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ORIGINAL ARTICLE

Potential and promising marker for serious bacterial infections in children: Delta neutrophil index

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Aim: This study aimed to evaluate the usefulness and accuracy of the delta neutrophil index (DNI), an index expressing the number of immature granulocytes as a proportion of the total, as an inflammatory marker in predicting serious bacterial infections (SBIs).

Methods: Paediatric patients admitted to our hospital with fever were divided into four groups: SBI, non-SBI, COVID-19 and control group. White blood cell count, absolute neutrophil count, C-reactive protein and the DNI were recorded, and their accuracy in predicting SBI was evaluated.

Results: Mean DNI was 4.96 ± 8.38 in the SBI group (150 patients), 0.67 ± 1.68 in the non-SBI group (397 patients), 0.29 ± 0.99 in the COVID-19 group (112 patients) and 0.14 ± 0.21 in the control group (102 patients). The DNI was significantly higher in the SBI group compared with the non-SBI ($P < 0.001$); the non-SBI group also had higher levels than the COVID-19 group ($P = 0.005$). One percent increase in the DNI increased the SBI rate 1.36 times (odds ratio 1.36 (95% confidence interval 1.23–1.49), $P < 0.001$). Based on the determined cut-off value (>2.5%), the DNI (odds ratio 6.27 (95% confidence interval 3.85–10.21), $P < 0.001$) significantly predicted SBIs with 90.4% specificity and 47.7% sensitivity.

Conclusions: SBIs in childrenare associated with an increase in DNI levels. Compared to other biomarkers, the DNI had higher specificity in predicting SBIs. The DNI may also be usefulin differentiating bacterial and non-bacterial infections in individualclinical syndromes. Currently, there is no evidence that serum DNI aids indifferentiating COVID-19 and upper respiratory tract infection.

Key words: children; delta neutrophil index; serious bacterial infection.

What is already known on this topic

1 The delta neutrophil index, an index expressing the number of immature granulocytes as a proportion of the total, has been accepted as an inflammatory marker, especially in sepsis.

What this paper adds

1 DNI has a higher specificity and lower sensitivity compared with conventional markers, including WBC, ANC and CRP, it may be a valuable tool in predicting SBI, especially when combined with the other markers.

Fever is an important clinical sign and a significant symptom of variable diseases. Many patients may manifest fever as the only sign of a major underlying infection. Especially in febrile young infants, clinicians should identify the patients who are at high risk of serious bacterial infections (SBIs), that is, meningitis, urinary tract infection (UTI), pneumonia and bacteraemia, because the rapid and accurate evaluation of an SBI is essential for early empiric antimicrobial therapy and hospitalisation.[1–4]

There are several clinical and laboratory prediction models and scoring systems to detect and diagnose SBIs via symptoms and infection markers, including C-reactive protein (CRP), white blood cell (WBC) count, absolute neutrophil count (ANC), erythrocyte sedimentation rate, procalcitonin, cytokines, chemokines, cell surface antigens and even immunoglobulins. Nevertheless, none of these markers alone is enough to diagnose SBIs, but a combination of them in patient clinics may facilitate early diagnosis.[1,5–8]

Contemporary technological advances in automated haematology cell analyzers enable the attainment of the delta neutrophil index (DNI), which presents the ratio of immature granulocytes in peripheral blood. It is counted automatically by the cytochemical myeloperoxidase reaction and light beam reflection method without any extra blood needed while the routine haemogram analysis was performed.[9]

Several recent studies have investigated the role of the DNI as a potential marker to predict SBIs, and some found it useful in sepsis diagnosis and mortality prediction. However, the DNI was studied mostly in adult patients, but studies in the paediatric population are limited, with the majority related to neonatal sepsis.[10–12] In children with SBIs, there have yet to be sufficient results

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divulged on the clinical usefulness of the DNI, and the predicted DNI values relative to traditional infection markers remain unclear.

Therefore, the aim of this study was to evaluate the usefulness and the accuracy of the DNI as an inflammatory marker in predicting SBI when compared with conventional infection markers, such as WBC, CRP and ANC, in paediatric patients.

Methods

Study design and population

We conducted this retrospective cross-sectional study at the Children's Hospital of the Ankara City Hospital, a tertiary paediatric hospital in Ankara, the Turkish capital, and among the biggest paediatric hospitals in Europe: about 450 000 patients visit our hospital annually. Our study population consisted of patients admitted to our hospital due to fever, and inpatients were followed up between 1 August 2020 and 30 April 2021. Patients 1 month to 18 years of age were retrospectively examined by using the file recording system and computerised hospital records. Inclusion criteria for this study were 1 month to 18 years of age, admission to hospital with fever, a suspected diagnosis of any type of infection, and having had haemogram and CRP tests carried out. We excluded patients who had primary or secondary immunodeficiency, had steroid therapies (a dose equivalent to either 2 mg/kg of body weight or a total of 20 mg per day of prednisone for two or more weeks), used antibiotics within 48 h of admission, were vaccinated within the last 3 days, and/or had malignancies, rheumatologic diseases, and other clinically important additional chronic diseases including chronic kidney disease, inflammatory bowel diseases, polycythemia and thalassemia that may alter the levels of inflammatory markers. We also excluded patients diagnosed with COVID-19-related multisystem inflammatory syndrome in children.

Clinical protocol

Patients were divided into four groups: SBI, non-SBI, COVID-19 and the control group, based on the diagnosis of infection made clinically, by laboratory, microbiologically or radiologically at the time of first presentation or at the next follow-up. Patients diagnosed with bacterial meningitis, bacteraemia, bacterial pneumonia (proven by radiological findings, including lobar infiltration, pneumatocele and effusion), osteomyelitis,

Table 1 Demographic features and diagnoses of patients

Demographic features	Patients with SBI ($n = 150$) (19.7%)	Patients with non-SBI ($n = 397$) (52.2%)	Patients with COVID-19 ($n = 112$) (14.7%)	Control Group ($n = 102$) (13.4%)
Age (years), mean ± SD	7.7 ± 5.5	5.9 ± 4.9	10.35 ± 5.64	9.86 ± 6.58
Gender, *n* (%)				
Male	94 (62.7)	234 (58.9)	60 (53.1)	56 (54.9)
Female	56 (37.3)	163 (41.1)	52 (46.9)	46 (45.1)
Length of hospital stay (days), mean ± SD	11.1 ± 8.7	6.7 ± 5.2	8.81 ± 3.88	
Diagnoses	***n* (%)**	***n* (%)**		
Upper respiratory tract infection	0 (0)	67 (8.8)		
Lower respiratory tract infection	0 (0)	90 (11.8)		
Acute otitis media	0 (0)	28 (3.7)		
Acute gastroenteritis	0 (0)	53 (7)		
Urinary tract infection	0 (0)	49 (6.4)		
Viral diseases with rash	0 (0)	15 (2)		
Cellulitis	0 (0)	22 (2.9)		
Stomatitis	0 (0)	11 (1.4)		
Lymphadenitis	0 (0)	57 (7.5)		
Viral meningitis	0 (0)	5 (0.7)		
Pyelonephritis	17 (2.2)	0 (0)		
Abscess	14 (1.8)	0 (0)		
Bacteraemia	13 (1.7)	0 (0)		
Invasive gastroenteritis	8 (1.1)	0 (0)		
Bacterial meningitis	11 (1.4)	0 (0)		
Osteomyelitis	10 (1.3)	0 (0)		
Peritonitis	34 (4.5)	0 (0)		
Pneumonia	26 (3.4)	0 (0)		
Deep neck infection	11 (1.4)	0 (0)		
Sepsis	6 (0.8)	0 (0)		

SBI, serious bacterial infections.

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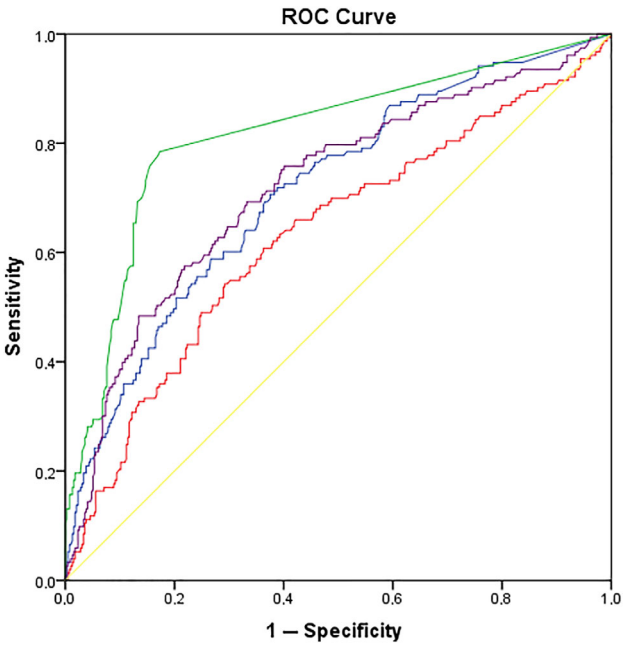


Fig. 1 Receiver operating characteristic (ROC) curves of inflammatory markers in serious bacterial infections. Source of the curve: (——), C-reactive protein; (——), delta neutrophil index; (——), white blood cell; (——), absolute neutrophil count; (——), reference line.

deep neck infection, abscess, intra-abdominal infection and peritonitis, invasive gastroenteritis, pyelonephritis and sepsis were included in the SBI group. Sepsis was diagnosed according to the International Pediatric Sepsis Consensus Conference definitions.[13] Patients diagnosed with upper respiratory tract infection, viral rash disease, acute gastroenteritis, stomatitis, acute otitis media (uncomplicated), lymphadenitis, non-complicated urinary tract infection, noninvasive soft tissue infection, viral meningitis and lower respiratory tract infection of viral origin (radiologically and clinically non-bacterial) were included in the non-SBI group. The diagnoses which were made by clinicians at the initial admission and during the follow-up were reviewed by the research team, which includes paediatricians and paediatric infectious disease specialists. In order to confirm these diagnoses, laboratory results, microbiology results, blood, urine, cerebrospinal fluid (CSF), abscess culture results and radiological imaging of each patient were retrospectively analysed one by one. However, no patient was excluded from the study at this stage since no discrepancy was found between the final diagnoses and the results. The control group was formed from the patients who did not have any complaints and chronic diseases, who applied to the hospital for routine control and for a reason other than fever, and who had haemogram and CRP examinations at their admission. In addition, a group was formed from COVID-19 patients who had positive COVID-19 respiratory PCR test results.

The study conformed with the principles of the Declaration of Helsinki and was approved by the local ethics committee and the Institutional Review Board of the Children's Hospital of the Ankara City Hospital.

Data collection

Patients' data were retrieved from computerised hospital records. Clinical data including demographics, length of hospital stay and diagnosis were recorded. CRP, ANC, DNI, neutrophil-to-lymphocyte ratio (NLR) and platelet counts at presentation to hospital were recorded from the laboratory data. The results of the tests, including urine, blood and CSF cultures, performed on the patients during follow-up were recorded as well as the radiological imaging. The DNI was automatically measured in complete blood count by a Siemens-ADVIA 2120 device in which the DNI was calculated as the ratio of immature granulocytes (myelocytes, metamyelocytes and promyelocytes) in peripheral blood over the total, including the neutrophils and expressed as a percentage (%).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM Corp, Armonk, NY, USA) was used to analyse the data. For descriptive statistics, categorical variables were expressed as number (n) and percentage (%) and continuous variables were expressed as mean ± standard deviation. The difference between groups in categorical variables was analysed using the χ^2 test. Comparison of means between two groups was examined by using a t-test, when the data fit a normal distribution, and by Mann–Whitney U test, when the data were non-normally distributed. For comparison of more than two groups, an ANOVA was used for normal distributions and the Kruskal–Wallis test for non-normal distributions. Receiver operating characteristic curve analysis, the Youden Index method, and area under the curve (AUC) calculation were used to determine the power of the variables to differentiate groups, to determine optimal cut-off values for WBC, ANC, CRP and the DNI for predicting SBIs, and to calculate significant sensitivity, specificity, and positive predictive and negative predictive values of each marker. The level of statistical significance was established as $P < 0.05$.

Results

The study population included 761 patients, 150 (19.7%) in the SBI group, 397 (52.2%) in the non-SBI group, 112 (14.7%) in the COVID-19 group and 102 (13.4%) in the control group. Among patients, 444 (58.3%) were male with a mean age of 6.7 ± 5.3 years and 317 (41.7%) were female with a mean age of 5.9 ± 4.8 years. While there was male dominance in all groups, there was no significant difference between the groups in terms of gender. The SBI group had a significantly longer length of hospital stay compared with the non-SBI and control group (11.1 ± 8.7 days vs. 6.7 ± 5.2 and 8.81 ± 3.88 days, respectively; $P < 0.001$). Among patients, 67 (8.8%) were diagnosed with upper respiratory tract infection, 90 (11.8%) with lower respiratory tract infection, 53 (7%) with acute gastroenteritis, 49 (6.4%) with urinary tract infections and 28 (3.7%) with acute otitis media. The demographic characteristics and diagnoses of the patients are listed in Table 1.

The most detected bacterial types in the blood cultures were *Staphylococcus* spp. ($n = 25$), *Micrococcus* spp. ($n = 4$), *Escherichia coli* ($n = 3$), *Klebsiella pneumoniae* ($n = 2$), *Acinetobacter* spp.

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Table 2 Mean values of infection markers according to diagnosis and groups

Diagnosis (*n*)	DNI (%)	WBC ($\times 10^9$/L)	ANC ($\times 10^9$/L)	CRP (mg/L)
SBI group[a] (150)	4.96 ± 8.38	13.79 ± 6.49	10.41 ± 5.62	94.31 ± 89.18
Sepsis (6)	14.97 ± 22.88	11.52 ± 5.91	7.63 ± 3.53	116 ± 75.89
Bacterial meningitis (11)	10.14 ± 15.57	17.18 ± 9.02	13.10 ± 8.76	140.7 ± 135.60
Invasive gastroenteritis (8)	6.61 ± 6.54	7.20 ± 3.34	5.31 ± 2.63	91.68 ± 63.39
Pyelonephritis (17)	6.52 ± 6.65	15.70 ± 6.29	12.40 ± 4.90	178.94 ± 109.1
Bacteremia (13)	4.87 ± 5.92	9.29 ± 3.63	5.90 ± 3.30	39.63 ± 53.21
Pneumonia (26)	4.49 ± 3.72	14.42 ± 6.27	11.17 ± 4.88	90.56 ± 77.67
Peritonitis (34)	3.76 ± 7.70	15.05 ± 6.51	12.43 ± 5.53	84.51 ± 72.02
Abscess (14)	2.70 ± 4.82	15.12 ± 5.19	10.82 ± 4.25	81.38 ± 80.90
Deep neck infection (11)	2.03 ± 1.32	15.84 ± 6.09	11.22 ± 4.95	82.66 ± 72.60
Osteomyelitis (10)	1 ± 1.82	9.25 ± 3.85	5.29 ± 3.86	33.50 ± 59.04
Non-SBI group[b] (397)	0.67 ± 1.68	11.21 ± 5.50	6.46 ± 4.45	41.03 ± 58.17
Cellutitis (22)	1.75 ± 2.93	13.26 ± 6.79	8.40 ± 6.36	57.84 ± 83.73
Acute gastroenteritis (53)	1.14 ± 2.35	10.12 ± 4.67	6.40 ± 3.97	51.31 ± 56.50
Lower respiratory tract infection (90)	0.84 ± 1.64	10.45 ± 4.68	6.02 ± 3.93	27.98 ± 46.73
Lymphadenitis (57)	0.58 ± 1.66	11.70 ± 5.79	6.75 ± 4.28	41.95 ± 51.26
Upper respiratory tract infection (67)	0.43 ± 1.39	10.95 ± 5.28	6.21 ± 3.76	57.90 ± 77.40
Urinary tract infection (49)	0.42 ± 1.06	12.09 ± 6.85	6.70 ± 5.76	34.97 ± 52.59
Viral diseases with rash (15)	0.20 ± 0.41	10.48 ± 4.85	5.10 ± 3.07	10.24 ± 13.46
Acute otitis media (28)	0.17 ± 0.37	12.55 ± 6.02	7.08 ± 5.72	48.31 ± 50.96
Stomatitis (11)	0.10 ± 0	12.73 ± 4.96	6.19 ± 2.58	22.30 ± 33.53
Viral meningitis (5)	0.10 ± 0	8.19 ± 2.91	5.13 ± 2.35	8.53 ± 7.38
COVID-19[c] (112)	0.29 ± 0.99	5.90 ± 3.01	3.50 ± 2.15	8.10 ± 17.07
Control group[d] (102)	0.14 ± 0.21	6.73 ± 2.22	3.57 ± 1.80	1.14 ± 1.07
p values between groups	$p^{a,b} < 0.001$	$p^{a,b} < 0.001$	$p^{a,b} < 0.001$	$p^{a,b} < 0.001$
	$p^{a,c} < 0.001$	$p^{a,c} < 0.001$	$p^{a,c} < 0.001$	$p^{a,c} < 0.001$
	$p^{a,d} < 0.001$	$p^{a,d} < 0.001$	$p^{a,d} < 0.001$	$p^{a,d} < 0.001$
	$p^{b,c} = 0.005$	$p^{b,c} < 0.001$	$p^{b,c} < 0.001$	$p^{b,c} < 0.001$
	$p^{b,d} = 0.003$	$p^{b,d} < 0.001$	$p^{b,d} < 0.001$	$p^{b,d} < 0.001$
	$p^{c,d} > 0.05$	$p^{c,d} < 0.001$	$p^{c,d} > 0.05$	$p^{c,d} < 0.001$

SBI, serious bacterial infections; DNI, delta neutrophil index; WBC, white blood cell; ANC, Absolute neutrophil count; CRP, C-reactive protein. [a]SBI group; [b]Non-SBI group; [c]COVID-19 group; [d]Control group.

Table 3 Infection markers' AUC, cut-off, sensitivity, specificity and predictive values for SBI

	Cut-off	AUC	Sensitivity	Specificity	PPV	NPV
DNI	2.5	0.82	47.7	90.4	65.8	81.7
WBC, $\times 10^9$/L	13	0.63	54.2	70.8	41.9	79.9
ANC, $\times 10^9$/L	6.5	0.72	75.8	60	42.2	86.4
CRP, mg/L	27	0.71	70.6	62.4	28.9	84.5

ANC, absolute neutrophil count; AUC, area under curve; CRP, C-reactive protein; DNI, delta neutrophil index; NPV, negative predictive value; PPV, positive predictive value; WBC, white blood cell.

($n = 2$) and *Pseudomonas aeruginosa* ($n = 2$). The most detected bacteria in urine cultures were *Escherichia coli* ($n = 21$), *Klebsiella* spp. ($n = 11$) and *Acinetobacter* spp. ($n = 2$). *Neisseria meningitidis* ($n = 2$), *Klebsiella pneumoniae* ($n = 1$), *Pseudomonas aeruginosa* ($n = 1$), *Staphylococcus aureus* ($n = 2$) and *Staphylococcus epidermidis* ($n = 2$) were identified in the CSF of eight patients. *Salmonella* spp. was identified in stool cultures from five invasive gastroenteritis patients. The upper and lower respiratory tract viral infections and viral gastroenteritis were the main causes of infection in non-SBI patients.

The mean DNI was 4.96 ± 8.38 in the SBI group, 0.67 ± 1.68 in the non-SBI group, 0.29 ± 0.99 in the COVID-19 group and 0.14 ± 0.21 in the control group. The DNI levels were significantly higher in the SBI group compared with the non-SBI ($P < 0.001$);

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Table 4 Logistic regression coefficients of inflammatory biomarkers to predict SBI

	Beta	SE	*P*	OR	95% CI for EXP(B)	
					Lower	Upper
DNI ≥ 2.5%	1.837	0.248	<0.001	6.276	3.857	10.213
ANC ≥ 6.5 × 10^9/L	1.116	0.240	<0.001	3.052	1.908	4.882
CRP ≥ 27 mg/L	0.812	0.233	<0.001	2.252	1.427	3.556

ANC, absolute neutrophil count; CI, confidence interval; CRP, C-reactive protein; DNI, delta neutrophil index; EXP(B), exponential beta; OR, odds ratio; SBI, serious bacterial infections; SE, standard error.

also non-SBI group had higher levels than the COVID-19 group ($P = 0.005$) and the control group ($P = 0.003$). There was no significant difference in the DNI levels between COVID-19 patients and the control group ($P > 0.05$). Similarly, the WBC count, ANC and CRP values were significantly higher in the SBI group ($P < 0.001$ for each). However, these markers' specificities for SBIs were lower than the DNI (Fig. 1 and Table 3).

Based on disease, the highest DNI was found in patients diagnosed with sepsis (DNI 14.97 ± 22.88) and bacterial meningitis (DNI 10.14 ± 15.57). The mean values of infection markers according to diagnosis and groups are shown in Table 2. The DNI showed significant differences on some specific clinical conditions. The mean DNI value was 6.52 ± 6.65 in pyelonephritis, while it was 0.42 ± 1.06 in non-complicated urinary tract infections ($P < 0.001$). Likewise, there was significant difference between pneumonia (4.49 ± 3.72) and lower respiratory tract infection (0.84 ± 1.64) ($P < 0.001$), bacterial (10.14 ± 15.57) and viral meningitis (0.10 ± 0) ($P < 0.001$), deep neck infection (2.03 ± 1.32) and lymphadenitis (0.58 ± 1.66) ($P < 0.001$) (Table 2). On the other hand, the mean DNI level was 0.29 ± 0.99 in COVID-19 patients, which has no difference with control group ($P > 0.05$) and upper respiratory tract infection patients ($P > 0.05$).

The AUC of the DNI to predict SBI was 0.82 (95% confidence interval (CI) 0.77–0.86). The corresponding AUC for CRP was 0.71 (95% CI 0.66–0.76), for ANC was 0.72 (95% CI 0.67–0.77) and for WBC was 0.63 (95% CI 0.57–0.68) (Fig. 1 and Table 3). The diagnostic performance of the DNI in SBI patients was evaluated and the cut-off value of the DNI was found to be 2.5 (AUC 0.82). When sensitivity, specificity and predictive values of infection markers were compared to the most appropriate cut-off values in predicting SBI, the DNI showed the highest specificity, but the lowest sensitivity (Table 3). The cut-off value was determined to be 2.5 for the DNI, and the sensitivity and specificity were 47.7% and 90.4%, respectively. Infection markers' AUC, cut-off, sensitivity, specificity and predictive values for SBI are shown in Table 3.

The DNI was statistically significantly associated with an increased likelihood of SBI per 1% absolute increase in the DNI (1.36-fold increased risk (95% CI 1.23–1.49)). Based on the determined cut-off values of the inflammatory markers, multiple logistic regression analyses showed the DNI (odds ratio 6.27, 95% CI (3.85–10.21), $P < 0.001$) and other markers, except for WBC, significantly predicted SBI. The odds ratio of the CRP was 2.52 (95% CI (1.42–3.55), $P < 0.001$) and the ANC was 3.05 (95% CI (1.91–4.88), $P < 0.001$) (Table 4).

Discussion

A thorough search of the relevant literature yielded only a few related articles, so our study, which evaluates the predictive value of the DNI in paediatric SBI, non-SBI and COVID-19 patients, is one of the very first and most comprehensive studies on this subject. Our study showed that since the DNI has a higher specificity and lower sensitivity compared with conventional markers, including WBC, ANC and CRP, it may be a valuable tool in predicting SBI, especially when combined with the other markers.

Early diagnosis and prompt therapy are essential to decreasing the morbidity and mortality rates of SBIs in paediatric patients. Nonetheless, there is no perfect marker for predicting SBIs, and elevated values of the most frequently used markers, including WBC count, CRP and ANC, are not specific for SBIs. Studies comparing the DNI with these markers have been conducted in predicting infection.[14–16] In a study which evaluated the diagnostic and prognostic power of the DNI and CRP in paediatric sepsis, Nam *et al.* found that CRP is not specific for sepsis, the DNI has the strongest prognostic power among WBC parameters, and the DNI has the most powerful diagnostic potential among the parameters tested. They found the cut-off level of the DNI for sepsis was 2.7, which is similar to ours (2.5).[17] In addition, Ann *et al.* showed in their meta-analysis that high DNI values are associated with mortality in adult patients with sepsis.[18] Sol *et al.* found that in paediatric intensive care unit(PICU) patients, as the admission DNI level increased, the ICU scoring system values also increased, and the proportion of survivors decreased. The DNI at PICU admission was also positively correlated with ICU scores, lactate and CRP levels and negatively correlated with platelet counts.[15] Similarly, we found the highest DNI value in sepsis patients in our study.

The DNI has a prognostic value not only in sepsis but also in other SBIs. Yoon *et al.* showed that the DNI had a moderate diagnostic capacity for detecting bacteraemia in infants with UTI.[19] Lee *et al.* found that the DNI can be an effective marker to differentiate APN from lower UTI in young children.[20] Similarly, our study found that the DNI may also help differentiate pyelonephritis and non-complicated urinary tract infections. As in the differential diagnosis of UTI and APN, we showed that in our

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study, the DNI could also be used to differentiate pneumonia with lower respiratory tract infection, bacterial meningitis with viral meningitis, and lymphadenitis with deep neck infection. This is potentially the most useful application of the DNI in the setting of a patient with sepsis, APN, bacterial meningitis, pneumonia, or deep neck infection. To the best of our knowledge, this is the first study evaluating the diagnostic value of the DNI in distinguishing these diseases.

Compared to conventional markers, the use of the DNI which has higher specificity as a predictive marker in SBI seems beneficial, but it should also be noted that it has a lower sensitivity. In studies conducted on paediatric patients with SBI, APN and acute appendicitis, it has been indicated that while DNI has higher specificity compared to conventional markers, its sensitivity is lower.[20–22] Similar results to the literature were reported in our study. Although the DNI is not a perfect diagnostic parameter, because its higher specificity, easiness to obtain and applicability in clinical practice, we consider that it would be convenient and practical in predicting SBI when used in combination with other infection markers.

In the present study, we also evaluated the DNI levels in paediatric COVID-19 patients. No difference was found between COVID-19 patients and upper respiratory tract infection patients. Currently, there is no evidence that serum DNI aids in differentiating between COVID-19 and upper respiratory tract infection. It is also one of the very first studies to evaluate the diagnostic value of the DNI in paediatric COVID-19 patients.

Our research had some limitations. It was designed as a retrospective and single-centre study. Secondly, the included clinical conditions showed a broad spectrum of heterogeneity. In addition, since procalcitonin is not usually requested at first application, it could not be compared with the DNI in terms of its diagnostic value since the procalcitonin values of the patients were not available. Furthermore, the risk of classification bias should not be disregarded since not all SBIs would be bacterial-proven. Multicentre and prospective studies would be helpful in elucidating the role of the DNI in predicting SBI in children. Nonetheless, this study contributes meaningfully to the literature due to the dearth of paediatric studies.

Conclusions

Our study suggests that SBI in children is associated with an increase in the DNI levels. Compared to other biomarkers, the DNI had higher specificity and lower sensitivity in predicting SBI. The DNI is easily measurable, fast, inexpensive and a highly specific marker; it also requires no extra blood study to complete blood count, and it can be used as an effective, facile and useful parameter for the early diagnosis of SBIs and differentiation of SBIs and non-SBIs. Finally, the DNI could be included in algorithms with other infection markers for better predicting SBIs.

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