

REVIEWS

DELTA NEUTROPHIL INDEX AND ITS FUTURE APPLICATION IN ORAL AND MAXILLOFACIAL SURGERY—A REVIEW ARTICLE

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ABSTRACT

INTRODUCTION: This report is dedicated to the delta neutrophil index (DNI) as a laboratory indicator reflecting circulating immature granulocytes, and its application as a diagnostic and prognostic marker in sepsis, severe infections and other acute inflammatory conditions.

AIM: The aim is to analyze, systematize and interpret data from the available scientific literature regarding the biological nature of DNI, its calculation method, clinical areas of application, its diagnostic accuracy, its prognostic value, and the main limitations in its interpretation in order to refine its use in the diagnosis and treatment of inflammatory diseases in the domain of oral and maxillofacial surgery.

MATERIALS AND METHODS: The text is a qualitative analytical review with a thematic synthesis of the used literature sources, including systematic reviews, meta-analyses, diagnostic studies, clinical observations, and publications on specific populations and acute clinical conditions.

RESULTS AND DISCUSSION: The reviewed sources show that DNI is an automatically generated indicator by certain hematology analyzers that reflects the fraction of immature granulocytes in peripheral blood. The cited scientific works consistently associate elevated DNI with severe infection, sepsis, and early inflammatory deterioration, and in many studies it has demonstrated high specificity and good prognostic value for severity and mortality, especially in sepsis and critically ill patients. However, the studies included in the review also show significant variability in diagnostic thresholds, as well as limitations related to nonspecific elevation of the indicator and its different effectiveness in individual clinical populations.

CONCLUSION: The available scientific literature supports the view that DNI is a rapid, automated and clinically useful marker for early recognition of severe infection and for assessing the prognosis in sepsis and other acute inflammatory conditions, but its interpretation should be done in the context of the clinical picture and in combination with other laboratory indicators, and not as a standalone diagnostic test. All this gives reason to assume that DNI can also be used in the diagnosis, treatment, and follow-up of patients with acute infectious diseases of the nature of oral and maxillofacial surgery.

Keywords: *delta neutrophil index, sepsis, immature granulocytes, diagnostic marker, prognostic marker, inflammation, critically ill patients*

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INTRODUCTION

Along with newer and more widely used markers of inflammation such as procalcitonin (PCT), neutrophil-to-lymphocyte ratio, mean platelet volume, evaluating mean platelet volume, the delta neutrophil index (DNI) has been established in a number of scientific publications as a laboratory indicator for the diagnosis of these diseases, many of which, if left untreated, can lead to serious complications and even death (1-4). In itself, it reflects the proportion of immature granulocytes in the peripheral blood and is used as an indirect marker of acute infection and inflammation (5,6). Its clinical significance is based on the fact that in severe bacterial infection, sepsis or a strong inflammatory process, the bone marrow releases a larger number of immature neutrophil forms, which leads to the so-called left shift of the granulocyte lineage (1,5-8). In this sense, DNI is not simply a quantitative indicator of the complete blood count, but a marker through which early and more intense activation of the innate immune response can be detected.

The cited scientific works emphasize that DNI is automatically generated by certain hematology analyzers and therefore combines several practical advantages: speed, low cost, and the possibility of inclusion in the routine examination of peripheral blood, without the need for a separate test, which would incur additional expenses (5,7,9-11). This is what makes it particularly useful in the context of emergency medicine, intensive care, surgery, and pediatric practice, where early assessment of the risk and severity of infection has direct clinical significance (12).

The analyzed sources outline several main thematic directions. First, the biological nature of DNI and the method of its automated calculation are examined. Second, its application in sepsis and severe bacterial infection is emphasized as the main clinical area of use. Third, the cited scientific works consider its role in other acute and critical conditions, including gastrointestinal emergencies, severe acute pancreatitis, poisoning, abdominal surgery, and localized purulent infections (7,13-16). Fourth, the available scientific literature draws attention to its application in pediatrics, including in serious bacterial infections, urinary tract infections, neonatal

sepsis, and multisystem inflammatory syndrome in children (MIS-C) (9-12). Fifth, the limitations of the indicator are discussed, related to the variability of threshold values, its different effectiveness in different populations, and the lack of absolute specificity for infection (5,21,22).

Systematization of the available data is necessary to assess the real place of DNI in modern clinical practice and to outline the conditions under which it has the greatest diagnostic and prognostic value.

AIM

The **aim** of this review article is to analyze, systematize and interpret the available scientific literature on the delta neutrophil index as a laboratory marker, with a focus on its biological basis, its diagnostic and prognostic application in sepsis, severe infections and other acute inflammatory conditions, its diagnostic accuracy, and the limitations of its clinical use.

MATERIALS AND METHODS

This text is a qualitative analytical review with a thematic synthesis of the literature sources used. By its nature, it is not an independent systematic review, as it does not include an independent search strategy in bibliographic databases, predefined selection criteria, or formalized assessment of the risk of systematic error. The report is structured as a review analysis of an already selected set of sources and therefore can most accurately be defined as a qualitative review report with an analytical-thematic approach.

The literature sources used include various types of scientific publications. There are systematic reviews and meta-analyses evaluating the diagnostic and prognostic value of DNI in infections, sepsis, and acute diseases. Also included are original clinical studies by other authors on sepsis, patients in intensive care units, suspected infection in emergency settings, pneumonia-induced sepsis, poisonings, surgical and gastrointestinal emergencies, as well as pediatric and neonatal populations. In addition, there are review publications focused on the clinical interpretation of DNI and its place among other inflammatory and hematological markers.

The main indicators considered in the cited scientific works include: diagnostic thresholds of

DNI; sensitivity, specificity and area under the curve (AUC); ability to distinguish between sepsis, non-infectious SIRS and milder infections; prognostic value for mortality, severity of disease, surgical complications and need for intensive care; as well as comparative value with C-reactive protein (CRP), procalcitonin (PCT), white blood cell count (WBC), and other inflammatory indicators.

RESULTS AND DISCUSSION

The analyzed sources define the delta neutrophil index as an automatically generated hematological indicator that assesses the fraction of immature granulocytes in the peripheral blood and essentially reflects the ratio of early neutrophil forms to the total neutrophil population (7,9,23). The reviewed publications indicate that the DNI is calculated by certain hematological analyzers, with the classical principle involving the difference between the fraction of myeloperoxidase-reactive leukocytes and the fraction of mature neutrophils, assessed by a nuclear lobularity channel (5,23–26). The biological basis of the indicator is associated with the release of immature granulocytes from the bone marrow during severe infection, sepsis, or severe inflammatory stress, which clinically corresponds to a left shift of the granulocyte line (1,5,7,8). The most widely used area of application of the DNI in the available scientific litera-

ed better prognostic value than CRP, lactate, white blood cell count, and absolute neutrophil count (5). The prognostic value of DNI in sepsis is another area of investigation. The studies included in the review showed that elevated values of the indicator are associated with 28-day mortality, severity of illness and adverse outcome, including pneumonia-induced sepsis (8,23,24). Some publications emphasize that serial values of DNI, including at follow-up up to 72 hours, can be particularly informative for assessing clinical dynamics (5,24).

In terms of diagnostic accuracy, the sources analyzed show that DNI has moderate sensitivity but high specificity for significant infection. A systematic review and meta-analysis by Park et al. (2017), including twelve studies, reported a pooled sensitivity of 0.67, specificity of 0.94, and AUC of 0.89 for the diagnosis of infection, which suggests a good ability to confirm a serious infectious condition. For the prediction of mortality in infected patients, the same meta-analysis reported a sensitivity of 0.70, specificity of 0.78, and AUC of about 0.84 (29). A meta-analysis by Ahn et al. (2018) in adults with sepsis showed an AUC of 0.82 for mortality and approximately balanced sensitivity and specificity around 0.70–0.72. These data support the view that DNI has substantial prognostic value, although not absolute (Table 1) (8).

Table 1. Diagnostic accuracy of DNI according to meta-analytic and key clinical data.

Indicator/Context	Main Results
Infection—general diagnostics (29)	Sensitivity = 0.67, Specificity = 0.94, AUC = 0.89
Mortality due to infection (29)	Sensitivity = 0.70, Specificity = 0.78, AUC = 0.84
Mortality in adults with sepsis (8)	Sensitivity = 0.70; Specificity = 0.72; AUC = 0.82
Severe sepsis/septic shock with DNI > 6.5% (29)	Sensitivity = 81.3%; Specificity = 91%

ture is sepsis and severe bacterial infection. The cited literature consistently shows that an elevated DNI can help distinguish between noninfectious systemic inflammatory response, sepsis, and more severe forms of infectious disease (5,27,28). Several studies have used cutoff values around 2–3% to differentiate sepsis from significant infection, with higher values being associated with greater severity and worse prognosis (23,28,29). In critically ill patients with a DNI > 6.5%, the index is associated with severe sepsis or septic shock and in some studies has demonstrat-

In addition to classical sepsis, the reviewed publications show the application of DNI in other acute and critical conditions. In acute gastrointestinal diseases and emergency abdominal surgery, the indicator is associated with the severity of the disease, surgical outcome, bacteremia, sepsis, and 30-day mortality (7,13). In acute pancreatitis, it is considered an early marker for the development of a severe form (27). In acute poisoning, serial DNI has been used as an early predictor of sepsis and bacteremia, and

in some studies it is superior to CRP, PCT, leukocyte count, and other indicators (14). Data are also available for its use in purulent infections of the neck and other localized inflammatory processes in the facial and cervical region (Table 2) (6,16,26,36).

Despite its wide clinical application, the cited scientific works clearly indicate the limitations of DNI. The indicator is not strictly specific for infection, as it can also be increased in non-infectious inflammation, critical stress, and some hematologi-

Table 2. Clinical role of DNI in the context of the relevant clinical condition.

Clinical Condition/Context	Clinical Role of DNI
Emergency abdominal surgery (13)	Prediction of bacteremia, sepsis, complications and 30-day mortality
Severe acute pancreatitis (27)	Early marker of severe course
Acute poisonings (14)	Early predictor of sepsis and bacteremia
Suppurative infections of the neck (6,16,26,36)	Assists in diagnosis and monitoring of deep suppurative processes

Pediatric and neonatal applications of DNI are also well documented in the literature, but with more mixed results. In children with serious bacterial infection, an elevated DNI, often around the 2.5% threshold, has been described as a highly specific marker that can help differentiate between bacterial and nonbacterial febrile conditions, although its sensitivity is more moderate (18). In MIS-C following COVID-19, DNI has been reported as a potential diagnostic marker with high specificity and correlation with the severity of the condition (19). In infants with febrile urinary tract infection, it has been shown to help differentiate between acute pyelonephritis and lower infections and has been associated with vesicoureteral reflux (17). In neonatal practice, some publications report high sensitivity and specificity at certain thresholds, especially in combination with CRP, while in very premature neonates with late neonatal sepsis, the effectiveness of the indicator may be more limited (Table 3) (20,30–32).

cal or neoplastic conditions (1,5,22). In addition, the threshold values vary considerably between individual studies and populations—from less than 1% to values around 9%—which makes it difficult to apply a single universal threshold (7,23,28,29). Some pediatric data also show that in certain febrile conditions without bacteremia, DNI is not superior to CRP and does not add significant diagnostic value (21).

The analyzed sources consistently show that DNI occupies a special place among modern hematological markers because it combines biological validity with high practical applicability. Unlike more traditional measures, such as the total leukocyte count, which reflects a more general response of the body, the DNI targets immature granulocyte forms and is therefore considered a more sensitive indicator of early activated granulocytopoiesis in severe infection and sepsis (5,7). It is this link between pathophysiology and laboratory accessibility that explains

Table 3. Primary role of DNI in the relevant study population with the relevant clinical condition.

Population/Clinical Condition	Main Role of DNI
Serious bacterial infections in children (18)	High specificity for differentiating bacterial infection
MIS-C (19)	Diagnostic aid marker and severity indicator
Febrile urinary tract infection in infants (17)	Differentiation of pyelonephritis from lower urinary tract infection; prediction of reflux
Neonatal sepsis (20,31,32)	Diagnostic and prognostic value, especially in combination with CRP
Late-onset sepsis in preterm infants (33)	Lower diagnostic value in some subgroups

the increased interest in the measure in emergency and intensive care medicine.

The data on the use of the DNI in sepsis are most convincing. Both meta-analytic and primary clinical studies show that an elevated value is useful both for distinguishing severe infection and for assessing prognosis. Of particular importance is the fact that in a number of publications, the DNI has demonstrated high specificity, suggesting a good diagnostic confirmation ability in clinically suspected infection (23,29). This means that at elevated values, the measure can strengthen the clinical suspicion of a serious infection, even when other parameters are not severely deviated.

However, the reviewed literature does not support the idea that DNI should be used in isolation. Although some studies have reported superiority over CRP or better early informativeness than total leukocyte count, the review and comparative data point to a more balanced interpretation: DNI is most useful as a complementary marker in combination with clinical assessment, CRP, PCT, and other indicators, and not as a standalone diagnostic test (10,22,33–36). An advantage of DNI is its applicability beyond classical sepsis. The cited scientific works show that the indicator may have a role in gastrointestinal emergencies, pancreatitis, acute poisoning, and surgical conditions, where early assessment of inflammatory severity and risk of complications is of great practical importance (7,13,14,27). This broadens the clinical profile of the marker and shows that its value is not limited to the classical infectious context, but is also related to the broader field of acute systemic inflammatory response.

Pediatric and neonatal data require more cautious interpretation. On the one hand, the studies included in the review show promising results in serious bacterial infections, MIS-C, urinary tract infections, and neonatal sepsis, including high specificity and good combined value with CRP (18–20). On the other hand, not all pediatric studies confirm the superiority of DNI, and in some populations it does not distinguish sufficiently from existing markers (21,32). This means that its application in childhood seems promising, but more dependent on the clinical context and characteristics of the specific population.

A particularly important result of the analysis is the variability of the threshold values. It is one of the most significant factors limiting the standard application of DNI in daily practice. When different studies use cutoff values from less than 1% to more than 6%, and in neonatal populations even in different ranges, it becomes clear that a universal diagnostic threshold can hardly be imposed without specific adaptation and consideration for the population, the analyst and the clinical setting (20,23,28,32). Therefore, the interpretation of the DNI should be adaptive, not mechanically applied.

CONCLUSION

The analyzed sources show that the delta neutrophil index is an automated laboratory indicator reflecting circulating immature granulocytes and is associated with the early granulocyte response in severe infection and inflammation. The available scientific literature supports its application mainly in sepsis, severe bacterial infections, and critical inflammatory conditions, where it has both diagnostic and prognostic value.

The available data show that the DNI is often characterized by high specificity and good prognostic value, especially in assessing the severity and mortality of sepsis, but at the same time demonstrates variability in diagnostic thresholds and inconsistent reliability in different clinical populations. The most reasonable conclusion is that the DNI should be considered as a useful complementary marker within the framework of a comprehensive clinical assessment, and not as an independent and universally applicable diagnostic criterion, including in the diagnosis and treatment of acute infections in oral and maxillofacial surgery.

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