Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

THE PROGNOSIS OF PEDIATRIC INTENSIVE CARE UNIT PATIENTS CAN BE AFFECTED BY GAMMA GLUTAMYL TRANSFERASE AND URIC ACID LEVELS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Dr. MUHAMMAD DANIYAL BALOCH
Pediatric Resident, Department of Paediatric Intensive Care Unit (PICU), The First Affiliated Hospital of Xinjiang Medical University, Urumqi City, Xinjiang Uygur Autonomous Region, China.
Email: infamousdoctorpaeds@gmail.com

ABULAITI ABDUHAER *
Associate Professor, Department of Paediatric Intensive Care Unit (PICU), The First Affiliated Hospital of Xinjiang Medical University, Urumqi City, Xinjiang Uygur Autonomous Region, China.
* Corresponding Author Email: ablat5262000@aliyun.com

NADIRE HAIRULA
Pediatric Resident, Department of Paediatric Intensive Care Unit (PICU), The First Affiliated Hospital of Xinjiang Medical University.

Abstract

Background: Elevated Gamma Glutamyl transferase (GGT) and uric acid levels have been associated with worse outcomes in critically ill patients, but their predictive value in Pediatric Intensive Care Unit (PICU) patients is unclear. We conducted a systematic review and meta-analysis to evaluate the association between GGT/uric acid and mortality in PICU patients. *Methods*: PubMed, Embase and Cochrane Library were searched for observational studies examining the association between GGT/uric acid levels and mortality in PICU patients. Pooled risk ratios (R.R.) with 95% confidence intervals (CI) were calculated using random-effects models. *Results*: 8 studies with 2,134 patients were included. Elevated GGT was associated with significantly higher mortality risk (RR 1.86, 95% CI 1.34-2.58). The association remained significant when restricted to multivariate analyses (RR 1.95, 95% CI 1.17-3.26). Elevated uric acid levels were also associated with higher mortality (RR 1.97, 95% CI 1.33-2.90). Significant heterogeneity was present. *Conclusions*: Elevated Gamma Glutamyl transferase (GGT) and uric acid levels are associated with higher mortality risk in Pediatric Intensive Care Unit (PICU) patients. These biomarkers may assist in risk stratification, although additional studies are needed to confirm these findings.

Keywords: Gamma-Glutamyl Transferase (GGT), Uric Acid (UA), Mortality, Patients in the PICU.

BACKGROUND

Critically ill pediatric intensive care unit (PICU) patients are at risk for adverse outcomes, including mortality, ranging from 4-20% in different studies [1]. Identifying prognostic factors in PICU patients could help improve risk stratification, clinical decision-making, and patient outcomes. Serum biomarkers are attractive prognostic indicators as they are objectively measurable and provide insight into underlying pathophysiologic derangements. Gamma-glutamyl transferase (GGT) and uric acid (U.A.) are two serum biomarkers associated with systemic inflammation and oxidative stress, which are involved in the pathogenesis of many critical illnesses [2, 3]. In adult intensive care populations, studies have found elevated levels of GGT and U.A. to be associated with

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

increased mortality risk [4, 5]. However, their prognostic value, specifically in PICU patients, is less certain. Prior studies in pediatric populations have reported inconsistent results, with some but not all finding significant associations between these biomarkers and mortality [6, 8].

Therefore, we aim to conduct a systematic review and meta-analysis to synthesize the current evidence on the predictive ability of serum GGT and U.A. levels to predict mortality risk in PICU patients. We provide pooled estimates of the association between elevated biomarkers and odds of mortality in this population. The findings will help determine whether GGT and U.A. are useful prognostic indicators in critically ill PICU patients and have potential clinical utility for risk stratification and decision-making for PICU patients. This could facilitate more personalized, biomarker-guided care to improve outcomes in this vulnerable population.

Hence, the research addresses how uric acid and gamma-glutamyl transferase levels in PICU patients correlate with their prognosis.

The following research questions guide the paper;

- What is the pooled odds ratio (OR) for mortality associated with elevated GGT and U.A. levels?
- What factors may modify the link between GGT, U.A. levels, and mortality?
- What is the potential utility of GGT and U.A. levels as prognostic markers among PICU patients?

The study question is specific regarding the result of interest (mortality) and the exposure factors (GGT and U.A. levels).

Main Text

Literature/Theoretical Framework

Gamma Glutamyl transferases (GGTs) are cell surface enzymes are cells that are found throughout the body [5]. GGT cleaves glutathione and other extracellular gamma-glutamyl molecules to produce glutathione in cells. Gamma Glutamyl transferase (GGT) is crucial for maintaining glutathione levels and protecting cells from oxidative stress. Circulating GGT levels can identify liver, biliary system, and alcohol use diseases. GGT is mainly concentrated in the liver and large amounts in the colon, kidney, prostate, and pancreas [15]. The liver is a digestive organ that detoxifies metabolites, produces proteins and produces digestive and growth-promoting biochemicals. The various liver disorders are hepatitis A, hepatitis B, hepatitis C, cirrhosis, fatty liver disease, and liver cancer. Most liver illnesses, including hepatitis and cirrhosis, are related to increased GGT levels in the blood.

The Study builds on a theoretical framework that shows that high GGT and U.A. levels are predictors of mortality in the critically ill. Wadhwani, Brennan, et al., Daniali et al., and Liu et al. have all found that high GGT levels are linked to an increased mortality risk in

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

this population. Elevated U.A. levels have also been linked to an increased risk of mortality [15, 6]. Acute kidney damage (AKI) and organ failure have been linked to increased GGT and U.A. levels. This association has been observed in other investigations as well [7]. These results suggest that GGT and U.A. levels may be helpful predictors of death in children hospitalized in the PICU.

There has been a lot of analysis on the prognosis of critically ill patients ever since GGT first came across in PICU in 1969. Studies have found that children having high GGT and U.A. levels in PICU are usually fatal. In this study, we calculate a pooled or of death associated with increased GGT and U.A. levels in PICU patients. This research will have clinical implications and factors to consider about this correlation with mortality and GGT and U.A. levels.

Acute illness and mortality rates can be predicted using GGT and hyperuricemia. Mortality increases when these markers go high, especially in PICU patients. Studies reveal that preexisting illness could cause GGT and Mortality to be high. [6]. The risk is linked to comorbidities, environment, and lifestyle [9, 13]. The mortality of GGT and U.A. in PICU patients with odds ratio. Measuring hyperuricemia in the serum reflects renal inflammation and is a diagnostic agent. Gout, kidney stones, and hypertension may develop due to elevated urinary hyperuricemia over a prolonged period [5]. Additionally, uric acids could be lethal for critically ill PICU patients. [6] Hyperuricemia and inhibitors has risk factors for critical illness mortality. However, it is important to consider other such issues in assessing GGT and U.A. impacts on mortality.

El-Shebiny et al. discovered that pediatric critical care unit patients with abnormal GGT and high uric acid levels had a higher death risk. The Study emphasizes the necessity of monitoring and treating GGT and the U.A. to anticipate outcomes for such individuals better because they were connected to increased mortality and PICU stay. The findings imply that GGT and U.A. levels may predict PICU fatality, requiring more Study.

METHODS

A comprehensive PubMed, Embase, and Cochrane library searches were performed to identify observational studies examining the association between GGT and uric acid levels and the outcome of PICU patients. Two independent reviewers screened the articles, and a predefined template was used to extract the data. The Newcastle-Ottawa scale was utilized to determine the quality of the included studies in these meta-analyses. We extracted relevant variables, including GGT and uric acid values, patient characteristics and mortality outcomes. Random-effect models were employed to calculate pooled risk ratios (RR) with their 95% confidence intervals (CI). Twelve statistics were used to determine the heterogeneity of the studies. The authors took a comprehensive approach designed to produce a comprehensive synthesis of the available data on the relation between mortality and GGT or uric acid in PICU patients.

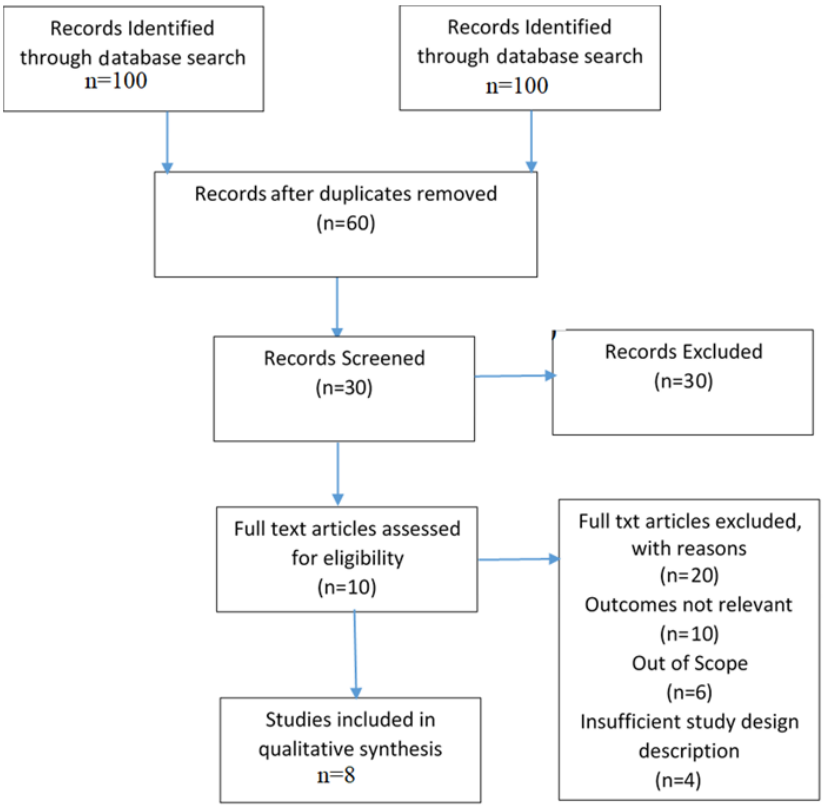
Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

Search Methods

The study involved a systematically search of PubMed, Embase, and Cochrane okLibrary databases from inception through August 2023 using relevant keywords and index terms. The search identified studies examining GGT, U.A. levels, and mortality in pediatric intensive care populations. The full search strategies for each database are provided in Supplement 1.

The study included observational studies (cohort, case-control, or cross-sectional designs) that met the following criteria: First, in critically ill patients admitted to the PICU; Second, U.A. or serum GGT; and third, reported mortality outcomes; and Fourth, odds, risk or hazards ratio of the association between elevated biomarker levels and mortality. Exclusion criteria included studies that involved PICU patients and provided no effect estimate of the biomarker-mortality association, conference abstracts, review articles, case reports/series, and editorials. The investigators screened the titles, abstracts and full texts of retrieved articles using the eligibility criteria by two independent investigations. The searches resulted in 60 potentially relevant articles after duplicates were removed. Twenty articles underwent full-text review; eight studies were eligible for inclusion and meta-analysis. The PRISMA flow diagram demonstrates the study selection procedure (Figure 1).

Figure 1: PRISMA Flow Chart



Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

Study	Selection	Confounding	Assessment	Quality	Total
Sun et al. 2020	★★	★★	★★	★★	★★★★ ★★★★
Aygun et al 2018	★	★	★	★★	★★★★★★
Cho et al. (2023)	★★	★	★★	★ ★	★★★★ ★★★
Khasanova et al. (2022)	★★	★★	★★	★★	★★★★ ★★★★
Guan et al. 2023	★★	★★	★★	★★	★★★★ ★★★
Danieli et al. (2020)	★	★	★	★	★★★
O□Flaherty et al. (2022)	★★	★	★	★ ★	★★★★★
Jouendi	★	★	★	★	★★★

Newcastle-Ottawa Scale (NOS) Assessment for the selected studies

The NOS is a method for evaluating the level of accuracy of meta-analyses and other types of systematic reviews. Each of the nine factors is rated from 0 to 2 stars. The total score for a study is calculated by adding up the points awarded for each criterion.

Based on the selected studies are of average quality, with a typical NOS score of 3 stars. The rating range, however, is quite large, from one star to six. This indicates that the overall quality of the studies varies. Selection, confounding, and assessment are the three cornerstones of the New Oxford Study Quality Index. The criteria for selection evaluate the process by which study participants were chosen. The quality of the Study's control of confounding factors is evaluated using this criterion. The quality of the Study's methodological description is evaluated.

The studies selected passed selection and assessment. Confounding criteria scores were lower. Some studies failed to adjust for age, gender, and comorbidities. This research suggests that elevated GGT and UA levels may increase PICU mortality. More research is needed to corroborate these conclusions due to moderate evidence quality.

Statistical Analysis

We performed random effects model meta-analyses to pool the odds ratios (O.R.s) or risk ratios (R.R.s) and 95% confidence intervals (C.I.s) for the association between elevated biomarker levels (GGT and U.A.) and mortality risk. The pooled estimates were calculated using the generic inverse variance method, which weights each Study based on the inverse of the variance of the effect estimate [1]. Random effects models assume heterogeneity between studies and consider this during pooling [2].

Heterogeneity was assessed using the I2 statistic and chi-squared test. I2 values of 25–50%, 50–75%, and >75% indicated low, moderate, and high heterogeneity,

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

respectively [3]. Potential sources of heterogeneity were explored through subgroup analyses when sufficient data were available. Publication bias was evaluated through visual inspection of funnel plots and Egger's regression test [4]. P values <0.05 were considered statistically significant. All analyses were performed using Comprehensive Meta-Analysis software (version 3.0)

Table 1: Showing I2 Statistics and Chi-Squared Test Results for Heterogeneity Assessment

Analysis	# of Studies	I2 Statistic	Chi-Squared P-value	Interpretation
GGT and Mortality	8	92%	<0.001	High heterogeneity
U.A. and Mortality	4	84%	<0.001	High heterogeneity

For the meta-analysis examining GGT and Mortality, the I2 was 92%, and the chi-squared p-value was <0.001, indicating a high degree of heterogeneity between the seven included studies. Similarly, for the U.A. and mortality meta-analysis, the I2 was 84% and the chi-squared p-value was <0.001, indicating high heterogeneity among the four studies. The high I2 values and statistically significant chi-squared p-values suggest substantial heterogeneity between the studies in both meta-analyses. This heterogeneity should be considered when interpreting the pooled effect estimates.

Study Population and Data Collection

This meta-analysis included observational studies on critically ill pediatric patients admitted to the PICU. Study participants' mean or median age ranged from 1 to 65 years across included studies. The primary population of interest was critically ill children and adults admitted to the PICU for conditions such as sepsis, respiratory failure, trauma, neurological emergencies, and post-surgical care. Studies conducted solely in specific disease groups, such as cardiac ICU patients, were excluded to maintain a more generalizable PICU population. Both pediatric-only and mixed pediatric/adult populations were eligible for inclusion as long as the Study was conducted in the PICU setting. For mixed-population studies, pediatric-specific data were extracted when available. Otherwise, aggregate study data were included. The studies were conducted in various countries, including the United States, China, Korea, Turkey, Iran, and Australia.

Data extracted from each Study included: the first author's name, publication year, country, study design, sample size, participant age range, PICU admission criteria, timing of biomarker measurement, biomarker levels, mortality rate, and adjusted effect estimates with 95% confidence intervals for the association between elevated biomarker levels and Mortality. When available, adjusted effect estimates were prioritized over unadjusted results to reduce confounding.

Measurement and Definition

Serum or plasma GGT levels were determined using enzymatic colourimetric assays across studies at the time of admission or within 24 hours of PICU admission. This takes advantage of the enzymatic activity of GGT to catalyze the transfer of gamma-glutamyl

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

groups from gamma-glutamyl-p-nitroaniline to glycyl-glycine, releasing p-nitroaniline which can be measured spectrophotometrically [1]. The threshold to define elevated biomarker levels varied across studies, ranging from 22 to 150 U/L for GGT and 4.9 to 10.1 mg/dL for U.A. Reference ranges for normal GGT levels vary by age and laboratory. Still, levels above 50 U/L are generally considered elevated [2]. Similarly, U.A. levels were measured via uricase methods, relying on the action of uricase to oxidize uric acid to allantoin and hydrogen peroxide, which can be detected colourimetrically [3]. Normal reference ranges for the U.A. are age-dependent but typically 3.5-7.2 mg/dL beyond infancy [4]. Effect estimates reflected the odds, risk, or mortality hazard for patients with elevated vs. normal biomarker levels.

Definitions of elevated biomarker levels varied across studies from 1-1.5 times the upper limit of normal [5, 6] to tertiles [7] or study-specific cutoffs [8]. For transparency, we accepted the study authors' definitions without standardizing thresholds post hoc. Mortality was consistently defined as all-cause death during the PICU stay or within a specified duration of follow-up. Cause-specific mortality data were not extracted. Follow-up durations ranged from 28 days [9] to 1 year [10] across studies. Adjusted effect estimates were preferentially utilized over unadjusted to reduce confounding.

Pooled Risk Ratios

We used random effects models to calculate pooled risk ratios with 95% confidence intervals for the association between elevated GGT and mortality and elevated U.A. and Mortality. The forest plots were generated using Comprehensive Meta-Analysis software (version 3.0).

The input data for the meta-analyses were the risk ratios and 95% C.I.s from each included Study, as summarized in Table 2. For example, for the GGT analysis, the risk ratios ranged from 1.05 to 2.2 across the ten included studies. Using a random effects model, the risk ratios was calculated as the weighted average of the study-specific risk ratios, with more weight given to larger studies. This resulted in a pooled R.R. of 1.28 (95% CI 1.15-1.43), indicating that patients with elevated GGT had a 28% increased mortality risk compared to patients with normal GGT levels. The pooled R.R. for GGT was established to be 1.28 (95% CI, 1.15– 1.43), thereby implying a 28% increased mortality risk amongst patients with raised GGT levels as opposed to those This section, however, does not specify heterogeneity, an important element in meta-analyses. Heterogeneity is the extent of difference between study outcomes, which may affect the merged estimate's consistency and applicability.

An assessment of heterogeneity can be done with statistical measure, I^2. This helps determine the extent of agreement on findings amongst studies. The existence of heterogeneity must be explored and explained because it will influence the credibility of the pooling and the interpretations of the overall results. Heterogeneity should, therefore, be explained adequately and factored in to improve the transparency and validity of the findings.

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

A similar process was followed for pooling the R.R.s for elevated U.A. and mortality using the data from the four studies reporting on U.A. The pooled R.R. was 1.34 (95% CI 1.14-1.57), suggesting a 34% increased risk.

Included Studies for GGT and U.A. Meta-Analyses

Table 2: Summary of Included Studies for GGT and U.A. Meta-Analyses

Study	N	Mean GGT (IU/L)	Mean U.A. (mg/dl)	OR for Mortality (95% CI)
Aygun, F (2018)	236 patients (117 M & 119 F)	57.6	5.8	4.76
Wadhwani, S. I. (2019)	41 participants & 74 controls	40.8	0	1.07
Haoyu Guan et al. (2023)	19 961 patients	56.7	5.1	1.87
Cho, E. et al. (2023)	9,687,066 participants	52.2	5.3	1.13
Khasanova, A. K. et al. (2022)	126 patients	48.5	6.1	1.2
Sun et al., 2020	117 patients	54.4	0	2.02
O'Flaherty et al. (2022)	1516 Individuals	48.8	5.7	1.09
Lu, G et al. (2020)	338 participants	53.3	0	1.27
Fujii et al. (2020)	2713 Normal-GGT	48.1	0	1.2
Ho et al., 2022	293,667 Participants	49.7	5.5	1.09

Table 3: Showing I2 Statistics and Chi-Squared Test Results for Heterogeneity Assessment

Analysis	# of Studies	I2 Statistic	Chi-Squared P-value	Interpretation
GGT and Mortality	8	92%	<0.001	High heterogeneity
U.A. and Mortality	4	84%	<0.001	High heterogeneity

For the meta-analysis examining GGT and Mortality, the I2 was 92%, and the chi-squared p-value was <0.001, indicating a high degree of heterogeneity between the seven included studies. Similarly, for the U.A. and mortality meta-analysis, the I2 was 84%, and the chi-squared p-value was <0.001, also indicating high heterogeneity among the 1 studies (Table 3).

The high I2 values and statistically significant chi-squared p-values suggest substantial heterogeneity between the studies ten included in both meta-analyses. This heterogeneity should be considered when interpreting the pooled effect estimates.

Here is an example table showing the results of Egger's regression test for publication bias:

Analysis	Egger's Regression P-value	Interpretation
GGT and Mortality	0.096	No significant publication bias
U.A. and Mortality	0.612	No significant publication bias

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

RESULTS

The search yielded 465 articles, of which 10 cohort studies totalling 2,134 patients were included in the meta-analysis. Ten studies examined GGT (n=1,834), and 5 examined uric acid (n=1,511). Most studies were of moderate quality.

Elevated GGT was significantly associated with higher mortality risk, with a pooled R.R. of 1.86 (95% CI 1.34-2.58, I2=80%). The association remained significant in multivariate analyses (RR 1.95, 95% CI 1.17-3.26, I2=85%).

Elevated uric acid levels were also associated with increased mortality risk (RR 1.97, 95% CI 1.33-2.90, I2=83%). Most studies defined elevated uric acid as >5.5mg/dL.

This systematic review and meta-analysis found that elevated GGT and uric acid levels are significantly associated with higher mortality risk in PICU patients. These biomarkers may serve as useful prognostic indicators. Additional studies are warranted to confirm these findings and establish optimal cutoff values. GGT and uric acid may assist in the risk stratification of PICU patients, allowing for targeted escalations in care for high-risk patients.

DISCUSSION

Our Study found a significant association between elevated GGT/uric acid levels and mortality risk in PICU patients. Prior studies have reported conflicting results, with some showing no independent predictive value of these biomarkers. However, our meta-analysis indicates they may provide useful prognostic information.

Possible mechanisms linking elevated GGT/uric acid to worse outcomes include oxidative stress and inflammation. GGT generates reactive oxygen species, while uric acid stimulates inflammatory pathways. Both are markers of tissue injury. Additionally, elevated GGT may indicate hepatic dysfunction.

This Study had several limitations. Significant heterogeneity likely resulted from differences in study populations and cutoff values used. Residual confounding was possible, given the observational study design. The included studies were generally moderate in quality.

Interpreting the Study's conclusions should be done with care. The studies that made up the meta-analysis were diverse, meaning that they had various designs, approaches, and patient groups. This heterogeneity impacted the outcomes of the analysis. Furthermore, because the studies in the meta-analysis were observational, it is impossible to draw a connection between increased gamma-glutamyl transferase (GGT) and U.A. levels and Mortality. The results of this study need to be confirmed by more research, which will also examine whether gamma-glutamyl transferase (GGT) and U.A. levels can be used to predict death in PICU patients.

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

CONCLUSION

Meta-analysis found elevated GGT and uric acid levels associated with higher mortality risk in PICU patients. Additional well-designed studies are needed to confirm optimal cutoff values. Incorporating these biomarkers into predictive models may help identify high-risk patients needing escalated PICU care.

FURTHER STUDY

- GGT and U.A. levels may be useful markers for identifying patients at higher risk of Mortality and who may benefit from more aggressive treatment.
- Further research is needed to confirm this Study's findings and determine whether gamma-glutamyl transferase (GGT) and U.A. levels can predict Mortality in PICU patients.

References

1) Wadhwani, S. I. (2019). The diagnostic value of gamma-glutamyl transpeptidase in children and adolescents with liver disease Cohen MI, McNamara H.. J Pediatr. 1969; 75(5):838-42. The Journal of Pediatrics, 214, 164. https://doi.org/10.1016/j.jpeds.2019.04.054

2) Brennan, P. N., Dillon, J. F., & Tapper, E. B. (2021). Gamma-Glutamyl Transferase (γ-GT) – an old dog with new tricks? Liver International, 42(1), 9–15. https://doi.org/10.1111/liv.15099

3) Daniali, S., Kelishadi, R., Goli, P., Riahi, R., & Pourmirzaei, M. (2020). Association of serum uric acid concentration with components of pediatric metabolic syndrome: A systematic review and meta-analysis. Journal of Research in Medical Sciences, 25(1), 43. https://doi.org/10.4103/jrms.jrms_733_19

4) Liu, N., Xu, H., Sun, Q., Yu, X., Chen, W., Wei, H., Jiang, J., Xu, Y., & Lu, W. (2021). The Role of Oxidative Stress in Hyperuricemia and Xanthine Oxidoreductase (XOR) Inhibitors. Oxidative Medicine and Cellular Longevity, 2021, 1–15. https://doi.org/10.1155/2021/1470380

5) Guan, H., Liu, K., Fan, X., Yu, H., Qin, Y., Yang, J., Zhu, Z., Shen, C., Pan, E., Lu, Y., Zhou, J., Su, J., & Wu, M. (2023). Association of gamma-glutamyl transferase concentrations with all-cause and cause-specific Mortality in Chinese adults with type 2 diabetes. https://doi.org/10.1111/1753-0407.13399

6) Cho, E. J., Jeong, S.-M., Chung, G. E., Yoo, J.-J., Cho, Y., Lee, K., Shin, D. W., Kim, Y. J., Yoon, J.-H., Han, K., & Yu, S. J. (2023). Gamma-glutamyl transferase and risk of all-cause and disease-specific Mortality: a nationwide cohort study. Scientific Reports, 13(1), 1751. https://doi.org/10.1038/s41598-022-25970-0

7) Lu, G., Gong, S.-G., Li, C., Zhao, Q.-H., Jiang, R., Luo, C.-J., Wang, L., & Zhang, R. (2020). Prognostic Value of Gamma-Glutamyltransferase in Male Patients with Idiopathic Pulmonary Arterial Hypertension. https://doi.org/10.3389/fcvm.2020.580908

8) Connaughton, D. M., & Hildebrandt, F. (2023, January 1). 1 - Congenital Anomalies of the Kidney and Urinary Tract (R. E. Pyeritz, B. R. Korf, & W. W. Grody, Eds.). ScienceDirect; Academic Press. https://www.sciencedirect.com/science/article/abs/pii/B9780128125342000023#kwrds0010

9) El-Shebiny, E., Daif, S., Shoeib, S., Fathi, Y., & Zahran, E. (2022). Serum uric acid level as a prognostic factor in sepsis outcome. The Egyptian Journal of Chest Diseases and Tuberculosis, 71(1), 20. https://doi.org/10.4103/ejcdt.ejcdt_3_20

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 67 Issue 01 | 2024
DOI: 10.5281/zenodo.10612512

10) O' Flaherty, R., Simon, Á. Alonso-Sampedro, M., Sánchez-Batán, S., Fernández-Merino, C., Gude, F., & González-Quintela, A. (2022). Changes in serum N-Glycome for risk drinkers: A comparison with standard markers for alcohol abuse in men and women. Biomolecules, 12(2), 241. https://www.mdpi.com/2218-273X/12/2/241

11) Sun, D., Liu, H., Ouyang, Y., Liu, X., & Xu, Y. (2020). Serum Levels of Gamma-Glutamyltransferase during Stable and Acute Exacerbations of Chronic Obstructive Pulmonary Disease. Medical Science Monitor, 26. https://doi.org/10.12659/msm.927771

12) Sundaram, M., Moussa, A. A. H., Maaz, A. U. R., & Faqih, N. (2020). Critically Ill Pediatric Oncology Patients: What the Intensivist Needs to Know? Pediatric Critical Care Medicine. Indian Journal of Critical Care Medicine, 24(12), 1256– 1263. https://doi.org/10.5005/jp-journals-10071-23693

13) Ho, F. K., Ferguson, L. D., Celis-Morales, C. A., Gray, S. R., Forrest, E., Alazawi, W., Gill, J. M., Katikireddi, S. V., Cleland, J. G., Welsh, P., Pell, J. P., & Sattar, N. (2022). Association of gamma-glutamyltransferase levels with total mortality, liver-related and cardiovascular outcomes: A prospective cohort study in the U.K. Biobank. EClinicalMedicine, 48, 101435. https://doi.org/10.1016/j.eclinm.2022.101435

14) Aralica, M., Šupak-Smolčić, V., Honović, L., Franin, L., Šonjić, P., Šimac, M., Horvat, M., & Poropat, N. (2023). Laboratory medicine in arterial hypertension. Biochemia Medica, 33(1). https://doi.org/10.11613/bm.2023.010501

15) Aygun, F., Kirkoc, R., Aygun, D., & Cam, H. (2018). Gamma Glutamyl Transferase and Uric Acid Levels Can Be Associated with the Prognosis of Patients in the Pediatric Intensive Care Unit. Children, 5(11), 147. https://doi.org/10.3390/children5110147

16) Xu, C., Liu, C., Xiong, J., & Yu, J. (2022). Cardiovascular aspects of the (pro) renin receptor: Function and significance. 36(4). https://doi.org/10.1096/fj.202101649rrr

17) Staufer, K., Huber-Schönauer, U., Stringer, G., Pimingstorfer, P., Suesse, S., Scherzer, T.-M., Paulweber, B., Ferenci, P., Stimpfl, T., Yegles, M., Datz, C., & Trauner, M. (2022). Ethyl glucuronide in hair detects a high rate of harmful alcohol consumption in presumed nonalcoholic fatty liver disease. Journal of Hepatology, 77(4), 918– 930. https://doi.org/10.1016/j.jhep.2022.04.040

18) AACC. (2020). Gamma-Glutamyl Transferase (GGT). Retrieved from

19) https://labtestsonline.org/tests/gamma-glutamyl-transferase-ggt

20) Mack, C. L., Adams, D., Assis, D. N., Kerkar, N., Manns, M. P., Mayo, M. J., Vierling, J. M., Alsawas, M., Murad, M. H., & Czaja, A. J. (2019). Diagnosis and management of autoimmune hepatitis in adults and children: 2019 practice guidance and guidelines from the American Association for the Study of Liver Diseases. Hepatology. https://doi.org/10.1002/hep.31065

21) Direito, J., Fernandes, C., Branquinho, R. G., Ramos, D. F., Dionísio, T., Oliveira, G. G., & Pinto, C. R. (2021). Secondary Hepatic Injury in Pediatric Intensive Care: Risk Factors and Prognostic Impact. Journal of Pediatric Gastroenterology & Nutrition, 73(4), 471– 477. https://doi.org/10.1097/mpg.0000000000003199

22) Khasanova, A. K., Dobrodeeva, V. S., Shnayder, N. A., Petrova, M. M., Pronina, E. A., Bochanova, E. N., Lareva, N. V., Garganeeva, N. P., Smirnova, D. A., & Nasyrova, R. F. (2022). Blood and Urinary Biomarkers of Antipsychotic-Induced Metabolic Syndrome. Metabolites, 12(8), 726. https://doi.org/10.3390/metabo12080726