

Laboratory parameters, clinical characteristics and hemogram-derived indices in adult patients with measles at tertiary hospital admission

Berina Hasanefendić^{1,2*}, Amila Muratspahić³, Semir Hrvo³, Emina Hajrović Hebibović¹, Lejla Avdagić¹, Almedina Moro⁴, Emir Šeherčehajić⁵, Amir Sandžić⁶

¹Clinical Biochemistry and Laboratory Medicine, Clinical Centre University of Sarajevo, Sarajevo, ²Department for Laboratory Technologies, Faculty of Health Studies, University of Sarajevo, Sarajevo, ³Clinic for Infectious Diseases, Clinical Centre University of Sarajevo, Sarajevo, ⁴Unit for Clinical Microbiology, Clinical Centre University of Sarajevo, Sarajevo, ⁵Department for Pathohistology and Cytology, ASA Hospital, Sarajevo, ⁶Institute for Transfusion Medicine of the Federation of Bosnia and Herzegovina, Sarajevo; Bosnia and Herzegovina

ABSTRACT

Aim To describe clinical and laboratory findings, as well as to examine the significance of novel hemogram-derived inflammatory indices in adult patients with measles admitted to a tertiary hospital.

Methods This prospective, descriptive, and analytical study included adult patients over 18 years of age with clinical signs of measles, admitted at the Clinic for Infectious Diseases, Clinical Centre of Sarajevo. Upon admission, medical history, physical examination, and laboratory analyses were conducted from February 2024 to 31 December 2024.

Results The study included 124 patients, 52 men and 72 were women with a mean age of 38.33±13.18 years. The most common symptoms in most patients were rash (95.97%) and cough (69.36%). Neutrophilia (63.7%) and lymphopenia (74.19%) were the main haematological features along with elevated C-reactive protein (CRP) (95.17%) and transaminase (75%) in the vast majority of patients. The results of laboratory analyses also indicated hyponatremia and hypokalaemia, with elevated values of the enzymes creatine kinase (CK) and lactate dehydrogenase (LDH). The CRP, as the most commonly elevated laboratory parameter, showed a significant positive correlation with the neutrophil-to-lymphocyte ratio (NLR) and the systemic inflammation response index (SIRI) ($p < 0.05$), as well as with the systemic immune-inflammation index (SII) and the aggregate index of systemic inflammation (AISII) ($p < 0.01$).

Conclusion Adult measles was associated with significant inflammation, hematologic changes, and organ involvement, with CRP showing strong correlations with hemogram-derived indices, suggesting that these indices may be useful in the diagnostics of measles.

Key words: biomarkers, infectious disease, inflammation, viremia

INTRODUCTION

The causative agent of measles is an RNA virus, from the family *Paramyxoviridae*, genus *Morbillivirus*. The virus is resistant in the external environment, and is found in nasopharyngeal secretions, urine and blood 2-3 days before the appearance of the disease symptoms and one day after the appearance of symptoms of the disease (1). Measles is a cosmopolitan disease and occurs sporadically or epidemically in all parts of the world. Newborns are protected in the first 6 months of life by passive, transplacental immunity transferred from the mother, if she had measles (2). The reservoir of infection are humans,

the source of infection is the nasopharyngeal secretion of an infected person. The route of spread of the infection is droplet transmission, and the entrance door of the infection is the mucous membrane of the conjunctiva and the upper parts of the respiratory tract. It occurs in an endemoepidemic form most often in children of preschool and early school age (3).

The incubation period for measles is 10-11 days. It proceeds without symptoms, and in the last third of the incubation period the patient is infectious. The symptoms that occur are cough, coryza, Koplik's spots and conjunctivitis. Patients go through a catarrhal, rash and convalescent stage of the disease (2). Measles can also have complications, the most common of which are pneumonia, diarrhea and ear infections (4).

Hemogram-derived indices (HDI) are new parameters obtained by simple mathematical calculation of inflammation indicators: the number of leukocytes, lymphocytes, neutrophils, monocytes, platelets, C-reactive protein (CRP), etc. (5).

*Corresponding author: Berina Hasanefendić

Clinical Biochemistry and Laboratory Medicine, Clinical Centre University of Sarajevo, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina

Phone: +387 33 297 664;

E-mail: bery-kurs@hotmail.com

ORCID ID: <https://orcid.org/0000-0002-9610-5020>

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HDI has a role in disease diagnostics, prediction of patient condition, disease and outcome prognosis and assessment of therapy success (6). A large number of studies have so far shown the usefulness of HDIs in respiratory infections such as COVID-19, respiratory syncytial virus (RSV) infection and *Mycobacterium pneumoniae* pneumonia (7,8). Given their demonstrated diagnostic potential in the viral infections, it would be worth testing them in measles as well.

The aim of this study was to describe clinical and laboratory findings and to examine the significance of novel HDIs in adult patients with measles admitted to a tertiary hospital.

PATIENTS AND METHODS

Patients and study design

This prospective, descriptive and analytical study included adult patients over the age of 18 who presented with symptoms of measles infection at the Clinic for Infectious Diseases, Clinical Centre University of Sarajevo, Bosnia and Herzegovina. Upon admission of patients with a referral diagnosis of measles, a medical history was obtained, a physical examination was performed, and blood samples were collected for laboratory analysis. Exclusion criteria included inadequate medical documentation, immunodeficiency, and autoimmune diseases. There were no pregnant women among the patients.

From February until the end of 2024, data on patients meeting the inclusion criteria were collected prospectively. Data on age, sex, symptoms, vaccination status and laboratory analysis values were obtained from the Hospital and Laboratory Information System. To ensure complete accuracy and completeness of patient data, two authors reviewed the database twice. The study was conducted with the approval of the Ethics Committee of the Clinical Center of the University of Sarajevo (No. 06-04-9-92174).

Methods

A venous blood sample was taken from all patients for biochemical, haematological, coagulation and serological analyses. Blood samples were collected from the cubital vein by venipuncture. Complete and differential blood counts were analysed from whole blood samples, basic biochemical and serological analyses from serum, and coagulation analyses from plasma. A DxH 900 haematology analyser (Beckman Coulter, USA) was used for haematological analyses, an Alinity biochemical analyser (Abbott, USA) for biochemical analyses, and a BCS CP (Siemens, Germany) for coagulation analyses. The reference interval for sodium (Na) was 135-145 mmol/l, potassium (K) 3.5-5.2 mmol/l, CRP 0-5 mg/l, aspartate aminotransferase (AST) 0-39 U/l, alanine aminotransferase (ALT) 0-37 U/l, creatine kinase (CK) 29-285 U/l and lactate dehydrogenase (LDH) 120-240 U/l. Serological analyses were performed using an ELISA (enzyme-linked immunosorbent assay) test to determine IgM (SERION ELISA classic Masern/Measles Virus IgM assay, Serion Diagnostics).

The neutrophil-to-lymphocyte ratio was calculated by dividing the absolute neutrophil count by the lymphocyte count (NLR = Neutrophils/Lymphocytes). The platelet-to-lymphocyte ratio was obtained by dividing the platelet count by the lymphocyte count (PLR = Platelets/Lymphocytes). The systemic immune-inflammation index was calculated as SII = (Platelets ×

Neutrophils)/Lymphocytes. The aggregate index of systemic inflammation is calculated as AISI = (Neutrophils × Monocytes × Platelets)/Lymphocytes. The systemic inflammation response index was calculated as SIRI = (Neutrophils × Monocytes)/Lymphocytes.

Statistical analysis

Continuous variables were presented as arithmetic means and standard deviations (SD), and categorical variables as absolute and relative numbers. Data analysis was focused on descriptive statistics and correlation testing. The correlation between HDI and the inflammatory parameter CRP was tested by Pearson's correlation test. The statistical significance threshold was set at $p < 0.05$.

RESULTS

The study initially included 270 patients and after the application of exclusion criteria 124 adult (>18 years) patients with clinically and serologically confirmed measles infection over a period of 11 months were included. Of the total number of patients, 52 (41.94%) were men and 72 (58.06%) were women with a mean age of 38.33 ± 13.18 years. The most common symptoms in most patients were rash (95.97%) and cough (69.36%). CRP had mean value 70.1 mg/L and it was elevated in 95.17% of patients. Liver transaminases (AST and ALT) were elevated in 75% of patients (Table 1).

Table 1. Demographic and clinical characteristics of adult patients with measles infection

Variables	No (%) of patients
Age (mean±SD) (years)	38.33±13.18
Gender	
Male	52 (41.94)
Female	72 (58.06)
Symptoms	
Rash	119 (95.97)
Cough	86 (69.36)
Koplik spot	80 (64.51)
Coryza	31 (25)
Conjunctivitis	20 (16.13)
Diarrhea	19 (15.32)
Vaccinated	
YES	34 (27.4)
NO	90 (27.4)
Laboratory findings (reference value)	
Leukopenia (<4 x 10 ⁹ /l)	16 (12.9)
Neutrophilia (>7 x 10 ⁹ /l)	79 (63.7)
Lymphopenia (<1 x 10 ⁹ /l)	92 (74.19)
Thrombocytopenia (<150 x 10 ⁹ /l)	49 (39.52)
Elevated transaminases (>50 U/l)	93 (75)
Elevated CRP (>5 mg/l)	118 (95.17)
IgM (mean±SD) (U/l)	451.25±345.83

CRP, C-reactive protein; IgM, immunoglobulin M

The results of laboratory analyses indicated hyponatremia and hypokalaemia, with elevated values of CRP, transaminases, and the enzymes CK and LDH (Table 2). Mean sodium and potassium levels of 135.71 mmol/L and 3.83 mmol/L were observed.

Table 2. Overview of main laboratory findings and hemogram-derived and inflammatory indices of adult patients with measles

Parameter (reference value)	Mean±SD
Na (135-145 mmol/L)	135.71±3.3
K (3.5-5.2 mmol/ L)	3.83±0.48
CRP (0-5 mg/l)	70.1±58.07
AST (8-34 U/l)	148.53±119.87
ALT (4-37 U/l)	201.16±189.56
AST/ALT ratio	1.05±1.12
CK (30-150 U/L for females and 40-250 U/L for males)	417.27±582.37
LDH (140-280 U/l)	503.68±253.99
NLR (0.78 to 3.53)	8.13±7.81
PLR (100-200)	278.95±185.17
SII (161-701)	1452.16±1754.98
AISI	929.09±1787,49
SIRI	4.58±8.32

CRP, C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; AST/ALT ratio, De Ritis ratio; CK, creatine kinase; LDH, lactate dehydrogenase; NLR, neutrophils/lymphocytes ratio; PLR, platelet/lymphocytes ratio; SII, systemic immune-inflammation index; AISI, aggregate index of systemic inflammation; SIRI, systemic inflammatory response index

CRP had positive, significant correlations with NLR, SIRI ($p < 0.05$) and with SII and AISI ($p < 0.01$) (Table 3). AST/ALT and PLR did not show a significant correlation.

Table 3. Correlation of hemogram-derived and inflammatory indices with C-reactive protein (CRP) in adults patients with measles

CRP	AST/ALT	NLR	PLR	SII	AISI	SIRI
rho	0.027	0.205*	0.183	0.397†	0.433†	0.250†
p	0.775	0.028	0.052	0.000	0.000	0.007

* $p < 0.05$; † $p < 0.01$

AST/ALT ratio, De Ritis ratio; NLR, neutrophils/lymphocytes ratio; PLR, platelet/lymphocytes ratio; SII, systemic immune-inflammation index; AISI, aggregate index of systemic inflammation; SIRI, systemic inflammatory response index

DISCUSSION

Bosnia and Herzegovina previously experienced two major measles epidemics: 1997–1999 and 2014–2015, with over 10,000 patients. In 2019, more than 700 cases were recorded, of which 92.5% were unvaccinated (9). The COVID-19 pandemic had a negative impact on routine vaccination programs. In the period from 2020 to 2022, DTP3 vaccine coverage decreased by 17.6%, while MMR1 coverage decreased by 26.7% (10). During the measles epidemic in 2024, a total of 7,477 cases were reported in the Federation of Bosnia and Herzegovina, of which 4,514 were reported in Sarajevo Canton (11). Therefore, the purpose of our study was to provide a comprehensive analysis of adult patients with confirmed measles infection at hospital admission, highlighting key clinical presentations, laboratory results, and the utility of determining hemogram-derived inflammatory indices.

The vaccine against measles is a basic preventive measure, which protects against the onset of infection or, in case of illness, the clinical picture is mild (1). However, even in immunized adults, it has been proven that its effectiveness and the concentration of IgG antibodies decrease over the years, which may

to some extent explain the emergence of this highly contagious viral infection, and thus increase the risk of an epidemic (12).

The vast majority of our patients exhibited classic measles symptoms, particularly rash and cough, aligning with the standard clinical presentation of measles in adults (13). Koplik’s spots, were present in more than half of the cases, which is similar to findings from China (14, 15).

Neutrophilia and lymphopenia were prominent hematologic findings, consistent with the known immunosuppressive effects of measles virus on lymphocyte populations (16). Casasoprana A et al also reported that 95% of patients had lymphopenia and 49 had thrombocytopenia in their study of 134 measles patients (17). Elevated CRP and liver transaminases were also observed, indicating a robust systemic inflammatory response and hepatic involvement. Similar hepatic abnormalities have been presented in other adult measles studies, suggesting that transient hepatitis may be a common complication (18,19).

Additionally, elevated levels of CK and LDH point toward muscle involvement and generalized cellular injury, possibly due to viral cytopathic effects or immune-mediated damage (20). Hyponatremia and hypokalaemia were also observed. These findings may be attributed to gastrointestinal symptoms (diarrhea and vomiting) or syndrome of inappropriate antidiuretic hormone secretion, both of which have been reported in adult viral infections (21).

This study evaluated novel hemogram-derived inflammatory indices - NLR, PLR, SII, AISI, and SIRI, all of which were markedly elevated. Their altered values, in this case elevated, were the result of changes in the differential blood count (6). These indices showed significant positive correlation with CRP, suggesting their potential role as biomarkers for the laboratory diagnostics of measles infection in adult patients. For comparison, in a study involving 71 patients with a moderate clinical picture, NLR had a mean value of 5.74 against our study where NLR was 8.13 among 124 patients (18). Previous studies have validated these markers in other viral and inflammatory diseases, emphasizing their prognostic relevance (6). Their use could assist clinicians in early identification of patients at risk for complications, especially in resource-limited settings (22). Therefore, these results are the first to describe the diagnostic potential of hemogram-derived indices in adult patients with measles.

The study has several important strengths and limitations. According to the available literature, our study included a relatively large number of adult patients with comprehensive clinical and laboratory data. Also, to our knowledge, this is the first study to examine the significance of using new hemogram-derived indices in measles diagnosis. Limitations of the study include its single-centre design, which may affect external validity. Additionally, data on IgG results, clinical outcomes, and long-term sequelae were not available this time and they should be studied further.

In conclusion, adult measles infection is associated with a pronounced systemic inflammatory response, as evidenced by frequent haematological abnormalities, elevated CRP, liver enzyme disturbances, and electrolyte imbalances. The strong correlation between CRP and hemogram-derived inflammatory indices such as NLR, SII, AISI, and SIRI suggests that these readily available markers may serve as useful parameters for adult patients at hospital admission. Early identification of patients with symptoms through simple laboratory indices could improve the management and outcomes in adult measles cases. Further research is

needed to validate the prognostic value of these inflammatory markers in larger and more diverse populations.

AUTHOR CONTRIBUTIONS

Conceptualization, B.H., A.M., S.H.; methodology, B.H.; validation, B.H., L.A., and E.H.H.; formal analysis, B.H., and E.Š.; data curation, B.H., A.P., A.M., and A.S.; writing—original draft preparation, A.M., S.H., and B.H.; writing - review and editing, B.H.; visualization, E.Š.; supervision, B.H., L.A.,

E.H.H., and A.P.; project administration, B.H. All authors have read and agreed to the published version of the manuscript.

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TRANSPARENCY DECLARATION

Conflict of interests: None to declare.

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