



# Evaluation of 20 Pediatric Cases Diagnosed with Measles in Diyarbakır Children's Hospital in 2019

2019 Yılında Diyarbakır Çocuk Hastanesinde Kızamık Tanısı Alan 20 Çocuk Olgunun İrdelenmesi

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## Abstract

**Objective:** Measles is a highly contagious viral disease which can cause serious complications and be prevented with vaccination. In this study, we evaluated the demographic, clinical and laboratory findings of 20 children diagnosed with measles in order to use these data to determine strategies for early detection, control and prevention of measles outbreaks.

**Material and Methods:** A total of 20 patients followed up with the diagnosis of measles in Diyarbakır Children's Hospital between 2<sup>nd</sup> April 2019 to 9<sup>th</sup> July 2019 were evaluated retrospectively. Data about patients' demographic characteristics, clinical and laboratory findings, treatments and complications were obtained from medical records.

**Results:** The age range of the patients was 5-214 months; median age was 11 months (8-27). Of the cases, 15 (75%) were males and 5 (25%) were females. Five (25%) cases had a history of contact with measles patients. Nineteen cases had no measles vaccination and 1 case had a single dose of measles vaccination. The most common clinical signs and symptoms were high fever (100%), catarrhal symptom and cough (95%), conjunctivitis (55%), maculopapular rash (45%), and Koplik's spots (30%). Laboratory tests revealed lymphopenia in 10 (50%) cases, leukopenia in 5 (25%) cases, and thrombocytopenia in 1 (5%) case. C-reactive protein was high in 8 (40%) cases, and the mean value was 28.75 mg/dL (9.95-39.3). Complications were bronchopneumonia in three cases, febrile convulsion in one case, diarrhea and acute dehydration in one case. All cases were discharged without sequel.

**Conclusion:** Measles is a highly contagious disease; prevention of outbreaks is possible by keeping vaccination rates of the population high.

## Öz

**Giriş:** Kızamık ciddi komplikasyonlarla seyredabilen aşı ile önlenebilen oldukça bulaşıcı viral enfeksiyon hastalığıdır. Bu çalışmada kızamık salgınlarının erken saptanması, kontrolü ve önlenmesi için strateji belirlenmesinde kullanılacak veri elde etmek amacıyla kızamık tanısı alan 20 çocuk olgunun demografik, klinik ve laboratuvar bulguları irdelendi.

**Gereç ve Yöntemler:** 2 Nisan-9 Temmuz 2019 tarihleri arasında Diyarbakır Çocuk Hastanesine başvuran, kızamık tanısı ile yatırılarak izlenen 20 çocuk olgu retrospektif olarak incelendi. Olguların demografik özellikleri, klinik ve laboratuvar bulguları, aldığı tedaviler ve gelişen komplikasyonları ile ilgili veriler tıbbi kayıtlardan elde edildi.

**Bulgular:** Hastaların yaş dağılımı 5-214 ay arasında, medyan yaş 11 ay (8-27), 15 (%75)'i erkek, 5 (%25)'i kız idi. Beş (%25) olguda temas hikayesi vardı. On dokuz olgu kızamık aşısı olmamış, bir olgunun tek doz kızamık aşılması mevcuttu. Başvuruda ön planda olan klinik belirti ve bulgular yüksek ateş (%100), nezle ve öksürük (%95), konjunktivit (%55), makülopapüler döküntü (%45) ve Koplik lekeleri (%30) idi. Laboratuvar tetkiklerinde 10 (%50)'unda lenfopeni, 5 (%25)'inde lökopeni, 1 (%5)'inde trombositopeni tespit edildi. C-reaktif protein 8 (%40) olguda yüksek medyan 28.75 mg/dL (9.95-39.3) idi. Gelişen komplikasyonlar üç olguda bronkopnömoni, birinde febril konvülsiyon, birinde ishal ve akut dehidratasyon idi, hepsi şifa ile taburcu edildi.

**Sonuç:** Kızamık, bulaşıcılığı oldukça yüksek bir enfeksiyon hastalığıdır, salgınlarının önlenmesi aşılama oranlarının yüksek tutulması ile mümkündür. Ek olarak salgın dönemlerinde kızamığın prodromal evredeki semptomlarını gösteren bir yaşından küçük duyarlı çocuklara şüphe

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In addition, during outbreaks of measles suspicious approach to children under 12 months who show prodromal symptoms of measles will provide early diagnosis. Early diagnosis will make possible early isolation, rapid management of their contacts, and so will significantly reduce outbreak.

**Keywords:** Measles, epidemic, isolation, maculopapular, rash, child

## Introduction

Measles is a highly contagious viral infection seen worldwide. The agent of the disease is an RNA virus from the morbillivirus group of the *paramyxoviridae* family. Infecting only humans, this virus becomes an epidemic in the end of winter and spring months since it can stay alive in low temperatures. Disease development rate in susceptible individuals after contact with the virus is 90%. Its period of contagiousness is accepted as 4 days before and 4 days after the start of rash (1). The incubation period of the disease is between 6 and 21 days, mean 13 days (2). Prodromal period is characterized with high fever, catarrh, cough, and conjunctivitis, and maculopapular rash developing afterwards. The rash begins from the hairy skin and face with an inclination to merge and spreads to the extremities but does not involve the palms and plantar and heals with hyperpigmentation after approximately 5-6 days. Lifelong immunization remains after having measles.

Vaccination is the most effective method of protection from measles. World Health Organization (WHO) recommends community immunization to increase up to 95% for the control of the disease, prevention of epidemics, and elimination of the disease. Vaccination rate, which was 98% in 2016 in our country, dropped to 96% in the years 2017 and 2018. Vaccination rates in Southeastern Anatolia, where the province Diyarbakir is also located, is again 96% (3). According to the data of the Ministry of Health, the number of cases in the years 2013, 2014, 2015, 2016, 2017, and 2018 was 7405, 565, 342, 9, 84, and 716, respectively. Along with the fact that data on the year 2019 has not been published yet, it is believed that there is a significant rise in the number of cases. Measles is still an endemic disease in Turkey and continues to cause epidemics once in 3-4 years.

ile yaklaşmak erken tanıyı sağlayacaktır, erken tanı ve temaslıların hızlı yönetimi, izolasyon önlemlerine sıkı uyulması bulaşıcılığı önemli ölçüde azaltacaktır.

**Anahtar Kelimeler:** Kızamık, salgın, izolasyon, makülopapüler, döküntü, çocuk

A significant increase in the number of cases in 2019 in our region and the fact that cases had received diagnosis as of April 2019 caught our attention, and with this study, it was aimed to determine factors that could be helpful in the prevention or control of the epidemic by examining the demographic, clinical, and laboratory characteristics of the patients diagnosed with measles.

## Materials and Methods

The study included hospitalized patients that presented to the Diyarbakir Children's Hospital between April 2-July 9, 2019 and fit the confirmed case description of the Measles, Rubella and Congenital Rubella Syndrome Surveillance (MRCS) Permanent Memorandum of the Ministry of Health (Table 1) (4). Data were obtained from patient files, medical records, and Ministry of Health Measles/Rubella Examination Form. Demographics of the patients, clinical and laboratory findings, the treatments they had received, and the complication that had developed were noted on the form prepared for the study. Laboratory tests were evaluated with age-appropriate reference range.

SPSS 22.0 package program was used for analysis. Continuous variables were presented as mean  $\pm$  standard deviation or median  $\pm$  interquartile range; and categorical variables were presented as number of cases and percentage (%).

The study was approved by Health Sciences University, Diyarbakir Gazi Yasargil Training and Research Hospital Ethics Board with date/number: 4.7.2019/325.

## Results

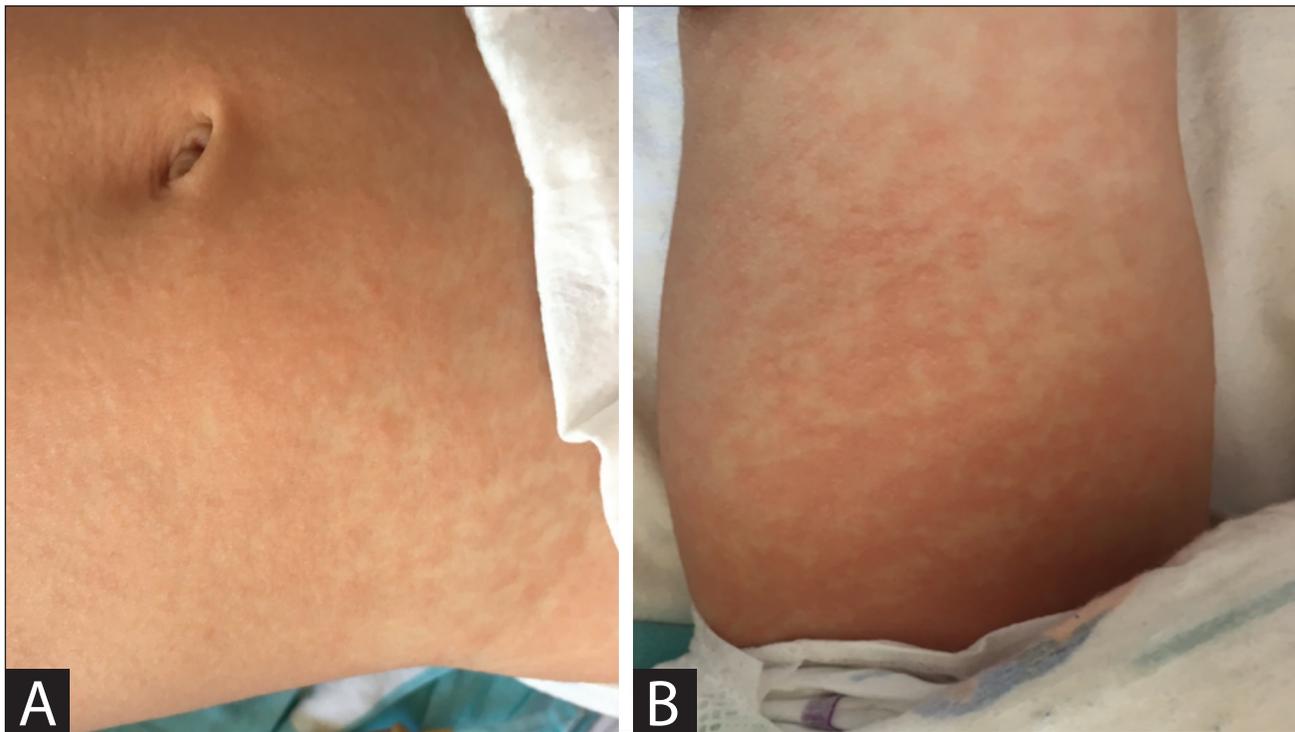
A total of 20 cases were included into the study. Fifteen (75%) were males and 5 (25%) were females. Age range

**Table 1.** Case identifications and classifications of Measles, Rubella and Congenital Rubella Syndrome Surveillance (MRCS) Permanent Memorandum of the Ministry of Health (4)

<p><b>Suspected Case:</b> Any disease presenting with maculopapular rash.</p> <p><b>Probable Measles Case (Clinical Case):</b> Case compatible with clinical description<sup>1</sup>.</p> <p><b>Definitive Measles Case:</b></p> <p><b>a. Laboratory-confirmed Case:</b> Probable Case confirmed with one of the criteria<sup>2</sup> needed for diagnosis or if vaccinated recently, case with an epidemiological relation to the laboratory-confirmed case.</p> <p><b>b. Epidemiology-related Case:</b> Probable Case with an epidemiology-related relation (time and place in terms of contact and incubation-contact 7-18 days prior to the start of symptoms) to a laboratory-confirmed case</p> <p>Not a Case: Negative laboratory tests in an individual with symptoms and signs compatible with the clinical definition of measles or case with an epidemiologic relation to a case confirmed by the laboratory of not having measles (for instance, (örn: roseola infantum, erythema infection, and etc)</p>
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<sup>1</sup> Fever higher than 38°C and maculopapular rash and cough or running nose or disease characterized by conjunctivitis.

<sup>2</sup> Detection of measles-specific IgM antibody or measles virus isolation or detection of measles viral RNA with RT-PCR or significant increase (at least 4 times) in measles-specific IgG antibody titer in serum samples taken at 2-4 weeks interval.



**Figure 1.** Maculopapular rashes in the abdomen region (A) and leg (B) of the case with measles.

was 5-214 months; median age was 11 months (range: 8-27 months). Thirteen (65%) of the cases were younger than 12 months and had not received their measles vaccination yet, 6 (30%) of the patients were older than 12 months and had not received any of the age-appropriate vaccinations, and 1 (5%) patient was older than 12 months and had the single

dose of measles vaccination. There were five cases who got into contact with measles patients, of whom 4 got into contact at hospital. Symptoms and signs of the cases at the time of presentation were fever (100%), catarrh and cough (95%), conjunctivitis (55%), maculopapular rash (45%), and Koplik's spots (30%) (Figure 1, 2). Eleven cases without any rashes on presentation experienced maculopapular rashes during follow-up. Table 2 summarizes the symptoms and clinical findings of the cases on presentation.

Laboratory tests revealed lymphopenia in 10 (50%) cases, leucopenia in 5 (25%) cases, and thrombocytopenia in 1 (5%) case. While aspartate aminotransferase (AST), alanine



**Figure 2.** Conjunctivitis in the case with measles, transverse marginal lines on the lower eye lids (Stimson sign).

**Table 2.** Clinical findings and symptoms of the cases on presentation

Symptoms	Number of patients n (%)
Fever	20 (%100)
Catarrhal symptom/cough/running nose/catarrh	19 (%95)
Lachrymation/photophobia	11 (%55)
Diarrhea	5 (%25)
<b>Findings</b>	
Maculopapular rash	9 (%45)
Koplik's spots	6 (%30)
Conjunctivitis	11 (%55)
Lymphadenopathy	3 (%15)

**Table 3.** Laboratory values of the cases

Hemogram	Mean value	Min-max value
Leucocyte (mm <sup>3</sup> )	8.26 ± 3.64	3.22-14.89
Neutrophil (mm <sup>3</sup> )	3.34 ± 1.96	1.16-6.95
Lymphocyte (mm <sup>3</sup> )	4.23 ± 3.02	0.77-11.9
Hemoglobin (g/dL)	11.38 ± 2.03	7.4-16.3
Thrombocyte (mm <sup>3</sup> )	315.22 ± 135.62	120-642
Biochemical values	Mean value	Min-max value
Alanine aminotransferase (U/L)	23.58 ± 10.15	10-43
Aspartate aminotransferase (U/L)	43.16 ± 11.38	17-67
Lactate dehydrogenase (U/L)	411 ± 86.39	347-552
Creatinine (mg/dL)	0.46 ± 0.11	0.4-0.8
C-reactive protein (mg/dL)	28.75*	2.3-142

\* Median

aminotransferase (ALT), blood urea nitrogen (BUN), and lactate dehydrogenase (LDH) were found normal in biochemical test, creatinine level in one patient with dehydration was found at the borderline with 0.8 mg/dL. C-reactive protein (CRP) (reference value < 5 mg/dL) was found high (40%) in 8 patients, and the median value was 28.75 mg/dL (range: 9.95-39.3). Erythrocyte sedimentation rate (ESR) was tested in two patients and found as 37 mm/hour and 9 mm/hour. In blood samples sent to Diyarbakir Provincial Public Health Laboratory for measles, measles IgM was found positive in all patients with the method Enzyme-Linked Immunosorbent Assay (ELISA). Laboratory values of the patients are summarized in Table 3.

All cases included into the study were inpatients of the Pediatric Clinic, whose tests and treatments were arranged as necessary. The first preliminary diagnosis of hospitalization was measles in 9 (45%), bronchiolitis in 7 (35%), and fever without a source in 4 (20%) patients. Kawasaki disease was simultaneously considered in two cases with fever without a source. Three cases developed bronchopneumonia, one developed diarrhea and dehydration and one developed febrile convulsion, all discharged with full recovery.

### Discussion

Age range of the cases in our study was 5-214 months, and median age was 11 months (range: 8-27 months). In a 2012 study of Metin et al. conducted in Ankara with 44 measles cases, age range was found as 4-191 months and median age as 58.6 ± 59.5 months (5). During the 2013-2014 epidemic in Istanbul, Türkkan et al. found the age range of 20 cases as 7-196 months and median age as 63.8 ± 44 months (6). In comparison to both studies, the median age determined in our study was younger, which was due to the fact that 65% of our cases consisted of those under the age of 12 months and

were not yet included into the routine vaccination calendar of the Ministry of Health. Two of the remaining cases were between 1-4 years, one between 5-9 years, and two between 10-18 years of age. Nineteen (95%) of our cases were not vaccinated, only one had a single dose of measles vaccination. These data indicate that susceptible individuals, particularly babies under 12 months without vaccination, are under serious risk at the event of an outbreak. In the event of an outbreak, an additional dose of vaccination administered at babies between 6-12 months would prevent the outbreak to expand, just like the mop-up practice performed in Istanbul in 2014. In the event of a serious increase in the number of cases in Turkey, an arrangement in the vaccination calendar with 3 doses at 9 months, 15 months, and first grade could also be taken into consideration as an option.

Fifteen (75%) of the 20 cases in our study were males and 5 (25%) were females, with a male/female ratio of 3/1. The male/female ration in Metin et al.'s and Türkkan et al.'s studies were found as 1.7/1 and 1/1.1, respectively (5,6). It is known that everyone at any age is susceptible to the disease without any sex discrimination unless there is measles immunization. All of our cases were Turkish citizens. The number of cases that had got into contact with measles patients was 5 (25%), and 4 of them had got into contact at hospital. The first contact-case in our hospital was examined in the same outpatient clinic 1.5 hours after the index case with complaints like cough and fever. After having being hospitalized with a preliminary diagnosis of bronchiolitis, this contact case had rashes 6 days later, and simultaneously the diagnosis of the index case became definite. While the first contact patient with rashes was isolated, 0.4 g/kg intravenous immunoglobulin (IVIG) was administered to the contact patients younger than 6 months and sharing the same room and measles vaccination was given to those older than 6 months without vaccination or

with single dose vaccination. Measles was seen despite IVIG administration in a 5-month old case among this secondary contact group (Second contact case). The third contact case was taken to the room of the contact patients who were isolated by his/her mother. Our fourth contact patient was referred to our clinic due to fever without a source, rashes were noticed during presentation and was hospitalized with a preliminary diagnosis of measles. The patient's history revealed that the patient with rash wandered around the corridors of the service in the previous healthcare center where the patient was hospitalized with a preliminary diagnosis of measles. When the attack rate of the disease is considered to be 90%, early suspicion, early isolation, strictly following isolation rules, and contact prophylaxis prove to be of utmost importance. Especially in endemic regions, inquiry and follow up must be carried out perfectly in epidemic periods when babies under the age of 12 months present with respiratory symptoms and fever, and in case of suspicion, the patient must be isolated and hospitalized. It was seen in two of our cases that isolation rules were not strictly followed, which emphasizes that informing the patient and next-of-kin and ensuring abidance are important parts of outbreak management.

The clinical progress of the disease can be atypical or modified, but it is not possible for the disease to progress without symptoms. Symptoms and clinical findings of our patients on presentation were fever, catarrh, cough, maculopapular rash, conjunctivitis, photophobia, and Koplik's spots (Table 1). High fever was the most definitive symptom in all of our patients and was taken as mean  $39.21 \pm 0.8$  (38.6-41)°C. Fever lasted for more than 5 days in three patients, and Kawasaki disease was considered for the differential diagnosis of the two patients but their acute phase negativities were found incompatible with this diagnosis. Eleven patients were in the prodromal period during presentation, they did not have rashes yet or the rashes were hardly visible. Therefore, hospitalization diagnosis of the patients was bronchiolitis in 7 (35%) and fever without a source in 4 (20%). During follow up, maculopapular rash was observed in all, and starting from the face and hairy skin, the rashes spread to the truncus and extremities. In two cases, the rashes were found more on the truncus rather than the face. Koplik's spots were observed in 6 (30%) patients, and they were less than anticipated since they persisted for 12-72 hours and disappeared prior to exanthema (7). These were detected when Koplik's spots were specifically searched for during examination after first measles cases were diagnosed.

Leucopenia and significant lymphopenia were found in laboratory studies of the patients. It has been indicated that leucopenia, thrombocytopenia, and T-cell lymphopenia can be observed during measles infection (8). In previous studies,

leucopenia and thrombocytopenia have been confirmed as 11.2-73% and 33.6-50%, respectively (9,10). CRP was slightly elevated in 40% of the cases. However, it was detected as 142 mg/dL in one case with bacterial pneumonia secondary to measles and between 6-39.3 mg/dL in other cases.

The most common complications of measles in children include otitis media, bronchopneumonia, croup, and diarrhea. Acute encephalitis causing permanent brain damage is seen at a rate of 0.1%. Mortality is encountered as a result of respiratory and neurologic complications at a rate of 0.1-0.3% (11). Three cases developed bronchopneumonia, one developed diarrhea and dehydration and one developed febrile convulsion, length of hospital stay was mean 3.8 days and all were discharged with full recovery.

In a society with insufficient measles vaccination rate, experiencing outbreaks is inevitable in the presence of susceptible persons. In our country, vaccination rate is 96% and not below the immunization rate recommended by WHO (3). Therefore, measles outbreaks seen in the region are most probably due to external migration. Hence, among the 716 measles cases reported in 2018, 304 were foreign and 412 were domestic.

Increasing vaccination rates should be the primary objective in the prevention of measles outbreaks. Additionally, early suspicion, isolation preventions with early diagnosis, and rapid contact management on site will be able to ensure the decrease in disease spread.

**Ethics Committee Approval:** The ethical approval for this study was obtained from Health Sciences University, Diyarbakir Gazi Yasargil Training and Research Hospital Ethics Board (Decision number: 325, Date: 04.07.2019).

**Informed Consent:** Verbal and written patient consent was obtained.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - SÖD; Design - SÖD; Supervision - SÖD; Resource - SÖD; Data Collection and/or Processing - SÖD, ÖA, SM, BY; Analysis and/or Interpretation - SÖD, GK, SM; Literature Search - SÖD; Writing - SÖD; Critical Review - All of authors.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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