specific consequences of alcohol use in older adults receiving pharmacological treatment. Previous evidence has shown that the concomitant use of alcohol and anxiolytics, hypnotics, antidepressants, and other central nervous system (CNS) depressants may increase the risk of sedation, cognitive impairment, and falls [42–45]. Likewise, the combined use of NSAIDs and alcohol has been associated with an elevated risk of gastric mucosal injury and gastrointestinal bleeding [46,47]. In men, who more frequently used cardiovascular medications, alcohol consumption in combination with these treatments has been associated with adverse outcomes such as hypoglycemia in patients receiving antidiabetic treatment [19], hypotension among individuals taking antihypertensive drugs [48,49], and increased bleeding risk in those treated with antiplatelet agents [28,50]. Overall, our findings suggest that older women with risky alcohol consumption may be particularly vulnerable to adverse effects resulting from the concomitant use of alcohol and CNS-active or anti-inflammatory medications, despite reporting lower levels of alcohol consumption than men. In contrast, older men may be more prone to alcohol-related complications associated with cardiovascular pharmacotherapy.

When we analyzed serological markers associated with alcohol consumption, mean ALT, AST, and GGT levels did not reach clinically relevant thresholds; however, significant sex-related differences were observed. Men showed higher GGT levels, consistent with previous studies reporting a stronger association between alcohol intake and GGT elevation in males [51]. In addition, the AST/ALT ratio (De Ritis ratio) was greater than 1 in both sexes and significantly higher in women, although values remained below those commonly associated with advanced alcohol-related liver disease [52,53]. Previous studies have shown that women may experience elevated GGT levels even with lower levels of alcohol consumption [51,54,55] and they may also have higher ALT/AST ratios [56]. These findings suggest that, although men showed higher absolute levels of biochemical markers of alcohol-related liver injury, the evidence of increased biological susceptibility in women indicates that the risk of liver-related damage should not be underestimated in older female drinkers.

Finally, alcohol consumption is a well-established risk factor for the development of fibrosis, cirrhosis and hepatocellular carcinoma (HCC) [28]. Biological and metabolic differences appear to make women more susceptible to alcohol-induced liver damage and, therefore, more likely to develop HCC than men [38]. We found a high proportion of participants that showed altered FIB-4 index values, particularly among men. To our knowledge, there are currently no precise data regarding the prevalence of liver fibrosis among adults aged >65 years with risky alcohol consumption. Previous studies have reported that, among risky drinkers without age restrictions, approximately 20% present markers of advanced fibrosis [28,57]. FIB-4 is a useful non-invasive marker to rule out advanced fibrosis [30], its accuracy may be limited by factors such as age, the presence of comorbidities, and the use of certain medications [58,59]. Consequently, the interpretation of these results should be regarded with caution within the context of the study.

This study has several limitations that should be considered when interpreting the findings. Firstly, it should be noted that the data originates from a cohort that was recruited more than a decade ago; therefore, they may not fully reflect current alcohol consumption and prescribing patterns. However, this is a well-characterized community sample and, despite the limited literature available on this population group, the results obtained are generally consistent with the evidence published to date. Secondly, the study was not originally designed to specifically characterize the pharmacological profile, comorbidities, or blood biochemistry parameters. This limitation limited the ability to explore associations in greater depth. Conversely, the absence of biochemical data on participants exhibiting risky consumption patterns and those who abstain from alcohol altogether hinders the capacity for direct comparisons between the various alcohol consumption groups. Thirdly, hepatic fibrosis was determined using non-invasive serological markers calculated retrospectively from previously collected variables and in light of the most recent scientific evidence. Consequently, a gold standard was not available to confirm these findings. The advanced age of the cohort, in conjunction with the aforementioned factors, may have led to an overestimation of the risk of liver fibrosis, particularly when employing indices such as FIB-4. Notwithstanding these limitations, the present study furnishes pertinent information regarding sex-based differences in the pharmacological profile, comorbidities, and hepatic biochemical parameters in older adults with risky alcohol consumption, thereby establishing the foundation for the development of future studies with a specific focus on sex.

5. Conclusions

A significant proportion of people aged 65 and older consume alcohol in amounts that pose a health risk while undergoing long-term medication treatment. The social normalization of alcohol consumption and the frequent use of medications in daily life can contribute to the risk of interactions between these two substances going unnoticed, both by the individuals affected and by healthcare professionals. In this context, our study provides relevant data for routine clinical practice, particularly in primary care, suggesting the need to systematically integrate the assessment of alcohol

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consumption into patients' medical histories, inform them of the potential health consequences, and periodically reassess pharmacological treatments to identify and prevent clinically significant interactions. Overall, these findings highlight the need for greater awareness of alcohol consumption and its potential interaction with medications in older adults, identifying sex differences in comorbidities, medication prescribing patterns, and laboratory biomarkers, and underscoring the importance of incorporating a sex-specific perspective into research and clinical practice.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author due to ethical and privacy restrictions.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

NSAIDs	Nonsteroidal anti-inflammatory drugs
PHC	Primary Health Care centers
PAPPS	Preventive Activities and Health Promotion Program
ICD-10	International Classification of Disease
SDU	Standard Drink Units
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
GGT	Gamma-glutamyl transferase
SIAP	Primary Care Information System
A3	Anxiolytics, antiepileptics and hypnotics
ANTH	Antihistamines antiallergics
H1	Antihistaminics H1 and antiemetics
OPIO	Morphine and opioids
HTA	Antihypertensive and alpha blockers
COPD	Chronic Obstructive Pulmonary Disease
ANAG	Analgesics
ADBT	Antidiabetics
ADP	Antidepressants
DIC	Dicoumarinics
NITR	Nitrates
APSY	Antipsychotics
APK	Antiparkinsonian
CNS	Central Nervous System
HCC	Hepatocellular Carcinoma

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