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*Sorumlu Yazar/Corresponding Author ,stasdemirmeister@gmail.com
KILIÇ E,F, ORCID: 0000-0002-0964-5572
TANRIVERDİ H, ORCID: 0000-0003-3208-2445
KOÇAK H,S,ORCID:0000-0003-1807-1280
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Araştırma Makalesi / Research Article

Evaluation of Laboratory and Demographic Data of Children Presenting with Hand, Foot and Mouth Disease

El, Ayak, Ağız Hastalığı ile Başvuran Çocukların Laboratuvar ve Demografik Verilerinin Değerlendirilmesi

Fedli Emre KILIÇ[1], Hüseyin TANRIVERDİ[1] , Hatice Serap KOÇAK[2]*

[1]Adıyaman Training and Research Hospital Pediatric Service, Adıyaman,
[2]*Faculty of Health Sciences, Department of Public Health Nursing, Gaziantep University, Gaziantep, Türkiye

ÖZ

El-ayak- ve-ağız hastalığı, enterovirüslerin neden olduğu yaygın bir çocukluk çağı hastalığıdır. El-ayak-ve-ağız hastalığında kan testleri etkilenebilir. Bu çalışmanın amacı el-ayak-ve-ağız hastalığı ile başvuran hastaların demografik ve laboratuvar verilerini sağlıklı çocuk grubuyla karşılaştırmak ve hastalığın etkisini belirlemektir. Bu çalışma geriye dönük olarak yapıldı. Araştırma 94 çocukla gerçekleştirilmiştir. El-ayak-ve-ağız hastalığına sahip 47 çocuk deney grubunu, diğer nedenlerle hastaneye başvuran 47 çocuk ise kontrol grubunu oluşturdu. Deney grubundaki çocukların hepsinde döküntü vardı. El-ayak-ve-ağız hastalığı olan çocukların kontrol grubu ve deney grubundakilari çocukların karşılaştırılmasında; deney grubundaki çocukların Beyaz Kan Hücresi (WBC) ve direkt bilirubin düzeyleri kontrol grubuna göre daha yüksekti ($p<0.05$). Çocukluk çağında viral hastalıklar yaygındır. Bu nedenle toplumun hastalığın yayılımı konusunda bilgilendirilmesi önemlidir.
Anahtar kelimeler: Döküntü, el, ayak ve ağız hastalığı, laboratuvar değerleri.

ABSTRACT

Hand-foot-and-mouth disease is a common childhood illness caused by enteroviruses. Blood tests may be affected in hand-foot-and-mouth disease.The aim of this study is to compare the demographic and laboratory data of the patients who applied with hand-foot-and-mouth disease with the healthy child group and to determine the effect of the disease on the laboratory values. This study was done retrospectively. The research was conducted with 94 children. 47 children with hand-foot-and-mouth disease constituted the experimental group and 47 children admitted to the hospital for other reasons constituted the control group. All of the children in the experimental group had a rash. The White Blood Cell (WBC) and direct bilirubin levels of the children in the experimental group were higher than those of the control group ($p<0.05$).In this study, it is seen that there is not much change in blood values in children with hand-foot-and-mouth disease compared to the control group. Viral diseases are common in childhood. Therefore, it is important to inform the society about the spread of the disease.
Key words: Rash, hand, foot and mouth disease, laboratory values.

1.Introduction

Skin rashes are caused by a group of diseases that are very common in childhood and have a very wide differential diagnosis. The presence of fever together with the rash increases the possibility of infectious disease (1). Hand-foot-and-mouth disease (HFMD) is a contagious viral infectious disease that can cause epidemics at varying rates depending on geographical regions and seasons. The disease was first described in 1957 in New Zealand (2). Its causative agents are known to be echovirus, coxsackievirus and enterovirus from the Picornaviridae family (3). Typical clinical findings are, after a short prodromal phase, erosive stomatitis and erythematous papulovesicular lesions on the palms and soles (4). Infected individuals can spread the virus through close contact, the respiratory tract (coughing or sneezing), contact with feces, and contaminated objects and surfaces. After an incubation period of 5-7 days, the virus causes lesions first in the mouth and then on the hands and feet (5). Lesions can also be seen in the knee, elbow, gluteal region and perioral region (4,5). All lesions usually heal on their own or with symptomatic treatment within 1-2 weeks. Despite being a mild and self-limiting disease, complications such as aseptic meningitis, encephalitis, myocarditis, pulmonary edema and/or hemorrhage, pleural effusion, acute flaccid paralysis and dehydration may also be encountered (3). To prevent the spread of the disease, society should be informed about personal hygiene and other basic health measures such as frequent hand washing and avoiding nail biting and thumb sucking. The aim of this study is to determine the effect of hand-foot-mouth disease on laboratory values by retrospectively comparing the demographic and laboratory data of patients presenting with hand-foot-mouth disease with the healthy child group.

2.Materials and methods

2.1.Study design

This study was conducted retrospectively.

2.2.Study Population and Sample

The population of the research consisted of pediatric patients who applied to XXX Training and Research Hospital. Since the study was conducted retrospectively, power analysis was not performed to determine the sample size. Pediatric patient files were examined, patients under the age of 18, diagnosed with hand-foot-and-foot disease and laboratory tests were performed were included in the experimental group. Children under the age of 18 who were admitted to the hospital for any reason, did not have any chronic disease, had laboratory tests and were not diagnosed with hand-foot-and-mouth disease were included in the control group. During the data collection phase, a total of 94 children were included, 47 in the experimental group and 47 in the control group.

2.3.Data collection

A retrospective file review of patients who presented to XXX Training and Research Hospital was performed between 1st May 2021 and 31st October 2022. Laboratory and demographic data of children with hand-foot-and-mouth disease entered with the code B08.4 (enteroviral vesicular stomatitis with exanthema) were analyzed.

Demographic and, if available, laboratory values (hemogram, biochemistry, C-reactive protein, sedimentation, vitamin B12, vitamin D, ferritin, folate, iron, iron binding capacity, and thyroid tests) of patients with hand-foot-and-mouth disease and healthy children were collected.

2.4.Data analysis

IBM SPSS Statistics for Windows version 22.0 was used to analyze the data, with the descriptive statistics of percentage, frequency, mean, standard deviation, and minimum and maximum values being calculated. The conformity of the data to normal distribution was examined with the Kolmogorov-Smirnov test. Independent groups t-test was used to compare normally distributed features. A *p* value lower than 0.05 was considered statistically significant.

2.5.Ethics

The necessary permission was obtained prior to the study in order to meet the ethical requirements for research. Ethical approval was obtained from XXX University Clinical Research Ethics Committee (Reference No:2022/8-14).

2.6. Limitation

The limitation of this study is that the study was conducted in a single center.

3.Results

A total of 94 patients were included in the study. There were 47 children in the patient group and 47 children in the control group. It was determined that 51.0% of the children in the experimental and control groups included in the study were male, and that their mean age was 42.38±6.20 months. There was no difference between the patient and control groups in terms of age and gender (p=0.49). It was found that 100.0% of the experimental group had a rash on their hands, feet and mouth, 40.4% had a rash on their buttocks, and 40.4% had fever. There were no physical findings such as fever or rash in the control group (Table 1).

Table 1. Distribution of experimental and control groups according to sociodemographic, rash and fever characteristics

Characteristics	Experimental		Control
	n	%	n
Gender			
Female	23	49.0	23
Male	24	51.0	24
Mean age (months)	42.38±6.20		42.38±6.20
Presence of rash on hand			
Rash present	47	100.0	0
Rash absent	0		47
Presence of rash on foot			
Rash present	47	100.0	0
Rash absent	0		47
Presence of rash on mouth			

Rash present	47	100.0	0
Rash absent	0		47
Presence of rash on buttocks			
Rash present	19	40.4	0
Rash absent	28	59.6	47
Presence of fever			
Fever present	19	40.4	0
Fever absent	28	59.6	47

The blood values of the experimental and control groups are given in Table 2. It was determined that the WBC value of the experimental group was 10498.36±518.697, while that of the control group was 9626.57±373.708, and this difference was statistically significant ($p<0.05$). The direct bilirubin value was determined as 0.1889±0.01262 in the experimental group, and 0.1372 ±0.01128 in the control group. This difference was found to be statistically significant ($p<0.05$). There was no statistically significant difference between HGB, HCT, PLT, RBC, PDW, MCH, MPV, MCV, PCT, MCHC, glucose, urea, creatinine, total bilirubin, AST, ALT, NA, K, CL, CA, ALP, FE, TIBC, vitamin D, B12, ferritin, TSH, T4 sedimentation levels of the children in the experimental and control groups ($p>0.05$,Table 2).

Table 2: Distribution of blood values of experimental and control groups

Blood values	**Experimental**	**Control**	**t-test**
	X±SD	X±SD	**p**
White Blood Cell (WBC) (/mm^3)	10498.36±518.697	9626.57±373.708	1.364 **0.012**
Hemoglobin (HGB) (gr/dl)	12.0196±0.17314	12.5315±0.14640	-2.258 0.457
Hematocrit (HCT) (%)	36.7947±0.41259	37.4051±0. 40201	-1.060 0.948
Platelets (PLT) ()	312.968±15.3588	333.898±13.7585	-1.015 0.264
RBC	4.9789±0.06273	4.8023±0. 07308	1.834 0.340
PDW	18.0830±0.25022	18.3187±0.28507	-.622 0.430
MCH	24.1279±0.37608	26.2645±0.39187	-3.934 0.516
MPV	6.1138±0.15569	7.0949±0.19193	-3.970 0.077
MCV	73.7494±0.74122	78.2562±0.84553	-4.008 0.517
PCT	0.1806±0.00738	0.2360±0.00981	-4.506 0.077
MCHC	32.4464±0.31666	33.5255±0.24930	-2.678 0.262
Glucose (mg/dL)	85.19±1.996	89.49±1.398	-1.764 0.431
Urea (mg/dL)	20.85±1.107	20.09±1.064	.499

			0.622
Creatinine (mg/dL)	0.3723±0.01127	0.3855±0.01224	-.793 0.445
TBIL	0. 4083±0.027	0.3330±0.0298	1.704 0.098
DBIL	0. 1889±0. 01262	0.1372±0.01128	2.637 **0.038**
AST (U/L)	32.66±1.519	39.57±1.772	2.963 0.144
ALT (U/L)	17.45±1.361	22.34±1.472	-2.441 0.903
NA (mmol/L)	139.70±0.388	138.91±0.308	1.588 0.330
K (mmol/L)	4.504±0. 0634	4.711±0.0659	-2.258 0.608
CL (mmol/L)	106.61±0. 683	105.78±0.339	1.084 0.261
CA (mmol/L)	9.045±0.0964	10.023±0.0967	-7.170 0.426
P	5.013±0.1158	5.315±0.103	-1.950 0.694
ALP	218.66±14.818	237.64±9.704	-1.071 0.255
FE	43.68±5.085	52.96±3.653	-1.071 0.134
TIBC	278.20±7.495	256.00±8.286	1.984 0.248
VIT D	32.8619±2.07401	42.2902±1.95303	-3.310 0.567
Folate	16.2581 ±0.88161	14.0006±0.92868	1.755 0.264
B12	266.35 ±23.838	302.38±17.070	-1.233 0.025
Ferritin	29.228 ±2.5235	30.217±2.3357	-.288 0.307
TSH	2.2955 ±0.17678	2.4194±0.15473	-.527 0.236
T4	0.8835 ±0.02355	0.8953±0.02078	-.377 0.292
Sedimentation	4.64 ±0.593	3.30±0. 594	1.586 0.418

4.Discussion

Hand-foot-and-mouth disease was first reported in 1957 in New Zealand and Canada, and in the following years, it became an important health problem threatening Asia-Pacific countries in particular (2,6,7). It is stated to have caused major epidemics in Taiwan, Singapore, Thailand, Vietnam, Korea, China and Japan. It is argued that the subtropical monsoon climate, in which heavy rainfall and humidity occur, facilitates the growth and spread of enteroviruses and that the ecology of enteroviruses is an important factor in the emergence of outbreaks of hand-foot-and-mouth disease (7). Hand-foot-and-mouth disease is commonly seen in the enteroviral disease group, and can often cause epidemics in summer and autumn. The most common causative agent is coxsackievirus A16. It is reported to be more common in summer and autumn in our country. Incidence increases between April and August and peaks twice in June and November (7).

Hand, foot and mouth disease mostly affects children under the age of five (8). In this study, the mean age of the children in the experimental and control groups was determined to be 42.38±6.20 months. In three different studies conducted in our country, the percentage of cases in children under the age of five was reported as 52.30%, 79% and 87.40%, respectively (6,9,10). In their study, Bucak et al. reported the percentage of patients under the age of five as 92.30% and the percentage of patients under the age of one as 15.30% (11). It is stated that the younger the child, the greater the severity of the disease (7,12). Gui et al. stated that 53% of 454,339 cases reported in China between 2008 and 2012 were in children aged 0-5 (8), while Liu et al. reported the percentage of cases in children under 5 years old as 92.90% (13). It was reported that 97.50% of cases in Thailand and 78.80% of cases in Singapore were under the age of 6 (14). The finding of our study is compatible with the literature.

Human enterovirus 71 infection and a peak body temperature of >39°C are associated with severe hand-foot-and-mouth disease (14). Symptoms of mild hand-foot-and-mouth disease are fever, papulovesicular rash on hands, feet, mouth and gluteal region, and rarely, anorexia and cough. As the diagnosis, the severity of the lesions is often determined according to the symptoms (7). In infectious diseases, one of the important reactions in the body is fever. In this study, it was determined that 40.4% of the children in the experimental group had fever, while none of the children in the control group had fever. In four different studies conducted in our country, the reported incidence of fever in children with hand-foot-and-mouth disease varied between 61.40% and 82.10% (6,9–11). The incidence of fever was lower in this study. In hand-foot-and-mouth disease, rashes first appear within one to three days after fever. This situation may have been caused by the fact that our study group consisted of patients with rashes. Since our study is a retrospective study, the incidence may be low due to the fact that patients presented to the hospital during the rash period after the fever had subsided. All children in our study group had rashes.

In children with hand-foot-and-mouth disease, a rash begins to appear after the symptom of fever. The most common reason why patients present to hospital is rashes (6). The disease is characterized by fever, oral ulcers, and skin manifestations affecting the palms, soles, and buttocks, and symptoms usually last less than a week (3). Rashes first appear on the throat. In this study, it was determined that all children had rashes on their hands, feet and mouth, while only 40.4% had a rash on their buttocks. There was no rash in any region of the control group. The palms have been reported as the most common site of involvement in the literature (11,15). Ghosh et al. reported that 61.10% of 62 patients aged 9 months-20 years were under the age of 12, that 16.10% had a family history of the disease, and that the most common site of involvement was the hand (16). Topkarcı et al. reported 80.90% gluteal involvement, while Kılınç and Akbaş reported gluteal lesion in only one patient in the study group (7,9). In the study by Kılınç and Akbaş, it was determined that 96.96% of patients had a rash on the hands and 72.72% in the mouth (7). In the same study, apart from the hands, feet and mouth, involvement of the knee, elbow, gluteal region and face was determined at a rate of 54.54% (7). These results were consistent with those of studies conducted abroad and in our country (2,6,9,10,13,17).

In this study, it was determined that WBC and direct bilirubin levels were higher in the experimental group, and that this difference was statistically significant. It is stated that laboratory work is not required in the diagnosis of hand-foot-and-mouth disease. A detailed medical history (anamnesis), physical examination, and characteristic rashes in the mouth, hands and feet are usually sufficient to diagnose the disease. Differential diagnosis should be made with diseases such as aphthous stomatitis, chicken pox, erythema multiforme and herpes simplex. Usually, no laboratory work is required. The leukocyte count ranges between 4000-16,000/ml. Occasionally, atypical lymphocytes are present. Recent studies show that C-reactive protein (CRP) and fasting blood glucose are significantly higher in severe cases than in mild cases (18). In this study, it was found that the blood values in laboratory tests of cases of hand-foot-and-mouth disease were not too negatively affected compared to the healthy group, and that the WBC value was higher than in the healthy children, just as in all cases of infection.

5.Conclusions

In this study, we investigated the effect of hand-foot-mouth disease on laboratory values by comparing the demographic and laboratory data of patients presenting with hand-foot-mouth disease with the healthy child group. Enteroviral disease is a disease that is seen especially in children aged 5 years and under, mostly in summer and autumn. Clinical findings are sufficient for diagnosis and the disease does not require specific treatment. Regarding disease transmission and prevention, the spread of the disease can be prevented to a great extent with personal and food hygiene, and early diagnosis of suspected cases. Especially the transmission routes and necessary isolation methods should be explained to patients and their relatives.

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