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RESEARCH ARTICLE

KALLISTATIN LEVELS IN CHILDREN DIAGNOSED WITH BRONCHITIS

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ABSTRACT

Purpose: The aim of this study is to evaluate the levels of kallistatin in the plasma of children diagnosed with bronchitis and to compare them with healthy control subjects.
Material and Methods: A total of 89 participants, including 16 patients diagnosed with bronchitis and taking medication with the diagnosis of tonsillitis (BT), 26 patients diagnosed with bronchitis only (B), and 47 healthy controls who attended the same outpatient clinic for routine control, were included in the study.
Results: When we looked at the differences by dividing the patient group into 2 groups (B, BT), we found that the kallistatin levels in the BT group were significantly higher than both the B group and the healthy control groups. There was no significant difference in kallistatin levels between the healthy controls and the B group. We found that the AUC for kallistatin was 0.631 in the ROC analysis performed between the patient (B+BT) and control groups.
Conclusion: Kallistatin levels were significantly higher in the patient group than in the control group. More comprehensive studies with repeated kallistatin measurements are needed to understand whether kallistatin levels are important in the diagnosis and management of patients with bronchitis and to confirm our findings.

Keywords: Bronchitis, enzyme-linked immunosorbent assay, kallistatin

INTRODUCTION

Bronchitis is an inflammation of the trachea and large airways characterised by coughing. While acute bronchitis is usually caused by upper respiratory tract infections, chronic bronchitis is the result of long-term exposure to irritants such as smoking. Acute bronchitis is a important reason of hospitalization among infectious diseases in children (1,2). Although viruses play a major role in the etiology of acute bronchitis at a high rate (about 90%), it is known that bacteria rarely (about 10%) also play a role. In general, as a result of inflammation caused by microbes such as viruses or bacteria, edema in the mucosa, thickening of the bronchial walls, and increase in bronchial secretion occur. The basis of treating acute bronchitis is symptomatic treatment. The incidence of the disease varies with age and season (1,3,4).

Kallistatin is an endogenous serine proteinase inhibitor that is naturally produced in the body and has many biological functions. Kallistatin has two structural domains, the active site and the heparin binding site. Through these domains, kallistatin exerts vasodilator, anti-angiogenic, antioxidant and anti-inflammatory effects (5,6). It regulates oxidative stress, cell apoptosis, the expression of several genes, and controls the activation of several signalling pathways (5,7). The active site of kallistatin stimulates the expression of endothelial nitric oxide synthase (eNOS) and sirtuin1 (SIRT1), thereby

inhibiting tissue kallikrein activity. Kallistatin forms a covalent complex with its heparin binding site to specifically inhibit human tissue kallikrein. The heparin-binding domain is required to inhibit vascular endothelial growth factor (VEGF)-induced angiogenesis and tumour necrosis factor-α (TNF-α)-induced inflammation (Figure 1) (6,7). Most studies have mentioned the protective effect of increasing kallistatin levels against disease. Studies have shown that the levels of kallistatin are reduced in patients with liver disease, septic shock, severe pneumonia, and acute respiratory distress syndrome also support this information (5,6,8,9). There are also studies reporting that plasma kallistatin levels decrease in sepsis and severe inflammation, and that low kallistatin levels are linked to mortality in community-acquired pneumonia (10,11).

Based on the information in the literature, we set out to evaluate the plasma kallistatin levels at the time of initial diagnosis in children with bronchitis and to compare the data we obtained with the kallistatin levels and other biomarkers of the healthy control group. We do not know of any other published in the literature evaluating kallistatin levels in children diagnosed with bronchitis. Thus, our study is original and contributes to the literatüre.

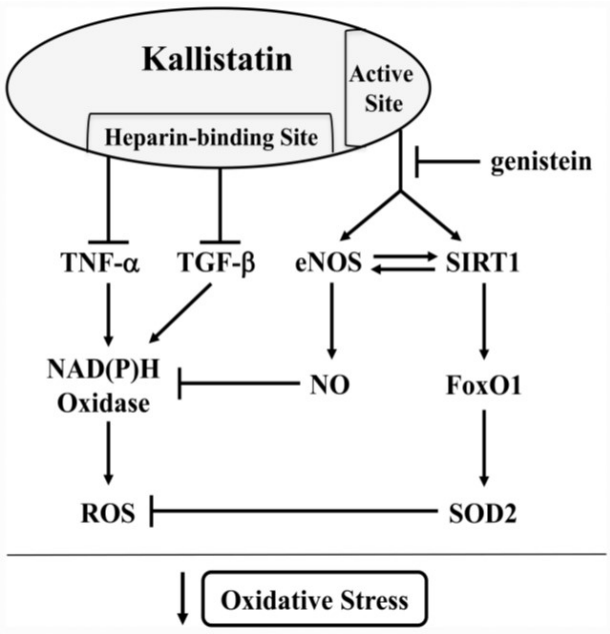

Figure 1. Structure and activity of kallistatin

MATERIAL AND METHODS

Study population

This study was conducted at Seydişehir State Hospital between 10 April 2023 and 10 July 2023. After obtaining the informed consent, the approval of the Ethics Committee and the institutional approval of the hospital, the sample collection procedures were performed. No invasive procedure were performed during the study. A total of 89 participants, including 16 patients diagnosed with bronchitis and taking medication with the diagnosis of tonsillitis (BT), 26 patients diagnosed with bronchitis only (B), and 47 healthy controls without any disease who attended the same outpatient clinic for routine control, were included in the study (Figure 2). The plasma samples of the patient and control groups were obtained from the blood that was taken during the routine analyses of these patients. Plasma samples processed in the laboratory were collected in Eppendorf tubes. It was kept at -80°C until kallistatin measurement. Age, gender, presence of additional diseases, medications and other laboratory information for the patient and control groups were obtained from the hospital's automated system and by interviewing the patients.

Patient group exclusion criteria: >18 years of age, presence of chronic diseases and any other disease (asthma, pneumonia, allergy, influenza, etc.).

Control group exclusion criteria: >18 years of age, presence of any disease such as asthma, pneumonia, allergy, influenza, bronchitis, tonsillitis, drug use etc.

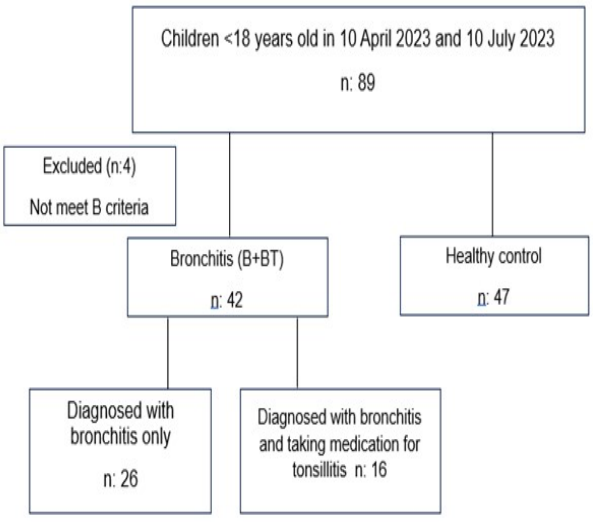

Figure 2. Flowchart used to select groups.

Table 1. Comparison of age and laboratory parameters between patient and control groups.

Variables	Patient (B+BT= n: 42)	Control (n: 47)	P value
[a]Age	2.43 (1.00-3.00)	2.9 (2.00-3.90)	0.71
[b]WBC ($10^3/mm^3$)	9.33±3.33	8.23±2.41	0.08
[b]HGB (g/dL)	12.01±1.33	13.12±1.16	0.00*
[b]RBC ($10^6/mm^3$)	4.65±0.56	4.91±0.46	0.01*
[b]MPV (fL)	9.34±0.79	9.49±0.75	0.34
[b]PDW (fL)	9.85±1.45	10.34±1.52	0.13
[b]PLT ($10^3/mm^3$)	337.07±112.74	329.12±74.35	0.70
[a]MCV (fL)	78.75 (76.27-83.22)	80.90 (78.30-86.60	0.02*
[a]MCH (pg)	26.15 (24.80- 27.70)	27.20 (26.00-28.40)	0.04*
[a]MON ($10^3/mm^3$)	0.77 (0.55-1.07)	0.59 (0.46-0.73)	0.00*
[a]EOS ($10^3/mm^3$)	0.14 (0.05-0.32)	0.18 (0.09-0.30)	0.31
[a]BAS ($10^3/mm^3$)	0.03 (0.02-0.05)	0.04 (0.03-0.05)	0.47
[a]Neutrophil ($10^3/mm^3$)	3.26 (1.39-4.38)	3.19 (2.22-4.04)	0.42
[a]Fasting glucose (mg/dL)	88.00 (85.00-93.00)	85.00 (80.00-89.00	0.07
[a]AST (U/L)	36.50 (30.75-41.25)	26.00 (20.00-32.02)	0.00**
[a]ALT (U/L)	16.00 (12.00-20.50)	15.00 (11.00-18.00)	0.18
[a]CRP (mg/L)	4.10 (1.00-7.50)	1.00 (1.00-3.00)	0.00*
[a]Albumin (g/L)	44.30 (42.54-45.36)	46.32 (44.52-47.22)	0.00**
[b]Urea (mg/dL)	18.13±6.78	19.26±5.70	0.13
[b]Creatinine (mg/dL)	0.39±0.10	0.46±0.12	0.06
[b]Na (mmol/L)	137.60±2.25	138.66±1.79	0.06
[b]K (mmol/L)	4.71±0.49	4.42±0.29	0.00*
[b]Ca (mg/dL)	9.88±0.52	9.95±0.51	0.57
[b]Mg (mg/dL)	2.21±0.20	2.15±0.21	0.06

*a: Mann-Whitney U test, b: Independent samples t-test, *p<0.05, **p<0.01*

Biochemical analysis

Enzyme-linked immunosorbent assay (ELISA) was used to measure plasma kallistatin levels. BT LAB brand Human Kallistatin, SERPINA4 ELISA Kit Catalog No: E3392Hu, Shanghai, China) was used. The manufacturer's instructions were followed for the ELISA study. The results of this study were read using a Multiskan Sky Thermo (A.B.D.) device. A Combi Wash (Human) washer was used in the study. Intra- and inter-assay variation were <5.5% and <10%, respectively. The minimum detectable concentration of kallistatin was 0.022 ng/mL, and the diagnostic interval of the assay was 0.05-20 ng/mL.

Table 2. Comparison of the groups with regard to the kallistatin levels.

Laboratory findings	Patient (B+BT = n: 42)		Control (n: 47)	p value
Kallistatin (ng/mL)	7.20 (4.45-17.10)		4.20 (3.10-8.90)	0.03*
	Patient (B, n: 26)	**Patient (BT, n: 16)**	**Control (n: 47)**	
Kallistatin (ng/mL)	[a, c] 5.45 (2.78-7.10)	[a, b] 19.50 (11.30-22.10)	[b, c] 4.20 (3.10-8.80)	a:<0.01** b: <0.01** c: >0.05

Data are expressed as median-IQR, Statistics for two groups: Mann-Whitney U, Statistics for three groups: Kruskal Wa Test, *p<0.05, **p<0.01

Statistical analysis

SPSS for Windows version 18.0 was used for data entry and statistical analysis (SPSS Inc. Chicago, IL, USA). The conformity of the data to the normal distribution was tested using visual and analytical methods. Arithmetic mean, standard deviation (SD), and median (1st quartile-3rd quartile (IQR)) were used to evaluate numerical data. Categorical data were summarised using frequencies and percentages. To compare categorical data, the chi-square test ($\chi 2$) was used. Non-normally distributed numerical data were compared using the Man-Whitney U test. The Kruskal-Wallis test was used for the evaluation of three or more groups with numerical data that were not normally distributed. Pairwise comparisons between groups with significant Kruskal-Wallis test results were post-hoc Man-Whitney U test with Bonferroni correction. The Spearman correlation coefficient has been used to analyse the correlations between numerical variables that are not normally distributed. Spearman correlation coefficients were considered to be highly correlated if they were less than 0.19, low if they were 0.20-0.39, moderate if they were 0.40-0.69, high if they were 0.70-0.89, and very high if they were greater than 0.90. The diagnostic decision-making properties of kallistatin levels in predicting disease were assessed using receiver operating characteristics (ROC) curves. Statistical significance has been defined as $p < 0.05$.

Ethical Approval

The KTO Karatay University, Faculty of Medicine, Ethics Committee for Non-Drug and Medical Device Research, has approved this study (Date: 31.03.2023, Number: 2023/011) in accordance with the tenets of the Declaration of Helsinki. The article complied with research and publication ethics.

RESULTS

Twenty-six (12F, 14M) patients diagnosed with bronchitis (B), 16 (10F, 6M) patients diagnosed with bronchitis and tonsillitis (BT), 47 (26F, 21M) healthy controls were included in this study. Among the patients diagnosed with bronchitis (n: 42), there were also patients (n: 16) who used drugs to treat tonsillitis. There were no other comorbidities in the patient group. Mean age of patients (B+BT) was 2.43 years, mean age of controls was 2.9 years. Between patient (B+BT) and control group there was no difference in age and gender ($p>0.05$).

When comparing the patient (B+BT) and control groups in terms of laboratory parameters, HGB, RBC, MCV, MCH, albumin were significantly lower, AST, CRP, K, monocytes, and kallistatin were significantly higher in the patient group compared to the control group ($p<0.05$). The kallistatin levels were 7.20 ng/mL (4.45 - 17.10) in the patient group and 4.20 ng/mL (3.10 - 8.90) in the control group. Table 1 and Table 2 show the laboratory data of the patient and control groups. When we compared the laboratory parameters of the patient group within themselves, there was no statistically significant difference between the B and BT patient groups in terms of any other parameter except kallistatin ($p>0.05$). The kallistatin levels in group B were 5.45 ng/mL (2.78-7.10), and kallistatin levels in group BT were 19.50 ng/mL (11.30-22.10).

Comparing the laboratory parameters of the 3 groups (B, BT and control), AST and CRP levels were significantly higher in both the B and BT groups than in the healthy control. In addition, kallistatin levels were significantly higher in the BT group than in the B

Table 3. Spearman's correlation coefficients of patient and control groups

	Correlations	Correlation coefficient (r)	Level	P value
Patient (B+BT= n: 42)	Age - Creatinine	0.740	High	p<0.01
	Age - Urea	0.710	High	
	Kallistatin - Creatinine	-0.469	Moderate	
	Kallistatin - Age	-0.397	Low	
Control (n: 47)	Kallistatin - Creatinine	-0.538	Moderate	
	Kallistatin - D vit	0.457	Moderate	
	Kallistatin - Mg	0.446	Moderate	
	Kallistatin - Age	-0.440	Moderate	
	Age - Creatinine	0.409	Moderate	

Statistics: Spearman's correlation test, p < 0.05 statistical significance

and control groups (p<0.01). There was no statistically significant difference in kallistatin between the B and control groups (p>0.05) (Table 2). When all participants' data were analysed for correlations, there was a moderately significant negative correlation between kallistatin and age (r: -0.554, p: 0.00), kallistatin and creatinine (r: -0.581, p: 0.00), a moderately significant positive correlation weakly significant positive correlation between kallistatin and vitamin D (r: 0.381, p: 0.009), kallistatin and WBC (r: 0.360, p: 0.001). Table 3 shows the significant correlation values of the patient and control groups.

We performed ROC curves and AUC analyses to investigate the predictive power of kallistatin. We found that the AUC for kallistatin was 0.631 (p=0.033, CI=0.512- 0.751) in the ROC analysis performed between the patient (B+BT) and control groups. Figure 3 shows the ROC analysis graph.

DISCUSSION

In this study, healthy controls and patients diagnosed with bronchitis were compared for kallistatin levels. Our findings showed that kallistatin levels were significantly higher in the patient groups than in the control groups.

Bronchitis is among the lower respiratory tract infections that are frequently seen at early ages. There is no specific laboratory parameter that can be used to diagnose bronchitis (3,12). There are studies that suggest a significant association between low hemoglobin levels and lower respiratory tract infections (13-15). In a 2021 study of 101 infants diagnosed with acute bronchiolitis and 62 healthy controls, HGB levels were found to be lower in the patient group and it has been reported that HGB levels and the severity of bronchiolitis have a significantly negative correlation (16). In our study, there was no patient diagnosed with anemia, but HGB, RBC, MCV and MCH levels were significantly lower in the patient group than in the healthy control group. When we compared the patient group as B and the BT group, there was no significant difference in laboratory parameters between the groups.

CRP is an acute phase reactant that increases in the blood during inflammatory reactions. CRP elevation is seen in most inflammatory diseases. In a study of 149 infants diagnosed with bronchiolitis, increased plasma CRP levels and the CRP/albumin ratio were associated with the need for advanced respiratory support in infants with acute bronchiolitis. Plasma albumin is a well-known negative acute phase reactant and its low level may indicate a poor prognosis. A study showing that hypoalbuminemia increases the risk of apnea in bronchiolitis supports this information. Another study showed an association between hypoalbuminemia and the need for neonatal intensive care (17). In our study, we found that the levels of CRP were higher and the levels of albumin were lower in the group of patients compared to the control group, which supports the literature.

Kallistatin is a protein produced naturally in the body and has many biological functions. Kallistatin is known to play an important role in the prevention of several diseases, through anti-angiogenic, anti-

inflammatory, anti-apoptotic and antioxidant effects. (6,7,18,19). Kallistatin levels are reduced in animal models of hypertension, septic shock, diabetes mellitus and liver neoplasia (20-23). However, in patients with diabetic vascular complications and rheumatoid disease, kallistatin levels have been shown to be elevated (24-26). Kallistatin has been studied in various diseases, but there is no literature investigating the relationship between bronchitis and kallistatin. If we look at the studies that have investigated kallistatin levels in community-acquired pneumonia, there are data that kallistatin levels are lower in such diseases than in the control group. A 2013 study of 54 patients with community-acquired pneumonia and 17 healthy controls reported that lower kallistatin levels were associated with more severe disease risk and increased mortality. A study investigating kallistatin in community-acquired pneumonia (CAP) found that kallistatin was significantly depleted in CAP patients (8.3 µg/mL) compared to healthy subjects (17.2 µg/mL). In the study, they found an AUC value of 0.683 for kallistatin levels measured on the first day of ICU admission between the surviving and non-surviving groups. In the study, low plasma kallistatin levels on day 1 were associated with the development of septic shock and acute respiratory distress syndrome in patients with severe CAP. In addition, it was stated in the study that there was a negative significant correlation between kallistatin levels and CRP levels (10). The results of another study, conducted in 2018 on 53 children and 55 healthy controls diagnosed with community-acquired pneumonia, reported that the kallistatin levels in the patient group at admission were significantly higher than in the control group. When this study made a comparison by dividing the patient group into 3 subgroups (hospitalised, those requiring mechanical ventilation and ex) according to their complications, it also reported that the kallistatin levels in these groups were significantly higher than in the healthy control group (27). The results of the study by Hangül M. et al. (27) are contrary to other information and expectations in the literature. To the best of our knowledge, this is the first study to show the role of kallistatin in children who have been diagnosed with bronchitis. Kallistatin levels were significantly higher in the patient group than in the control group in our study. In the ROC analysis performed between the patient (B+BT) and control groups, we found that the AUC for kallistatin was 0.631. When we looked at the differences by dividing

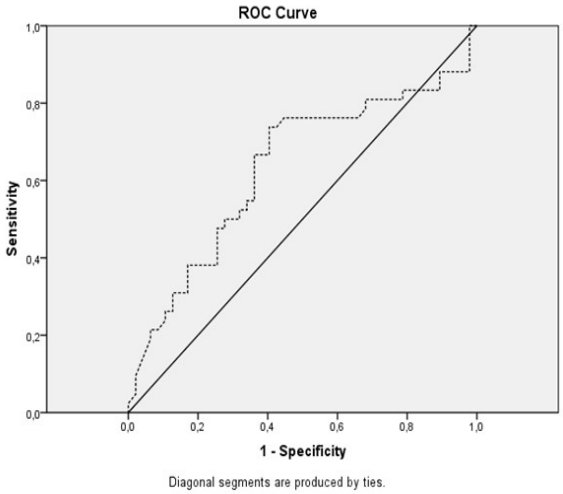

Figure 3. The ROC analysis for kallistatin (AUC: 0.631).

the patient group into 2 groups (B, BT), we found that the kallistatin levels in the BT group were significantly higher than both the B group and the healthy control groups. Between the healthy controls and the B group, there was no significant difference in kallistatin levels. We believe that the significantly higher kallistatin levels in the BT group compared to the other two groups may be due to the use of antibiotics to treat tonsillitis in patients in the BT group, or that kallistatin levels may have increased during the recovery period. We could not find any information in the literature on the effect of antibiotic use on kallistatin levels to compare with our study.

Study limitations

The low number of patients in the study and the fact that some patients diagnosed with bronchitis were treated for tonsillitis are important limitations. Most studies have emphasised the need for repeated measurements for kallistatin. Another limitation of our study is the use of plasma samples taken at the time of initial diagnosis and the inability to perform repeated measurements of kallistatin.

CONCLUSION

We designed this study expecting kallistatin levels to be lower in the group of patients with bronchitis, but the fact that kallistatin levels were not statistically different in the patient group compared to the healthy control group showed that kallistatin measurement was not useful for the diagnosis and follow-up of bronchitis. As a result, kallistatin levels were significantly higher in the patient group than in the

control group. The high kallistatin levels in the patient group were due to the high kallistatin levels in the group of 16 patients (BT) with bronchitis who were treated for tonsillitis. There was no difference in kallistatin levels between the group diagnosed with bronchitis only and the healthy control group. More comprehensive studies with repeated kallistatin measurements are needed to understand whether kallistatin levels are important in the diagnosis and management of bronchitis and to confirm our findings.

Author Contributions: KY, SID planned to work. KY, TD did ELISA's work of plasma. KY, SID, TD designed the study and wrote the paper. SID obtained clinical data. KY performed statistical analysis. KY sent the article to the journal. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Conflict of Interests: No competing interests declared.

Ethical Approval: The Ethics Committee for Non-Drug and Medical Device Research of KTO Karatay University, Faculty of Medicine, has approved this study in accordance with the tenets of the Declaration of Helsinki (Decision Date: 31.03.2023, Number: 2023/011). The article complied with research and publication ethics. Informed consent was obtained from all of the individuals who participated in this study.

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REFERENCES

1. Kinkade S, Long NA. Acute bronchitis. Am Fam Physician 2016;1;94(7):560-5.
2. Clark TW, Medina MJ, Batham S, Curran MD, Parmar S, Nicholson KG. Adults hospitalised with acute respiratory illness rarely have detectable bacteria in the absence of COPD or pneumonia; viral infection predominates in a large prospective UK sample. J Infect 2014;69(5):507-15.
3. Fretzayas A, Moustaki M. Etiology and clinical features of viral bronchiolitis in infancy. World J Pediatr 2017;13(4):293-9.
4. Sung FC, Wei CC, Muo CH, et al. Acute bronchitis and bronchiolitis infection in children with asthma and allergic rhinitis: A retrospective cohort study based on 5,027,486 children in taiwan. Viruses 2023;15(3):1-10.
5. Lin WC, Chen CW, Chao L, Chao J, Lin YS. Plasma kallistatin in critically ill patients with severe sepsis and septic shock. PLoS One 2017;12(5):1-15.
6. Wang G, Zou J, Yu X, Yin S, Tang C. The antiatherogenic function of kallistatin and its potential mechanism. Acta Biochim Biophys Sin (Shanghai) 2020;52(6):583-9.
7. Chao J, Li P, Chao L. Kallistatin: double-edged role in angiogenesis, apoptosis and oxidative stress. Biol Chem 2017;398(12):1309-17.
8. Lin WC, Chen CW, Huang YW, et al. Kallistatin protects against sepsis-related acute lung injury via inhibiting inflammation and apoptosis. Sci Rep 2015;12463:1-16.
9. Liu Y, Bledsoe G, Hagiwara M, Shen B, Chao L, Chao J. Depletion of endogenous kallistatin exacerbates renal and cardiovascular oxidative stress, inflammation, and organ remodeling. Am J Physiol Renal Physiol 2012;303(8):1230-8.
10. Lin WC, Lu SL, Lin CF, et al. Plasma kallistatin levels in patients with severe community-acquired pneumonia. Crit Care 2013;17(1):1-10.
11. Kim T, Suh GJ, Kwon WY, Kim KS, Jung YS, Shin SM. Lower serum kallistatin level is associated with 28-day mortality in patients with septic shock. J Crit Care 2018;48:328-33.
12. Mahowald M, Shahan B, Forbes D. Respiratory conditions: Lower respiratory tract infections. FP Essent 2019;486:19-25.
13. Behairy O, Mohammad O, Elshaer O. Iron-deficiency anemia as a risk factor for acute lower respiratory tract infections in children younger than 5 years. Egypt J Bronchol 2018;12(3):352-7.
14. Mourad S, Rajab M, Alameddine A, Fares M, Ziade F, Abou MB. Hemoglobin level as a risk factor for lower respiratory tract infections in Lebanese children. N Am J Med Sci 2010;2(10):461-6.
15. Ramakrishnan K, Harish PS. Hemoglobin level as a risk factor for lower respiratory tract infections. Indian J Pediatr 2006;73(10):881-3.
16. Celik E, Celik SF, Güngör S, Dursun A. Impact of anaemia on the severity of acute bronchiolitis in infants. Journal of Nepal Paediatric Society 2021; 41(1): 73-9.
17. Rodriguez-Gonzalez M, Estepa-Pedregosa L, Estalella-Mendoza A, et al. Routine laboratory test to assess the need of respiratory support in acute bronchiolitis. Pediatr Pulmonol 2022;57(5):1339-47.
18. Gao L, Yin HS, Smith RJ, Chao L, Chao J. Role of kallistatin in prevention of cardiac remodeling after chronic myocardial infarction. Lab Invest 2008;88:1157-66.
19. Miao RQ, Agata J, Chao L, Chao J. Kallistatin is a new inhibitor of angiogenesis and tumor growth. Blood 2002;100:3245-52.

20. Chao J, Chai KX, Chen LM, et al. Tissue kallikrein-binding protein is a serpin. I. Purification, characterization, and distribution in normotensive and spontaneously hypertensive rats. J Biol Chem. 1990;265:16394-16401.
21. Shen B, Hagiwara M, Yao YY, Chao L, Chao J. Salutary effect of kallistatin in salt-induced renal injury, inflammation, and fibrosis via antioxidative stress. Hypertension. 2008;51:1358-1365.
22. Chao J, Chen LM, Chai KX, Chao L. Expression of kallikrein-binding protein and alpha 1-antitrypsin genes in response to sex hormones, growth, inflammation and hypertension. Agents Actions Suppl. 1992;38(1):174-181.
23. Luo Q, Siconolfi-Baez L, Annamaneni P, Bielawski MT, Novikoff PM, Angeletti RH. Altered protein expression at early-stage rat hepatic neoplasia. Am J Physiol Gastrointest Liver Physiol. 2007;292:1272-1282.
24. McBride JD, Jenkins AJ, Liu X, et al. Elevated circulation levels of an antiangiogenic SERPIN in patients with diabetic microvascular complications impair wound healing through suppression of Wnt signaling. J Invest Dermatol. 2014;134:1725-1734.
25. Jenkins AJ, McBride JD, Januszewski AS, et al. Increased serum kallistatin levels in type 1 diabetes patients with vascular complications. J Angiogenes Res. 2010;2:19:1-8.
26. Wang CR, Chen SY, Shiau AL, et al. Upregulation of kallistatin expression in rheumatoid joints. J Rheumatol. 2007;34:2171-2176.
27. Hangul M, Ozturk D, Keti DB, Demirkan FG, Kose M. Plasma kallistatin levels in children with community-acquired pneumonia. Pediatr Allergy Immunol Pulmonol 2018;31(3):146-50.