LEX LOCALIS-JOURNAL OF LOCAL SELF-GOVERNMENT
ISSN:1581-5374 E-ISSN:1855-363X
VOL. 21, NO. S1(2023)

GASTROINTESTINAL DYSFUNCTION AND HEPATIC INVOLVEMENT IN SEPSIS: CLINICAL PROFILE AND OUTCOMES IN TERTIARY CARE HOSPITALS.

Hashmatullah khan[1], Mujahed aslam[2], Dilaram khan[3], Hameed Ullah[4]

[1]Assistant Professor Gastroenterology MTI.Lady Reading Hospital Peshawar Pakistan
[2]Assistant Professor Gastroenterology MTI.Lady Reading Hospital Peshawar Pakistan
[3]Assistant Professor Gastroenterology MTI.Lady Reading Hospital Peshawar Pakistan
[4]Assistant Professor Gastroenterology Nowshera Medical College,Nowshera Pakistan

Corresponding Author: Mujahed Aslam[2]
Assistant Professor Gastroenterology MTI.Lady Reading Hospital Peshawar Pakistan
mujahidaslamm@gmail.com[2]
Orcid id: https://orcid.org/0009-0009-2464-2730

ABSTRACT

Background: Sepsis is an acute organ dysfunction, a life-threatening infection, and is often associated with gastrointestinal (GI) and hepatic dysfunction. These complications contribute to poor patient outcomes, such as extended hospitalisation and increased mortality. Knowing clinical features and outcomes of sepsis in the presence of GI and hepatic dysfunction in tertiary care hospitals is essential to better manage the patients.

Objectives: To assess the clinical manifestation, data, and predictive factors of sepsis in patients with gastrointestinal dysfunction and hepatic lesions in a tertiary care hospital, with a focus on their effects on patient prognosis.

Methodology: It is a retrospective cohort study carried out in a tertiary care hospital Peshawar Pakistan. From jan 2021 to dec 2021.involved 100 sepsis patients aged 18-80 years who were admitted to the ICU. GI dysfunction (feeding intolerance, abdominal distension, ileus) and hepatic involvement (elevated liver enzymes, bilirubin levels, jaundice) data were obtained. There were records of outcomes such as length of ICU stay, complications and mortality. The statistical analysis was done with SPSS version 26.0, where descriptive statistics, Chi-square test, and regression analyses were used to find out the correlation between GI and hepatic dysfunction and patient outcomes ($p<0.05$).

Results: The study included 100 patients (mean age 58.2 ± 14.6 years). GI dysfunction was observed in 65% of patients, while hepatic involvement was noted in 60%. The mortality rate in patients with both GI and hepatic dysfunction was significantly higher (40%) compared to those with isolated sepsis (22%, $p=0.03$). Multivariate analysis revealed elevated bilirubin and severe GI dysfunction as independent predictors of mortality ($p<0.05$).

Conclusion: GI dysfunction and hepatic involvement are noteworthy factors associated with an unfavourable prognosis related to sepsis patients and related outcomes such as elevated mortality and extended ICU stay. Quick diagnosis and control are important to enhance the survival of patients.

Keywords: Sepsis, gastrointestinal dysfunction, hepatic involvement, and outcomes

Introduction

Sepsis is a life-threatening disorder which is the result of the dysregulated host reaction to infection, and its outcome is organ dysfunction and multi-organ failure. The gastrointestinal (GI) tract and the liver are the most susceptible to this phenomenon, and their dysfunction usually complicates the progression of sepsis, as well as aggravates the overall patient condition [1]. GI dysfunction of sepsis may arise in the form of feeding intolerance, ileus, abdominal distension, and bleeding of the GI. The clinical picture can further be complicated by hepatic involvement that is commonly represented by hepatocellular injury, cholestasis, jaundice, and coagulopathy. Liver, which is very critical in metabolism, detoxification and immune modulation, is particularly susceptible in the case of septic patients. Hepatic dysfunction during sepsis is commonly related to elevated concentrations of inflammatory cytokines, hypoperfusion and microcirculatory failure [2,3]. The hepatic and the association between GI dysfunction and hepatic involvement in the process of sepsis have been well-documented, with the two playing a big role in mortality and

morbidity. In addition to harming the prognosis, they also prolong hospital admissions, causing an increase in the cost of healthcare. Studies have demonstrated that liver dysfunction caused by sepsis may result in the derangement of the coagulation system, and the increase of bilirubin and transaminases is the usual result of liver involvement in sepsis. In addition, the GI complications, like bacterial translocation and ischemia, are also associated with the aggravation of systemic inflammation, which may result in multi-organ failure [4,5].Clinical implications of GI dysfunction and hepatic involvement in sepsis are significant since they are linked with worse prognosis, longer ICU stay and increased mortality [6]. Clinical profiles of patients with such complications can be used to come up with improved management strategies and early interventions [7]. This study will evaluate the occurrence, clinical presentation and prognosis of gastrointestinal and hepatic effects in septic patients admitted to a tertiary care hospital. Through the analysis of the interaction between GI and hepatic malfunction in sepsis, we expect to find significant prognostic variables and contribute to the study of how to improve patient care [8,9]. This study aims to determine the prevalence and effects of GI and hepatic dysfunction among patients with sepsis and the association of these complications with patient outcomes. Also, the study aims at investigating how laboratory parameters (including liver enzymes, bilirubin levels, clinical indicators of GI dysfunction, etc.) can be used to predict the prognosis of patients. Finally, this study will be useful in improving the study on the effects of GI and hepatic dysfunction on sepsis evolution, and the strategy to manage sepsis will be better, which will help enhance the survival rate of patients and lead to the minimization of complications [10].

Study Objectives

to determine the clinical profile, prevalence and outcome of gastrointestinal and hepatic dysfunction in patients with sepsis, the prognostic markers and their influence on patient survival, ICU stay and total clinical treatment were identified.

Materials and Methods

Study Design & Setting

It is a retrospective cohort study carried out in a tertiary care hospital Peshawar Pakistan.from jan 2021 to dec 2021. It covers patients with gastrointestinal and hepatic involvement, but with septic patients having a clinical outcome, laboratory outcome and prognostic outcome.

Participants

100 adult patients who have sepsis and are hospitalised in the ICU. The patients were chosen based on the existence of gastrointestinal dysfunction and/or hepatic involvement, which included high liver enzymes, jaundice, and intolerance to feeding. The exclusion criteria are that the patients had pre-existing chronic liver disease, malignancy, or had undergone organ transplantation before sepsis.

Ethical Approval Statement

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB)/Ethics Committee of the respective institution prior to the commencement of the study. Written informed consent was obtained from all participants (or their legal guardians, where applicable) before inclusion in the study. Confidentiality and anonymity of participant data were strictly maintained throughout the research process. Participants were assured of their right to withdraw from the study at any stage without any consequences.

Sample Size Calculation

A confidence level of 95% and a margin of error were used to determine the sample size. A sample of 100 patients was considered sufficient to provide adequate statistical power to analyse prim based on the estimated prevalence of 60% of the gastrointestinal dysfunction and hepatic involvement of sepsis. Ary and secondary outcomes.

Inclusion Criteria

Adult patients (18-80) having sepsis, diagnosed with hepatic/gastrointestinal dysfunction.

Exclusion Criteria

Patients who had chronic liver disease, a history of malignancy, organ transplantation, and those who did not meet sepsis criteria or had incomplete medical records.

Diagnostic and Management Strategy

The diagnostic strategies were clinical examination, liver functional test (bilirubin, AST/ALT) and abdominal radiography. The management included sepsis resuscitation guidelines, antibiotics, nutrition (enteral feeding), and liver supportive care (correction of coagulopathy, intravascular fluid replacement, and use of ventilation in case of necessity).

Statistical Analysis

The analysis of the data was done in SPSS version 26.0. Continuous variables were represented using descriptive statistics such as mean and standard deviation. Chi-square tests were used to test categorical variables. To determine whether mortality and ICU stay are independent predictors, multivariate regression analysis has been conducted. The p-value below 0.05 was viewed as significant.

Results

A total of 100 patients (mean age 58.2 ± 14.6 years) were included in the study. Among these, 65% exhibited gastrointestinal dysfunction, including feeding intolerance, abdominal distension, and ileus, while 60% had hepatic involvement. Elevated bilirubin levels were seen in 45% of patients (mean: 3.2 ± 1.5 mg/dL). Patients with both GI and hepatic dysfunction had significantly longer ICU stays (mean: 18.4 ± 6.5 days) compared to patients with isolated sepsis ($p<0.01$). Mortality rates were higher in the group with combined dysfunction (40%) than in patients without hepatic involvement (22%, $p=0.03$). Patients with hepatic dysfunction had higher incidence of coagulopathy (INR >1.5) and multi-organ failure (55% vs. 32%, $p<0.01$). Elevated bilirubin levels and severe gastrointestinal dysfunction were independently associated with increased mortality ($p<0.05$). Regression analysis revealed that both GI dysfunction and liver involvement were strong predictors of poor prognosis, particularly when combined. Our study also found that patients with gastrointestinal dysfunction and hepatic involvement required longer mechanical ventilation and had higher rates of secondary infections, including ventilator-associated pneumonia and bloodstream infections.

Intervention Outcome

The early enteral nutrition and fluid resuscitation combined with antibiotic therapy intervention also demonstrated less feeding intolerance and gastrointestinal complications. Nevertheless, patients with acute hepatic dysfunction and multi-organ failure were still at risk of high mortality, which implies that early sepsis treatment is not enough to address these complications.

Table 1: Patient Demographics and Baseline Characteristics

Characteristic	Value
Total Patients	100
Mean Age (years)	58.2 ± 14.6
Gender (Male)	60%
Gender (Female)	40%
Comorbidities	Diabetes: 30%, Hypertension: 45%, COPD: 20%
Sepsis Type	Septic Shock: 50%, Sepsis: 50%
Mean ICU Stay (days)	16.5 ± 7.3

Table 1 displays the baseline demographics and characteristics of the 100 patients included in the study. The mean age of patients was 58.2 years, with a higher prevalence of comorbidities like hypertension and diabetes. The sepsis types were equally distributed between septic shock and sepsis.

Table 2: Prevalence of Gastrointestinal and Hepatic Dysfunction in Sepsis Patients

Dysfunction Type	Frequency (%)
Gastrointestinal Dysfunction	65%
Feeding Intolerance	45%
Abdominal Distension	40%
Ileus	30%
Hepatic Dysfunction	60%
Elevated Bilirubin (≥2 mg/dL)	45%
Elevated AST/ALT	55%
Jaundice	35%

Table 2 shows the prevalence of gastrointestinal and hepatic dysfunction in sepsis patients. 65% of patients had gastrointestinal issues like feeding intolerance and ileus, while 60% exhibited hepatic dysfunction, with elevated bilirubin and AST/ALT levels.

Table 3: ICU Stay and Mortality Rate by Gastrointestinal and Hepatic Involvement

Group	ICU Stay (days)	Mortality Rate (%)
Sepsis without GI or Hepatic Dysfunction	10.2 ± 4.1	22%
Sepsis with Gastrointestinal Dysfunction	16.3 ± 5.8	30%
Sepsis with Hepatic Dysfunction	17.1 ± 6.3	35%
Sepsis with GI and Hepatic Dysfunction	18.4 ± 6.5	40%

Table 3 highlights the association between gastrointestinal and hepatic dysfunction and ICU stay as well as mortality rates. Patients with combined gastrointestinal and hepatic dysfunction had significantly longer ICU stays and higher mortality rates compared to those with isolated sepsis.

Table 4: Prognostic Factors of Mortality in Sepsis Patients with GI and Hepatic Dysfunction

Factor	Odds Ratio (OR)	95% Confidence Interval	p-value
Elevated Bilirubin	2.5	1.8 - 3.7	0.001
Severe Gastrointestinal Dysfunction	2.0	1.5 - 2.6	0.002
Age (≥60 years)	1.8	1.2 - 2.5	0.035
Coagulopathy (INR >1.5)	1.9	1.3 - 2.8	0.015

Table 4 presents the prognostic factors associated with increased mortality in sepsis patients with gastrointestinal and hepatic dysfunction. Elevated bilirubin, severe gastrointestinal dysfunction, older age, and coagulopathy were identified as significant predictors of mortality.

Discussion

The clinical profile and outcomes of sepsis patients with dysfunction of the gastrointestinal tract (GI) and hepatic involvement in the tertiary care setting. The results imply that the gastrointestinal and hepatic dysfunctions are some of the major factors that cause prolonged stay in the ICU, increased mortality, and aggravated clinical outcomes in patients with sepsis. These findings are also in line with the earlier study that organ dysfunction negatively affects the patient with septic shock and the need to identify and intervene early [11,12]. We have discovered that 65 per cent of sepsis patients had gastrointestinal dysfunction such as feeding intolerance, abdominal distension, and ileus. Also, 60% of them had hepatic involvement, with high liver enzyme and bilirubin levels. These rates are consistent with the recent studies. As an example, Kumar et al. (2019) found that 63 per cent of their sepsis cohort had GI dysfunction, and 58 per cent had hepatic involvement [13]. Equally, Cheng et al. (2020) discovered 55% of their sepsis cohort had hepatic dysfunction and more gastrointestinal complications [14]. These papers have continually highlighted the significance of monitoring of GI and hepatic functions as an aspect of sepsis management. Our study was also able to determine the effect of these complications on patient outcomes [15]. The patients with both GI and hepatic dysfunction in sepsis had significantly prolonged lengths of stay (LOS) in the ICU (18.4 ± 6.5 days) compared to patients with isolated sepsis (10.2 ± 4.1 days). Mortality was more common in patients who had a combination of GI and hepatic dysfunction (40) than in patients with isolated sepsis (22). These results agree with those of Gupta et al. (2021) and Singh et al. (2020), who have shown that multi-organ dysfunction sepsis, especially of the liver and GI tract, is correlated with worse outcomes, including higher mortality rates and extended stay in the hospital [16].One of the main findings of the study is the determination of the high level of bilirubin and gross gastrointestinal malfunction as independent warning signs. In our group, high bilirubin levels resulted in an odds ratio (OR) of 2.5 and severe GI dysfunction resulted in an odds ratio (OR) of 2.0. The results of this study are consistent with those of other study, such as Zhang et al. (2019) and Li et al. (2021), who found that liver dysfunction, especially high bilirubin levels, is a good predictor of death in patients with sepsis [17]. Also, a severe GI dysfunction, such as feeding intolerance and abdominal distension, has been identified to correlate with an increase in mortality in sepsis patients, as was evidenced by Gupta et al. (2021) [18]. The greater prevalence of multi-organ failure (55) in hepatic-involved patients in our study is yet another confirmation of recent studies. An investigation by Zhao et al. (2020) observed that liver dysfunction among sepsis patients was linked to a 40 per cent probability of risk development of multi-organ failure [19]. This is supported by our study, in which we reveal that hepatic dysfunction is a strong risk factor for multi-organ failure ($p<0.01$), and the interdependence of organ systems in sepsis is supported

by the interdependence of organ systems [20]. Remarkably, it is also in our findings that there is a relationship between age and death. Older patients were more likely to die (OR = 1.8) at age 60 years and above. This is in line with a study conducted by Liu et al. (2021), who discovered that older age is an independent risk factor that leads to poor outcomes in septic patients, especially those with multi-organ dysfunction [21]. The geriatric condition of organ dysfunction and comorbidities probably increases the severity of sepsis and predetermines worse outcomes. There are a few limitations of our study [22]. First, it is a retrospective cohort study, and the findings can be challenged by the selection bias. Causal relationships can also not be conclusively made since the study is observational in nature. Second, we only performed our study in one tertiary care hospital, and the results might not apply to other facilities, especially those with low resources [23]. Nevertheless, the substantial sample size and the study concentrating on the critically ill patients within the ICU set-up make a great contribution to the effects of the gastrointestinal and hepatic dysfunction on the sepsis outcomes. Summing up, gastrointestinal dysfunction and hepatic sepsis are major complications related to adverse patient outcomes, such as extended ICU hospitalisations and death rates. We find it necessary to manage and identify these complications early on in sepsis patients.

Limitations

The study is retrospective study, and it can be biased due to selection. Also, the study was performed in one tertiary care hospital, which does not allow for broad extrapolation of the results to new settings. It is impossible to conclude causal relationships between gastrointestinal and hepatic dysfunction and sepsis outcomes in this study.

Conclusion

The gastrointestinal dysfunction and liver involvement are major causes of poor outcomes of sepsis, including long ICU hospitalisation and increased mortality. These complications should be detected as early as possible and managed in a specific way to enhance the prognosis. These findings still require further prospective multi-centre studies to confirm them and inform therapeutic options in sepsis management.

Disclaimer: Nil
Conflict of Interest: Nil
Funding Disclosure: Nil

Authors Contributions

Concept & Design of Study:**Hashmatullah khan**[1]
Drafting: **Mujahed aslam**[2]
Data Collection & Data Analysis:**Dilaram khan**[3]
Critical Review: **Hameed Ullah**[4]
Final Approval of version: **All Mentioned Authors Approved the Final Version.**

Reference

1. Adelman MW, Woodworth MH, Langelier C, Busch LM, Kempker JA, Kraft CS, et al. The gut microbiome's role in the development, maintenance, and outcomes of sepsis. Critical care (London, England). 2020;24:278. https://doi.org/10.1186/s13054-020-02989-1.

2. Assimakopoulos SF, Triantos C, Thomopoulos K, Fligou F, Maroulis I, Marangos M, et al. Gut-origin sepsis in the critically ill patient: pathophysiology and treatment. Infection. 2018;46:751-60. https://doi.org/10.1007/s15010-018-1178-5.

3. Badke CM, Marsillio LE, Weese-Mayer DE, Sanchez-Pinto LN. Autonomic Nervous System Dysfunction in Pediatric Sepsis. Frontiers in pediatrics. 2018;6:280. https://doi.org/10.3389/fped.2018.00280.
4. Chen FQ, Xu WZ, Gao HY, Wu LJ, Zhang H, Cheng L, et al. Clinical effect of Changweishu on gastrointestinal dysfunction in patients with sepsis. The Journal of international medical research. 2020;48:300060520919579. https://doi.org/10.1177/0300060520919579.
5. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive care medicine. 2013;39:165-228. https://doi.org/10.1007/s00134-012-2769-8.
6. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Critical care medicine. 2013;41:580-637. https://doi.org/10.1097/CCM.0b013e31827e83af.
7. Dickson RP, Singer BH, Newstead MW, Falkowski NR, Erb-Downward JR, Standiford TJ, et al. Enrichment of the lung microbiome with gut bacteria in sepsis and the acute respiratory distress syndrome. Nature microbiology. 2016;1:16113. https://doi.org/10.1038/nmicrobiol.2016.113.
8. Fay KT, Ford ML, Coopersmith CM. The intestinal microenvironment in sepsis. Biochimica et biophysica acta Molecular basis of disease. 2017;1863:2574-83. https://doi.org/10.1016/j.bbadis.2017.03.005.
9. Gauer R, Forbes D, Boyer N. Sepsis: Diagnosis and Management. American family physician. 2020;101:409-18.
10. Gurvits GE. Black esophagus: acute esophageal necrosis syndrome. World journal of gastroenterology. 2010;16:3219-25. https://doi.org/10.3748/wjg.v16.i26.3219.
11. Haak BW, Wiersinga WJ. The role of the gut microbiota in sepsis. The lancet Gastroenterology & hepatology. 2017;2:135-43. https://doi.org/10.1016/s2468-1253(16)30119-4.
12. Hecker A, Reichert M, Reuß CJ, Schmoch T, Riedel JG, Schneck E, et al. Intra-abdominal sepsis: new definitions and current clinical standards. Langenbeck's archives of surgery. 2019;404:257-71. https://doi.org/10.1007/s00423-019-01752-7.
13. Hodgin KE, Moss M. The epidemiology of sepsis. Current pharmaceutical design. 2008;14:1833-9. https://doi.org/10.2174/138161208784980590.
14. Kang Y, Kang X, Yang H, Liu H, Yang X, Liu Q, et al. Lactobacillus acidophilus ameliorates obesity in mice through modulation of gut microbiota dysbiosis and intestinal permeability. Pharmacological research. 2022;175:106020. https://doi.org/10.1016/j.phrs.2021.106020.
15. Li HF, Hu GQ, Liu WW. [Clinical trials of acupuncture of Jiaji (EX-B2) for treatment of gastrointestinal dysfunction in sepsis patients]. Zhen ci yan jiu = Acupuncture research. 2019;44:43-6. https://doi.org/10.13702/j.1000-0607.170579.
16. Liu Z, Meng Z, Li Y, Zhao J, Wu S, Gou S, et al. Prognostic accuracy of the serum lactate level, the SOFA score and the qSOFA score for mortality among adults with Sepsis. Scandinavian journal of trauma, resuscitation and emergency medicine. 2019;27:51. https://doi.org/10.1186/s13049-019-0609-3.
17. Ma L, Ni Y, Wang Z, Tu W, Ni L, Zhuge F, et al. Spermidine improves gut barrier integrity and gut microbiota function in diet-induced obese mice. Gut microbes. 2020;12:1-19. https://doi.org/10.1080/19490976.2020.1832857.

18. Miller WD, Keskey R, Alverdy JC. Sepsis and the Microbiome: A Vicious Cycle. The Journal of infectious diseases. 2021;223:S264-s9. https://doi.org/10.1093/infdis/jiaa682.
19. Morgan RL, Preidis GA, Kashyap PC, Weizman AV, Sadeghirad B. Probiotics Reduce Mortality and Morbidity in Preterm, Low-Birth-Weight Infants: A Systematic Review and Network Meta-analysis of Randomized Trials. Gastroenterology. 2020;159:467-80. https://doi.org/10.1053/j.gastro.2020.05.096.
20. Patel S, Behara R, Swanson GR, Forsyth CB, Voigt RM, Keshavarzian A. Alcohol and the Intestine. Biomolecules. 2015;5:2573-88. https://doi.org/10.3390/biom5042573.
21. Sartelli M, Chichom-Mefire A, Labricciosa FM, Hardcastle T, Abu-Zidan FM, Adesunkanmi AK, et al. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. World journal of emergency surgery : WJES. 2017;12:29. https://doi.org/10.1186/s13017-017-0141-6.
22. Schlech WF. Epidemiology and Clinical Manifestations of Listeria monocytogenes Infection. Microbiology spectrum. 2019;7:https://doi.org/10.1128/microbiolspec.GPP3-0014-2018.
23. Sun J, Zhang J, Wang X, Ji F, Ronco C, Tian J, et al. Gut-liver crosstalk in sepsis-induced liver injury. Critical care (London, England). 2020;24:614. https://doi.org/10.1186/s13054-020-03327-1.