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Review

Alcohol Consumption and Its Effect on Liver Function Test—A Systematic Review and Meta-analysis

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Abstract: Around 2.3 billion people globally consume alcohol, with Europe leading at 9.8 litres per capita. This high level of alcohol consumption significantly contributes to liver diseases, including alcoholic hepatitis, cirrhosis, and liver cancer. This review explores alcohol consumption's impact on liver function, focusing on alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) levels to understand liver health, disease progression, and influencing factors. The study used multiple databases and manual searches, with eligibility criteria including original research articles from diverse demographics and regions. Two independent reviewers conducted the screening process, minimizing bias and enhancing reliability. The Joanna Briggs Institute's critical appraisal checklist assessed the quality and risk of bias in the studies. Meta-Mar v3.5.1 was used for data analysis, with descriptive statistical tests and a random-effects model to synthesize findings across studies. Subgroup analyses were conducted to explore regional variations. The meta-analysis, incorporating data from 27 datasets across 13 studies, demonstrated a significant overall risk of alcohol consumption impacting liver function tests (LFTs). The pooled relative risk (RR) was 1.33 (95% CI: 0.97–1.82), as determined using a random-effects model ($z/t = 1.86$, $p = 0.007$). Higgins' I^2 statistic was extremely high at 99.4% (95% CI: 99.4%–99.5%), with an H value of 13.23 (95% CI: 12.49–14.01), confirming substantial heterogeneity ($Q = 4550.29$, $df = 26$, $p = 0$). The findings revealed that alcohol consumption increases the relative risk of elevated liver enzyme levels: ALT had a RR of 1.2625 (95% CI: 0.8459–1.8842), AST had an RR of 1.1783 (95% CI: 0.4851–2.8621), and GGT had a RR of 1.7645 (95% CI: 0.8241–3.7782). The observed outcomes regarding the effects of alcohol consumption on ALT, AST, and GGT were not significantly influenced by publication bias, as confirmed by Egger's regression analysis with no significant publication bias ($t = 0.06$, $df = 25$, $p = 0.9558$). Alcohol consumption negatively impacts LFTs, leading to elevated levels of key enzymes like ALT, AST, and GGT. This risk is consistent across geographical areas, suggesting the need for consideration in assessing alcohol's impact on liver health.

Keywords: alcohol consumption; alcohol-related liver disease (ALD); hepatocellular carcinoma (HCC); alanine aminotransferase (ALT); aspartate aminotransferase (AST); gamma-glutamyl transferase (GGT); liver function tests (LFTs)

1. Introduction

Globally, 2.3 billion people consume alcohol, with an average annual per capita consumption of 6.4 litres [1,2]. Europe leads with 9.8 litres per capita, while the Americas have 8.0 litres per capita [3]. Regional differences exist, with Southern

Africa having higher consumption rates [4,5]. Men consume almost three times more alcohol than women, with high-income countries typically showing higher consumption [6,7]. The widespread alcohol consumption significantly contributes to the global burden of liver diseases, which account for approximately 3 million deaths annually, or 5.3% of all deaths worldwide [1,8,9]. Alcohol-related liver disease (ALD) encompasses conditions such as alcoholic hepatitis, cirrhosis, and liver cancer, notably hepatocellular carcinoma (HCC), all of which are strongly associated with heavy alcohol intake [10,11].

Excessive alcohol consumption is closely associated with various liver diseases and significantly impacts the levels of key liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) [12–15]. These enzymes serve as crucial biomarkers for assessing liver function and health [16]. ALT, which is primarily found in the liver, becomes elevated when liver cells are damaged, indicating hepatocellular injury typically seen in conditions like fatty liver disease and alcoholic hepatitis [17,18]. AST, present in both the liver and other tissues, such as the heart and muscles, is also elevated in response to liver damage from heavy alcohol intake [13,19]. The AST/ALT ratio is particularly useful in diagnosing alcohol-related liver conditions, with a ratio greater than 2:1 often suggesting alcoholic hepatitis [20,21].

GGT, an enzyme found in the liver and bile ducts, is highly sensitive to alcohol consumption and liver dysfunction, with elevated levels frequently observed in chronic drinkers, serving as a marker for liver damage and alcohol use [22,23]. Chronic excessive alcohol intake leads to sustained liver damage, manifesting as elevated levels of ALT, AST, and GGT, which are indicative of a range of alcohol-induced liver diseases, from fatty liver to cirrhosis and liver cancer [24,25]. These enzymes not only reflect liver damage but also provide critical insights into the severity and progression of liver disease [26], underscoring the importance of regular monitoring and early intervention to mitigate alcohol-related liver damage and improve liver health outcomes.

Although individual studies have investigated the association between alcohol consumption and liver enzyme levels, their findings are often inconsistent or limited to specific populations or regions. There is currently no up-to-date, comprehensive global synthesis of these studies that accounts for variables such as drinking level, gender, and geographic differences. This systematic review and meta-analysis is necessary to consolidate these fragmented findings and provide an evidence-based understanding of global patterns in alcohol-induced liver enzyme alterations.

The primary aim of this systematic review and meta-analysis is to evaluate and quantify the impact of alcohol consumption on liver function as assessed by liver function tests (LFTs), specifically focusing on the levels of ALT, AST, and GGT. This study seeks to synthesize existing evidence to understand the extent to which alcohol consumption contributes to alterations in these liver enzymes, which are critical indicators of liver health and disease progression. Furthermore, the analysis aims to explore the variability in liver enzyme responses due to different levels of alcohol consumption, including heavy and moderate drinking, and to identify potential factors such as gender, geographical region, and alcoholic status that may influence these effects. By systematically reviewing and meta-analyzing relevant studies, the goal is

to provide a comprehensive overview of the relationship between alcohol consumption and liver function, thereby offering insights that could inform public health strategies, clinical practice, and future research on alcohol-related liver disease.

2. Materials and Methods

2.1. Literature Search Strategy

The literature search strategy for this systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [27]. It aimed to identify relevant peer-reviewed articles on the effects of alcohol consumption on liver function tests. The search spanned multiple electronic databases, including PubMed, ScienceDirect, and Cochrane, covering articles published from January 2000 to December 2023. Using the Boolean operator "AND" in search queries for "alcohol" AND ("AST" OR "ALT" OR "GGT"), the review focused on full-text articles published in English and openly accessible. Additionally, a manual search via Google Scholar complemented the electronic search to capture potentially missed studies. Screening involved evaluating titles and abstracts for relevance, followed by a thorough assessment of the full texts of qualifying articles. Bibliographies of selected studies were also reviewed to identify additional pertinent citations, ensuring comprehensive coverage of the literature. This meticulous approach facilitated a robust compilation of data on the influence of alcohol consumption on liver function tests.

2.2. Study Eligibility Criteria

The study screened and selected original research articles investigating the effects of alcohol consumption on liver function tests across diverse demographics and regions. Exclusions encompassed non-human studies, review articles, duplicates, and irrelevant publications. The primary objective was to compile comprehensive data elucidating the impact of alcohol consumption on liver function tests.

2.3. Study Selection and Data Extraction

This study employed a systematic and rigorous approach to ensure comprehensive and reliable results regarding the effects of alcohol consumption on liver function tests (LFTs). The methodology followed standard systematic review guidelines, including transparent selection, screening, and extraction procedures.

1. Literature Search and Initial Screening

a) An exhaustive search was conducted across multiple electronic databases to identify all relevant articles on alcohol consumption and liver function.
b) Duplicate studies were identified and removed to ensure that only unique records were retained for further screening.
c) This initial step enhanced the efficiency and focus of the review by minimizing redundancy in the dataset.

2. Screening Process

a) Two independent reviewers screened titles and abstracts based on predefined inclusion and exclusion criteria.

b) This dual-review process was designed to minimize selection bias and ensure that only relevant studies were included.
c) Disagreements between reviewers during screening were resolved through discussion or, when necessary, by consultation with a third reviewer.

3. Full-Text Review and Eligibility Assessment

a) Full-text articles were retrieved and carefully assessed for eligibility using the same inclusion criteria.
b) The reviewers focused on studies reporting data on liver enzyme levels (AST, ALT, and GGT) in relation to alcohol consumption.

4. Data Extraction

Data were extracted using a standardized form covering:

a) Publication details: Author(s), journal, and year of publication.
b) Study characteristics: Geographic location, design, sample size, and study setting.
c) Population demographics: Age, sex, and classification of drinking status (e.g., moderate, heavy).
d) Outcome measures: Levels of liver enzymes (ALT, AST, and GGT) reported in the context of alcohol consumption.

5. Quality Control and Dispute Resolution

a) Two independent reviewers carried out data extraction to ensure accuracy and reliability.
b) Any discrepancies in data extraction or study eligibility were resolved by a third reviewer through consensus.
c) This multi-reviewer system served as a safeguard against individual bias and enhanced the methodological quality of the review.

2.4. Assessment of Study Quality and Risk of Bias

The study employed the Joanna Briggs Institute's critical appraisal checklist to rigorously assess the quality and risk of bias in the included studies [28]. This standardized tool facilitated a systematic evaluation of each study, ensuring a comprehensive appraisal of methodological strengths and weaknesses. Two independent reviewers conducted the critical appraisal process, which was pivotal in reducing bias and enhancing the overall reliability of the study. By involving two reviewers, the study benefited from multiple perspectives and insights, thereby minimizing the risk of subjective influence in the assessment. In cases where discrepancies arose between the reviewers during the appraisal, consensus discussions were employed to resolve differences and reach a unified decision. This collaborative approach not only ensured thoroughness but also reinforced the study's validity by addressing potential inconsistencies through dialogue and mutual agreement. Overall, the study's adherence to a standardized and systematic appraisal framework contributed significantly to the credibility of its conclusions, enhancing the trustworthiness of the included literature and bolstering the reliability of its analysis.

2.5. Data Analysis

The study employed a rigorous and structured statistical approach to analyze data on the effects of alcohol consumption on liver function tests (LFTs). Data were initially organized using Microsoft Excel to ensure systematic entry and management.

Meta-analysis was conducted using Meta-Mar v3.5.1 (University of Marburg, Marburg, Germany) (https://meta-mar.shinyapps.io/meta-analysis-calculator/), a tool designed specifically for meta-analytic computations. The software supports a range of statistical tests suited for combining results across multiple studies.

Descriptive statistics were performed, including the calculation of risk estimates using dichotomous models and average effect sizes via log risk ratios. A random-effects model was adopted to account for between-study variability, yielding conservative and generalizable estimates of the overall effect size.

To examine geographic differences, subgroup analyses were conducted based on the regions where the studies were performed. This helped uncover potential regional variations in the impact of alcohol consumption on liver enzyme levels.

Heterogeneity among studies was assessed using:

1. Forest plot visual inspection;
2. Cochran's Q test;
3. Higgins' I^2 statistic, with values above 50% considered indicative of substantial heterogeneity.

Where high heterogeneity was detected, further analysis was conducted to identify possible sources of variation.

Overall, this robust and comprehensive statistical strategy allowed for meaningful synthesis of the data, providing critical insights into how alcohol consumption affects liver health across diverse populations.

2.6. Publication Bias

The study employed proactive measures to ensure the robustness and reliability of its findings on the effects of alcohol consumption on liver function tests, addressing both publication bias and heterogeneity. Publication bias, the tendency for studies with significant results to be published more readily, was rigorously evaluated using several methods. The study employed a fail-safe N calculation using the Rosenthal Approach to estimate the number of unpublished studies needed to nullify observed effects, providing insights into potential publication bias impacts. Additionally, funnel plots were utilized to visually assess the symmetry of the effect size distribution, with asymmetry potentially indicating publication bias. Egger's test was applied to quantitatively evaluate funnel plot asymmetry. To assess heterogeneity between studies, Higgins' I^2 statistic was employed, quantifying the proportion of total variation across studies due to heterogeneity rather than chance. Sensitivity analyses were conducted to examine the influence of large studies on meta-analyses, exploring potential sources of variation and bias. These comprehensive approaches provided a thorough evaluation of biases and variations in the data, strengthening the validity and credibility of the study's conclusions regarding alcohol consumption's effects on liver function tests.

3. Results

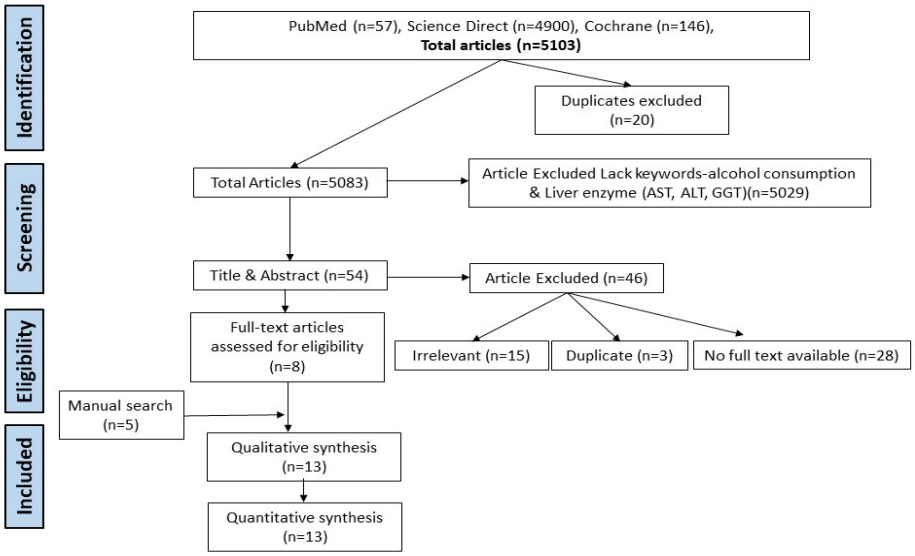
3.1. Study Characteristics

A comprehensive search across three electronic databases, PubMed, Science Direct, and Cochrane, initially identified 5,103 articles related to the effects of alcohol consumption on liver function tests. After the removal of duplicates and the screening of titles and abstracts, 8 full-text articles met the criteria for inclusion. Additionally, a manual search on Google Scholar added 5 more articles, bringing the total to 13 studies included in the quantitative synthesis [29–41]. These studies, published between 2000 and 2023, involved a collective total of 521,132 participants. This review underscores the variability in how alcohol consumption affects liver function tests, reflecting a broad range of findings across different populations and study designs (Table 1, Figure 1a). The synthesis highlights the complexity and variability in liver enzyme responses to alcohol consumption, pointing to the need for a nuanced understanding and interpretation of liver function test results in the context of alcohol use.

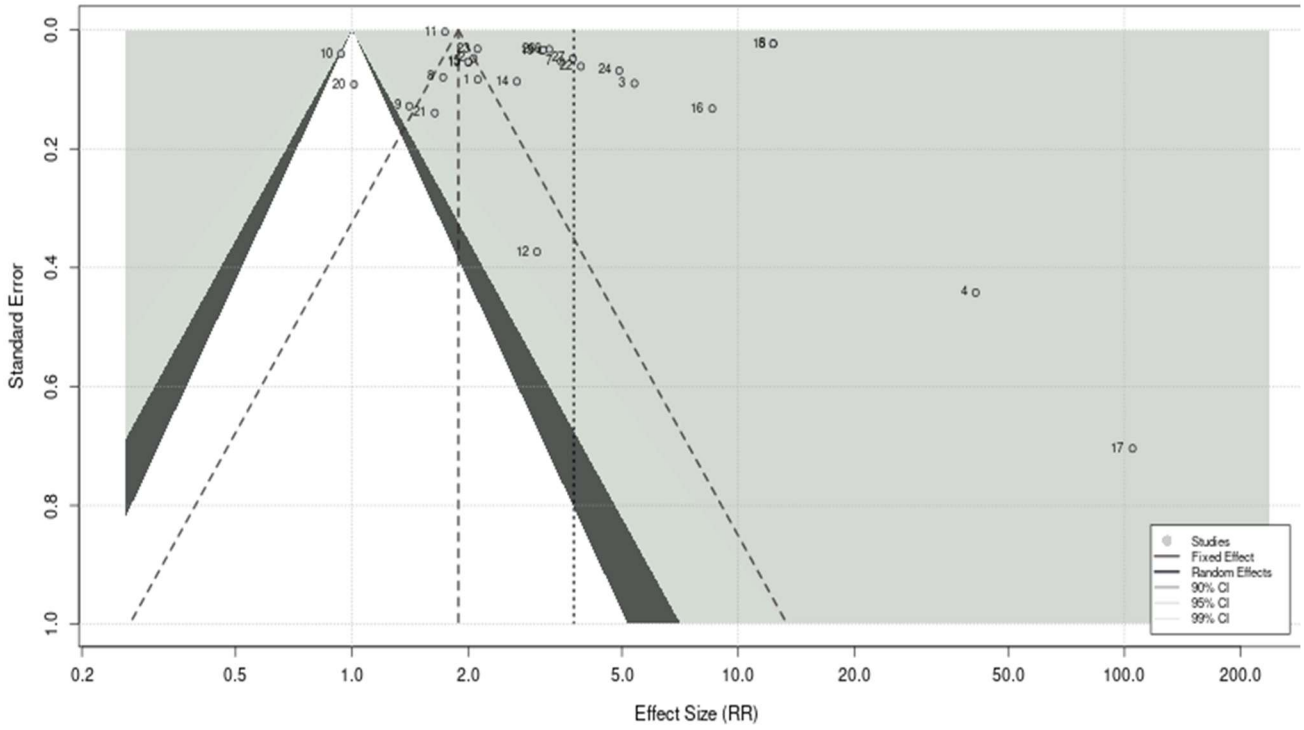
Table 1. Demographic characteristics of the eligible studies included in the quantitative meta-analysis.

Study	Country	Number of Participants	Methodology	Statistical Analysis	Conclusion
Park et al., 2013	South Korea	5946	Blood serum liver enzyme test	Multiple regression analysis	-
Liangpunsakul et al., 2010	India	8,708	Blood serum liver enzyme analyzer (Hitachi 737 Analyzer)	Analysis of variance and chi-square, Univariate and multivariate logistic regression analyses	A large U.S. study found limited evidence supporting the effectiveness of blood tests used as heavy drinking markers in detecting such issues.
Rossof et al., 2019	South Korea	1519	Blood serum liver enzyme analysis	Multivariable logistic regression analysis of variance, Kruskal-Wallis, and $\chi 2$ or Fisher's exact tests	Additional days of level II or III drinking increase clinically high levels of ALT, AST, and GGT, but individual biomarkers' performance for distinguishing hazardous drinking patterns is poor.
McDonald et al., 2013	Russia	1023	Blood serum ALT and AST by Humalyzer 2000 analyzer, GGT by the kinetic colorimetric method	Multivariable logistic regression, Multivariable logistic regression	Additional days of level II or III drinking increase clinically high levels of ALT, AST, and GGT, but individual biomarkers' performance for distinguishing hazardous drinking patterns is poor.
Argawal et al., 2016	America	13,104	Blood serum ALP, ALT, AST, and GGT were measured by spectrophotometricall y, kinetic enzymatic methods	Dunnett's significant difference post-hoc test	Alcohol had a graded linear effect on several liver enzymes. At low and moderate doses, the benefits as well as risks of alcohol intake may be related to liver function.
Alatalo et al., 2008	Finland	2164	Serum ALT, AST, and GGT test	Spearman's rank correlation, z-test for correlation coefficient, chi-square, 2 and 3 factor analyses by (SPSS v. 14.0.8 statistical software (SPSS Inc., Chicago, IL, USA)	Research is needed to understand the correlation between ethanol intake, BMI, and liver enzyme responses in nonalcoholic populations and early stages of fatty change.
Niemela et al., 2023	Finland	8743	Serum liver enzymes (ALT and GGT) were	Chi-square test, spearman's rank correlation	The study found that older men over 40 years of age showed higher

			measured using (Abbott Architect clinical chemistry analyzer)		levels of increased liver enzyme GGT, while younger men often exceeded the upper limit of ALT activity.
Freiman et al., 2021	Uganda	1301	Venous blood samples AST, ALT test	Multiple logistic regression models, calculated odds ratios (OR)	Consuming alcohol within the past three months increased the likelihood of transaminase elevations, with male sex also showing a significant association.
Degertekin et al., 2020	Turkey	259	Liver ultrasound, transient elastography, routine serum liver enzyme test	Cox regression hazards model (SPSS v. 14.0.8 statistical software (SPSS Inc., Chicago, IL, USA)	Coffee positively impacts liver histology and enzyme levels in healthy individuals, chronic alcohol users, NAFLD, and NASH patients, especially those who consume coffee regularly for over five years.
Balali et al., 2022	Iran	31,050	Laboratory blood sample ALT analysis	Multivariate logistic regression analyses	-
Sinn et al., 2022	Korea	367612	Screening by blood sample	Cox's proportional hazard regression model performed using STATA version 14 (StataCorp LP, College Station, TX, USA).	Individuals with elevated ALT levels were found to have increased liver-related and all-cause mortality rates due to a small amount of alcohol intake.
Tervo et al., 2022	Finland	66	Blood serum liver function testing	Mann-Whitney U-test, Chi-square, spearman's rank correlation (IBM SPSS v27.0)	At the control visit, 41.1% of patients displayed biomarker-based signs of recent alcohol consumption.
Zhang et al., 2015	China	3769	AST and ALT levels were measured from Blood serum samples using a special kit	Statistical analysis was performed with SPSS 17.0	The study suggests that the new upper cut-off values for serum ALT and AST are significantly lower than current standards, potentially aiding in the assessment of liver function.



(a)



(b)

Figure 1. (a) PRISMA flow diagram for systematic and meta-analysis; **(b)** Funnel plot showing asymmetrical distribution and assessing publication bias based on risk ratio analysis on the influence of alcohol consumption on liver function tests among 27datasets from 13 studies. **1**. Park et al., 2013; **2**. Liangpunsakul et al., 2010; **3**. Rossof et al., 2019; **4**. Helen et al., 2013; **5**. Argawal et al., 2016; **6**. Pailivikki et al., 2008; **7**. Niemela et al., 2023; **8**. Freiman et al., 2021; **9**. Degertekin et al., 2020; **10**. Pargol et al., 2022; **11**. Sinn et al., 2022; **12**. Tervo et al., 2022; **13**. Zhang et al., 2015; **14**. Park et al., 2013; **15**. Liangpunsakul et al., 2010; **16**. Rossof et al., 2019; **17**. Helen et al., 2013; **18**. Argawal et al., 2016; **19**. Pailivikki et al., 2008; **20**. Freiman et al., 2021; **21**. Zhang et al., 2015; **22**. Park et al., 2013; **23**. Liangpunsakul et al., 2010; **24**. Rossof et al., 2019; **25**. Helen et al., 2013; **26**. Pailivikki et al., 2008; **27**. Niemela et al., 2023.

3.2. Influence of Alcohol Consumption on Liver Function Tests

The meta-analysis, incorporating data from 27 datasets across 13 studies, demonstrated a significant overall risk of alcohol consumption impacting liver function tests (LFTs). The pooled relative risk (RR) was 1.33 (95% CI: 0.97–1.82), as determined using a random-effects model (z/t = 1.86, p = 0.007). The analysis encompassed a total of 521,132 observations and 144,455 events, indicating a substantial dataset. Most studies within the meta-analysis reported an elevated risk ratio, suggesting that alcohol consumption adversely affects LFT outcomes. However, a few studies indicated a lower risk. For instance, McDonald et al., 2013 [32] reported an RR of 0.32 (95% CI: 0.18–0.55), Freiman et al., 2021 [36] found RRs of 0.40 (0.30–0.52) and Liangpunsakul et al., 2021 [30] reported 0.85 (0.71–1.01) for the ALT; Freiman et al., 2021 [36] reported 0.15 (95% CI: 0.11–0.20), McDonald et al., 2013 [32] reported 0.82 (0.25–2.74), Liangpunsakul et al., 2021 [30] reported 0.84 (0.70–1.01) and Alatalo et al., 2016 [34] reported 0.94 (0.91–0.98) for AST and Liangpunsakul et al., 2021 [30] reported 0.91 (0.82–1.00) and Alatalo et al., 2016 [34]

reported 0.96 (0.93–0.99) for GGT (Figure 2). Despite these outliers, the majority of the datasets pointed towards a greater risk of alcohol consumption negatively influencing ALT, AST and GGT outcomes. The heterogeneity analysis revealed significant variability across the pooled study datasets. This was evidenced by Cochran's Q statistic ($Tau^2 = 0.605$, $Chi^2 = 4550.29$, df = 26, p = 0). Furthermore, Higgins' I^2 statistic was extremely high at 99.4% (95% CI: 99.4%–99.5%), with an H value of 13.23 (95% CI: 12.49–14.01), confirming substantial heterogeneity (Q = 4550.29, df = 26, p = 0) (Figure 3). This high degree of heterogeneity underscores considerable variability across the datasets, likely due to differences in LFT measurements, populations, and geographical locations. The observed variability necessitates a cautious interpretation of the results, as it reflects the diverse contexts and methodological approaches of the included studies. Thus, the meta-analysis highlights a significant association between alcohol consumption and adverse effects on liver function, although the high heterogeneity suggests that this relationship varies across different contexts. The findings underscore the importance of considering individual study characteristics and population differences when assessing the impact of alcohol on liver health.

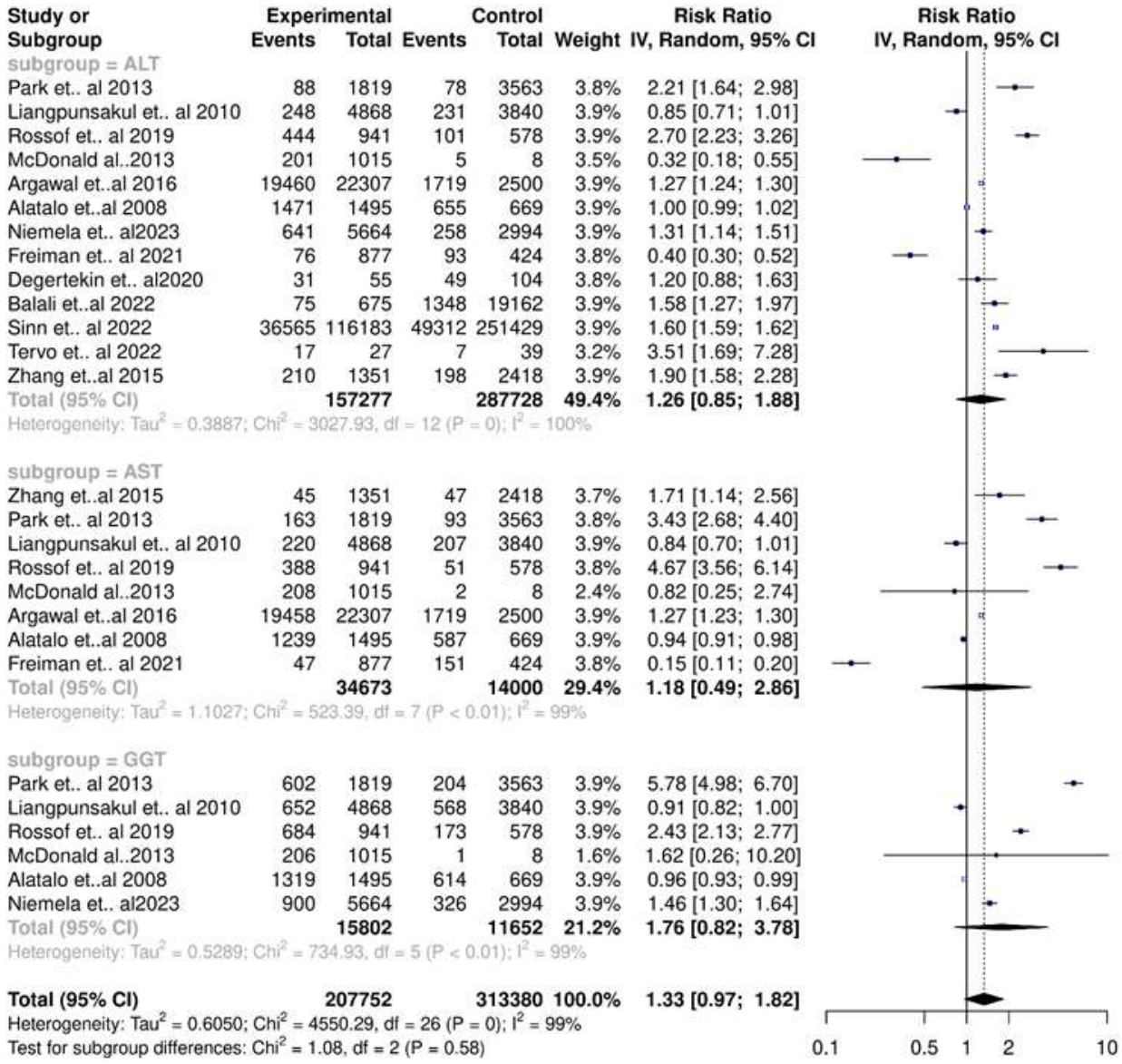


Figure 2. Forest plot showing the risk ratio of effects of alcohol consumption on liver enzymes in LFTs.

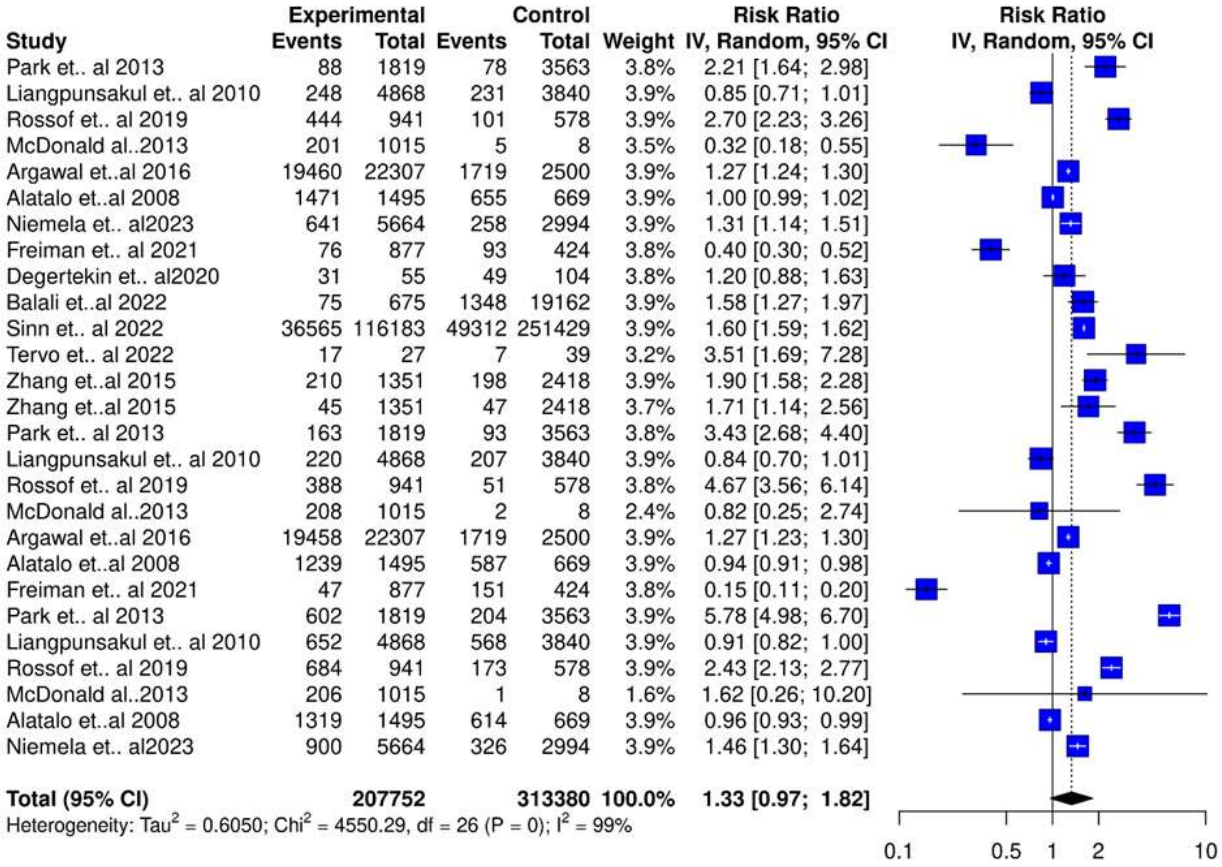


Figure 3. Forest plot showing the risk ratio of influence of alcohol consumption on liver function tests among 27 datasets from 13 studies

3.3. Effect of Alcohol Consumption on Liver Function Tests: ALT, AST, and GGT

Alcohol consumption significantly affects liver function, as evidenced by changes in liver enzyme levels. Key liver enzymes such as Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Gamma-Glutamyl Transferase (GGT) are typically monitored in Liver Function Tests (LFTs) to assess liver health. Elevated levels of these enzymes often indicate liver damage or disease. The analysis examined the relative risk (RR) of alcohol consumption on these enzymes across multiple datasets. The findings revealed that alcohol consumption increases the relative risk of elevated enzyme levels: ALT had an RR of 1.2625 (95% CI: 0.8459–1.8842) across 13 datasets, AST had an RR of 1.1783 (95% CI: 0.4851–2.8621) across 8 datasets, and GGT had an RR of 1.7645 (95% CI: 0.8241–3.7782) across 6 datasets. Although the confidence intervals are broad, suggesting variability and a potential lack of statistical significance for some enzymes, the overall trend indicates that alcohol consumption is associated with higher enzyme levels and possible liver damage. The study also shows a high heterogeneity among the datasets, with Tau² values indicating substantial variability: 0.3887 for ALT, 1.1027 for AST, and 0.5289 for GGT. This variability might be due to differences in study populations, alcohol consumption patterns, and measurement methods. However, a subgroup analysis showed no significant heterogeneity between the groups (Q = 1.08, df = 2, p = 0.5823), suggesting that the

effect of alcohol on these enzymes is relatively consistent. In terms of weighted contributions to the pooled analysis, ALT contributed 49.4% with an I^2 of 100%, AST contributed 29.4% with an I^2 of 99%, and GGT contributed 21.2% with an I^2 of 99%, indicating high heterogeneity and variability in the data (Figure 2). These findings highlight the impact of alcohol consumption on liver health, emphasizing the need for monitoring and managing liver enzyme levels in individuals who consume alcohol. The consistent trend of elevated enzyme levels underscores the harmful effects of alcohol on liver function, despite the variability across different studies. This analysis suggests that alcohol consumption poses a significant risk for liver damage, reinforcing the importance of public health interventions to mitigate the adverse effects of alcohol on liver health.

3.4. Meta-Regression Analysis Summary for the Effects of Alcohol Consumption on Liver Enzymes in LFTs

A meta-regression analysis using a mixed effects model with restricted maximum likelihood (REML) was conducted on 27 datasets ($k = 27$) to investigate the residual heterogeneity in the effects of alcohol consumption on liver enzymes measured in liver function tests (LFTs). The results demonstrated significant residual heterogeneity, with Tau^2 (SE) estimated at 0.6343 (0.1934) and Tau at 0.7964, indicating substantial variability between the studies. This high level of unexplained heterogeneity is underscored by the ratio of residual heterogeneity to unaccounted variability (I^2) being 99.91%, suggesting that nearly all variability remains unexplained by the model. The unaccounted variability to sampling variability ratio (H^2) was 1058.78, reflecting significant between-study variability that the model could not account for. Furthermore, the percentage of accounted heterogeneity (R^2) was 0.00%, indicating that the model failed to explain any of the heterogeneity observed. The heterogeneity test (QE) yielded a highly significant result ($df = 24$, $QE = 4286.2472$, $p < 0.0001$), reinforcing the notion of a consistently high risk of alcohol's effects on various liver enzymes (Figures 2 and 3). This suggests that factors other than those included in the model are likely driving the variability. When examining the regression coefficient for the various liver enzymes compared to ALT, the coefficient was 0.2334 (SE = 0.2232), with a 95% confidence interval ranging from −0.2272 to 0.694. This implies a 0.23 unit increase in the log relative risk of the effects of alcohol consumption on liver enzymes, although this increase was not statistically significant ($t = 0.06$, $df = 25$, $p = 0.9558$) (Figure 2). The lack of statistical significance and the wide confidence interval suggest that the model did not capture a meaningful difference in the effects of alcohol consumption across different liver enzymes.

This high level of unexplained heterogeneity may be attributed to several factors not captured in the model, such as differences in study design (e.g., cross-sectional vs. longitudinal), participant demographics (age, sex, ethnicity), varying definitions of alcohol use (e.g., frequency, quantity, type of alcohol), and inconsistent measurement protocols for liver enzymes. Such methodological and contextual differences can significantly influence study outcomes, leading to residual heterogeneity. To improve the model’s explanatory power, future research should consider including a broader set of covariates such as alcohol intake patterns (e.g., binge vs. chronic consumption),

body mass index, comorbidities (e.g., viral hepatitis, metabolic syndrome), and lifestyle factors (e.g., diet, smoking). Moreover, subgroup analyses stratified by region, gender, age group, or study setting may uncover important moderators that help explain variations in liver enzyme responses to alcohol.

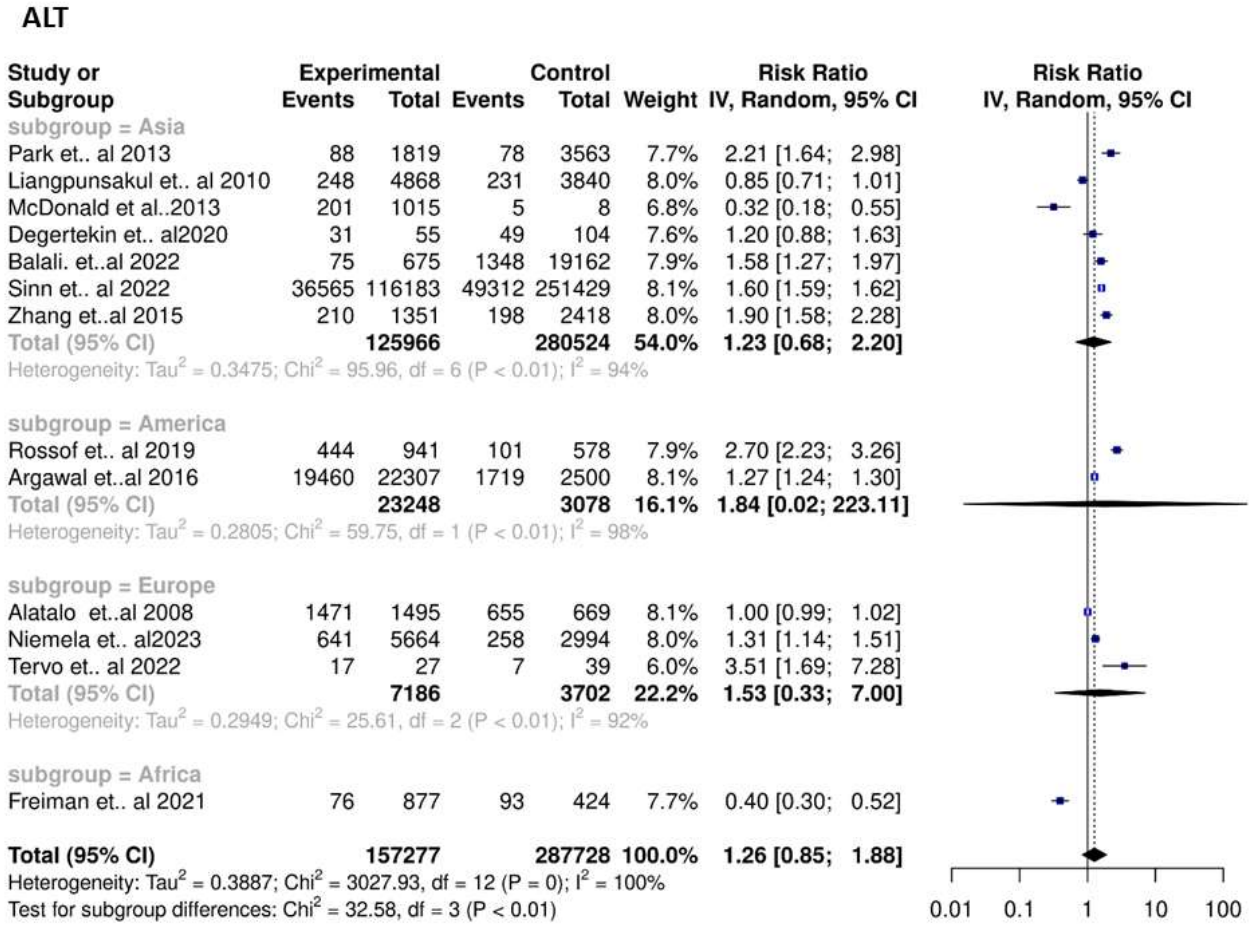
These findings highlight the importance of developing more nuanced models that integrate both clinical and socio-demographic variables. Such refinements could provide a deeper understanding of alcohol's differential impact on liver health across populations and improve the predictive accuracy of meta-analyses on liver-related outcomes.

3.5. Examination of Publication Bias and Robustness of Observations in Alcohol Consumption Effects on Liver Enzymes

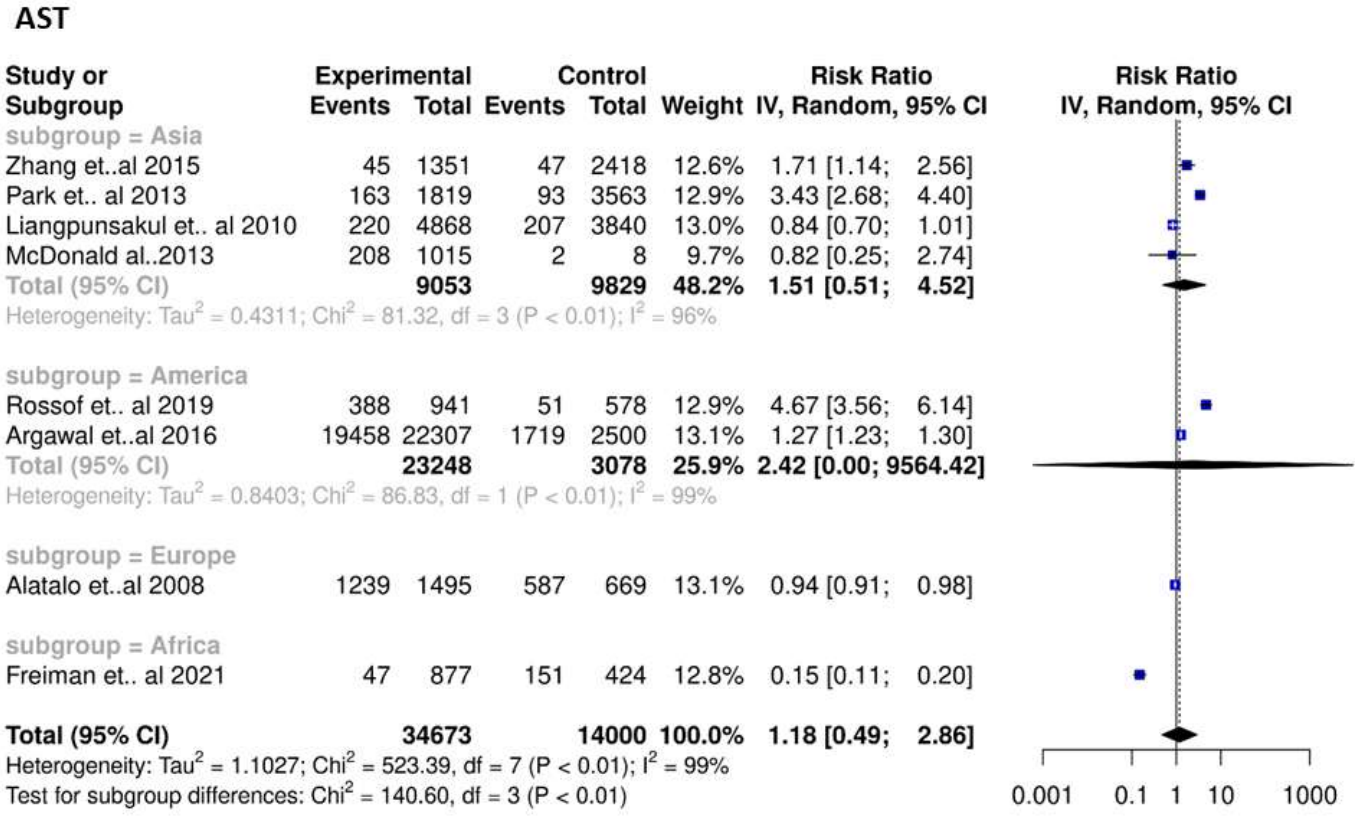
The observed outcomes regarding the effects of alcohol consumption on liver enzymes (ALT, AST, and GGT) were not significantly influenced by publication bias. This conclusion is supported by the fail-safe N calculation using the Rosenthal approach, which yielded a fail-safe N of 12,277. This implies that it would require 12,277 null result studies to bring the combined effect size to non-significance ($p < 0.0001$ compared to the target level of $p = 0.05$). This high fail-safe N indicates a robust effect, reinforcing the reliability of the observed significant levels despite potential unpublished studies that might show no effect. In addition, a funnel plot analyzed using the Trim and Fill method suggested some apparent publication bias, as visual inspection of the plot typically reveals an asymmetrical distribution of studies, indicating that smaller or null studies may be underrepresented. However, this apparent bias was not substantiated by statistical tests for publication bias. Egger's regression analysis, which tests for funnel plot asymmetry, revealed no significant publication bias ($t = 0.06$, $df = 25$, $p = 0.9558$) (Figure 1b). This statistical result suggests that the asymmetry observed in the funnel plot does not significantly impact the robustness of the findings. The lack of significance in Egger's test implies that any observed asymmetry might be due to factors other than publication bias, such as heterogeneity in study design or population differences. The sample estimates did indicate some bias with a standard error of 0.1745 (3.1196), suggesting variability in the estimates. The multiplicative residual heterogeneity variance (Tau^2) was estimated at 181.9889, highlighting the presence of considerable residual heterogeneity. This significant variance underscores the complexity and diversity of the study populations and conditions, suggesting that multiple factors contribute to the observed effects beyond just the presence of publication bias. Overall, there was no indication of publication bias, the statistical analyses, including the high fail-safe N and the results from Egger's test, suggest that the observed effects of alcohol on liver enzymes are robust and not significantly compromised by publication bias. The substantial residual heterogeneity points to the need for further exploration into the diverse factors influencing these outcomes, but it does not diminish the observed significant impact of alcohol on liver enzyme levels. The study, therefore, examines the geographical and gender influences on the effects of alcohol consumption on liver enzymes.

3.6. Geographical Influence on the Effects of Alcohol Consumption on the Liver Enzymes (ALT, AST, and GGT)

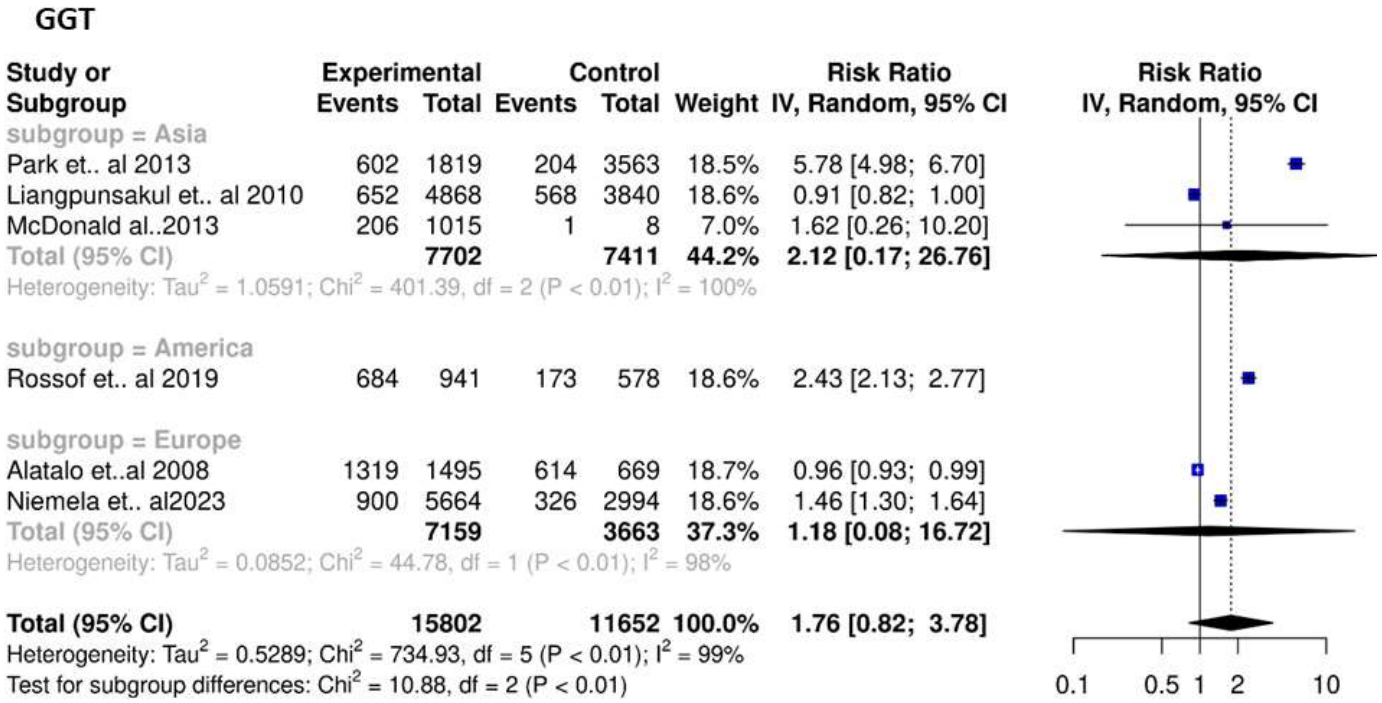
The geographical influence on the effects of alcohol consumption on liver enzymes, ALT, AST, and GGT showed substantial regional variability, contributing to the significant heterogeneity observed in the pooled datasets. The analysis indicates that geographical differences in study populations and alcohol consumption patterns play a crucial role in how alcohol affects liver enzyme levels. For ALT, studies from Asia, America, and Europe displayed considerable variability, with relative risks (RR) indicating different impacts across regions: 1.2270 in Asia, 1.8397 in America, and 1.5263 in Europe. The heterogeneity was significant, both between groups ($Q = 2846.61$, $df = 3$, $p = 0$) and within groups ($Q = 181.31$, $df = 9$, $p < 0.0001$), suggesting that regional factors such as genetic predisposition and lifestyle differences influence ALT levels (Figure 4a). In terms of AST, the common effect model also showed high variability between geographical groups ($Q = 218.9$, $df = 2$, $p < 0.0001$) and within groups ($Q = 304.49$, $df = 5$, $p < 0.0001$). Asian studies had an RR of 1.5124, American studies showed a much higher RR of 2.4169, and European studies had a lower RR of 0.3795, reflecting differences in baseline liver health and alcohol consumption patterns across regions. The heterogeneity was most pronounced in European studies, potentially due to a broader range of alcohol-related behaviours and genetic factors affecting liver enzyme levels (Figure 4b). For GGT, the analysis highlighted significant heterogeneity between geographical areas ($Q = 288.76$, $df = 2$, $p < 0.0001$) and within regions ($Q = 446.17$, $df = 3$, $p < 0.0001$). The RR for GGT was highest in American studies (2.4286), followed by Asian (2.1229) and European studies (1.1795), indicating regional differences in the impact of alcohol on this enzyme (Figure 4c). These findings underscore the importance of considering geographical context when assessing the effects of alcohol on liver health, as factors such as genetic diversity, dietary habits, and healthcare practices vary widely across regions. This variability suggests that public health interventions should be tailored to address specific regional needs to effectively mitigate the adverse effects of alcohol on liver function. It is important to note that significant heterogeneity does not necessarily confirm meaningful or causal regional differences. High heterogeneity may also result from differences in study design, sample size, alcohol classification methods, or laboratory procedures for measuring liver enzymes. For example, some studies may have included participants with pre-existing liver conditions, varying levels of alcohol dependence, or unmeasured lifestyle factors such as smoking and diet, which could influence liver enzyme outcomes independently of geographic location. Acknowledging these limitations provides a more nuanced interpretation of the results and cautions against over-attributing observed differences solely to regional effects. Future analyses could control for these confounders or conduct stratified analyses based on standardized alcohol use metrics and health backgrounds.


ALT
Study or Subgroup | Experimental Events Total | Control Events Total | Weight | Risk Ratio IV, Random, 95% CI
subgroup = Asia
Park et.. al 2013 88 1819 78 3563 7.7% 2.21 [1.64; 2.98]
Liangpunsakul et.. al 2010 248 4868 231 3840 8.0% 0.85 [0.71; 1.01]
McDonald et al..2013 201 1015 5 8 6.8% 0.32 [0.18; 0.55]
Degertekin et.. al2020 31 55 49 104 7.6% 1.20 [0.88; 1.63]
Balali. et..al 2022 75 675 1348 19162 7.9% 1.58 [1.27; 1.97]
Sinn et.. al 2022 36565 116183 49312 251429 8.1% 1.60 [1.59; 1.62]
Zhang et..al 2015 210 1351 198 2418 8.0% 1.90 [1.58; 2.28]
Total (95% CI) 125966 280524 54.0% 1.23 [0.68; 2.20]
Heterogeneity: Tau² = 0.3475; Chi² = 95.96, df = 6 (P < 0.01); I² = 94%
subgroup = America
Rossof et.. al 2019 444 941 101 578 7.9% 2.70 [2.23; 3.26]
Argawal et..al 2016 19460 22307 1719 2500 8.1% 1.27 [1.24; 1.30]
Total (95% CI) 23248 3078 16.1% 1.84 [0.02; 223.11]
Heterogeneity: Tau² = 0.2805; Chi² = 59.75, df = 1 (P < 0.01); I² = 98%
subgroup = Europe
Alatalo et..al 2008 1471 1495 655 669 8.1% 1.00 [0.99; 1.02]
Niemela et.. al2023 641 5664 258 2994 8.0% 1.31 [1.14; 1.51]
Tervo et.. al 2022 17 27 7 39 6.0% 3.51 [1.69; 7.28]
Total (95% CI) 7186 3702 22.2% 1.53 [0.33; 7.00]
Heterogeneity: Tau² = 0.2949; Chi² = 25.61, df = 2 (P < 0.01); I² = 92%
subgroup = Africa
Freiman et.. al 2021 76 877 93 424 7.7% 0.40 [0.30; 0.52]
Total (95% CI) 157277 287728 100.0% 1.26 [0.85; 1.88]
Heterogeneity: Tau² = 0.3887; Chi² = 3027.93, df = 12 (P = 0); I² = 100%
Test for subgroup differences: Chi² = 32.58, df = 3 (P < 0.01)
Risk Ratio IV, Random, 95% CI
0.01 0.1 1 10 100

(a)


AST
Study or Subgroup | Experimental Events Total | Control Events Total | Weight | Risk Ratio IV, Random, 95% CI
subgroup = Asia
Zhang et..al 2015 45 1351 47 2418 12.6% 1.71 [1.14; 2.56]
Park et.. al 2013 163 1819 93 3563 12.9% 3.43 [2.68; 4.40]
Liangpunsakul et.. al 2010 220 4868 207 3840 13.0% 0.84 [0.70; 1.01]
McDonald al..2013 208 1015 2 8 9.7% 0.82 [0.25; 2.74]
Total (95% CI) 9053 9829 48.2% 1.51 [0.51; 4.52]
Heterogeneity: Tau² = 0.4311; Chi² = 81.32, df = 3 (P < 0.01); I² = 96%
subgroup = America
Rossof et.. al 2019 388 941 51 578 12.9% 4.67 [3.56; 6.14]
Argawal et..al 2016 19458 22307 1719 2500 13.1% 1.27 [1.23; 1.30]
Total (95% CI) 23248 3078 25.9% 2.42 [0.00; 9564.42]
Heterogeneity: Tau² = 0.8403; Chi² = 86.83, df = 1 (P < 0.01); I² = 99%
subgroup = Europe
Alatalo et..al 2008 1239 1495 587 669 13.1% 0.94 [0.91; 0.98]
subgroup = Africa
Freiman et.. al 2021 47 877 151 424 12.8% 0.15 [0.11; 0.20]
Total (95% CI) 34673 14000 100.0% 1.18 [0.49; 2.86]
Heterogeneity: Tau² = 1.1027; Chi² = 523.39, df = 7 (P < 0.01); I² = 99%
Test for subgroup differences: Chi² = 140.60, df = 3 (P < 0.01)
Risk Ratio IV, Random, 95% CI
0.001 0.1 1 10 1000

(b)



(c)

Figure 4. Forest plot showing the random effect model of geographical influence on the effects of alcohol consumption on the liver enzymes. **(a)** Effects of geographical influence on Alanine Aminotransferase (ALT); **(b)** Effects of geographical influence on Aspartate Aminotransferase (AST); **(c)**Effects of geographical influence on Gamma-Glutamyl Transferase (GGT).

4. Discussion

Studies have suggested that small amounts of alcohol, particularly red wine, may have health benefits, including cancer prevention and improved cardiovascular health [42,43]. These potential benefits are often attributed to the presence of antioxidants such as resveratrol in red wine, which are thought to have protective effects against heart disease by improving cholesterol levels and reducing inflammation [42–44]. Observational studies have noted an association between moderate alcohol consumption and a reduced risk of coronary heart disease and certain types of cancer [45,46]. However, it is important to note that these findings are primarily based on epidemiological studies, which can show associations but cannot establish causality. In fact, while observational studies suggest associations, they are vulnerable to confounding variables and selection bias, thereby limiting their ability to demonstrate a direct causal relationship between alcohol intake and health outcomes.

Despite these promising observational data, clinical trials in humans have not provided strong corroborative evidence for these benefits [47–49]. The complexities of conducting long-term, controlled trials on alcohol consumption and its health effects make it difficult to draw definitive conclusions [50,51]. This highlights a critical gap in the literature: the absence of randomized clinical trial evidence confirming the protective effects of moderate alcohol consumption, which weakens

the strength of public health recommendations based on observational findings. Moreover, alcohol consumption carries potential risks, including an increased risk of certain cancers (such as breast and liver cancer), liver disease, and other health issues, particularly with higher levels of intake [52,53]. Therefore, while some studies suggest the possible benefits of moderate alcohol consumption, including red wine, the lack of robust evidence from clinical trials means that these purported health benefits should be interpreted with caution. The potential risks associated with alcohol consumption must be carefully weighed against any possible benefits, and individuals are generally advised to follow guidelines that promote minimal or moderate alcohol intake for overall health and well-being [54]. This systematic review and meta-analysis aimed to evaluate and quantify the impact of alcohol consumption on liver function as assessed by LFTs, specifically focusing on the levels of ALT, AST, and GGT.

The pooled risk analysis demonstrated a significantly elevated risk ratio, indicating that alcohol consumption has an impact on LFTs. This suggests that alcohol consumption negatively influences LFT outcomes, with outliers highlighting an even greater risk of harm. The study revealed substantial variability across the pooled datasets, confirming significant heterogeneity. This variability is likely attributable to differences in LFT measurements, populations studied, and geographical locations, which underscores the complex interplay of factors influencing liver function [55]. Notably, the observed heterogeneity may stem from multiple sources, including genetic polymorphisms affecting alcohol metabolism (such as Alcohol Dehydrogenase (ADH) and Aldehyde Dehydrogenase (ALDH) variants), individual lifestyle choices (such as diet, exercise, and smoking), socioeconomic status, and varying health care access. These factors can modify the degree of liver enzyme elevation and complicate cross-study comparisons. Despite these differences, the analysis established a significant association between alcohol consumption and adverse effects on liver function, as evidenced by elevated levels of key liver enzymes such as ALT, AST, and GGT [13,56]. The findings emphasize the need for careful consideration of the impact of alcohol on liver health across diverse populations and settings.

Studies have shown that alcohol is responsible for a substantial burden of disease globally, particularly in terms of liver cirrhosis and liver cancer [57–59]. Alcohol-attributable liver cirrhosis caused 493,300 deaths and 14,544,000 disability-adjusted life years (DALYs), with a significant impact on both men and women. Alcohol-attributable liver cancer led to 80,600 deaths and 2,142,000 DALYs [60]. The ALT, AST, and GGT are key diagnostic markers for liver cirrhosis and liver cancer [61,62]. Elevated ALT indicates liver damage, while AST indicates liver damage [63]. GGT, a sensitive marker for liver dysfunction, is associated with alcohol-related diseases [13,21]. These enzymes aid in early detection, monitoring, and management [64,65]. ALT is a vital enzyme in LFTs for assessing liver health and diagnosing liver diseases [66]. ALT is primarily found in hepatocytes, where it plays a role in amino acid metabolism [63,67]. When liver cells are damaged, ALT leaks into the bloodstream, making it a sensitive marker for liver injury [68]. Monitoring ALT levels helps clinicians assess liver damage severity, track disease progression, and evaluate treatment effectiveness [69].

AST is a vital biomarker in LFTs for liver health assessment [68]. Elevated AST levels indicate liver cell damage, aiding in the diagnosis of conditions like hepatitis, cirrhosis, and drug-induced liver injury [70]. AST/ALT ratio helps differentiate between liver diseases, with higher ratios suggesting alcoholic liver disease [71]. AST levels are monitored over time to assess treatment response [71]. GGT is a crucial LFT marker due to its sensitivity and specificity in detecting liver dysfunction [64,66]. Elevated GGT levels indicate liver damage, fatty liver disease, alcoholic liver disease, and liver cirrhosis [21]. GGT is also useful in clinical practice for distinguishing liver-related causes of elevated alkaline phosphatase levels [72]. Regular monitoring helps assess treatment efficacy and disease progression [73].

This study highlights a significant risk association between alcohol consumption and elevated levels of the liver enzymes ALT, AST, and GGT, accompanied by considerable heterogeneity among the findings. The analysis underscores that alcohol intake is linked to increased levels of these enzymes, which are indicative of liver damage and dysfunction. The observed heterogeneity across the studies suggests variations in populations studied, alcohol consumption patterns, and possibly different methodologies for assessing liver enzyme levels. To improve the interpretation of these findings, future research should attempt to disaggregate data by known modifiers of enzyme levels, such as body mass index, comorbid conditions (e.g., diabetes, hepatitis), and socioeconomic status. Accounting for these potential confounders could enhance the comparability of studies and reduce residual heterogeneity. Despite these variations, the overall trend indicates a consistent association between alcohol consumption and adverse effects on liver health, emphasizing the importance of monitoring and mitigating the impact of alcohol on liver enzymes through targeted interventions and public health measures [74,75].

The risk association between alcohol consumption and liver enzymes ALT, AST, and GGT appears consistent across different geographical areas, as indicated by this study. Despite variations in study populations and alcohol consumption patterns across regions, the overall findings suggest that alcohol intake consistently correlates with elevated levels of ALT, AST, and GGT. This uniformity implies that the detrimental effects of alcohol on liver health, reflected in these enzyme markers, transcend geographical boundaries [76]. The lack of significant changes in risk across different regions underscores the global impact of alcohol consumption on liver function, emphasizing the need for universal strategies to mitigate these health risks [77,78]. However, for public health policies to be most effective, regional customization is essential. Interventions should consider local drinking norms, access to care, and cultural perceptions about alcohol. Community-specific education campaigns, taxes on alcohol products, and screening programs integrated into primary care can be valuable in high-burden settings. Efforts aimed at reducing alcohol consumption and promoting liver health should therefore be prioritized on a global scale to address this widespread public health concern effectively [79,80]. Emerging data from the COVID-19 pandemic reveal a 30% reduction in alcohol-related emergency service (ES) calls in Italy, particularly among adults aged 25–44, likely due to economic hardship, social restrictions, and heightened health concerns. However, minimal reductions were seen among adolescents and older adults, and surveys indicated increased alcohol use among those with pre-existing alcohol problems, reflecting

varied behavioural responses [81]. Fear of COVID-19 exposure led to fewer hospital admissions, while pharmacological treatment with metadoxine, especially among adolescents, was limited to higher-severity cases to manage emergency resources efficiently. Rising polydrug use among adults further complicated emergency response efforts [81]. Meanwhile, Managed Alcohol Programs (MAPs) helped reduce alcohol-related harms, stabilize consumption, and improve housing and healthcare access among vulnerable populations, though some participants reported increased use of other substances [82].

The previous study found that GGT and AST are not reliable indices of alcohol intake due to significant between-person variation and weak correlation [83,84]. Factors like genetics, liver health status, and lifestyle affect their consistency and accuracy in the ALT, AST, and GGT diagnoses of alcohol related liver damage [85]. Despite their usefulness for liver function, their utility for directly measuring alcohol intake remains limited [86]. A meta-analysis found varying associations between alcohol consumption and liver cancer incidence, mortality, disease-related mortality, and overall mortality [52]. Low to moderate alcohol consumption increased risks for liver cancer and mortality, while higher alcohol consumption significantly increased liver disease-related mortality and overall mortality [52]. This highlights the importance of considering alcohol intake in public health strategies.

5. Study Limitations

This study has several key limitations. Most included studies were observational, limiting the ability to establish causality due to potential confounding and bias. There was significant heterogeneity in study design, populations, alcohol consumption patterns, and liver function test methods, making comparisons difficult. Alcohol intake was often self-reported, introducing recall and misclassification bias. Many studies did not control for important confounders like hepatitis infections, obesity, and smoking. Some were cross-sectional, preventing assessment of long-term effects. Underrepresentation of certain regions limits generalizability, and a lack of data stratification by genetic and lifestyle factors may obscure important subgroup differences. Finally, the absence of randomized controlled trials weakens the strength of conclusions about the causal impact of alcohol on liver health.

In conclusion, the study found that alcohol consumption negatively impacts liver function tests (LFTs), with elevated levels of key liver enzymes such as ALT, AST, and GGT. The risk association was consistent across different geographical areas, indicating that the detrimental effects of alcohol on liver health transcend geographical boundaries.

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