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Research Article / Araştırma Makalesi

Severe Measles Cases Requiring Pediatric Intensive Care Unit Admission

Çocuk Yoğun Bakım Ünitesine Yatış Gerektiren Ağır Kızamık Vakaları

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Abstract

Measles is a vaccine-preventable disease, and the disease burden is reduced with widespread pediatric measles immunization. Sporadic and severe cases might be observed during local outbreak situations, especially among unvaccinated people or vaccine non-eligible age groups, including infancy. In this study, we retrospectively evaluated the clinical and laboratory findings, and outcomes of children with measles requiring pediatric intensive care unit admission. We retrospectively evaluated medical records of 14 children with measles, who were followed up in the pediatric intensive care unit of Sanliurfa Training and Research Hospital between January 1st and June 30th, 2019. The median age was 9.5 months (range between one and 120 months). The most common reasons for admission to the pediatric intensive care unit were bronchopneumonia (n: 10) and/or sepsis. Two were diagnosed with pediatric acute respiratory distress syndrome, four patients had sepsis, and one patient had meningoencephalitis. The mortality rate was 14.2%. Risk factors associated with intensive care unit admission included being unvaccinated, being malnourished, having an underlying condition, and the development of bronchopneumonia as a complication. The mortality rate of measles, which is a preventable disease despite early treatments in the pediatric intensive care unit, is high, especially in unvaccinated children and those who have underlying conditions.

Keywords: Children; outbreaks; Measles; Mortality; Bronchopneumonia; Pediatric intensive care unit.

Özet

Kızamık aşı ile önlenebilir bir hastalıktır. Yerel salgın durumlarında, özellikle aşılanmamış kişilerde sporadik ve ciddi vakalar gözlenebilir. Bu çalışmada, çocuk yoğun bakım ünitesinde yatış gerektiren kızamık tanısı kesin olan çocukların klinik ve laboratuvar bulgularını ve sonuçlarını geriye dönük olarak değerlendirdik. 1 Ocak-30 Haziran 2019 tarihleri arasında Şanlıurfa Eğitim ve Araştırma Hastanesi çocuk yoğun bakım ünitesinde izlenen 14 kızamık tanılı çocuğun tıbbi kayıtları geriye dönük olarak değerlendirildi. hastaların median yaşı 9,5 aydı (1 ile 120 ay arasında değişiyordu). Pediatrik yoğun bakım ünitesine en sık yatış nedenleri bronkopnömoni (n: 10) ve/veya sepsis idi. İki hastada pediatrik akut solunum sıkıntısı sendromu, dört hastada sepsis ve bir hastada meningoensefalit tanısı konuldu. Mortalite oranı %14,2 idi. Yoğun bakım ünitesine kabul ile ilişkili risk faktörleri arasında aşılanmamış olma, yetersiz beslenme, altta yatan bir durumun olması ve komplikasyon olarak bronkopnömoni gelişimi yer almaktadır. Önlenebilir bir hastalık olan kızamık nedeniyle yoğun bakım yatışı gereksinimi olan çocuklarda ölüm oranı erken müdahalelere rağmen yüksektir.

Anahtar Kelimeler: Çocuk, salgınlar, Kızamık, Ölüm, Bronkopnömoni, Çocuk yoğun bakım ünitesi

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1. Introduction

Measles is an acute highly transmissible viral infection associated with morbidity and mortality among unvaccinated or vaccine-ineligible populations. The most common complication of measles is otitis media, while other severe complications, such as pneumonia or neurological conditions, can cause severe clinical conditions that result in admission to the pediatric intensive care unit (PICU) (1).

According to WHO, the measles vaccine has saved the lives of nearly 31.7 million people around the World since 2000 (2). There are also local outbreaks of measles. The annual recorded incidence of measles decreased by 88% between 2000 and 2016, from 145 to 18 cases per million people, but increased to 120 in 2019 before decreasing to 22 in 2020. In 2020, 26 major and disruptive outbreaks (more than 20 cases per million) were recorded throughout five WHO regions; 17 (65%) of these outbreaks occurred in African nations (3). Between 2000 and 2010 reported measles-containing vaccine first dose (MCV1) coverage improved globally from 72 percent to 84 percent between 2000 and 2010, peaked at 86 percent in 2019, and then decreased to 84 percent in 2020 during the COVID-19 pandemic (3). Measles deaths have been reduced by 94 percent since 2000. However, measles remains an important public health problem.

This study aims to assess the clinical and laboratory data of patients with measles requiring pediatric intensive care unit admission in 2019 in Sanliurfa, Turkey.

2. Materials and Methods

In this study, medical records of patients with measles requiring PICU admission, have been retrospectively evaluated in the Ministry of Health Sanliurfa Training and Research Hospital between January 1st and June 30th, 2019. The diagnosis of measles has been confirmed with laboratory tests (ELISA tests, specific IgM, and IgG antibodies) in cases that fulfill the criteria for definitive diagnosis, in addition to clinical findings (fever, malaise, cough, coryza, and conjunctivitis, Koplik spots, a maculopapular rash). Ethics approval was obtained from the Harran University Local Ethical Committee. Age, gender, anthropometric measurements, vaccination status, socioeconomic status, history of contact with a measles case, diagnosis upon admission to the intensive care unit, receipt of treatment (vitamin A, antibiotics), and complications were evaluated. From medical records, complete blood counts, peripheral blood smears, serum C-reactive protein (CRP) and procalcitonin levels, arterial blood gas analysis, and blood culture results were noted. Pediatric risk of mortality (PRISM) scores were recorded for all patients with the worst clinical and laboratory data within the first 24 hours (4). Supportive extracorporeal therapies such as renal replacement therapy and plasma exchange therapy were recorded. The outcomes of the patients have been classified as ”died” or “discharged”.

3. Results

Clinical and laboratory parameters of 14 children (8 boys and 6 girls) requiring PICU admission have been evaluated (Table 1-3). The median age of the patients was 9.5 months (range between one and 120 months). Three children (21.4%) were aged between 0-3 months, eight children (57.1%) were aged between 3-12 months, and three children were above 12 months (15 months, 69 months, and 120 months, respectively).

Four children (28.5%) have had contact with a patient who had a measles-like rash, while one patient had contact with a patient who had been diagnosed with measles in another city. All of the patients were positive for measles IgM. One patient had a serological test three weeks after being admitted because of technical difficulties; the results showed that this patient had measles IgG. All of our patients received vitamin A supplements (age-appropriate doses) after the diagnosis of measles.

Eleven children with measles were younger than the age for the measles-containing vaccine in the National Immunization Program of the Ministry of Health Turkey, and two children (> 1 year) had missed their MMR vaccine Schedule (unvaccinated refugees). In three cases, siblings of the patients had a history of measles. Five patients (35.7%) were immigrants with Syrian backgrounds, and one of these was a resident of an immigrant camp. One patient had albinism, three patients had neuromotor retardation and epilepsy, and one of them had a ventricular septal defect and aortic coarctation. Anthropometric measurements (weight-for-age) of five patients (35.7%) were lower than the 3rd percentile for age, and two patients were between the 3-10th percentile for (14.2%).

Table 1. Demographical findings, clinical findings of 14 children with measles

Case Number	Age (Months)	Gender	*Vaccine status*	Underlying disease	GCS	*Complications*
1	1	M	unvaccinated	-	10	Septic shock, PARDS, acute renal injury
2	3	F	unvaccinated	-	15	Bronchopneumonia
3	8	F	unvaccinated	-	15	Bronchopneumonia
4	12	M	unvaccinated	NMR, epilepsy	13	Bronchopneumonia
5	6	F	unvaccinated	-	15	Bronchopneumonia
6	5	M	unvaccinated	-	15	Bronchopneumonia
7	10	F	unvaccinated	NMR, epilepsy	13	Sepsis
8	12	M	unvaccinated	-	15	Bronchopneumonia
9	120	F	unknown	NMR, epilepsy, severe malnutrition	9	Bronchopneumonia, Empyema, Sepsis
10	2	F	unvaccinated	-	13	Sepsis
11	15	M	unvaccinated	Albinism	8	Bronchopneumonia, TAMOF
12	10	M	unvaccinated	VSD, AoC	13	Bronchopneumonia, PARDS
13	9	M	unvaccinated	-	15	Bronchopneumonia
14	69	M	unvaccinated	-	9	Status epilepticus, Suspected Meningitis

CRP: C- reactive protein; GCS: Glasgow coma score; Gender F: Female, M: Male; AoC: Aortic Coarctation; NMR: Neuromotor retardation; PARDS: Pediatric Acute Respiratory Distress Syndrome; PCT: Procalcitonin; TAMOF: Thrombocytopenia-associated multiple-organ failure; WBC: White blood cell; VSD: Ventricular septal defect

Table 2. Laboratory findings of 14 children with measles

Case Number	WBC (mm^3)	Platelet (mm^3)	Lactate (mmol/L)	CRP (mg/dL)	PCT (ng/mL)
1	32,290	20,000	12.1	283	100
2	27,000	429,000	0.7	69	2
3	30,000	380,000	1	39	0.5
4	25,000	221,000	0,6	32	0.6
5	10,300	473,800	0.8	61	0.5
6	18,000	547,000	1.6	86	1.5
7	33,000	230,000	3.8	157	30
8	21,500	365,000	2	76	0.5
9	19,690	325,000	3.9	180	100
10	19,100	266,700	3.5	82	55
11	23,000	44,000	6	53	85
12	17,500	274,000	2.0	70	0,6
13	24,000	690,000	0.8	16	0.7
14	28,120	234,000	1.8	277	1

CRP: C- reactive protein, PCT: Procalcitonin; WBC: White blood cell

Table 3. Clinical interventions in PICU, PRISM score, predicted mortality and outcome of 14 children with measles

Case Number	Antibiotic	ECT	Mechanical Ventilation	PRISM score	Predicted Mortality	Length of PICU stay (days)	Outcome
1	Cefotaxime Linezolid	Peritoneal dialysis	IMV	19	30%	14	Discharged
2	none	-	-	13	11%	7	Discharged
3	none	-		10	6.2%	3	Discharged
4	none	-	-	13	11%	5	Discharged
5	none	-	-	15	11.7%	4	Discharged
6	none	-	-	9	5.1%	3	Discharged
7	Cefotaxime Vancomycin	CVHDF	-	18	25.8%	5	Discharged
8	none	-	-	5	1.7%	3	Discharged
9	Meropenem Vancomycin	-	IMV	23	49.5%	21	Died
10	Cefotaxime	-	-	18	25.8%	4	Discharged
11	Cefotaxime Vancomycin	PLEX, CVVHDF	IMV	36	93.5%	12	Died
12	Cefotaxime Vancomycin	-	IMV	21	39.3%	10	Discharged
13	none	-		13	11%	3	Discharged
14	Cefotaxime Vancomycin	-		16	18.7%	6	Discharged

CVVHDF: Continuous veno-venous hemodiafiltration; ECT: Extracorporeal Treatment; IMV: Invasive mechanical ventilation; PICU: Pediatric intensive care unit; PLEX: Therapeutic plasma exchange; PRISM: Pediatric risk of mortality

All patients were admitted to isolated rooms in the PICU. Fever and a maculopapular rash were the most common presenting symptoms for all the patients. The period between the onset of symptoms and presentation varied between 12 and 72 hours. Ten children were admitted from the Pediatric Emergency Unit and four patients were admitted from the inpatient wards. PRISM scores vary between 5 and 36, and predicted mortality according to PRISM scores was between 1.7 and 93.5%. Ten patients were admitted with respiratory distress due to bronchopneumonia, requiring oxygen supplementation. Two children were diagnosed with pediatric acute respiratory distress syndrome (pARDS). A 69-months-old boy presented with a seizure, a lumbar puncture was performed for suspected meningoencephalitis; the cerebrospinal fluid (CSF) protein level was 60 mg/dL and the glucose level was 50 mg/dL. CSF gram staining was negative, but measles serology could not be confirmed in the CSF sample. Two patients had culture-negative sepsis. During the intensive care unit stay, one patient had pancytopenia and two patients had ARDS secondary to bronchopneumonia and sepsis (Figure 1). Two patients required chest tube drainage due to pneumothorax and empyema.

The length of PICU admission varied from 3–21 days, and hospital admission were 5–41 days. One patient who had albinism and presented with atypical symptoms of measles was treated in the PICU unit for 12 days and needed continuous venovenous hemodiafiltration (CVVHDF) and plasma exchange therapy because of multiorgan failure caused by pARDS and septic shock. Despite all supportive therapies, the patient died. One patient, who needed to be admitted to the intensive care unit twice during the clinical course, died three weeks after acute presentation with empyema and sepsis.

In this study, we present 14 cases of measles who needed to be admitted to an intensive care unit, two of whom died because of complications from measles.

In our study, 11 patients were under the age of vaccination for measles-containing vaccines according to the National Immunization Program. Metin et al. evaluated 44 pediatric measles cases in Ankara, Turkey, between 2012 and 2013, and they showed that all of these patients either missed scheduled vaccinations or were smaller than the age of vaccination as in our study (9). In 2014, in a study carried out in the USA, Gastanaduy et al. showed that among 178 cases of measles, only 10% had received the measle vaccine (10).

The primary method of protecting children under the age of vaccination is through high immunization rates in the population (11). Yörük et al. showed that the region with the highest vaccination rejection rate is Southeastern Anatolia Region where Sanlıurfa is located. The biggest reason for vaccine rejection is the fear that the ingredients in the vaccine may cause undesirable effects (12). Reduced vaccination rates make neonates and infants high-risk groups for measles, which can cause problems that necessitate hospitalization to an intensive care unit and, in some cases, death. In our case series, two children missed their measles-containing vaccine schedule. Missing the vaccine shot for a disease in which vaccination is the principal method for prevention, is the underlying etiology of the infection in these patients.

Complications have been reported in 30% of measles cases. It is known that the risk of severe complications is higher in infants younger than one year of age and adults. One to six percent of the patients who have measles have pneumonia, 6% have gastroenteritis, 7–9% have severe otitis media, and loss of sight and encephalitis are each encountered in one in 1000 cases (13). In our study, ten of the patients in the PICU had bronchopneumonia, three had sepsis, and one had meningoencephalitis. One patient had pancytopenia, two patients had pARDS secondary to bronchopneumonia and sepsis. Two of our patients needed CVVHDF and plasma exchange therapy because of sepsis-associated organ dysfunction with thrombocytopenia-associated multiple organ failure. In our study, although they were in contact with the measles case, none of the patients were vaccinated or received intravenous immunoglobulin (IVIG) treatment (14).

One of every 20 measles cases results in mortality in developing countries (15). Donadel

et al. tried to determine the mortality risk factors of measles cases in infants and children under the age of 59 months. They found that 93% of the patients who died, were not vaccinated with an age-appropriate dose of measles-containing vaccine. The presence of malnutrition and children with bronchopneumonia have an increased risk for mortality (16). In our study, none of our patients were vaccinated, 50% had malnutrition (underweight/ low weight-for-age), 35.7% had an underlying disease, and 71.4% of patients developed bronchopneumonia. Despite all treatment modalities, the mortality rate was 14.2 % in the PICU. In our study, one patient died during a measles infection and another died when s/he was admitted to the PICU two weeks after the acute infection. We enrolled only children with severe conditions requiring PICU, and the predicted mortality regarding pediatric risk of mortality at admission was higher than 20% in six out of 14 cases.

Our study has some limitations. This is a retrospective, short-term interval, single-center experience and includes only children requiring PICU.

4. Conclusion

Respiratory tract infections, ARDS, and sepsis are among the important clinical states that cause mortality and morbidity in measles patients admitted to the intensive care unit. Despite early treatment, the mortality rate of measles is high, particularly in unvaccinated children and those with underlying conditions. Complications and high mortality observed in intensive care patients highlight the importance of maintaining a high measles vaccine coverage, with enhanced targeting of the unvaccinated population.

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Ethics

Ethics Committee Approval: The study was approved by Harran University Local Ethical Committee (Number: 20, Date: 23.11.2020).

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

Authorship Contributions: Surgical and Medical Practices: EK Concept: EK Design: EK Data Collection or Processing: EK Analysis or Interpretation: EK, AFY Literature Search: EK Writing: EK, AFY.

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