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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

PNÖMONİ TANISI ALAN ÇOCUK HASTALARDA KAN KÜLTÜRÜ VE KAN PARAMETRELERİNİN DEĞERLENDİRİLMESİ

ASSESSMENT OF BLOOD CULTURE AND BLOOD PARAMETERS IN PEDIATRIC PATIENTS DIAGNOSED WITH PNEUMONIA

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ÖZET

AMAÇ: Pnömoni tanısı alan çocuk hastalarda kan kültürü testi alınması önerilmektedir. Ancak, kan kültürü testlerinde üretilen patojen mikroorganizma oranı oldukça düşüktür. Bu çalışmada; pnömoni tanısı ile hastaneye yatırılan çocuk hastalarda kan kültürü sonuçları ve bazı kan testi parametreleri araştırıldı.

GEREÇ VE YÖNTEM: 2016 - 2018 tarihleri arasında ICD10 kodlamasına uygun olarak pnömoni tanısı ile hastaneye yatırılan ve kan kültürü testi alınan 643 hasta çalışmaya dahil edildi. Kan kültür sonuçları, kan testi parametreleri (WBC (White Blood Count), ANC (Absolute Neutrophil Count), AMC (Absolute Monosite Count), trombosit sayısı, MPV (Mean Platelet Volume), PDW (Platelet Distribution Wide), PCT (Plateletcrit)) ve CRP (C-Reaktif Protein) değerlendirildi.

BULGULAR: Ortalama yaş 27.1±38.2ay, %41,8'i kız cinsiyet idi. %4,0 oranında (n=26) kan kültürü sonucu pozitifti. Kan kültürü pozitif olan hastaların trombosit sayısı (307.3/mL) kan kültürü negatif olanlardan (360.2/mL) daha düşüktü (p=0.035), ancak; CRP (p=0.095), toplam beyaz küre sayısı (p=0.069) ve MPV (p=0.846) sonuçları ile fark bulunamadı. Kan kültür sonucu pozitif olanlarda PDW (%12,7±2,6) negatif olanlardan (%10,4±1.7) daha yüksek bulundu (p<0.001). En sık izole edilen patojen Stafilokok Hominis (n=8, %36,4) idi.

SONUÇ: Pnömoni tanısı ile hastaneye yatırılan çocuk hastalarda kan kültürü testinde patojen mikroorganizmanın gösterilme oranı oldukça düşük seviyededir. Bu hastalarda; kan kültürü testinde patojen bakterinin gösterilmesi hastalığın tedavisi ve ampirik antibiyoterapi seçimi için kıymetlidir. Çocuklarda pnömoni tanı, tedavi ve klinik izleminde diğer kan parametrelerinin kullanımı konusunda çalışmalara ihtiyaç vardır.

ANAHTAR KELİMELER: Pnömoni, Kültür, Patojen, Kan testi, Pediatri

ABSTRACT

OBJECTIVE: It is recommended to take a blood culture test in pediatric patients diagnosed with pneumonia. However, the rate of pathogenic microorganisms produced in blood culture tests is quite low. In this study, the results of blood culture tests and some blood test parameters in pediatric patients hospitalized with pneumonia diagnosis were evaluated.

MATERIAL AND METHODS: 643 patients who were hospitalized and diagnosed with pneumonia in accordance with ICD10 coding and whose blood culture test was taken between 2016 and 2018 were included in the study. The results of blood culture tests and blood test parameters ((WBC (White Blood Count), ANC (Absolute Neutrophil Count), AMC (Absolute Monosite Count), MPV (Mean Platelet Volume), PDW (Platelet Distribution Wide), PCT (Plateletcrit)) and CRP (C-Reaktif Protein)) were evaluated.

RESULTS: The mean age of the patients was 27.1±38.2 months and 41.8% of the patients were female. Blood culture results were positive in 4.0% of the patients (n=26). The platelet count of the patients with positive blood culture (307.3/ml) was lower than those with negative blood culture (360.2/ml) (p=0.035) but no differences were found in the CRP levels (p = 0.095), total white blood cell count (p = 0.069) and MPV (p= 0.846) values. PDW level was found higher (p <0.001) in patients with positive blood culture (12.7±2.6%) than those with negative blood culture (10.4±1.7%). The most frequently isolated pathogen was Staphylococcus Hominis (n=8, 36.4%).

CONCLUSIONS: The rate of detection of pathogenic microorganisms in the blood culture test in pediatric patients hospitalized with the diagnosis of pneumonia is at a very low level. In these patients, the demonstration of pathogen bacteria in the blood culture test is valuable for the treatment of the disease and choice of empirical antibiotherapy. It is necessary to conduct studies on the use of other blood parameters in the diagnosis, treatment and clinical follow-up of pneumonia in children.

KEYWORDS: Pneumonia, Culture, Pathogen, Blood test, Children.

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INTRODUCTION

Pneumonia is among the causes of infection in children under five years old and causes the death of approximately 2400 children in one day. In 2016, a total of 880.000 children under the age of five, most of whom were <2 years old, have been reported to die from pneumonia (1). CDC (Centers for Disease Control and Prevention (2015)) reported that pneumonia was the cause of 70% of hospitalizations in children under 5 years of age (2). In Turkey, the results of TNSI (Turkish National Statistic Institution) health surveys in 0-6 years of age group report that the rate of those diagnosed with lower respiratory tract infections such as pneumonia in the last six months increased by 10.1% in 2014 and 11.1% in 2016 (3). Current guidelines from the American Academy of Pediatrics, Committee on Infectious Diseases for the detection of etiological pathogen recommend that blood culture should be taken from children diagnosed with moderate-severe bacteremia who are hospitalized for community-acquired pneumonia (CAP) (4). However, bioavailability is considered to be low due to the growth of uncommon microorganisms in blood cultures and the fact that they rarely change antibiotherapy (5). In recent studies, the prevalence of bacteremia in children hospitalized for CAP has been reported to be 1.1-7.0%(6,7) and antibiotic change according to blood culture results are 4.6% (8). Although low bioavailability of blood culture has been reported, it has been reported that it is frequently taken in pediatric patients hospitalized with a diagnosis of pneumonia in the clinic and may cause unnecessary vascular access and antibiotic use (7).

On the other hand, in the diagnosis and treatment response of some infections and inflammations, many bacteria are recently capable of interacting with platelets and the changes may be a direct or indirect interaction between a bacterial surface protein and a platelet receptor (9). Mean platelet volume (MPV), the most commonly used measure of platelet size, is an index of platelet activation and is available in clinical practice (10) and Platelet distribution width (PDW), another platelet index, indicates variation in platelet size which may be an indicator of active platelet release and normal values of PDW are between 10% and 17.9% (11). In a study conducted in newborns, reported that high levels of MPV and PDW have 95 % and 79 % specificity in the detection of bacteremia, respectively (12). It has been reported that increased risk and severity of bacterial infection correlates with clinical abnormalities in platelet quantity and quality. In these respects, the molecular and cellular roles of platelets in host defense against bacterial pathogens are explored with attention on advances in platelet immunobiology (13).

The highlight of all information, the pathogens identified in the previous blood cultures should be known and the relationship between the culture results and blood parameters should be investigated in the diagnosis and treatment of pneumonia in children. For this purpose, we examined the blood culture results and blood-infection parameters of the patients hospitalized with a diagnosis of pneumonia and who received blood culture.

MATERIAL AND METHODS

Between 2016 and 2018, the laboratory results of 643 patients who were admitted to the pediatric unit with the diagnosis of any pneumonia according to ICD10 (International Statistical Classification of Disease and Related Health Problems) codes (J10-J18) and received blood culture were evaluated retrospectively. The inpatients who had blood count, blood culture, and CRP(C-Reactive Protein) tests were included but inpatients who had not had blood tests or blood culture or CRP test were not included. Blood counts have been taken into EDTA tubes and blood cultures have been taken into aerobic and anaerobic culture bottles (Becton, Dickinson and Company Sparks, MD 21152 USA). Before the blood culture sampling, the related skin site has been wiped with a sterile sponge and antiseptic solution and dried with a sterile gauze sponge. And then the blood sample has been taken with a 1ml syringe and inoculated into a blood culture tube at the point of care and transferred to the laboratory. The results of hemoglobin levels (Hb), total white blood cell count (WBC), absolute neutrophil count (ANC), absolute monocyte count (AMC), absolute lym-

phocyte count (ALC), platelet count, MPV, PDW, Plateletcrit (PCT) and CRP levels were evaluated in blood tests.

Ethical Committee

Ethical committee approval for this study was obtained from Istanbul Training and Research Hospital (2011-KAEK-50).

Statistical Analysis

For the comparison of the culture and test results, Student's t-test was used for variables with normal distribution, and the Mann-Whitney U test was used for variables with non-normal distribution. The Chi-square test was used to compare categorical variables. For blood culture positivity, logistic regression analysis was performed to determine risk factors as measured by the 95% confidence interval. A $p<0.05$ value was considered statistically significant. SPSS V21.0 (SPSS Inc, Chicago, IL) was used for statistical analysis.

RESULT

The mean age was 27.1±38.2 months and 41.8% were female. Demographic characteristics have been presented in **Table 1** (n=384) 59.7% of the blood culture tests had been taken after the patients were hospitalized in the pediatric unit and 40.3% (n=259) had been taken at the pediatric emergency department.

Table 1: Demographic features

Variables	N	Mean±SD
Age (months)	643	26.9±38.2
Hgb (g/dL)	642	11.0±1.4
Hct	642	33.0±3.9
MCH	643	26.1±3.3
MCHC	643	33.4±1.8
MCV	643	78.0±7.9
MPV	628	9.5±0.9
RDW	642	15.2±8.4
WBC(10^3/mm^3)	637	6.0±7.5
PLT(10^3/mm^3)	642	358.1±125.3
PCT(%)	625	0.3±0.2
PDW(%)	626	10.5±1.7
CRP(mg/dL)	641	33.6±56.5
Lymphocyte (%)	642	40.5±20.2
ALC (10^3/mm^3)	643	4.8±3.4
Neutrophil (%)	643	47.5±23.0
ANC (10^3/mm^3)	643	6.6±5.6
Monocyte (%)	643	9.6±5.5
AMC (10^3/mm^3)	643	1.2±1.4
Eosinophil (%)	568	2.1±3.4

The blood culture was positive in 4.0% (n = 26) of patients. While 6% (n = 23) of the blood cultures obtained in the pediatric unit were positive, but only 1.2% (n = 3) of the blood cultures taken in the pediatric emergency department were positive (p=0.002). There was no difference between the age of blood culture positive (18.7±27.7 months) and negative (27.3±38.6 months) groups (p=0.261). The platelet count of the patients with positive blood culture (307.3/ml) was lower than those with a negative blood culture (360.2/ ml) (p=0.035). There was no statistical difference with CRP levels (p=0.095), total WBC (p=0.069) and MPV (p=0.846) values **(Table 2)**.

Table 2: Correlation of blood culture results with the variables

	Culture (-)		Culture (+)		
Variables	**N**	**Mean±SD**	**N**	**Mean±SD**	**p**
Age (months)	617	27.3±38.6	26	21.5±27.3	.446*
CRP(mg/dL)	615	33.3±54.4	26	41.0±93.9	.095^m
WBC(10^3/mm^3)	611	6.1±7.6	26	2.5±4.4	.069^m
ANC(10^3/mm^3)	617	6.6±5.6	26	5.9±6.0	.520*
ALC(10^3/mm^3)	617	4.9±3.4	26	4.8±2.6	.944*
AMC(10^3/mm^3)	617	1.2±1.4	26	1.1±0.6	.706*
Hgb(g/dL)	616	11.0±1.4	26	10.9±1.8	.719*
PLT(10^3/mm^3)	616	360.2±124.4	26	307.3±136.5	.035*
MPV	605	9.5±0.8	21	9.6±1.2	.813*
PCT(%)	604	0.3±0.1	21	0.7±1.2	.867^m
PDW(%)	605	10.4±1.7	21	12.7±2.6	<.001^m

*=Student's t-test, m= Mann-Whitney U Test

The most frequently isolated pathogens were Staphylococcus Hominis (n=8, 1.2%), Staphylococcus Epidermidis (n=4, 0.6%), Streptococcus Mitis (n=3, 0.5%) and Streptococcus Pyogenes (n=2, 0.3%). A negative correlation of MPV values with the age (rho=-0.159, p<0.001) and ANC (rho=-0.145, p<0.001), but positive correlation of ALC (rho=0.088, p=0.027) and no correlation with total WBC (rho=0.036, p=0.367) were found. While MPV was observed a positive correlation with PDW% (rho=0.852, p<0.001), it had negative correlation between platelet count (rho=-0.109, p=0.007) and CRP levels (rho=-0.089, p=0.025).

In the logistic regression analysis was analyzed by taking the dependent variable as a result of blood culture, and independent factors including age, CRP, WBC, Hgb, PLT, MPV, PCT, PDW, RDW, ALC, and AMC, it was determined that MPV and PDW% values affected the blood culture results independent of the other variables **(Table 3)**.

Table 3: Regression analysis computer output

		95% CI for EXP(B)	
Variables	B	Lower-Upper	p
Age (months)	.001	.982-1.020	.958
CRP(mg/dl)	-.008	.975-1.010	.400
WBC(10^3/mm^3)	-.026	.886-1.071	.591
Hgb(g/dL)	.133	.746-1.750	.540
PLT(10^3/mm^3)	-.003	.988-1.006	.471
MPV	-.931	.196-.793	.009
PCT(%)	1.862	.003-12713.765	.631
PDW (%)	.577	1.356-2.338	.000
RDW (%)	-.005	.717-1.380	.976
ALC	.099	.927-1.315	.267
AMC	-.395	.224-2.030	.483

Although MPV was not found a difference between blood culture positive and negative groups, it could be any risk factor on the result

of blood culture, it was included as an independent factor at logistic regression analysis. And ROC analysis provided an area under the curve (AUC) of 0.758 (95% CI:0.645-0.872, p<0.001) to predict blood culture positivity using the PDW% values **(Figure1)**.

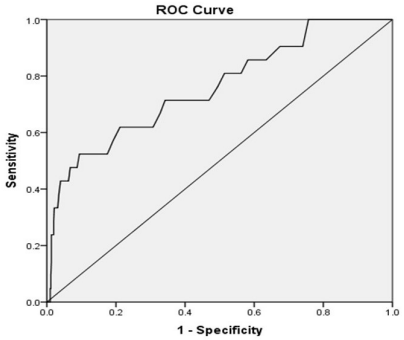

Figure 1: ROC analysis for PDW%

A cut-off value of 12.3 provided a sensitivity of 52% and a specificity of 91%. But ROC analysis for MPV, AUC was 0.510 and (95% CI: 0.376-0.645, p=0.873) **(Figure 2)**.

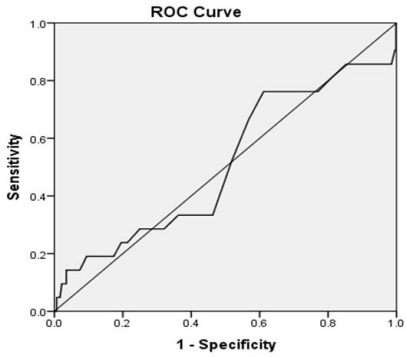

Figure 2: ROC analysis for MPV

DISCUSSION

We determined the positivity rate of blood culture as 4.0% in children who were hospitalized with a diagnosis of pneumonia and 1.2% in blood cultures obtained in the pediatric emergency department. Previous studies reported such as our result, low rates of bacteremia in children with pneumonia evaluated in the emergency department with 1.2%–2.7% (14). Based on of meta-analysis, children with CAP had positive blood cultures in 5.14% of cases (15). In another study of 535 hospitalized children <36 months of age with radiographic evidence of uncomplicated pneumonia, 2.2% had positive blood culture results, all of which were considered contaminants (16). In our study, It has shown that isolated pathogens with blood cultures are mostly coagulase-negative staphylococci which are the most common etiology of nosocomial bacteremia as well as the most common blood culture contaminant both in children and in adults (17). Moreover, isolated Streptococcus Mitis and Pyogenes are associated chiefly in the respiratory tract, bloodstream, and skin infections (18). Especially, Streptococcus Pyogenes infections encompass some clinical syndromes, most prominently infection of the skin, soft tissues, joints, or lower respiratory tract as well as bacteremia without a focus of infection (19). In a study that assessed 7509 children hospitalized with a diagnosis CAP, it was reported that the rate of bacteremia was very low, isolated pathogens were usually penicillin-susceptible, and most children hospitalized with a diagnosis CAP did not require a blood culture test (20).

The low rate of pathogen growth in blood cultures may be due to technical problems such as sampling technique conditions, the volume of the blood material inoculated, delivery to the laboratory. On the other hand, vaccination programs, high consumption of antimicrobial agents (before blood culture test), mixed infections of viral agents should also be considered.

Studies performed after licensure of the conjugated pneumococcal vaccine have shown low rates of bacteremia in pediatric patients hospitalized with a diagnosis CAP (2, 21). As a result of routine pneumococcal immunization in childhood, recommended by the World Health Organization (WHO) since 2006, the burden of disease in children has begun to decrease significantly. In Turkey, the 7-valent pneumococcal conjugate vaccine (PCV7), which was introduced in 2008, was included in the Expanded Programme on Immunization for use in children in 2008; thereafter PCV13 replaced PCV7 in 2011 (22). Thanks to immunization programs, we believe that the frequency and severity of S. Pneumonia in the diagnosis of pneumonia in children has a decreasing trend and affects blood culture results. Although the frequency of S. Pneumonia decreases in the etiology of CAP in children, S. Pneumoniae remained the predominant pathogen isolated from positive blood cultures even after the introduction of PCV. However, in the post-PCV era, S. Pneumo-

niae isolates made up 2.4% of all blood cultures obtained in pediatric CAP compared with 5.6% pre-PCV (15). However, we know that use of antibiotics and co-infections with viruses may also affect blood culture results. However, antibiotics are at the first rank among the most frequently used medications and they are most frequently used in childhood (23). Moreover, the sensitivity of blood cultures declines significantly if antibiotic therapy has been initiated, or when fastidious or slow-growing pathogens are cultured (24). To improve the blood culture utilization, it is recommended to collect at least two samples from different peripheral regions before the initiation of antibiotic therapy (25).

Moreover, it has been reported that the rate of mixed infections caused by a bacterial-viral agent, bacteria-atypical bacteria or dual viral agent (respiratory syncytial virus (RSV)-influenza) in lower respiratory tract infections during childhood was 16-34% and the rate of mixed bacterial-viral infection alone was 30-50% (26).

The high rate of mixed infections makes it difficult to interpret the identified agents (27). For blood culture positivity, we found the MPV value recommended for clinical follow-up of the patients for infection to be a negative predictor and the PDW value to be a positive predictor. As indicated in the literature, MPV may be a useful predictor for diagnosed CAP but has low specificity (28). But, rising MPV with inpatients with CAP has been reported as a powerful predictor and long-term mortality and suggested that repeated MPV determinations may improve risk stratification for CAP and patients with pneumonia in the patients (29, 30). And not only MPV, MPV/PCT, PDW/Platelet count, and MPV/Platelet count have been reported as predictors of mortality and could predict 65-67% of deaths accurately (31) Higher PDW levels have been reported in blood culture positive group and found as a risk factor for positivity of blood culture in our study. The combination of the three parameters of RDW, PDW, and neutrophil-lymphocyte ratio demonstrated a high diagnostic performance similar to that of procalcitonin and the combination of these three tested parameters could be considered as a marker to distinguish bacteremia (32).

And increased PDW levels have been reported to be associated with specific disorders (33, 34). Although the treatment of CAP is initiated empirically, it is very important to determine the causative pathogen in blood culture in cases where the clinical response cannot be obtained, especially in the presence of antibiotic resistance. Therefore, the yield of blood cultures should be improved. Also, further investigation is needed for cost-effective and practical laboratory markers such as PDW for the diagnosis and follow-up of CAP in children.

Limitation

In this study, antibiotherapy used before hospitalization and the co-infection of any viral pathogen was not questioned.

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