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Erythrocyte sedimentation rate and red blood cell indices association in pediatrics patients with fever and cough: A cross-sectional study

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Abstract

Background and Aims: The erythrocyte sedimentation rate (ESR) is an essential inflammatory marker in treating some patients, particularly children. The level of ESR can be affected by red blood cell (RBC) indices, and not considering this can complicate the interpretation of ESR and the treatment and follow-up of patients. The study aimed to assess the association between ESR and RBC indices in children hospitalized with fever and cough in the pediatric ward of Imam Khomeini Hospital, Jiroft, in 2023.

Methods: A cross-sectional study was conducted to measure the association between ESR and RBC indices in children hospitalized with fever and cough in the pediatric ward of Imam Khomeini Hospital, Jiroft, in 2023. A total of 156 patients participated in the study. SPSS software was used for statistical analysis.

Results: The mean age of participants was 27.26 ± 3.14 months. The results showed that there is a significant negative correlation between ESR and RBC, $r = -0.282$ ($p < 0.001$), and ESR and hematocrit (HCT), $r = -0.215$ ($p = 0.007$). Also, the results demonstrated that there is a significant positive correlation between ESR and mean corpuscular volume (MCV), $r = 0.159$ ($p = 0.048$), ESR and mean corpuscular hemoglobin (MCH), $r = 0.214$ ($p = 0.007$), and ESR and mean cell hemoglobin concentration (MCHC), $r = 0.209$ ($p = 0.009$). There was a negative correlation between ESR and hemoglobin (Hb), $r = -0.98$ ($p = 0.225$), but this correlation was insignificant.

Conclusion: This study showed an association between ESR and RBC indices in hospitalized children with complaints of fever and cough. So, it is necessary that physicians and treatment staff pay attention to the RBC indices while interpreting and following up the results of ESR to complete the treatment process of patients.

KEYWORDS

cough, erythrocyte sedimentation rate, fever, pediatrics, red blood cell indices

1 | INTRODUCTION

Inflammation is a response of immune tissue to an external stimulus that occurs in many infectious and noninfectious diseases.[1] There are many inflammatory indices to measure inflammation and follow-up of inflammatory diseases. One of the nonspecific parameters indicating inflammation is the erythrocyte sedimentation rate (ESR), which can indirectly estimate the function of inflammatory cytokines.[2,3] The ESR is determined by the sedimentation rate of a blood sample after 1 h.[4] ESR is a valuable parameter for detecting inflammation. Also, it is practical in diagnosing infection, trauma, tumors, and malignancy, as well as showing the progression of the disease or treatment.[2,4] Various factors can affect the ESR. These include cellular factors, such as the size, concentration, and accumulation ability of cells, as well as plasma proteins like haptoglobin, glycoprotein α1, and globulin, which can affect plasma viscosity.[5] However, new inflammatory biomarkers with higher sensitivity are being discovered; ESR remains one of the most commonly used inflammatory biomarkers due to its affordability and simplicity.[6,7] Previous studies have shown that erroneous results in the interpretation of ESR may occur due to abnormal RBC shape, low room temperature, and excessive use of anticoagulants.[8]

Red blood cell (RBC) indices measure the size, shape, and quality of RBCs. RBC, hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC) are RBC indices.[9–11] As mentioned, the ESR is affected by various factors, including the size and ability of RBC. A literature review has shown that the level of blood inflammatory indices such as ESR can be influenced by RBC indices. Some studies have shown that more giant RBCs cause higher ESR.[12–14] Therefore, to have a correct interpretation of the ESR level in the treatment and follow-up of patients, it is necessary to know the effect of RBC indices on it.

Even though in some previous studies, the association between ESR and some RBC indices has been measured, these studies were mainly conducted in adults, and this association has not been definitively investigated in children. Since the normal range of inflammatory markers and the level of erythrocyte indices in children and adults are different because the level of them is age-dependent, the results of previous studies on the relationship between ESR and erythrocyte indices in adults cannot be generalized to the pediatric population, so the relationship between ESR and RBC indices in the pediatric should also be studied. Also, previous studies have investigated the relationship between ESR and RBC indices mainly in healthy populations. At the same time, it should be seen if the person is involved in a disease, what will be the relationship between ESR and RBC indices. In children who are hospitalized with symptoms of fever and cough, one of the basic tests requested for them is ESR and RBC indices, so the present study aims to determine the association between ESR and RBC indices. The present study was performed on children hospitalized with fever and cough in the pediatric ward of Imam Khomeini Hospital, Jiroft, in 2023 to assess the association between ESR and RBC indices.

2 | MATERIALS AND METHODS

2.1 | Design, settings, and participants

This cross-sectional study was conducted on the target population of children admitted to the pediatric ward of Imam Khomeini Hospital, Jiroft, between June 11, 2023 and July 21, 2023. The study aims and objectives were clearly explained to the participants and their legal guardians before they entered the study. This study was conducted following the Helsinki Declaration. The inclusion criteria were[1] age under 16 and[2] hospitalization for fever and cough. Exclusion criteria were having a known underlying disease or long-term use of certain drugs. All study participants met the inclusion criteria, and no one was excluded.

2.2 | Data collection procedure

ESR and complete blood count (CBC) tests were requested by the attending physician for the patients who entered the study. RBC indices included RBCs, Hb, HCT, MCV, MCH, and MCHC. After the test results were prepared, they were placed in the patient file records, and then the researchers extracted the required data based on the information in the patient file records. A total of 156 patients participated in the study.

2.3 | Sample size

A convenience sampling method was used with a 5% level of significance and 80% power to detect a minimum of 5% difference. All the children hospitalized for fever and cough in the pediatric ward of Imam Khomeini Hospital, Jiroft, between June 11, 2023 and July 21, 2023 were assessed. A total of 156 patients participated in the study.

2.4 | Data analysis

The computer package SPSS (version 23.0) was used for statistical analysis. The Kolmogorov–Smirnov test was performed to find out whether the data followed a normal distribution or not. For data with a non-normal distribution, Spearman's correlation test was used, and for data with a normal distribution, Pearson's correlation test was used. Also, the mean of the two groups was compared using Student's *t* test (for data with normal distribution) or Mann–Whitney *U* test (for data with non-normal distribution). Regression analysis was used to investigate the relationship between independent and dependent variables.

3 | RESULTS

One hundred and fifty-six people (63 females + 93 males) participated in the study. The mean age of participants was 27.26 ± 3.14 months. Based on the findings, the mean ESR level in the studied population was 31.23 ± 18.8. The patient's CBC blood test showed that the RBC = 4.56 ± 0.65, Hb = 10.66 ± 1.16, HCT = 33.53 ± 4.14, MCV = 74.32 ± 9.86, MCH = 23.58 ± 3.8, MCHC = 31.48 ± 2.93, platelets (PLT) = 443.1 ± 165.6, and WBC = 19.24 ± 8.77 (Table 1).

A Spearman's rank correlation coefficient was performed to determine the association between ESR and RBC indices. The results showed that there is a significant negative correlation between ESR and RBC, $r = -0.282$ ($p < 0.001$), and ESR and HCT, $r = -0.215$ ($p = 0.007$). Also, the results demonstrated that there is a significant positive correlation between ESR and MCV, $r = 0.159$ ($p = 0.048$), ESR and MCH, $r = 0.214$ ($p = 0.007$), and ESR and MCHC, $r = 0.209$ ($p = 0.009$). There was a negative correlation between ESR and Hb, $r = -0.98$ ($p = 0.225$), but this correlation was insignificant. As a secondary objective, the correlation between ESR, WBC, and PLT was also measured, and it was found that there is a significant positive correlation between ESR and WBC, $r = 0.258$ ($p = 0.001$) as well as ESR and PLT, $r = 0.194$ ($p = 0.015$) (Table 2).

TABLE 1 The level of ESR, red blood cell indices, WBC, and PLT in the blood test of the studied population.

Variable	Mean	Std. deviation
ESR	31.23	18.8
RBC	4.56	0.65
Hb	10.66	1.16
HCT	33.53	4.14
MCV	74.32	9.86
MCH	23.58	3.8
MCHC	31.48	2.93
WBC	19.24	8.77
PLT	443.1	165.6

Abbreviations: ESR, erythrocyte sedimentation rate; Hb, hemoglobin; HCT, hematocrit; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; MCHC, mean cell hemoglobin concentration; PLT, platelets; RBC, red blood cell.

Among the RBC indices, only RBC and Hb had a normal distribution, and data analysis showed that there is no significant relationship between ESR and RBC in different gender groups $t(154) = 0.434$ ($p = 0.665$), but there is a significant relationship between ESR and Hb in separate gender groups $t(154) = 2.425$ ($p = 0.016$) (Table 3).

In investigating the association between ESR and HCT, MCV, MCH, and MCHC, which had abnormal distributions, in different gender groups, it was found that among the mentioned parameters, only HCT has a significant difference with ESR in separate gender groups ($p = 0.044$). The two variables WBC and PLT also had a non-normal distribution, and their association with ESR in separate gender groups was insignificant.

4 | DISCUSSION

The clinical care of many inflammatory or noninflammatory disorders depends significantly on the ESR, a commonly used laboratory test. The erythrocyte variables affecting ESR, however, are not well understood. This study aimed to investigate the association between ESR and RBC indices in pediatric patients hospitalized with complaints of fever and cough. Previous studies for exploring the relationship between ESR and RBC indices had been mainly conducted in adults. The current study population was children admitted to the hospital with symptoms of fever and cough. Since inflammatory markers and RBC indices in children are fundamentally different from those in adults, and even the typical ranges of these markers and indices are different in children compared with adults, the importance of investigating the relationship between ESR and RBC indices in the pediatric population is twofold. Also, previous studies have investigated the relationship between ESR and RBC indices mainly in healthy populations. At the same time it should be

TABLE 3 The association between ESR and red blood cell indices based on gender.

	t	*df*	*p* Value
RBC	0.434	154	0.665
Hb	2.425	154	0.016

Note: Correlation is significant at the 0.05 level.

Abbreviations: ESR, erythrocyte sedimentation rate; Hb, hemoglobin; RBC, red blood cell.

TABLE 2 The association between erythrocyte sedimentation rate and red blood cell indices and WBC and PLT.

	RBC	Hb	HCT	MCV	MCH	MCHC	WBC	PLT
ESR	$r = -0.282$ ($p < 0.001$)	$r = -0.98$ ($p = 0.225$)	$r = -0.215$ ($p = 0.007$)	$r = 0.159$ ($p = 0.048$)	$r = 0.214$ ($p = 0.007$)	$r = 0.209$ ($p = 0.009$)	$r = 0.258$ ($p = 0.001$)	$r = 0.194$ ($p = 0.015$)

Note: Correlation is significant at the 0.05 level.

Abbreviations: ESR, erythrocyte sedimentation rate; Hb, hemoglobin; HCT, hematocrit; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; MCHC, mean cell hemoglobin concentration; RBC, red blood cell.

seen if a person is involved in a disease, what is the relationship between ESR and RBC indices.

The results of this study showed that the level of ESR increases in hospitalized children with complaints of fever and cough. ESR level in these patients has a negative relationship with some RBC indices, including RBC and HCT. Also, it has a positive relationship with some other RBC indices, including MCV, MCH, and MCHC. However, according to the findings, ESR level is unrelated to Hb.

In Taşkın et al. (2019) study, they showed that ESR with all RBC indices, including (RBC, HCT, Hb, MCV, MCH, and MCHC, have a negative association,[15] while in the present study, it was found that ESR has a negative association only with RBC and HCT. The population studied by Taşkın et al. were people between 18 and 50 years old, while in the present study, children were evaluated. So, it can be concluded that age is one of the influencing factors in the association between ESR and RBC indices. Although Taşkın et al. also measured this association in a group of patients, they did not specify the patient's disease. However, in the present study, children with complaints of fever and cough were discussed. Based on the analysis of Kanwal et al. (2021), it can be concluded that the type of disease affects the association of ESR and RBC indices.[16] Kanfer et al.'s study showed a significant negative correlation between ESR and Hb.[17] In the current study, the results showed that ESR and Hb have a negative association, but this association was not significant in the population of the recent study.

This finding is notable because, in our investigation, ESR, RBC, and HCT are significantly correlated. Still, ESR and Hb were not significantly correlated, even though Hb, HCT, and RBC counts all follow the rule of three in hematology. In explanation of this finding, it can be concluded that sometimes something happens in some cases called Hb and HCT mismatch or Hb and RBC count mismatch. Based on the evidence that is currently available, it is probable that the hematological rule of three is not followed by RBC count, Hb, and HCT.

Hemolysis, cold agglutinins (CAs), lipemia, dehydration, thalassemia, hyperleukocytosis, hyperbilirubinemia, and so on, are common diseases that cause the condition in patients.[18,19] Our study population was children who complained of fever and cough, so there was probably an infection in them. The presence of infection is one of the possible reasons that can cause hemolysis in some samples. Also, uremia is the cause of hemolysis, and patients may have had uremia during their illness.

Also, according to evidence, some polyclonal immunoglobulin M (IgM) CAs arise in association with infections with Mycoplasma pneumoniae, infectious mononucleosis, influenza B, and human immunodeficiency virus (HIV), as well as with other infections.[20,21] Considering that the children in our study were patients with complaints of fever, cough, and possible infection, there is a risk of occurrence of CAs in some of them. Many of the studied children have received glucocorticoids and antiretroviral drugs during their treatment.

These drugs can cause lipemia. Pediatrics are very susceptible to dehydration during illness, and it is a common finding in them. It is possible that some of the studied children had a hematological disorder called thalassemia, which caused a mismatch in the correlation of blood parameters. Also, hyperbilirubinemia can cause Hb in a child with hyperbilirubinemia to be much lower than expected,[18] and some samples may have had hyperbilirubinemia during our study. Finally, considering the possibility of hemolysis, CA, lipemia, dehydration, thalassemia, and hyperbilirubinemia in our study population, the occurrence of Hb and HCT mismatch or Hb and RBC count mismatch is not far from expected. It can explain our different findings in this study.

In Vayá et al. study, it was shown that RBC distribution width is related to inflammatory indicators. RBC distribution width is a parameter dependent on MCV,[22] so it can be concluded that MCV is associated with inflammatory markers, which is in line with the findings of the present study, which showed that MCV is correlated with ESR, which is an inflammatory marker.

The results of the present study showed that the relationship between ESR and, Hb as well as ESR and, HCT is gender-dependent. The Rabe et al. study showed that in Chorea-Acanthocytosis patients, ESR and the number of acanthocytes are related to the mechanical-morphological characteristic of RBCs.[23] We know that the mechano-morphological feature of RBCs affects many RBC indices. The findings of our study showed that ESR and RBC indices are related to each other; in some cases, there is a positive relationship and in others, there is a negative relationship. So, it can be concluded that Rabe et al.'s study has raised the reason for confirming the relationship between ESR and RBC indices. These findings were in line with our study results.

Previous research has demonstrated that racial differences affect ESR, although this effect is not dependent on Hb concentration. Thus, it is evident that racial disparities in ESR have no impact on the correlation between ESR and Hb concentration.[24,25] However, some specific conditions, such as being infected with malaria, can disrupt the relationship between ESR and RBC indices, because, according to previous studies,[26] malaria infection causes a decrease in Hb and an increase in ESR. Therefore, it should be noted that in a situation where the patient is suffering from a disease that has specific hematological effects, it is not possible to find a correlation between ESR and RBC indices. According to the study of Rabe et al., cell shape and rigidity of RBCs can affect ESR in addition to changes in RBC indices.[23] The study of Constantino also confirms that changes in the morphology of RBCs affect ESR.[27]

Factors affecting the ESR value include plasma fibrinogen and globulin levels, rouleaux formation, erythrocyte size and shape, and mechanical and technical aspects. The prevalence of inherited diseases of erythrocyte size and shape determines the relationship between ESR and RBC indices in a healthy population. If the majority is high, ESR should be negatively correlated with RBC indices, and this correlation becomes stronger with diseases like infection. If the majority is low, there should be a clear difference in the correlation of ESR with RBC indices in healthy and diseased populations.[28] Malaria endemicity affects the steady-state Hb of the people, contributing to high ESR.[29] Malaria endemicity also affects the agglutination of

parasitized RBCs, which contributes to rouleaux formation and increases ESR.[30] Infectious diseases appear to further strengthen the negative correlation between ESR and HCT and RBC counts in malaria-endemic populations. However, in people with low or no malaria disease, the relationship between ESR and RBC indices will be different in apparently healthy and diseased people.[31,32]

Therefore, it can be concluded that in disorders that disrupt the morphology of RBCs, such as hereditary spherocytosis, elliptocytosis, and sickle cell disease, based on the findings of our study, can change ESR and RBC indices correlation, than this correlation in the healthy hematological population. This means that first, to check the relationship between ESR and RBC indices, we must make sure that the patient does not have a specific hematological disorder affecting the shape and size of RBCs.

Considering that the relationship between ESR and RBC indices was only measured in a limited number of people in the current study, future research should aim to measure this relationship in various age groups and diseases, particularly hematological disorders. Also, in our research, we did not investigate the exact cause of RBC and HCT versus Hb mismatch, which was one of the limitations of our research. It was suggested that future studies be carried out in a similar population that, at the same time as examining the CBC test, additional detailed hematological tests, liver function tests, renal function tests, and lipid profile analysis should be performed.

5 | CONCLUSION

The present study showed an association between ESR and RBC indices in hospitalized children with complaints of fever and cough. In some RBC indices, there is a positive association (MCV, MCH, and MCHC), and in others, there is a negative association (RBC, HCT). So, it is necessary that physicians and treatment staff pay attention to the RBC indices while interpreting and following up the results of ESR to complete the treatment process of patients. The accurate interpretation of laboratory tests causes that, in addition to better treatment of patients, lower costs are imposed on patients and the health care system.

AUTHOR CONTRIBUTIONS

Mohammad Pourfridoni: Conceptualization; data curation; methodology; supervision; writing—original draft; writing—review & editing. **Hamidreza Farhadi Rad**: Data curation; writing—original draft. **Faezeh Mirzaee**: Writing—original draft; writing—review & editing. **Seyede Mahsa Abbasnia**: Data curation; writing—original draft; writing—review & editing. **Mehran Nikvarz**: Conceptualization; writing—original draft. **Elham Sharifi**: Conceptualization; writing—original draft. **Shohreh Shafiei**: Formal analysis; software. **Yousef Baghcheghi**: Writing—original draft; writing—review & editing. **Asma Amiri Domari**: Writing—review & editing. **Hedyeh Askarpour**: Conceptualization; supervision; writing—original draft; writing—review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The study was approved by the Research Ethics Committee (REC) of the Jiroft University of Medical Sciences, Jiroft, Iran (Ethical Approval Number: IR.JMU.REC.1402.028).

TRANSPARENCY STATEMENT

The lead author Hedyeh Askarpour affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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