Evaluation of serum Lipocalin-2 Level as potential biomarkers for respiratory bacterial infection.

Abstract:

Background: Lipocalin-2 (LCN2) is an innate immune protein that provides protection against bacteria. The aim of the study to evaluate the potential diagnostic power of serum LCN2 in bacterial respiratory infections.

Methods: The study included 90 cases of bacterial respiratory infection and 90 healthy controls. The cases were identified based on the type of bacteria causing their infection, i.e., *Streptococcus pneumoniae* (n=36), *Pseudomonas aeruginosa* (n=23), *Klebsiella pneumoniae* (n=18), *and Haemophilus influenzae* (n=13). Serum LCN2 levels were determined for all subjects, and comparisons were made between cases and controls.

Results: Serum LCN2 levels were statistically significantly higher in patients with bacterial respiratory infection (mean=180.45±55.32 ng/ml) as compared to the control group of healthy subjects (mean=75.28±28.46 ng/ml; t=16.69; P<0.001). There were no statistically significant differences in serum LCN2 concentrations between the different types of bacteria causing the respiratory infections, although there was a slight numerical trend for S. pneumoniae infections to produce the highest average serum LCN2 concentrations (mean=190.42±54.36 ng/ml) followed by P. aeruginosa (mean=181.63±49.51 ng/ml), K. pneumoniae (mean=174.28±46.74 ng/ml) and H. influenzae (mean=168.46±43.83 ng/ml; F=0.82; P=0.487). ROC analysis indicated that serum LCN2 had fair-to-good diagnostic accuracy for identifying bacterial respiratory infection, with an AUC of 0.83 (P=0.02). At a cut-off point of 69.55 ng/ml, serum LCN2 exhibited 78% sensitivity and 62% specificity.

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Conclusion: Serum LCN2 is significantly higher in patients with bacterial respiratory infection than in healthy control individuals. However, serum LCN2 was not different among groups based on the identification of a specific type of bacteria. Additional research will be necessary to confirm the diagnostic utility and clinical value of serum LCN2.

Keywords: LCN2, Bacterial Respiratory Infection, Innate Immune Response, AUC

Introduction

Respiratory Tract Infection (RTI) is one of the most common causes of morbidity and health care use throughout the world. RTIs can be anything from very minor upper respiratory tract infections to severe lower respiratory tract infections such as pneumonia and bronchopneumonia (Saleri & Ryan, 2019). Respiratory Tract Infection can be caused by many different types of viruses, bacteria and occasionally fungi; however, bacterial RTIs are especially significant due to the possible development of severe complications, systemic inflammatory response syndrome (SIRS), hospital admission and even death (Reed, 2015). Some examples of common bacterial respiratory pathogens include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *and Klebsiella pneumoniae*(File, 2012). Many of the clinical signs and symptoms of bacterial RTIs are similar to those of viral RTIs, therefore, it is often difficult to determine if an RTI is due to a bacterium or a virus based solely upon clinical assessment. Therefore, the ability to correctly identify if an RTI is due to a bacterial pathogen is critical in order to administer the correct antimicrobial treatment, prevent complications, and reduce the number of inappropriate antibiotic prescriptions, which greatly contributes to the development of antimicrobial resistance (Venge et al., 2017).

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Conventional laboratory tests, such as total white blood cell count (total leukocyte count), neutrophil count, C-reactive protein (CRP), and procalcitonin (PCT), can help confirm whether or not a person has a bacterial infection. There are some disadvantages to using these tests to determine if someone has a bacterial infection. Some of those include: CRP is an acute phase protein that will increase in concentration in response to numerous types of inflammation; including both bacterial and viral infections (Velur et al., 2025). PCT levels will differ based upon how serious the infection is, how far along the disease process is, and other factors specific to each individual patient (Lee, 2013). Also, microbiological studies, such as bacterial cultures and molecular diagnostics, can identify which organism(s) are causing the infection; however, they require more time for processing, require specialized laboratory equipment, and require relevant clinical samples. Due to these limitations, researchers have investigated alternative host-derived biomarkers that may offer additional insight into the existence and characteristics of infectious processes (Venge et al., 2017; Mills et al., 2025).

Lipocalin-2 (LCN2) is a protein within the lipocalin family, and it plays a critical role in the innate immune response. The protein is primarily produced by activated neutrophils and epithelial cells, and it is present in multiple types of body fluids such as serum, plasma, and urine. LCN2 acts as part of the host's defense system through binding bacterial siderophores; specifically, iron-binding molecules used by bacteria to obtain iron (Lu et al., 2019). Through restricting the amount of iron available to bacteria for growth, LCN2 participates in nutritional immunity - a key component of the innate immune response against bacteria. In addition togoving bacteriostatic actions, LCN2 is also involved in the regulation of inflammation, cell migration, and modulating the immune system during infection (Guardado et al., 2021).

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During bacterial infection, the production and release of LCN2 may increase in response to inflammatory mediators and microbial stimuli. The activation and degranulation of neutrophils are major sources of circulating LCN2. Serum levels of LCN2 can be used as a measure of the extent to which the innate immune system has been activated in response to bacteria (Li et al., 2018). While LCN2 is primarily related to bacterial infection, it can also be expressed during tissue injury, systemic inflammation, and renal dysfunction. Therefore, its circulating concentration should be interpreted in relation to the patient's clinical condition and other laboratory findings (Guardado et al., 2021).

The usefulness of LCN2 as a potential biomarker for both diagnosis and prognosis of respiratory infections has been evaluated by several studies. Yeh et al. (2013) evaluated circulating LCN2 concentrations in 61 adult subjects who had been hospitalized with community acquired pneumonia (CAP) as well as 60 age/sex matched healthy controls. The results of their study showed that LCN2 concentrations correlated with pneumonia severity, i.e., they significantly correlated with Pneumonia Severity Index (PSI), CURB-65, and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores. Additionally, circulating LCN2 concentrations declined after initiation of antimicrobial therapy, which may suggest a correlation between circulating LCN2 concentrations and the host inflammatory response to bacterial pneumonia. Therefore, it appears that LCN2 may provide another biomarker to assess respiratory infection and its severity(Boix-Palop et al., 2023).

Similarly, Huang et al. (2014) conducted a study in children with pneumonia enrolled in Gambia and Kenya to identify biomarkers associated with disease severity and bacterial etiology. They reported that lipocalin-2 emerged as one of the most promising protein biomarkers, demonstrating an area under the receiver operating characteristic curve (AUC) of 0.71 for severe pneumonia. Furthermore,

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LCN2 demonstrated considerable predictive potential for bacteremia and pneumococcal bacteremia. These findings highlighted its possible application in identifying patients with bacterial respiratory infections and distinguishing severe disease from less severe clinical presentations.

Further evidence was provided by Esposito et al. (2016), who investigated serum LCN2 and syndecan-4 concentrations in children hospitalized with community-acquired pneumonia. Their findings supported the potential usefulness of these inflammatory biomarkers in differentiating bacterial from viral respiratory infections. In another investigation, Venge et al. (2017) evaluated human neutrophil lipocalin in activated whole blood among patients with respiratory tract infections. Their study demonstrated that activated HNL had a higher diagnostic performance than CRP and PCT in distinguishing bacterial from viral infections, with an AUC of 0.91 in patients whose infection etiology was supported by microbiological investigations. These findings emphasized the potential diagnostic importance of neutrophil-derived lipocalins in the assessment of respiratory bacterial infections.

More recently, Boix-Palop et al. (2023) studied plasma LCN2 concentrations among 130 adult patients who had community-acquired pneumonia. The patients included those with a known cause (bacterial, viral, or undetermined) of their pneumonia. The authors found that there were statistically significant differences in the concentration of LCN2 in patients with bacterial vs. non-bacterial pneumonia. While the authors' study showed that LCN2 could be used as a marker for identifying community-acquired pneumonia caused by bacteria, they stated that LCN2 had a limited capacity for distinguishing community-acquired pneumonia caused by bacteria from community-acquired pneumonia caused by other types of organisms, with an AUC of 0.62.More recently, there have been additional studies emphasizing the need to consider biological and demographic characteristics of a

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patient as part of the interpretation process for LCN2 measurements. Mills et al. (2025) developed age-specific reference ranges for LCN2 and several other novel biomarkers of infection in healthy children. These researchers found that circulating LCN2 levels increased progressively with age; therefore, researchers must account for these age-related changes when assessing the utility of LCN2 as a diagnostic tool in pediatric patients. In addition, experimental evidence from Sheldon et al. (2022) demonstrated an important protective role for LCN2 in the innate immune response against Acinetobacter baumannii, a clinically significant pathogen associated with healthcare-acquired infections and ventilator-associated pneumonia.

Therefore, the present study aims to evaluate serum lipocalin-2 concentrations in patients with respiratory bacterial infections compared with healthy controls and using it as an additional biomarker in the diagnosis and evaluation of respiratory bacterial infections.

Patients and Methods

Study Design and Setting

The study was carried out in Al-Hilla Teaching Hospital, Babylon, Iraq, during the period of March 2026 through August 2026. This study aimed to assess serum LCN2 levels among those who were diagnosed with respiratory bacterial infection and compare these findings to a group of seemingly healthy individuals. Al-Hilla Teaching Hospital is a significant health care facility in Babylon Governorate and provides services for patients from Babylon and adjacent regions.

Study Population

A total of 180 subjects (90 subjects in the patient group and 90 subjects in the control group) were included in this study. The patient group was comprised of subjects who had been diagnosed with respiratory bacterial infection. These

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subjects presented to the hospital with symptoms of respiratory tract infection such as cough, fever, sputum production, dyspnea, chest discomfort, and abnormal respiratory examination findings.

The bacterial pathogens that were diagnosed included the following: *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *and Haemophilus influenzae*. The control group was made up of individuals who appeared to be in good health and had no history of an acute respiratory illness at the time of the assessment or prior to the assessment. Both the treatment group and the control group were evaluated for demographics that would relate to their participation in the study. These variables included age and gender.

Inclusion and Exclusion Criteria

Inclusion criteria for the patient group:

• Patients who present symptoms indicative of an upper respiratory tract infection.

• Microbiologically confirmed bacterial respiratory infection.

The availability of a sufficient number of blood and respiratory samples to allow for laboratory studies.

• Willingness to participate and provision of informed consent.

Exclusion criteria for the patient group:

• Patients who have been diagnosed with a viral or fungal infection of their respiratory system and do not have an additional diagnosis of a bacterial infection.

• Patients who are experiencing an additional type of bacterial infection, such as a urinary tract infection or a gastrointestinal infection.

• Individuals with chronic kidney disease or acute kidney injury, as the presence of renal impairment can independently alter the concentration of LCN2 in circulation.

• Patients who suffer from autoimmune disease, malignancy, or other serious systemic inflammatory conditions.

• Patients receiving immunosuppressive therapy.

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• Patients with insufficient clinical or laboratory information.

For both groups, participants who recently underwent major surgery or suffered severe tissue damage were excluded from the study in order to reduce the possibility of other variables influencing serum LCN2 levels.

Clinical and Microbiological Examination

Whenever possible, respiratory specimens (primarily sputum) were obtained using aseptic techniques prior to antibiotics being administered. The quality of the specimen was evaluated by Gram staining; specifically, assessing the number of inflammatory cells present and whether there was an excessive amount of squamous epithelial cells. Those specimens that met quality criteria were then inoculated onto specific bacteriological media and incubated appropriately.The bacteria were identified based upon their colonial appearance, how they stained with a Gram stain, and standard biochemical assays.

1. *Streptococcus pneumoniae*: This bacterium was identified based on its Gram-positive, lancet shaped diplococcal appearance. Its identity was confirmed through alpha hemolysis on blood agar, its susceptibility to optochin, and its solubility in bile.
2. *Pseudomonas aeruginosa*: This species has been identified as Gram-negative, oxidase-positive bacilli that usually produce characteristic pigments when grown on suitable culture media. This identification can be confirmed by using biochemical methods.
3. *Klebsiella pneumoniae*: This is a Gram-negative, lactose fermenting, encapsulated bacillus that produces a mucoid colony on MacConkey agar and is biochemically confirmed.
4. *Haemophilus influenzae*: A type of Gram-negative coccobacilli that requires both X (hemin) and V (NAD) factors to be present in order to grow. This is confirmed through use of a valid identification procedure.

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Sample Collection

For biochemical analysis, approximately 3–5 mL of venous blood was obtained from each subject in an aseptic manner with the use of sterile disposable syringes. Serum was then separated from the cellular elements of the blood through centrifugation of the sample at approximately 3000 rpm for 10 minutes after being allowed to clot at room temperature. The separated serum was carefully transferred into sterile Eppendorf tubes using micropipettes and stored at −20°C until biochemical analysis. Repeated freezing and thawing were avoided to preserve sample integrity.

Measurement of Serum Lipocalin-2

Serum lipocalin-2 concentrations were quantitatively determined using a commercially available human lipocalin-2/neutrophil gelatinase-associated lipocalin (NGAL) enzyme-linked immunosorbent assay (ELISA) kit (Human Lipocalin-2/NGAL ELISA Kit, Catalog No. EHLCN2; Invitrogen, Thermo Fisher Scientific, Waltham, Massachusetts, USA). The kit is designed for quantitative measurement of human LCN2 in serum and plasma samples. The assay was performed according to the manufacturer's instructions using the sandwich ELISA technique. Briefly, serum samples and standard solutions were added to the antibody-precoated microtiter plate wells. Following incubation, the wells were washed to remove unbound substances. Biotin-conjugated detection antibody was subsequently added, followed by streptavidin-horseradish peroxidase (HRP). After further incubation and washing, tetramethylbenzidine (TMB) substrate was added to develop the colorimetric reaction. The reaction was terminated using the supplied stop solution.

The absorbance was read by an ELISA microplate reader at 450 nm. To determine serum LCN2 levels, a calibration curve was created using the known concentration levels of the provided standards and then the corresponding optical density value

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for each sample was used to calculate its serum LCN2 level. All results are expressed in pg/mL. According to the manufacturer, the analytical sensitivity is 4 pg/mL and has an assay range of 4.1 – 1000 pg/mL.

Ethical Considerations

The study's design/protocol has been evaluated for ethical considerations, as well as the health regulations established within the Babylon governorate. Prior to participating in the study, participants provided written approval to be included. Participants that did not have the capability to make an independent decision regarding providing written approval, received written approval from their legal representative, if applicable. All information gathered during the study will remain confidential; additionally, each participant’s identity will remain protected throughout the entirety of the study.The institutional ethics committee name and approval number should be inserted according to the actual approval document.

Statistical Analysis

All statistical analyses were performed using SPSS software, version 26 (IBM Corp., Armonk, NY, USA). Differences in demographic characteristics between patients and controls were evaluated by chi-square (χ^2) test for categorical variables.Serum LCN2 concentrations were compared between the patient and control groups using the independent-samples t-test. One-way analysis of variance (ANOVA), followed by Tukey's post hoc test, was used to compare serum LCN2 concentrations among patients infected with different bacterial species.Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of serum LCN2 in differentiating patients with bacterial respiratory infections from healthy controls. The area under the curve (AUC), sensitivity, specificity, and optimal cutoff value were calculated.

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Results

Demographic analysis showed that the patient and control groups were relatively well matched with respect to study variables. The majority of participants in both groups were young and middle-aged (24-43 years of age), with only a small proportion of participants older than 43 years of age. Both groups had a higher proportion of males than females, reflecting the higher risk of exposure and prevalence of bacterial respiratory infection in men. In terms of residence, there were slightly more participants from urban areas than from rural areas, which is consistent with the higher transmission rates frequently reported in densely populated areas. Although it borderlines the significance at (p value <0.07), and reported more smokers among patients (37.8% vs 26.7 for control) the difference smoking habits is considered non-significant (Table 1).

Table 1.Demographic distribution of both healthy control and patientswith bacterial respiratory infection

Indicators		`Patients (No. = 90)		Control (No. = 90)		Chi Square	P value (Sig.)
		Freq.	%	Freq.	%		
Age/Years	25-34	24	26.7	27	30	0.262	0.65 (NS)
	35-44	29	32.2	27	30		
	> 45	37	41.1	36	40		
Sex	Male	51	56.7	48	53.3	0.202	0.58 (NS)
	Female	39	43.3	42	46.7		
Residence	Urban	58	64.4	54	60	0.378	0.39 (NS)
	Rural	32	35.6	36	40		
Smoking	Yes	34	37.8	24	26.7	2.544	0.07 (NS)
	No	56	62.2	66	73.3		

NS: Non-significant at P>0.05

The distribution of bacterial causative species in respiratory infection among patients indicates that the *Streptococcus pneumoniae*was the most common,

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accounting for 36 cases (40%), followed by *Pseudomonas aeruginosa*with 23 cases (25.56%), *Klebsiella pneumoniae* was 18 cases (20%) and finally *Haemophilus influenzae* constituted 13 cases (14.44%), as shown in (Figure 1).

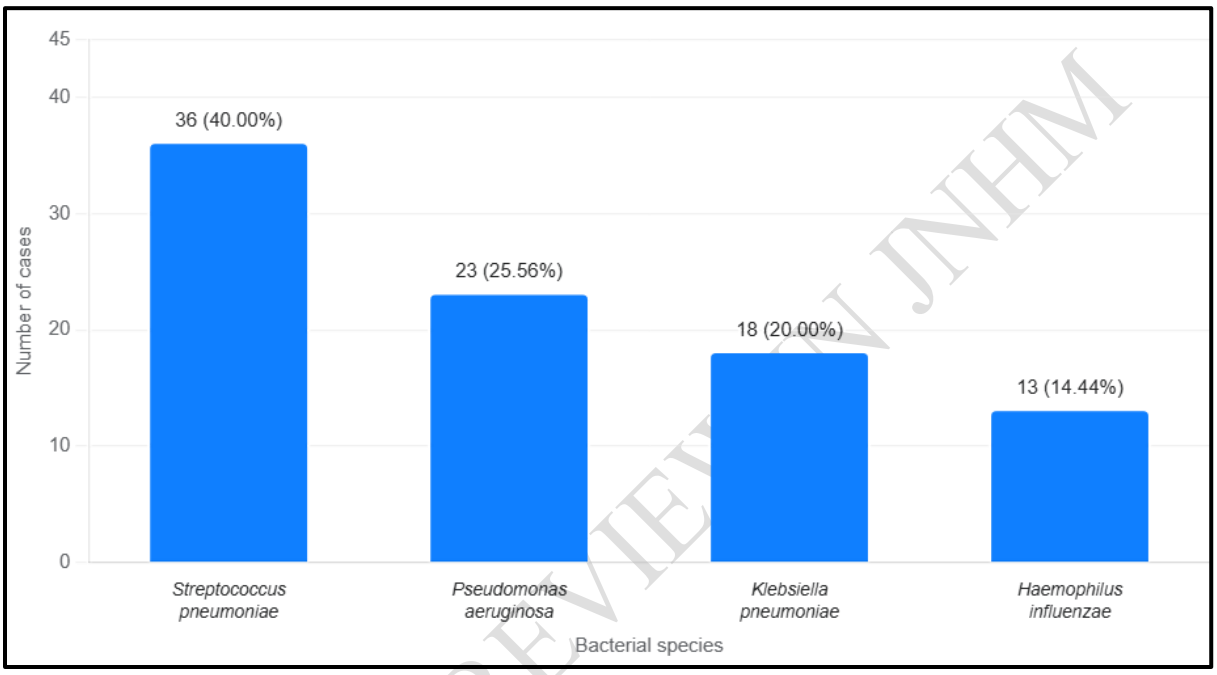

Figure 1. Distribution of patients according to bacterial causative species in respiratory infection

The results in table 2 revealed that the mean serum LCN2 level was considerably higher among patients with bacterial respiratory infections (180.45 ng/mL) compared with control participants (75.28 ng/mL). The independent-samples t-test demonstrated a highly significant difference between the two groups ($t = 16.69$, $P < 0.001$).

Table 2.Comparison ofserum LCN2 levels between patients with bacterial respiratory infectionand controlparticipants

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Groups	No.	Serum LCN2 (ng/mL) Mean ± SD	T Test (P Value)
Patient	**90**	**180.45 ± 55.32**	**16.69**
Control	**90**	**75.28 ± 28.46**	**P < 0.001 (HS)**

HS: High significant at P<0.001

There were slight differences in the levels of serum LCN2 in those who had infections from different bacteria. Those who were infected with *Streptococcus pneumoniae* had the highest average amount of serum LCN2 at 190.42 ng/mL, followed by those who were infected with *Pseudomonas aeruginosa* at 181.63 ng/mL, those who were infected with *Klebsiella pneumoniae* at 174.28 ng/mL, and those who were infected with *Haemophilus influenzae* at 168.46 ng/mL. One-way ANOVA showed that there were no statistically significant differences between the four groups (F = 0.82, P = 0.487).

Table 3.Differences inSerum LCN2in patients' groups according to site of infection

Age Sub-groups	Freq.	Serum LCN2 (ng/mL) Mean ± S.D	F test	T test P-value
Streptococcus pneumoniae	**36**	**190.42 ± 54.36**	**0.82**	**0.89 (NS)**
Pseudomonas aeruginosa	**23**	**181.63 ± 49.51**		
Klebsiella pneumoniae	**18**	**174.28 ± 46.74**		
Haemophilus influenzae	**13**	**168.46 ± 43.83**		

NS: High significant at P<0.001

ROC curve analysis demonstrated that serum LCN2 had an area under the curve (AUC) of 0.83, indicating good discriminatory ability between patients with

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bacterial respiratory infections and healthy controls. At an optimal cut-off point of 69.55 ng/mL, serum LCN2 showed a sensitivity of 78% and a specificity of 62%. The AUC was statistically significant (P = 0.02) (Table 4, figure 2).

Table 4. Receiver operating characteristic (ROC) analysis of Serum LCN2for the diagnosis of bacterial respiratory infection

Biomarker	(AUC)	p-value	Cut-off Point	Sensitivity (%)	Specificity (%)
Serum LCN2	**0.83**	**0.02**	**69.55**	**0.78**	**0.62**

AUC: Area Under the curve

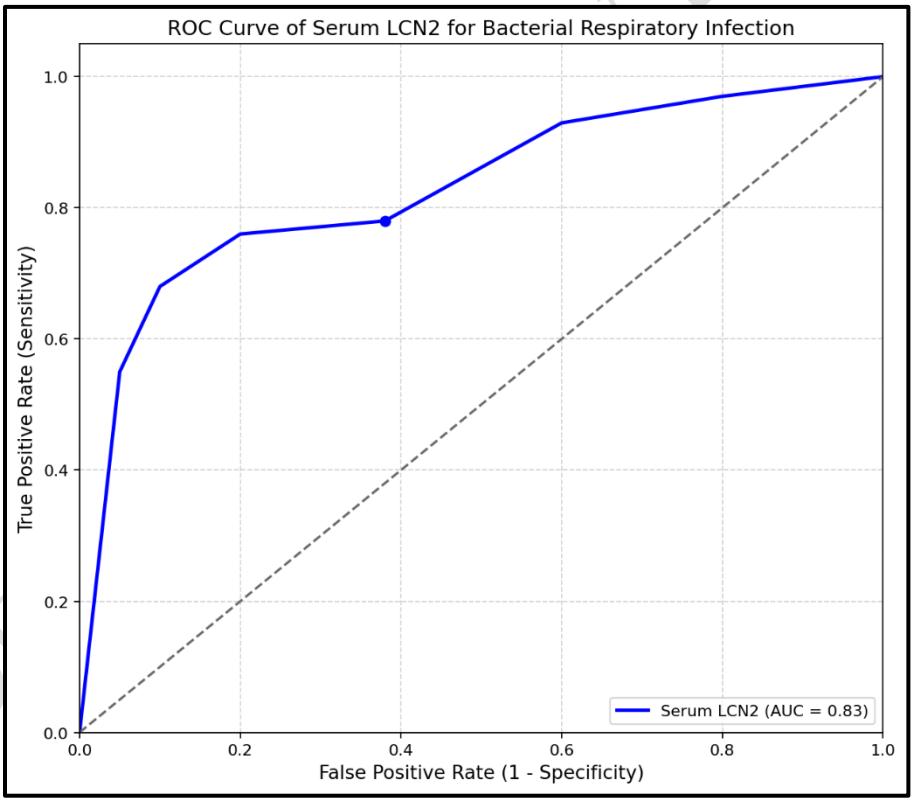

Figure 2. ROC Curve of Serum LCN2 Levels for Diagnosing Bacterial respiratory infection

Discussion

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Serum levels of LCN2 were significantly higher in patients with bacterial respiratory infection than in healthy control subjects. Serum levels of LCN2 averaged 180.45 ng/mL in patients, while they averaged 75.28 ng/mL in control subjects; thus, there was a large difference between these two groups ($P<0.001$). Elevated serum levels of LCN2 could result from the biological function of LCN2 as a primary component of the innate immune system involved in the inflammatory response and antimicrobial defense (Xu et al., 2015). The LCN2, or neutrophil gelatinase-associated lipocalin (NGAL), is secreted by activated neutrophils and can be synthesized by epithelial cells after exposure to proinflammatory cytokines. One of the main roles of LCN2 as an antimicrobial agent is its ability to bind bacterial siderophores and thereby reduce the availability of iron for use by bacteria during their replication (Chakraborty et al., 2012).

The results found in this study are consistent biologically with those published by Warszawska et al. (2013) who reported significantly higher levels of LCN2 in the lungs of humans suffering from bacterial pneumonia. Additionally, they also showed that LCN2 was related to macrophage function and may therefore have an effect on how the body responds to inflammation caused by pneumococcal infection. From the other hand, Yeh et al. (2013) examined plasma LCN2 levels in 61 people suffering from community-acquired pneumonia and 60 individuals without disease. They determined that LCN2 levels decreased after being treated with antibiotics; thus, confirming that LCN2 is part of the body's response to inflammation associated with respiratory infections. In the same line, Yeh et al. (2013) showed that LCN2 levels were positively correlated with numerous pneumonia severity index (PSI) and CURB-65 scores used to assess the severity of pneumonia.

In terms of how serum LCN2 levels are distributed across different types of bacteria, there were clear numerical differences across the four bacterial categories

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identified in this study. Patients who had infections caused by *Streptococcus pneumoniae* had the highest average concentration of serum LCN2 (190.42 ng/mL), followed by patients with infections caused by *Pseudomonas aeruginosa* (181.63 ng/mL), patients with infections caused by *Klebsiella pneumonia*e (174.28 ng/mL) and patients with infections caused by *Haemophilus influenzae* (168.46 ng/mL). However, none of these differences reached statistical significance (F=0.82, p=0.487).The fact that there are no statistically significant differences implies that while individual species of bacteria may initiate varied types of inflammatory responses, the overall systemic LCN2 response that each bacterial infection produces may be similar (Yeh et al., 2013). This finding is significant since LCN2 production is not limited to a single type of bacterial pathogen, but can instead be produced by multiple innate immune signaling pathways that are activated in response to bacterial infection. In this line, Warszawska et al. (2013) demonstrated that LCN2 was involved in pneumococcal pneumonia, and also found that there were elevated levels of LCN2 in the lungs of people who had developed bacterial pneumonia. Furthermore, these researchers suggested that LCN2 could be involved in regulating macrophage polarization and inflammation. In a similar vein, the experimental study conducted by Bachman et al. (2009) established a vital role for LCN2 as a protective agent against pulmonary *Klebsiella pneumoniae* infection, as it has been shown to assist with the removal of bacteria via iron sequestration.While previous studies demonstrate that LCN2 is involved in response to various types of respiratory pathogens, there are few studies that make direct comparisons among multiple bacterial species. Therefore, the numerical differences identified in this study do not provide evidence that any single bacterial species causes significantly higher levels of LCN2 production compared to all other bacterial species (Huang et al., 2022).

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The ROC curve analysis of serum LCN2 in this study resulted in an AUC of 0.83, which was statistically significant with a p-value of 0.02. These results show that serum LCN2 can be used to distinguish between patients who have bacterial respiratory infections and those who are healthy. With a cut-off value of 69.55 ng/mL, the biomarker has a sensitivity of 78% and specificity of 62%. Although the high sensitivity of serum LCN2 will allow for identification of many of the infected individuals, the moderate specificity of serum LCN2 will result in identification of some individuals who do not have bacterial respiratory infection as having elevated levels of serum LCN2.The findings of this study have some support from the research conducted by Huang et al. (2014) on potential biomarkers for pneumonia in African children. The researchers found LCN2 to be an important protein that correlates with severe cases of pneumonia; they reported an AUC of 0.71 when comparing severe vs. non-severe cases of pneumonia. Additionally, LCN2 was shown to have significant correlation with bacteremia and pneumococcal bacteremia. While the AUC reported in the previous studyby Huang et al. (2014) was lower than what we have found in our study, both studies show that LCN2 could be a relevant biomarker in identifying individuals at risk for developing respiratory infections.

In addition, Boix-Palop et al. (2023) measured plasma LCN2 levels in 130 adult patients admitted for community-acquired pneumonia. While they found that patients who had been diagnosed as having bacterial pneumonia had significantly higher plasma LCN2 levels (122.0 ng/mL) than did patients who were diagnosed as having non-bacterial pneumonia (89.7 ng/mL), the difference between the two groups was not statistically significant. Their assessment of the discriminative power of plasma LCN2 as a marker of bacterial infection was modest, as indicated by an AUC of 0.62. These findings contrast with the much larger AUC (0.83) that we obtained in our current study. It is possible that these discrepancies could arise

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from variations in the characteristics of the study populations, the types of samples used for analysis, the laboratory procedures employed for measuring LCN2, the nature of the diseases studied, and the makeup of the comparison groups. For example, comparing patients with documented bacterial infections to healthy individuals would likely provide greater discriminatory power than would comparing patients with bacterial pneumonia to patients with viral or other types of non-bacterial respiratory disease. On the other hand, Esposito et al. (2016)studied serum LCN2 in hospitalized pediatric patients who had contracted community acquired pneumonia. What they found was that serum LCN2 levels dropped significantly within five days of beginning treatment. However, serum LCN2 could not be used to distinguish between bacterial and viral pneumonia as it had a low AUC value (0.51). These results indicate that serum LCN2 may represent a measure of the patient's overall inflammatory status and not necessarily the specific etiology of the infection.

In addition, Venge et al. (2017) studied human neutrophil lipocalin (HNL) in whole blood that was stimulated by activation in patients with respiratory tract infections. The authors reported that the HNL was able to discriminate well between bacterial and viral respiratory tract infections, as indicated by an AUC of 0.91. While HNL and serum LCN2 are both associated with the same neutrophil protein system, they vary significantly in how they are measured and their respective biological properties. This means that although the results of this study are complementary to the results of the serum LCN2 study, they do not directly validate them; instead, they add weight to the idea that neutrophil-derived lipocalins may play an important role in assessing respiratory tract infections.

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Conclusion

The present study showed a much higher amount of serum LCN2 in those who had bacterial respiratory tract infections than what was found in the control group of healthy people. The elevation of serum LCN2 may indicate the activation of both innate immune responses and inflammatory reactions due to bacterial infection. While there were some numerical differences in serum LCN2 levels among various bacterial species, they did not reach statistical significance. The ROC curve analysis demonstrated that serum LCN2 had high discriminatory power with moderate specificity. These results imply that serum LCN2 could serve as a valuable additional biomarker in assessing bacterial respiratory infections; however, additional studies will be needed to confirm this.

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