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ORIGINAL ARTICLE

Predictive value of clinical findings and complete blood count parameters for measles diagnosis in pediatric patients: A retrospective cross-sectional study

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ABSTRACT

Objective: Diagnosing measles, a highly contagious viral infection characterized by fever and a characteristic rash, can be challenging due to the similarity of the clinical presentation to other diseases. Confirmatory laboratory testing is critical to accurately identify measles cases, as different pathogens and medications can produce comparable symptoms. The objective of this study was to evaluate the predictive value of clinical findings and complete blood count parameters for the diagnosis of measles in pediatric patients presenting with fever and maculopapular rash.

Material and Methods: This study was conducted in our clinic between January 1, 2023, and October 1, 2023. Patients with fever and maculopapular rash were divided into two groups: the study group consisting of patients diagnosed with measles, and the control group consisting of patients without measles.

Results: A total of 140 pediatric patients presenting with fever and maculopapular rash were included in the study. In the measles group, 34.4% (31/90) of patients had Koplik's spots. In our study, vaccination rates were similar between the measles group (34%, 31/90) and the non-measles group (40%, 20/50) (p=0.513). However, vaccine refusal was significantly higher in the measles group (40%, 36/90) compared to the non-measles group (14%, 7/50) (p=0.001). Comparing symptoms between the groups, cough (p<0.001), conjunctivitis (p=0.004), coryza (p<0.001), and lymphadenopathy (p=0.02) were statistically significantly more common in the measles group. Cough significantly increased the likelihood of measles, with patients exhibiting this symptom being 8.94 times more likely to have the disease. A platelet-to-lymphocyte ratio cutoff of 89.2 yielded a sensitivity of 65% and a specificity of 72%. For the neutrophil-to-lymphocyte ratio, a cutoff of 0.28 demonstrated a sensitivity of 94% but a lower specificity of 40%.

Conclusion: Clinical findings, particularly the presence of cough alongside fever and maculopapular rash, aid in strengthening measles diagnosis. However, we believe that markers derived from complete blood counts are not strong diagnostic tools for measles.

Keywords: Blood cell count, Koplik's spot, maculopapular rash, Measles virus.

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INTRODUCTION

Measles is a highly contagious viral infection characterized by high fever and maculopapular rash, and it is preventable through vaccination.[1] The causative agent of the infection is the measles virus (MeV), classified in the genus Morbillivirus within the family Paramyxoviridae. Before the development of the vaccine, measles caused an estimated 2.6 million deaths annually, occurring in epidemics every 2–3 years. Today, it continues to be a significant cause of morbidity and mortality.[2]

According to the World Health Organization (WHO) report, more than 300,000 measles cases were recorded globally in 2023. The number of reported cases in 2024 so far suggests that this year's total is projected to surpass that of the previous year.[3]

Clinicians often suspect measles when a patient presents with fever and maculopapular rash accompanied by additional symptoms such as cough, coryza, and conjunctivitis.[2] However, the causes of fever and rash are numerous, and many present with similar clinical symptoms, which can lead to misdiagnosis. Confirmatory laboratory tests are essential for accurately diagnosing suspected measles cases, as other pathogens and even certain medications can cause similar symptoms.[4]

The detection of specific IgM antibodies against MeV using enzyme-linked immunosorbent assay is widely used for laboratory diagnosis of suspected cases, especially in areas where measles is endemic. IgM antibodies can be detected as early as 3 days after the rash appears and remain detectable for approximately 2 months.[1,5] In areas with high vaccination coverage, the positive predictive value of IgM serology is lower, making real-time PCR (RT-PCR) detection of MeV RNA a preferred method for confirming measles cases.[1]

Measles is a systemic inflammatory disease that includes immunosuppression lasting several months after the acute infection.[6] The virus replicates in lymphoid tissues, leading to lymphopenia.[7] Recent studies have found that inflammatory indices derived from complete blood count (CBC) are associated with diagnosis and prognosis in various inflammatory conditions such as trauma, sepsis, bronchiolitis, and malignancy.[8–11] However, studies investigating the role of these inflammatory markers in the diagnosis and prognosis of measles are limited. One study found a relationship between mean platelet volume (MPV) and inflammation in measles, while another identified an association between platelet-to-lymphocyte ratio (PLR) and outcomes in children with measles.[12,13] In contrast, a study examining the relationship between inflammatory indices derived from peripheral blood cell counts and complicated measles did not yield significant results.[14]

We hypothesize that if clinical features and routine laboratory tests can reliably indicate measles at any stage of the disease, the dependency on additional laboratory tests for diagnosis could be reduced. The objective of this study was to ascertain whether clinical symptoms and inflammatory indices derived from complete blood count (CBC) can be utilized to predict measles infection in children presenting with fever and maculopapular rash.

MATERIAL AND METHODS

This retrospective cross-sectional study included all pediatric patients admitted to our pediatric emergency department with fever and maculopapular rash between January 1, 2023 and October 1, 2023. The ethical principles of the Declaration of Helsinki were adhered to throughout the study period. Ethical approval was obtained from the local ethics committee (Date: 22/12/2023, Number: 2023/12/16/093).

Patient data were retrieved from our hospital's electronic record system. Patients presenting with only rash, those who had received a measles vaccination within the last six weeks, those with a history of corticosteroid use (for more than two weeks), and those diagnosed with hematologic diseases or immunodeficiencies were excluded from the study.

Patients with fever and maculopapular rash at the first presentation to the pediatric emergency department were divided into two groups: the study group consisting of patients diagnosed with measles, and the control group consisting of patients without measles.

The diagnosis of measles was confirmed in patients presenting with fever, maculopapular rash, and additional symptoms, through the presence of measles IgM antibodies and positive MeV RNA by RT-PCR.[1]

As part of the Türkiye Public Health Institution's Measles Elimination Program, a measles case notification form was completed for all suspected measles cases, and blood, nasopharyngeal swabs, and urine samples were sent to the district health directorate. Measles IgM antibodies and positive MeV RNA by RT-PCR were performed by WHO-registered national public health laboratories.

Demographic data (age, gender, and race), measles vaccination status, presenting symptoms (fever, rash, cough, coryza, lymphadenopathy, conjunctivitis), and complications were recorded. Laboratory tests were obtained during the initial encounter in the emergency department. Laboratory findings included measles RT-PCR, IgM, CBC, lymphocytes, neutrophils, platelets, MPV, neutrophil-to-lymphocyte ratio (NLR), PLR, C-reactive protein (CRP), procalcitonin, and albumin. Leukopenia was defined as a white blood cell (WBC) count <4000/μL, neutropenia as a neutrophil count <1500/μL, and lymphopenia as a lymphocyte count <1500/μL.

In the study, pneumonia, acute otitis media (AOM), and acute gastroenteritis (AGE) were considered complications of measles if they occurred alongside fever and rash in the measles group.[1]

According to the national immunization program in our country, two doses of the measles, mumps, and rubella (MMR) vaccine are administered (the first dose at 12 months of age and the second dose at 6 years).[15] Since July 1, 2020, the national immunization program has included two doses of the MMR vaccine administered at 12 months and 48 months. Additionally, an extra dose is given at 9 months in areas at risk of outbreaks.[16] Vaccination status was obtained from the vaccination cards issued by the Ministry of Health of the Republic of Türkiye or the electronic health record system "e-nabız" created by the Ministry of Health. Patients who had completed both doses of the measles vaccine were considered vaccinated.

Table 1: Comparison of clinical and demographic findings of study groups

	Measles group (n=90) n (%)	Control group (n=50) n (%)	Total (n=90) n (%)	p
Age (months) median (75–25)	43 (102–10)	12.5 (60–9)		**0.02**[1]
Gendern				
Male	46 (51)	29 (58)	75 (53.5)	0.434[2]
Female	44 (49)	21 (42)	65 (46.5)	
Ethnicity				
Turkish	68 (75)	45 (90)	113 (80)	**0.038**[2]
Syrian	22 (25)	5 (10)	27 (20)	
Vaccination status				
Vaccinated	31 (34)	20 (40)	51 (36)	0.513[2]
Unvaccinated	59 (66)	30 (60)	89 (64)	
Vaccine refusal	36 (40)	7 (14)	43 (47.8)	**0.001**[2]
Symptoms				
Cough	70 (78)	17 (34)	87 (62)	**0.000**[2]
Conjunctivitis	48 (53)	14 (28)	62 (44)	**0.004**[2]
Coryza	65 (72)	19 (38)	84 (60)	**0.000**[2]
Myalgia	6 (7)	1 (2)	7 (5)	0.225[2]
Lymphadenopathy	9 (10)	0	9 (6)	**0.02**[2]
Complicated measles	44 (48.8)			
Complications				
Acute gastroenteritis	29 (65.9)			
Acute otitis media	13 (29.5)			
Pneumonia	13 (29.5)			

1: Mann-Whitney U test; 2: Chi-Square, shown in bold if p<0.05.

Statistical Analysis

The statistical analysis was performed using SPSS version 29.0. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were assessed for normality and compared using the Mann-Whitney U test or independent t-test. The significance level was set at p<0.05. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic performance of inflammatory indices derived from CBC parameters. Sensitivity, specificity, and cut-off values were determined. Multivariate logistic regression analysis was used to identify independent predictors of measles diagnosis.

RESULTS

A total of 140 pediatric patients who presented with fever and maculopapular rash and met the inclusion criteria (90 patients in the measles group and 50 patients in the control group) were included in the study over a 9-month period. More than half (53.5%, 75/140) of the patients were male, and gender distribution was similar across the groups (p=0.434). Seventy-five percent (75/90) of the cases in the measles group and 90% (45/50) of the control group were Turkish citizens. The incidence of measles was statistically significantly higher among Syrian refugees compared to Turkish citizens (p=0.038) (Table 1).

Thirty-four percent (31/90) of the measles group and 40% (20/50) of the non-measles group were vaccinated, and vaccination rates were similar between the groups (p=0.513). In our study, the overall vaccine refusal rate was determined to be 48.8% (43/140). A comparison between groups revealed that the refusal rate was significantly higher in the measles group (40%, 36/90) compared to the non-measles group (14%, 7/50) (p=0.001).

Cough (p<0.001), conjunctivitis (p=0.004), coryza (p<0.001), and lymphadenopathy (p=0.02) were statistically significantly more common in the measles group. In the measles group, 34.4% (31/90) of patients had Koplik's spot, and detailed comparisons of symptoms are shown in Table 1.

In the measles group, 44 patients (48.8%) developed complications, with AGE in 29 patients, AOM in 13 patients, and pneumonia in 13 patients (Table 1).

Table 2: Comparison of laboratory findings of study groups

	Measles group	Control group	p
WBC (x10^3/ml), Median (min–max)	5.37 (2.2– 23.6)	8.4 (4.3–21.6)	**<0.001**[1]
Neutrophile (x10^3/ml), Median (min–max)	2.9 (0.31–16.9)	3.2 (0.29–18.9)	0.473[1]
Lymphocyte (x10^3/ml), Median (min–max)	2.1 (0.28–9.7)	4.9 (1–10.7)	**<0.001**[1]
Platelet (x10^3/ml), Median (min–max)	244.5 (101–695)	288 (119–644)	0.087[1]
CRP, mg/L, Median (min–max)	6.8 (0.5–140)	2.4 (0.3–115)	0.301[1]
Procalcitonin, ng/mL, Median (min–max)	0.19 (0.02–19)	0.12 (0.3–1.3)	0.288[1]
MPV, fl, Mean±SD	9.6±1	9.1±0.85	**0.07**[2]
Albumin, g/dL, Mean±SD	4.1±0.33	4.26±0.36	0.126[2]
NLR, Median (min–max)	1.5 (0.1–10.2)	0.7 (0.04–12.3)	**0.013**[1]
PLR, Median (min–max)	116.8 (29.5–878.5)	65.1 (19.6–211)	**<0.001**[1]
Leukopenia, n (%)	32 (36)	0	**0.000**[3]
Neutropenia, n (%)	15 (17)	20 (40)	**0.002**[3]
Lymphopenia, n (%)	36 (40)	0	**0.000**[3]

1: Mann Whitney-U test; 2: Student t-Test; 3: Chi-Square, shown in bold if p<0.05. WBC: White blood cells; MPV: Mean platelet volume; CRP: C-Reactive protein; NLR: Neutrophile-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; Min: Minimum; Max: Maximum; SD: Standard deviation.

Table 3: ROC curve analyses of laboratory findings in predicting measles diagnosis

	Cut-off value	AUC	AUC – %95 CI	Sensitivity (%)	Specifity (%)	p
PLR	≥89.2	0.739	0.657–0.809	65	72	**<0.001**
NLR	≥0.28	0.680	0.597–0.757	94	40	**<0.001**
MPV	≥10	0.628	0.542–0.708	36	86	**0.008**

PLR: Platelet-lymphocyte ratio; NLR: Neutrophile-lymphocyte ratio; MPV: Mean platelet volume; AUC: Area under curve; CI: Confidence interval. Shown in bold if p<0.05.

The median WBC count in the measles group was significantly lower than the control group (5.37 [2.2–23.6] vs. 8.4 [4.3–21.6]) (p<0.001). The lymphocyte count was also significantly lower in the measles group (2.9 [0.31–16.9] vs. 4.8 [1.0–10.7]) (p<0.001). CRP, procalcitonin, albumin, neutrophil, and platelet counts were similar across the groups (p>0.005 for all). Regarding inflammatory indices derived from CBC, the mean MPV was significantly higher in the measles group (9.6±1.0 vs. 9.1±0.85) (p=0.07). Similarly, median NLR was significantly higher in the measles group (1.5 [0.1–10.2] vs. 0.7 [0.04–12.3]) (p=0.013). Median PLR was also significantly higher in the measles group (116.8 [29.5–878.5] vs. 65.1 [19.6–211]) (p<0.001). The number of patients with leukopenia and lymphopenia was significantly higher in the measles group (36% vs. 0% and 40% vs. 0%) (p<0.001 and p<0.001). On the contrary, neutropenia was significantly lower in measles (17% vs. 40%) (p=0.002) (Table 2).

ROC analysis of laboratory findings used to predict measles diagnosis is shown in Figure 1. For PLR, a cut-off value of 89.2 had a sensitivity of 65% and a specificity of 72%. For NLR, a cut-off value of 0.28 had a sensitivity of 94% and a specificity of 40%. For MPV, a cut-off value of 10 had a sensitivity of 36% and a specificity of 86% (Table 3, Fig. 1).

Parameters that could be used to predict measles diagnosis in patients with fever and rash were identified as the presence of cough (p<0.001) and the absence of neutropenia (p=0.040). Patients with cough had 8.94 times higher likelihood of having measles, while patients without neutropenia had a 4 times higher likelihood of having measles (Table 4).

DISCUSSION

In children, the causes of fever and maculopapular rash are diverse. Besides the MeV, these clinical symptoms can be associated with rubella virus, group A streptococci causing scarlet fever, parvovirus B19, enteroviruses, adenoviruses, and human herpesvirus type 6.[17] In our study, 64.2% (90/140) of patients presenting with fever and maculopapular rash to our pediatric emergency department over a 9-month period were diagnosed with measles. In a study conducted in Belarus, during a period of high measles incidence in Europe in 2011, MeV was detected in 13.1% of children with maculopapular rash.[18] The proportion of patients diagnosed with measles among those suspected of having the disease varies across countries, with

Table 4: Logistic regression analysis of parameters predicting measles diagnosis

	B	SE	Wald	df	p	Exp(B)
Cough	2.191	0.568	14.848	1	**<0.001**	8.940
Conjunctivitis	0.393	0.583	0.455	1	0.500	1.482
Coryza	0.682	0.564	1.462	1	0.227	1.979
Lymphadenopathy	22.175	10510.126	0.000	1	0.998	4272296418.828
Lymphopenia	21.317	5054.374	0.000	1	0.997	1810221539.569
Neutropenia	-1.384	0.673	4.236	1	**0.040**	0.251
Leukopenia	18.424	5331.802	0.000	1	0.997	100317011.659
NLR	0.323	0.232	1.927	1	0.165	1.381
PLR	-0.004	0.008	0.304	1	0.581	0.996
Constant	-62.200	12823.320	0.000	1	0.996	0.000

NLR: Neutrophile-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; B: Beta coefficient; SE: Standard error; df: Degrees of freedom; Significant p values shown as bold.

rates reported at 76% in India, 91% in Indonesia, and 54.9% in the Mediterranean region of Türkiye.[19–21] These differences can be attributed to various factors, but we believe the primary reason is related to vaccination rates within the populations.

The typical symptoms of measles include fever and rash accompanied by cough, conjunctivitis, and coryza.[2] The combination of these clinical features, especially in high-risk patients or during an outbreak, strengthens the clinical suspicion of measles. Early suspicion allows clinicians to intervene in outbreaks and manage cases more effectively. However, in periods when measles is not prevalent, these symptoms may not immediately raise suspicion, leading to delays in diagnosis and outbreak response. Therefore, the use of serological tests becomes important in such scenarios.[4,19] In our study, cough was the most common symptom observed in 78% (70/90) of patients with measles, followed by coryza in 73% (65/90) and conjunctivitis in 53% (48/90). Additionally, the presence of cough along with fever and rash increased the likelihood of a measles diagnosis by 8.94 times. In the study by Husada et al.,[19] cough was the most common symptom after fever and rash, followed by coryza and conjunctivitis in half of the patients, which is consistent with our findings. Tuncay et al.[22] reported cough in 31.4% of measles cases, with conjunctivitis as the second most common symptom. Another study from Türkiye found similar results, with cough observed in 75% of cases and conjunctivitis in 47.5%.[23]

The severity of inflammation associated with infection can be measured through various hematological and biochemical tests. Neutrophils and lymphocytes play an important role in the inflammatory process, and temporary changes in their numbers are observed during this process.[9] Although there are specific biomarkers for measles, they are time-consuming and costly. While confirmatory tests are necessary for measles diagnosis in addition to clinical findings, the isolation of suspected cases is important in preventing transmission during the initial encounter. Therefore, clinicians need to have clinical indicators for rapid decision-making. Studies addressing this issue in the literature are limited, and when these studies are evaluated, the results are insufficient.[12–14,19]

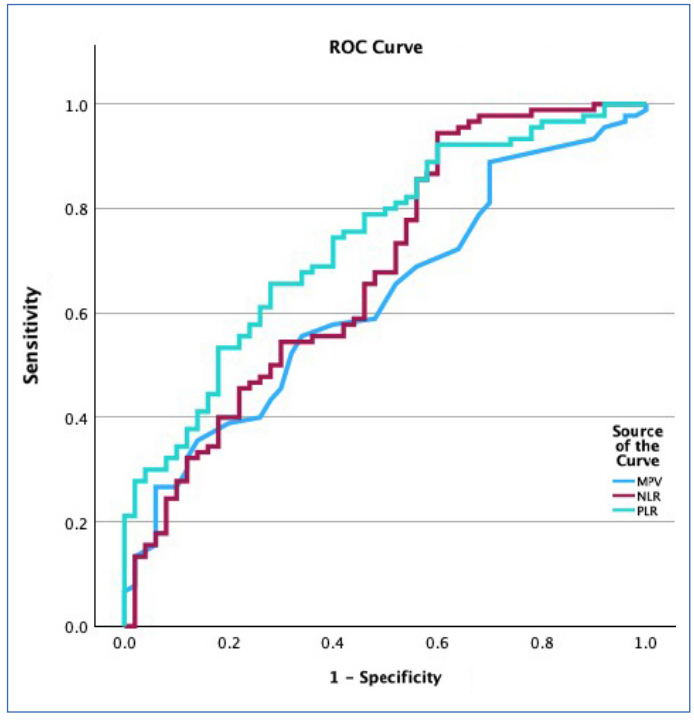

Figure 1: Predictive values of MPV, NLR and PLR for the diagnosis of measles.

In a study by Solmaz et al.[12] examining the role of NLR in measles diagnosis, no significant results were obtained when measles and healthy children were compared for NLR. In the study by Güzelçicek and Demir,[13] NLR was found to be significantly lower in measles children, but its predictive power for measles was found to be low. Considering all likelihood ratios for these positive and negative predictions, we found that an NLR of 0.28 was the best cut-off point for predicting the diagnosis of measles in children (area under the receiver operating characteristic (AUC): 0.680, sensitivity: 94%, specificity: 40%).

In a previous study, no relationship was found between the PLR value and measles,[12] while in several studies, the PLR value was found to be associated with the severity of measles cases.[13,14] In our study, PLR was significantly higher in the measles group and performed well in predicting measles diagnosis (cut-off point >89.2, AUC: 0.739, sensitivity: 65%, specificity: 72%). However, similar to NLR, we found that PLR was not a good predictor of measles diagnosis in linear regression analysis. We believe that the contribution of elevated lymphopenia in measles children to both PLR and NLR being higher compared to the control group is significant. We believe that both NLR and PLR cannot be used independently as individual indicators to strengthen the preliminary diagnosis of measles in febrile and rash-presenting children.

Thrombocytopenia is a common finding following many viral infections or during infection. Clinically, mild thrombocytopenia accompanied by lymphopenia in a patient exhibiting signs of acute illness raises suspicion of a viral infection.[24] MPV, used to measure the size of platelets, is also a laboratory test indicating platelet reactivity.[25] Studies investigating the role of MPV in measles diagnosis, like other inflammatory markers obtained from complete blood counts, are limited in the literature. In our study, we found lower platelet counts and higher MPV values in the measles group compared to the control group. Additionally, we found that a cut-off point 10 performed best in predicting measles diagnosis (AUC: 0.628, sensitivity: 36%, specificity: 86%). While Solmaz et al.[12] found lower MPV values in measles children, another study found lower platelet counts in the measles group compared to the control group but no difference in MPV.[14] In adult studies, mild thrombocytopenia has been reported as a common finding in measles patients, sometimes associated with minor bleeding complications.[24] Overall, both the literature and our findings indicate that MPV does not have a strong predictive power in measles diagnosis.

MeV, when entering the human body through the respiratory tract, initiates viremia via lymphocytes in lymphoid tissues and subsequently leads to the consumption of infected lymphocytes.[6] In our study, we identified significant relationships between changes in peripheral blood cell counts and measles infection. WBC and lymphocyte counts were found to be lower in measles cases, with leukopenia observed in one-third of measles patients and lymphopenia in 40%, both significantly higher compared to the control group. Looking at some previous studies, we found that the rates of leukopenia and lymphopenia in our study were quite high.[23,26,27] However, a study conducted in Italy on 249 children hospitalized due to measles reported similar rates; leukopenia was observed in 40.6% of patients and lymphopenia in 38.5%.[28] Another study from Türkiye also found significantly lower leukocyte and lymphocyte counts in measles patients compared to the control group, with lymphopenia detected in 40.5% of measles cases.[22]

In our study, complications were observed in approximately half of the patients, with AGE being the most common at 65.9% (29/44). Acute otitis media and pneumonia were observed at rates of 29.5% each. Previous studies have reported complication rates in measles patients ranging from 35% to 85%.[23,26–28] Lo Vecchio et al.[28] found complications in 85% of hospitalized children, with pneumonia being the most common at 23.3%. Us et al.[23] reported a complication rate of 37.5%, with AGE being the most common at 40%. The high complication rate in our study may be due to our status as a tertiary care center and the central hospital in our region. The most common complications vary across studies, which can be explained by differences in patient age distributions, the presence of comorbid chronic diseases, and vaccination rates. The reason for the high incidence of AGEs in the measles group is that these patients may have been diagnosed with a bacterial upper respiratory tract infection during the febrile prodrome before the onset of the characteristic rash and consequently treated with antibiotics. However, our data do not provide sufficient evidence to support this hypothesis. Therefore, we interpreted the observed rate of acute gastroenteritis as a potential complication of measles and considered this uncertainty as a limitation of our study.

Before 2020, the first dose of the measles vaccine was administered at 12 months and the second dose at 6 years of age in Türkiye.[15] However, following an increase in measles cases, changes were made to the national immunization program. According to the updated vaccination schedule, the MMR vaccine is now administered at 12 and 48 months, with an additional dose at 9 months in areas with a high number of cases.[16] Full vaccination is defined as receiving at least two doses of the measles vaccine, with a reported efficacy of 97% for two doses.[15,29] The measles vaccination coverage in Türkiye was reported as 95% according to the 2022 WHO report.[30] In our study, 36% (51/140) of all cases and 31% (34/90) of measles cases were fully vaccinated. We found no statistically significant difference in vaccination status between the measles and non-measles groups. In the study conducted by Tuncay et al.,[22] the rate of full vaccination for MeV was found to be 22.2%, while this rate was 7.8% among measles cases. In a study from Mersin, a city in Türkiye with a high population of Syrian refugees, 79.7% of suspected measles cases were unvaccinated.[21] In studies conducted in Europe, the proportion of measles cases that were unvaccinated ranged from 35% to 95%.[27,31–33] The low vaccination rate in our study can be attributed to the low socioeconomic status of the local population, the high number of refugees and undocumented immigrants in our region, and the increasing vaccine hesitancy in Türkiye. Recently, vaccine hesitancy has surged due to a court ruling requiring parental consent for vaccination and the frequent media coverage of anti-vaccine rhetoric.[34]

The most significant limitation of the study is that the non-measles etiology of fever and maculopapular rash in the control group was not investigated. Another important limitation is that the onset and distribution of rashes could not be accurately reported by families, leading to their exclusion from the study. To our knowledge, no similar study has been published previously, which strengthens the significance of our research.

CONCLUSION

Fever and rash are common in childhood and often cause concern among parents. This clinical presentation can result from a variety of conditions, ranging from benign viral rashes to serious illnesses. The differentiation of measles, a highly contagious disease that can lead to severe complications, from other diseases poses a significant challenge. Our study found that the presence of cough in addition to fever and rash significantly strengthens the diagnosis of measles. Furthermore, the presence of neutrophilia can serve as a valuable laboratory indicator, aiding in the exclusion of measles. Consequently, we conclude that markers derived from complete blood counts are not robust diagnostic tools for measles.

Statement

Ethics Committee Approval: The Bağcılar Training and Research Hospital Non-Interventional Clinical Research Ethics Committee granted approval for this study (date: 22.12.2023, number: 2023/12/16/093).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Conflict of Interest: The authors have no conflict of interest to declare.

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