Article

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The Impact of High-Intensity Noise on Liver Damage in Septic Rats

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Background: Previous studies have shown that sepsis induces systemic inflammation, affecting liver function. Additionally, noise exposure, as an environmental stressor, can exacerbate inflammation and contribute to organ damage. However, the combined effects of noise exposure and sepsis on liver injury have not been extensively studied. This study aimed to investigate the impact of exposure to different noise intensities on lipopolysaccharide (LPS)-induced liver damage in septic rats.

Methods: Healthy 6–8-week-old Wistar rats were randomly assigned to five groups: control, LPS, noise exposure (NE)-45, NE-75, and NE-105, with 20 rats per group. Rats in the experimental groups received intraperitoneal injection of LPS (5 mg/kg) to induce sepsis, followed by exposure to noise at 0, 45, 75, or 105 dB for 1 hour daily over 7 consecutive days. Within 24 hours after the final noise exposure, blood samples were collected for the assessment of liver function-related biochemical parameters. The expression levels of inflammatory factors and related proteins in liver tissue were determined using Enzyme-Linked Immunosorbent Assay (ELISA) and western blot assays. The liver weight/body weight ratio was calculated for each group to evaluate relative changes in liver mass.

Results: Compared to the LPS group, the survival rate of rats in the NE-105 group was significantly reduced to 5–10% ($p < 0.01$). Serum and liver biochemical tests showed significant increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, as well as in the liver weight/body weight ratio ($p < 0.01$). Activities of superoxide dismutase (SOD) and glutathione (GSH) were significantly decreased ($p < 0.01$), while malondialdehyde (MDA) levels were significantly elevated ($p < 0.01$). ELISA and western blot analyses indicated significant increases in tumor necrosis factor-α (TNF-α) and interleukin 1β (IL-1β) levels in both serum and liver tissue of rats in the NE-105 group ($p < 0.01$), accompanied by significant upregulation of Toll-like receptor 4 (TLR4), myeloid differentiation primary response gene 88 (MyD88), and phosphorylated nuclear factor kappa-light-chain-enhancer of activated B cells p65 (p-NF-κB p65) protein levels ($p < 0.01$).

Conclusions: High-intensity noise may exacerbate inflammatory responses and oxidative stress in septic rats through the activation of the TLR4/MyD88/NF-κB signaling pathway, thereby significantly aggravating liver damage.

Keywords: noise exposure; inflammatory response; liver injury; oxidative stress

Introduction

Prolonged exposure to high-intensity noise environments not only causes auditory damage but also adversely affects various systems of the body through multiple mechanisms [1]. Recent studies suggest that noise exposure is closely associated with a range of health issues, including cardiovascular diseases, metabolic syndrome, and neurodegenerative disorders [2–4]. Noise exposure activates the sympathetic nervous system, triggering stress responses that result in increased secretion of stress hormones such as cortisol and adrenaline. These hormones can significantly impact the immune system function and inflammatory responses [5]. Epidemiological studies have shown a strong correlation between long-term exposure to high-intensity noise environments and the occurrence of numerous health problems, including hypertension, insomnia, cardiovascular diseases, and psychological stress [6,7]. Noise affects health through several mechanisms. First, it directly stimulates the central nervous system via the auditory system, activating the sympathetic nervous system, releasing stress hormones, and eliciting physiological responses such as increased heart rate and elevated blood pressure [8]. Second, noise exposure can disrupt the function of the hypothalamic-pituitary-adrenal (HPA) axis, leading to endocrine disorders and impaired immune function [9]. Furthermore, noise exacerbates pathological states by inducing oxidative stress and inflammatory responses. Specifically, through the activation of the sympathetic nervous system and the release of stress hormones, noise exposure increases the production of oxidative stress and inflammatory mediators, thereby intensifying inflammatory responses and tissue damage [10].

While extensive research has focused on the impact of noise on the nervous and cardiovascular systems, relatively little attention has been given to its effects on the liver, a vital organ involved in detoxification and metabolic functions. Sepsis, a systemic inflammatory response syndrome caused by infection, is associated with high incidence and mortality rates [11]. The pathogenesis of sepsis is complex, primarily involving pathogen invasion, excessive immune system activation, and subsequent multi-organ dysfunction [12]. Notably, the liver is often severely affected during sepsis, leading to hepatic dysfunction or even liver failure [13]. Inflammatory mediators generated during sepsis not only target pathogens but can also cause significant damage on the host tissues and organs, particularly the liver [14]. As a key organ for detoxification and metabolism, the liver's role is often compromised during sepsis, often resulting in dysfunction or failure [15]. The excessive release of inflammatory mediators induces oxidative stress and inflammation in hepatocytes, leading to cellular injury and necrosis. This can progress to liver failure, causing toxin accumulation, further deterioration of the patient's condition, and the onset of systemic complications [16]. While there is extensive research on the health effects of noise, most studies have focused on its impact on the nervous and cardiovascular systems. In contrast, relatively few studies have investigated the effects of noise exposure on the liver, an essential organ involved in detoxification and metabolic processes [17]. This knowledge gap highlights the need for further investigation into how environmental stressors, such as noise, may exacerbate liver damage, particularly in conditions like sepsis.

This study aims to address this gap by establishing a sepsis rat model and exposing it to different noise intensities to assess liver function, levels of inflammatory factors, and oxidative stress responses in liver tissue. By analyzing the relationship between noise intensity and liver injury, this study seeks to elucidate how different intensities of noise exacerbate liver damage in septic rats. The research will provide new insights into the potential mechanisms underlying noise-induced liver injury in sepsis and offer valuable information for optimizing the management of environmental factors, particularly noise, in the clinical treatment of sepsis.

Materials and Methods

Establishment of a Sepsis Model

Healthy Wistar rats (6–8 week-old, weighing 180–250 g) were obtained from Central South University (Changsha, China). Only animals exhibiting no congenital or acquired diseases were included in the experiment [18]. A total of 100 rats were used in the study. Prior to the start of the experiment, all rats underwent a one-week acclimatization period under controlled conditions: constant temperature (22 $\pm$ 2 °C), constant humidity (55% $\pm$ 5%), and a 12-hour light/dark cycle. During this period, rats had free access to food and water to maintain normal physiological conditions. After acclimatization, the animals were randomly divided into five groups: control, lipopolysaccharide (LPS), noise exposure (NE)-45, NE-75, and NE-105, with 20 rats in each group [19].

Sepsis was induced in the experimental groups by intraperitoneal injection of LPS solution (5 mg/kg) to simulate the pathological state of sepsis in humans [20,21]. Rats in the control group received an equivalent volume of saline (1 mL) via the same intraperitoneal injection method. Each rat in the experimental group received a 1 mL intraperitoneal injection of LPS. Following LPS administration, the rats were monitored for general behavior and physical condition to ensure normal activity; any abnormal behavior was promptly recorded and addressed. Euthanasia was performed by intraperitoneal injection of pentobarbital sodium (150 mg/kg), prepared as a 3% (w/v) solution in sterile saline. The solution was administered using a 1 mL syringe and a 25 G needle, and the dosage was calculated based on each animal's body weight to ensure rapid and painless euthanasia. Cessation of respiration and heartbeat was confirmed before tissue collection. This method was selected due to its high reliability and minimal distress to the animals. All procedures were conducted in accordance with the guidelines of the Animal Laboratory Ethics Committee of The First People's Hospital of Jiashan and were approved to ensure animal welfare and ethical compliance (Ethics approval number: 2024-39-529).

Noise Exposure and Sample Collection

The noise exposure experiment was conducted in a specialized chamber using an ultrasonic acoustic device (Model: JY99-IIDN, Ningbo Scientz Biotechnology Co., Ltd., Ningbo, China), which was calibrated according to the manufacturer's instructions before each experiment [22]. The noise generated by this device was narrowband ultrasonic noise, with a central frequency of approximately 20–25 kHz. The distance between the sound source and the animals was maintained at approximately 20 cm. The control and LPS groups were kept in a quiet environment without noise exposure. The other three experimental groups were exposed to ultrasonic noise at 45, 75, and 105 dB for 1 hour daily over 7 consecutive days. All noise exposure sessions were conducted at the same time each day. The rats' behavior was observed and recorded to ensure that stress responses remained manageable.

Within 24 hours after the final noise exposure, 1–2 mL of blood was collected from the tail vein using a sterile syringe and transferred into pre-chilled centrifuge tubes. All animals were fasted for 12 hours prior to blood collection to minimize dietary interference. Blood samples were collected in the morning (between 8:00 and 10:00 AM) under light isoflurane anesthesia to reduce stress and ensure consistency. Samples were centrifuged at 1000 $\times$g for 10

minutes to separate the serum, which was then stored at –80 °C for subsequent biochemical analysis of liver function and Enzyme-Linked Immunosorbent Assay (ELISA) testing. After euthanizing the rats, liver tissue was quickly excised and weighed with an electronic balance. The total body weight of each animal was also recorded. Approximately 100 mg of liver tissue was homogenized in pre-chilled phosphate-buffered saline (PBS, C0221A, Beyotime, Shanghai, China). The homogenate was centrifuged at 13,400 ×g for 10–15 minutes at 4 °C, and the supernatant was collected for subsequent ELISA and western blot analyses.

Determination of Survival Rate

Throughout the experiment, the survival rates of each rat group were closely monitored during both the noise exposure and post-exposure recovery phases. Health checks were conducted at least twice daily, once in the morning and once in the evening, to ensure comprehensive monitoring of the rats' well-being. During these checks, parameters such as activity level, appetite, coat condition, and respiratory function were evaluated. Any deviations from normal health status were promptly recorded, and appropriate measures were taken to address any concerns. This regular monitoring ensured that the rats maintained stable physiological conditions during the noise exposure period. In the event of mortality, immediate necropsies were performed to determine the cause of death. The necropsy included a thorough examination of major organs, especially the liver, heart, and lungs, with all pathological changes potentially related to the experimental conditions recorded. The necropsy results were used to assess the impact of the experimental treatments on survival and to provide additional data for the analysis of survival rates.

Assessment of Hepatic Function via Biochemical Analysis

The levels of alanine aminotransferase (ALT) (C009-2, Beyotime, China) and aspartate aminotransferase (AST) (C010-2, Beyotime, China) were quantified using specific assay kits. Reagents were prepared according to standardized protocols. Serum samples and standards were dispensed into designated wells of 96-well plates with precise volumes. ALT and AST substrate working solutions were then added, followed by incubation at 37 °C. After incubation, a color developer was introduced, and absorbance was measured at 510 nm. ALT and AST activities were calculated and expressed as concentrations in U/L. The liver weight/body weight ratio was determined to evaluate relative changes in liver mass. Additionally, the levels of total superoxide dismutase (SOD) (BC0175, Servicebio, Wuhan, China), reduced glutathione (GSH) (BC1175, Servicebio, China), and malondialdehyde (MDA) (BC0025, Servicebio, China) in liver tissues were quantified using the respective assay kits, following standardized procedures [23]. SOD and GSH levels were measured using a microplate reader (Multiskan FC, Thermo Fisher Scientific, Waltham, MA, USA) at 450 nm, while MDA levels were assessed at 532 nm.

Enzyme-Linked Immunosorbent Assay (ELISA) Detection

The levels of tumor necrosis factor-α (TNF-α) and interleukin 1β (IL-1β) in serum and liver tissue were assessed using ELISA kits (ml107050, Meimian Biotechnology, Shanghai, China) [24]. TNF-α (PT516, Beyotime, China) and IL-1β (PI303, Beyotime, China) levels were measured according to the manufacturer's instructions. First, serum and liver tissue samples were prepared following standard protocols. Liver tissues were homogenized in phosphate-buffered saline (PBS), and the resulting homogenates were centrifuged to collect the supernatant for analysis. All reagents, including standards and detection antibodies, were prepared according to the kit instructions. For each assay, 100 µL of either sample or standard was added to the wells of the pre-coated ELISA plates and incubated at 37 °C for 2 hours to allow antigen-antibody binding. The wells were then washed with wash buffer to remove unbound substances, followed by the addition of the detection antibodies and a further incubation at 37 °C for 1 hour. Subsequently, streptavidin-horseradish peroxidase (HRP) reagent was added, and the plates were incubated at 37 °C for 30 minutes. The wells were washed again, and the substrate solution was added for color development, which was stopped after 15 minutes by adding the stop solution. Absorbance was measured at 450 nm using a microplate reader (SpectraMax iD3, Molecular Devices, San Jose, CA, USA). The concentrations of TNF-α and IL-1β in the samples were calculated by comparing the absorbance values to the standard curve generated from known concentrations of the respective standards. The results were expressed in pg/mL, and statistical analysis was performed to compare the levels of TNF-α and IL-1β across the different experimental groups.

Western Blot Analysis

Total protein was extracted from liver tissues using Radioimmunoprecipitation Assay (RIPA) lysis buffer (#89900, Thermo Fisher Scientific), supplemented with 1 mM phenylmethylsulfonyl fluoride (PMSF) and 1x protease/phosphatase inhibitor cocktail (Thermo Fisher Scientific). The tissue was homogenized in 500 µL of RIPA buffer per 100 mg of tissue. Protein concentration was determined using the bicinchoninic acid (BCA) assay. For sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), 20 µg of protein per sample was loaded and run for 120 minutes. Proteins were then transferred to a polyvinylidene difluoride (PVDF) membrane (#LC2005, Thermo Fisher Scientific, USA) using wet transfer and blocked with 5% non-fat milk for 1 hour at room tem-

perature. The membrane was then incubated with primary antibodies at 4 °C overnight. After washing three times with TBST, the membrane was incubated with secondary antibodies at room temperature for 1 hour. Following three washes with TBST, images were captured using a protein immunoblot imaging system (#12003153, Bio-Rad, Hercules, CA, USA), and the exposure results were quantitatively analyzed using ImageJ software (version 1.54f, National Institutes of Health, Bethesda, MD, USA). The antibodies used were as follows: Toll-like receptor 4 (TLR4) antibody (1:500, sc-293072, Santa Cruz Biotechnology, Dallas, TX, USA), myeloid differentiation primary response gene 88 (MyD88) antibody (1:2000, ab133739, Abcam, Cambridge, UK), phosphorylated nuclear factor kappa-light-chain-enhancer of activated B cells p65 (Phospho-NF-κB p65) antibody (1:1000, 3033, Cell Signaling Technology, USA), nuclear factor kappa-light-chain-enhancer of activated B cells p65 (NF-κB p65) antibody (1:1000, 8242, Cell Signaling Technology, USA), β-actin (1:1000, A1978, Sigma-Aldrich, USA), anti-rabbit secondary antibody (HRP-conjugated) (1:1000, 7074, Cell Signaling Technology, USA), anti-mouse secondary antibody (HRP-conjugated) (1:1000, 7076, Cell Signaling Technology, USA). Protein bands were visualized using the Pierce ECL Western Blotting Substrate (Thermo Scientiffc, CA, USA).

Statistical Analysis

Experimental data were analyzed using SPSS 22.0 statistical software (IBM Corp., Armonk, NY, USA). Results are presented as mean $\pm$ standard deviation (SD) to ensure the reliability and comparability of the findings. One-way analysis of variance (ANOVA) was used for inter-group comparisons. LSD post-hoc tests were conducted to identify specific group differences. Survival data were analyzed using Kaplan-Meier survival curves, and group comparisons were conducted using the log-rank test. Statistical significance was defined as $p < 0.05$.

Results

High-Intensity Noise Significantly Reduces Survival Rates in Septic Rats

To assess the impact of noise exposure on the survival of septic rats, we recorded and calculated the survival rates of each group subjected to different noise intensities. The rats were divided into five groups: control, LPS, NE-45, NE-75, and NE-105. The control group, which did not receive any treatment, exhibited a 100% survival rate. In contrast, the survival rate in the LPS group, which underwent sepsis induction without noise exposure, was significantly reduced (Fig. 1). Compared to the LPS group, the survival rates in the NE-45 and NE-75 groups, exposed to moderate noise intensities of 45 dB and 75 dB, respectively, were slightly lower, but these differences were not statistically significant (Fig. 1). Notably, the survival rate in the NE-105 group, which was exposed to high-intensity noise (105 dB), was significantly reduced and was notably lower than those in the NE-45 and NE-75 groups (Fig. 1). These results suggest that, under septic conditions, exposure to low and moderate-intensity noise has minimal impact on survival rates, whereas high-intensity noise significantly exacerbates survival crises, severely impairing the survival of the rats.

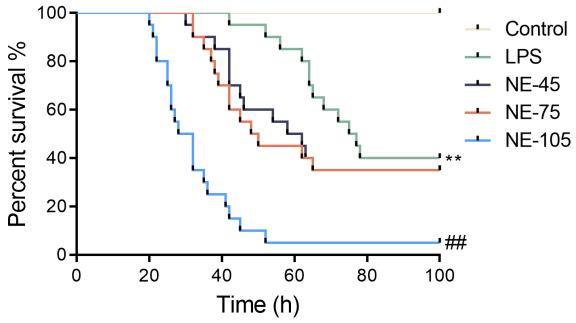

Fig. 1. Effects of different noise intensities on the survival rates of each group of rats. $^{**}p < 0.01$ *vs* the control group; $^{\#\#}p < 0.01$ *vs* the LPS group. LPS, lipopolysaccharide; NE, noise exposure.

High-Intensity Noise Exacerbates Liver Function Damage and Oxidative Stress Response in Septic Rats

Following the assessment of survival rates, we further examined the impact of noise exposure on liver function and oxidative stress in septic rats. Liver function was first evaluated by measuring the liver weight/body weight (LW/BW) ratio. The control group displayed a stable LW/BW ratio, indicating normal liver function. However, the LPS group showed a significant increase in this ratio ($p < 0.01$), suggesting liver swelling and damage due to sepsis. The NE-45 and NE-75 groups, exposed to low and moderate noise levels, respectively, showed minor increases in the LW/BW ratio; however, these changes were not statistically significant ($p > 0.05$). In contrast, the NE-105 group, exposed to high-intensity noise, exhibited a markedly elevated LW/BW ratio ($p < 0.01$), significantly higher than that observed in the LPS group, indicating that high-intensity noise further exacerbated liver damage (Fig. 2A).

Biochemical analyses showed that serum ALT and AST levels were significantly elevated in the LPS group compared to the control group ($p < 0.01$) (Fig. 2B,C). In the NE-105 group, these enzyme levels were even higher than those in the LPS group ($p < 0.01$), suggesting that high-intensity noise exacerbated liver dysfunction under septic conditions. In contrast, the NE-45 and NE-75 groups showed slight, non-significant increases in ALT and AST levels compared to the LPS group ($p > 0.05$).

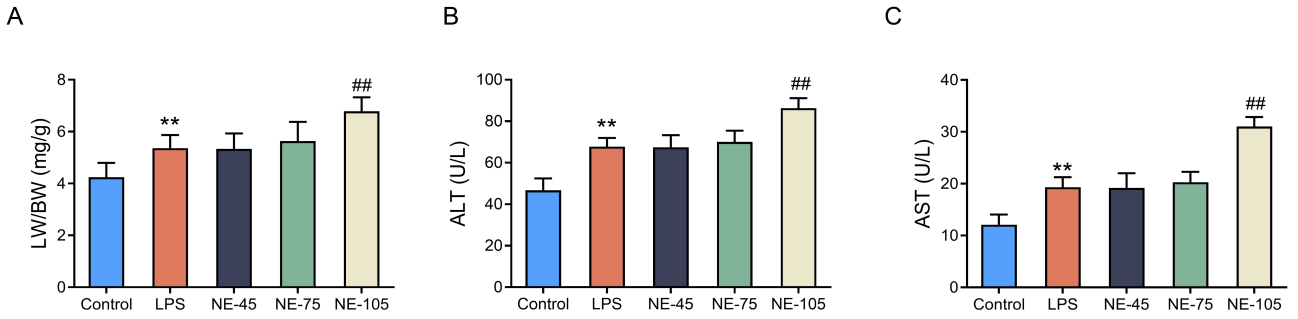

Fig. 2. Effect of liver function in each group of rats exposed to different noise intensities. (A) Comparison of liver weight/body weight ratios in each group of rats. (B) Serum ALT levels in each group of rats. (C) Serum AST levels in each group of rats. $^{**}p < 0.01$ *vs* the control group; $^{\#\#}p < 0.01$ *vs* the LPS group. LW/BW, liver weight/body weight; ALT, alanine aminotransferase; AST, aspartate aminotransferase (n = 3).

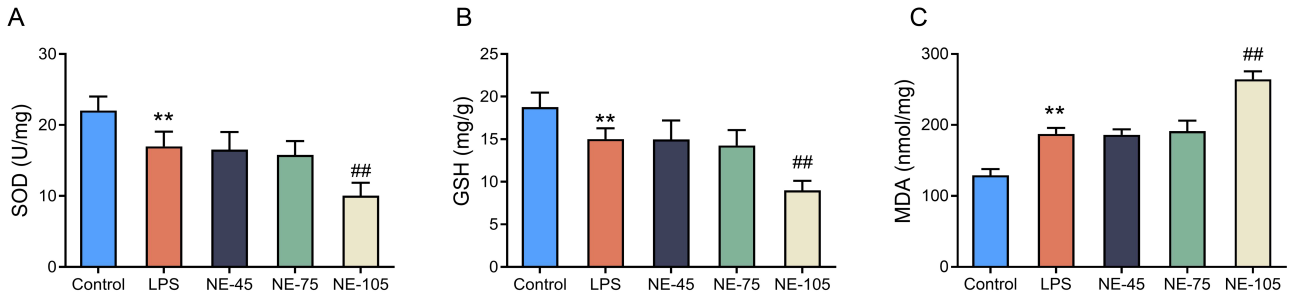

Fig. 3. Effects of different noise intensities on the oxidative stress response of rat liver tissue. (A) SOD activity in liver tissues of each group of rats. (B) GSH activity in the liver tissues of each group of rats. (C) MDA levels in the liver tissues of each group of rats. $^{**}p < 0.01$ *vs* the control group; $^{\#\#}p < 0.01$ *vs* the LPS group. SOD, superoxide dismutase; GSH, glutathione; MDA, malondialdehyde (n = 3).

Additionally, biochemical analysis of liver tissues showed that, compared to the control group, the LPS group had significantly reduced activities of SOD and GSH, along with significantly increased levels of MDA ($p < 0.01$). In the NE-105 group, SOD and GSH activities were further reduced, and MDA levels were significantly higher ($p < 0.01$) (Fig. 3A–C), indicating that high-intensity noise exacerbated oxidative stress in liver tissues. These findings suggest that the combined effects of sepsis and high-intensity noise lead to a more severe oxidative stress response, thereby amplifying liver damage.

High-Intensity Noise Exacerbates Inflammatory Response in Septic Rats

To further evaluate the impact of high-intensity noise on inflammation in septic rats, we performed ELISA analyses to measure the levels of key inflammatory mediators. Compared to the control group, the LPS group showed significantly elevated levels of TNF-α and IL-1β in both serum and liver tissues ($p < 0.01$) (Fig. 4A–D), indicating an active inflammatory response due to sepsis. In the NE-105 group, which was exposed to high-intensity noise, the levels of TNF-α and IL-1β were significantly higher than those in the LPS group ($p < 0.01$), suggesting that high-intensity noise further exacerbated the inflammatory response in septic conditions.

Additionally, the protein expression levels of key inflammatory markers, including TLR4, MyD88, and p-NF-κB p65, were significantly elevated in the liver tissues of the LPS group compared to the control group ($p < 0.01$) (Fig. 5A,B), indicating that LPS-induced sepsis activated the inflammatory response through the TLR4/MyD88/NF-κB signaling pathway. In the NE-105 group, the protein levels of these markers were significantly higher than those in the LPS group ($p < 0.01$), further confirming that high-intensity noise exacerbated the inflammatory response in septic rats. Interestingly, there were no significant differences in the levels of these markers between the NE-45 and NE-75 groups and the LPS group ($p > 0.05$), highlighting that only high-intensity noise (105 dB) leads to a substantial enhancement of the inflammatory response.

Discussion

This study demonstrates that high-intensity noise significantly exacerbates liver damage, oxidative stress, and inflammatory responses in LPS-induced septic rats. The primary findings include markedly elevated levels of ALT

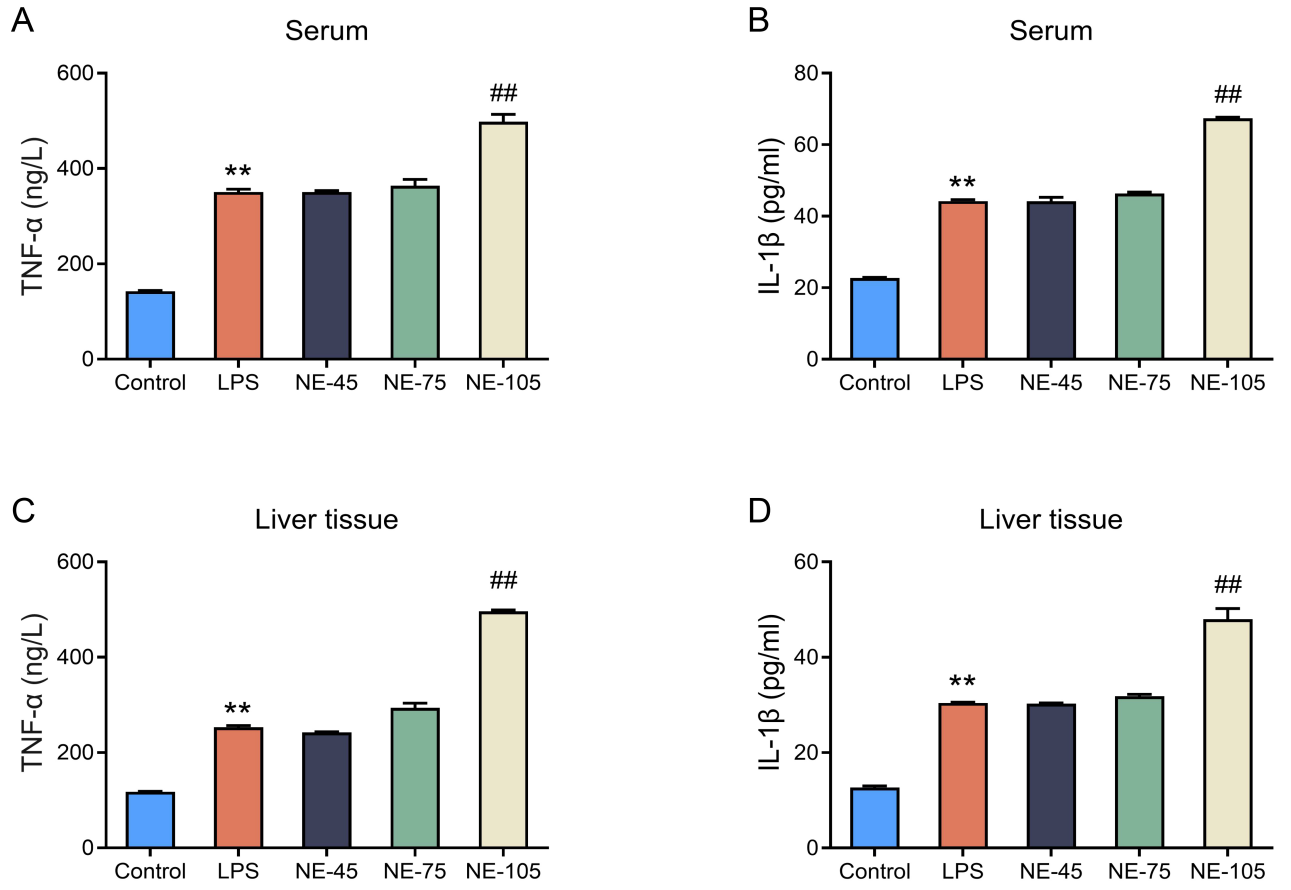

Fig. 4. Effects of different noise intensities on serum and liver tissue levels of inflammatory factors in rats. (A) Serum TNF-α levels in each group of rats. (B) Serum IL-1β levels in each group of rats. (C) TNF-α levels in the liver tissues of each group of rats. (D) IL-1β levels in the liver tissues of each group of rats. $^{**}p < 0.01$ *vs* the control group; $^{\#\#}p < 0.01$ *vs* the LPS group. TNF-α, tumor necrosis factor alpha; IL-1β, interleukin-1 beta (n = 3).

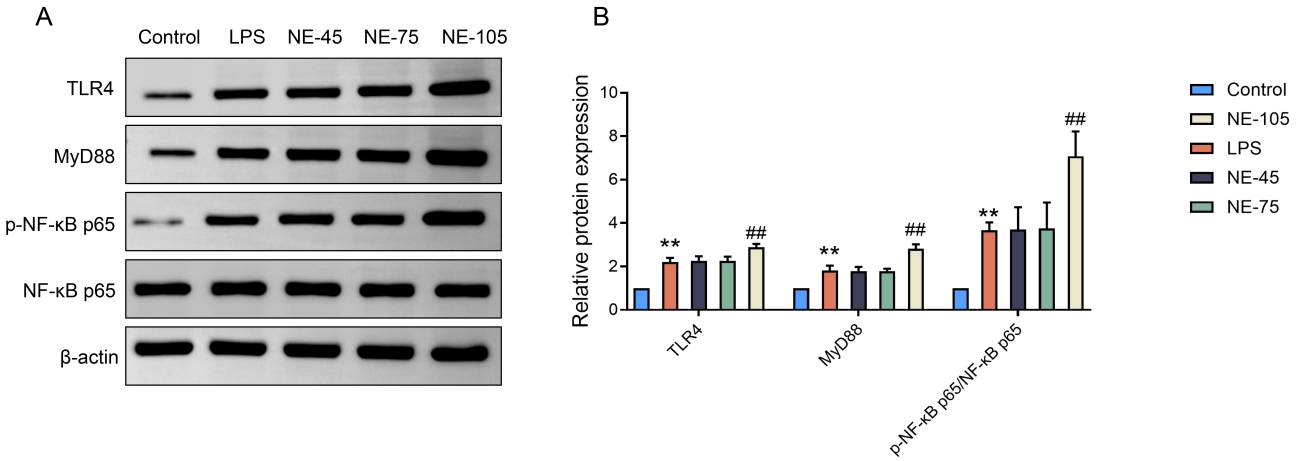

Fig. 5. Effects of different noise intensities on the NF-κB pathway in rat liver tissue. (A) Protein levels of TLR4, MyD88, p-NF-κB p65, and NF-κB p65 in liver tissues of each group of rats. (B) Ratios of TLR4, MyD88, and p-NF-κB p65/NF-κB p65 protein levels in liver tissues of each group of rats. Relative protein expression levels of TLR4, MyD88, and p-NF-κB p65/NF-κB p65. Data were normalized to the control group (expression level set to 1). $^{**}p < 0.01$ *vs* the control group; $^{\#\#}p < 0.01$ *vs* the LPS group. TLR4, Toll-like receptor 4; MyD88, myeloid differentiation primary response gene 88; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; p-NF-κB p65, phosphorylated nuclear factor kappa-light-chain-enhancer of activated B cells p65 (n = 3).

and AST, increased oxidative stress markers such as reduced SOD and GSH activities, and heightened MDA levels. Additionally, the inflammatory cytokines TNF-α and IL-1β were significantly elevated in both serum and liver tissues of rats exposed to high-intensity noise. This exposure further activated the TLR4/MyD88/NF-κB signaling pathway. These results highlight the critical impact of environmental noise on the progression and severity of sepsis-related liver damage. Clinically, these findings suggest that managing noise pollution in healthcare settings could be an important strategy for improving outcomes in sepsis patients by mitigating additional stress-induced liver injury and systemic inflammation.

Noise exposure may exacerbate the severity of sepsis through multiple mechanisms. As a potent environmental stressor, noise triggers stress responses in the body, activating the sympathetic nervous system and promoting the release of stress hormones such as cortisol and adrenaline [25,26]. These hormones not only affect cardiovascular stability but also suppress normal immune function, impairing the body's ability to effectively respond to infection [27]. The increased production of pro-inflammatory mediators, such as TNF-α and IL-1β, further exacerbates inflammatory responses, leading to greater tissue damage and organ dysfunction [28]. Elevated ALT and AST levels, which are indicators of liver function, are typically associated with hepatocyte membrane damage and necrosis when increased [29,30]. In this study, the significant decline in survival rates, changes in liver function indicators, and activation of oxidative stress responses under noise exposure indicate that septic rats are more susceptible to infection and experience substantial hepatocyte damage.

Additionally, noise exposure significantly enhanced inflammatory responses, as evidenced by significantly elevated levels of TNF-α and IL-1β, as well as increased protein expression of TLR4, MyD88, and p-NF-κB p65 [31]. TLR4, a critical receptor for pathogen-associated molecular patterns (PAMPs) like LPS, activates downstream MyD88-dependent signaling pathways, ultimately leading to NF-κB activation [32,33]. MyD88, the main adaptor molecule in TLR4 signaling, mediates signal transduction to NF-κB, a key transcription factor that regulates pro-inflammatory genes such as TNF-α and IL-1β [34,35]. These mediators exacerbate both local and systemic inflammatory responses, thereby contributing to further damage to the liver and other organs [36]. Moreover, noise exposure not only activates inflammatory pathways but also exacerbates liver injury by inducing oxidative stress responses [36]. Noise exposure increases the production of reactive oxygen species (ROS), leading to lipid peroxidation of cellular membranes and disruption of their integrity and function. Oxidative stress can also activate multiple signaling pathways, including the TLR4/MyD88/NF-κB pathway, further amplifying the inflammatory response [32,33]. Studies have shown that oxidative stress can directly damage hepatocytes and activate liver immune cells like Kupffer cells, leading to the release of additional inflammatory factors and exacerbation of liver inflammation and tissue damage [35,37,38]. Thus, the activation of the TLR4/MyD88/NF-κB pathway and oxidative stress response induced by noise exposure may represent a key mechanism underlying its detrimental effects.

Compared to previous studies, the findings of this study are consistent with most research results, indicating that noise exposure can exacerbate disease progression through inflammatory and oxidative stress mechanisms [39,40]. However, few studies have investigated the relationship between noise exposure and liver damage during sepsis progression. This study has some limitations, firstly, the experiments were conducted at specific noise intensities and exposure durations, without exploring the effects of different noise frequencies or exposure patterns on septic rats. Additionally, the study mainly focused on the TLR4/MyD88/NF-κB signaling pathway, without comprehensively exploring other potential molecular mechanisms. The inflammatory dynamics following LPS injection, such as the peak time of TNF-α, were not validated, which may limit the interpretation of inflammatory responses at the selected sampling time point. Moreover, the experimental results are based on animal models, limiting the extrapolation of the findings to humans; therefore, further validation in clinical practice is needed. Finally, the relatively small sample size may also affect the generalizability and reliability of the results. Furthermore, the lack of comparison with baseline models or existing methods weakens the argument for the effectiveness of the proposed approach. Future studies should investigate the effects of different noise frequencies and exposure patterns on septic rats and further elucidate the mechanisms of noise-induced liver damage in sepsis. Moreover, attention should be given to other potential signaling pathways and molecular mechanisms. More studies should be conducted to verify the impact of noise on liver function in sepsis patients, thereby providing a scientific basis for the development of effective prevention and treatment strategies.

Conclusions

This study suggests that high-intensity noise may exacerbate liver injury in septic rats by enhancing oxidative stress and inflammatory responses, possibly through the activation of the TLR4/MyD88/NF-κB signaling pathway. These findings highlight the potential aggravating effect of noise on the progression of sepsis. Future studies should further investigate the impact of different noise exposures on sepsis and validate these results in clinical settings.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

WF, Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Writing - Review and Critically Revising; MX, Formal Analysis, Resources, Writing - Review and Critically Revising; MS, Data Curation, Software, Writing - Review and Critically Revising; CP, Data Curation, Writing - Review and Critically Revising; FY, Data Curation, Writing - Review and Critically Revising, Supervision. All authors have given final approval of the version to be published. All authors have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All procedures were carried out in accordance with the guidelines of the Animal Laboratory Ethics Committee of The First People's Hospital of Jiashan and were approved to ensure animal welfare and ethical compliance (Ethics approval number: 2024-39-529). At the end of the experiment, the rats were humanely euthanized, and samples were collected for analysis.

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Conflict of Interest

The authors declare no conflict of interest.

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