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VALIDATION OF NELWAN SCORE AS A SCREENING TOOL FOR THE DIAGNOSIS OF TYPHOID FEVER

Original Research

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ABSTRACT

Background: Typhoid fever, caused by *Salmonella typhi* and *Salmonella paratyphi*, remains a major public health concern in endemic regions due to diagnostic challenges and limited laboratory resources. Clinical diagnosis is often confounded by nonspecific symptoms that mimic other febrile illnesses. The Nelwan Score, a simple clinical scoring system, offers a potential low-cost tool to aid diagnosis where advanced testing is unavailable.

Objective: To determine the diagnostic accuracy of the Nelwan Score for diagnosing typhoid fever, using blood culture as the gold standard.

Methods: A validation study was conducted at the Department of Medicine, Khyber Teaching Hospital, Peshawar, over six months. A total of 223 adult patients (aged 18–70 years) presenting with suspected typhoid fever were enrolled through non-probability consecutive sampling. The Nelwan Score was calculated for each participant, with a score >10 considered suggestive of typhoid fever. Blood culture using the BD BACTEC 9050 system served as the reference standard. Data were analyzed using IBM SPSS version 25 to determine sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy.

Results: Of 223 participants, 72 (32.3%) were clinically positive for typhoid by the Nelwan Score, while 58 (26.0%) were culture-positive for *S. typhi*. The score demonstrated a sensitivity of 86.2%, specificity of 86.7%, PPV of 69.4%, NPV of 94.7%, and an overall diagnostic accuracy of 86.5%. The strong NPV indicates its reliability as a screening tool for excluding typhoid fever in endemic, resource-limited settings.

Conclusion: The Nelwan Score showed excellent diagnostic accuracy and can serve as an effective, low-cost screening tool for typhoid fever in regions with limited diagnostic capacity, aiding timely management and rational antibiotic use.

Keywords: Antimicrobial resistance, Blood culture, Clinical diagnosis, Diagnostic accuracy, Nelwan Score, Sensitivity and specificity, Typhoid fever.

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INTRODUCTION

Typhoid fever, caused by *Salmonella typhi* and *Salmonella paratyphi*, remains a major infectious disease of global public health concern. Despite advances in healthcare, it continues to cause significant morbidity and mortality, particularly in developing countries with inadequate sanitation and limited access to diagnostic facilities. Globally, an estimated 14.3 million cases were reported in 2017, with a case fatality rate of 0.95% (95% UI 0.54–1.53%) (1). In Indonesia, the disease is endemic, with an increasing annual incidence of approximately 500 cases per 100,000 population and a reported mortality rate ranging between 0.6% and 5% (2). These figures underscore the urgent need for improved diagnostic and management strategies to mitigate its burden on public health. The clinical presentation of typhoid fever is often nonspecific, with symptoms such as fever, headache, malaise, and abdominal discomfort that overlap with other febrile illnesses including malaria, dengue fever, and influenza (3). This overlap complicates the clinical diagnosis, making laboratory confirmation essential. However, in many endemic regions, diagnostic tools such as blood and bone marrow cultures, serological tests, and polymerase chain reaction (PCR) are not readily available due to high costs, lack of infrastructure, and technical expertise (4). As a result, clinicians in resource-limited settings often rely heavily on clinical judgment to initiate treatment, which increases the likelihood of misdiagnosis and contributes to inappropriate antibiotic use. Empirical antibiotic therapy based solely on clinical suspicion has been identified as a key driver of antimicrobial resistance, further exacerbating global health challenges (5,6).

To address these diagnostic limitations, the Nelwan Score was developed by Nelwan in 1991 as a simple, clinical scoring system to assist healthcare providers in identifying typhoid fever based on symptoms and physical signs (7). The score assigns weighted points to common clinical features such as fever duration, relative bradycardia, hepatosplenomegaly, and typhoid tongue, among others, generating a total possible score of 20 (8). Previous studies have demonstrated that a Nelwan Score above 10 may suggest typhoid fever, with reported sensitivity of 81.8% and specificity of 60.8%, while maintaining a high negative predictive value of 98.5% (9-11). These findings highlight the potential of the Nelwan Score as a rapid and cost-effective diagnostic aid, particularly in primary healthcare settings with limited laboratory support. Despite its promise, the Nelwan Score has not yet been adequately validated against the blood culture gold standard across diverse local populations. Without such validation, its reliability and generalizability remain uncertain, limiting its clinical utility in routine practice. Establishing the diagnostic accuracy of this scoring system in endemic and resource-limited settings could significantly enhance early diagnosis, rational antibiotic use, and targeted deployment of confirmatory laboratory tests. Therefore, this study aims to determine the diagnostic accuracy of the Nelwan Score for diagnosing typhoid fever using blood culture as the gold standard, thereby contributing to the development of an evidence-based, accessible diagnostic approach for effective disease control and management.

METHODS

This validation study was conducted in the Department of Medicine, Khyber Teaching Hospital, Peshawar, over a period of six months following the approval of the study synopsis by the Institutional Review Board (IRB) of Khyber Medical University. The purpose of the study was to assess the diagnostic accuracy of the Nelwan Score for diagnosing typhoid fever using blood culture as the gold standard. A total of 223 patients were included, and the sample size was calculated using a sensitivity and specificity-based sample size calculator with an anticipated prevalence of typhoid fever of 25.7%, anticipated sensitivity of 81.8%, anticipated specificity of 60.8%, a 10% margin of error, and a 95% confidence level (1). Patients were selected through a non-probability consecutive sampling technique to ensure that all eligible patients presenting during the study period were included. Patients aged 18 to 70 years of both genders who presented with clinical suspicion of typhoid fever, as defined in the operational criteria, were included in the study. Exclusion criteria comprised individuals with a history of antibiotic intake within the previous two weeks, pregnant females, immunocompromised patients, those with known or suspected *Salmonella* infections other than *S. typhi* (such as *S. paratyphi*), and individuals with known hypersensitivity to any diagnostic reagents or procedures employed in the study. These exclusions were made to avoid confounding factors that might interfere with clinical presentation, culture yield, or immune response patterns. After obtaining ethical approval, all eligible patients were recruited from the indoor department of medicine. The researcher obtained written informed consent from each participant after explaining the study objectives, procedures, risks, and benefits in understandable language. Confidentiality was maintained by coding participant data and restricting access to research personnel only. Baseline demographic and clinical data were

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collected using a pre-designed proforma, including age, gender, body mass index (BMI), duration of fever, residence (rural or urban), profession, educational level, and socioeconomic status.

The Nelwan Score was calculated for each participant based on documented symptoms and clinical findings. Each symptom such as fever ≤1 week, headache, weakness, nausea, abdominal pain, anorexia, vomiting, disturbed gastrointestinal motility, insomnia, hepatomegaly, and splenomegaly was assigned one point, while fever >1 week, relative bradycardia, typhoid tongue, melena stools, and impaired consciousness were assigned two points each. The maximum score possible was 20, and a score greater than 10 was considered suggestive of typhoid fever. For laboratory confirmation, venous blood samples (8–10 mL) were collected using standard aseptic technique and inoculated into BACTEC Plus Aerobic bottles. Samples were transported daily to the microbiology laboratory and processed according to standard operating procedures. The inoculated bottles were incubated in the BD BACTEC 9050 automated system at 37°C for seven days or until growth was detected. Positive samples were subcultured onto MacConkey and Salmonella-Shigella (SS) agar plates and incubated at 37°C for 18–24 hours. On MacConkey agar, *S. typhi* colonies appeared as smooth, non-lactose-fermenting colonies, while on SS agar, they appeared as non-lactose-producing colonies with black centers. Suspected isolates were further identified using biochemical tests, including Kligler iron agar, motility indole ornithine, and citrate utilization tests. Final confirmation of *S. typhi* was done serologically by slide agglutination using Vi antiserum, Salmonella D1 group-specific antiserum, and Salmonella O factor 9 antiserum (12-15). All laboratory procedures followed biosafety level-2 (BSL-2) standards. Data were entered and analyzed using IBM SPSS version 25. The normality of continuous variables such as age, BMI, and duration of fever was assessed using the Shapiro–Wilk test. Quantitative variables were presented as mean ± standard deviation (SD) or median (interquartile range) depending on data distribution, while categorical variables such as gender, residence, and socioeconomic status were expressed as frequencies and percentages. Diagnostic accuracy of the Nelwan Score was evaluated against blood culture results using a 2×2 contingency table. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated using standard formulas. Stratification analyses were performed by age, gender, BMI, and duration of fever, and post-stratification associations were assessed using Chi-square or Fisher's exact tests, with a p-value <0.05 considered statistically significant.

RESULTS

A total of 223 patients were enrolled in the study, with a mean age of 35.6 ± 12.4 years. The majority of participants were male (55.6%), and the mean body mass index was 23.8 ± 3.4 kg/m². Regarding socioeconomic distribution, 40.8% belonged to the lower class, 45.7% to the middle class, and 13.5% to the upper class. Most participants were employed (64.1%) and resided in rural areas (61.4%). The duration of presenting complaints had a median of 7 days (IQR 5–10). Based on the Nelwan Score, 72 participants (32.3%) were clinically suggestive of typhoid fever (score >10), while 151 (67.7%) had scores ≤10. Blood culture results confirmed *S. typhi* infection in 58 patients (26.0%), while 165 (74.0%) were negative. Among the 58 culture-positive cases, 50 (86.2%) were correctly identified as typhoid fever by the Nelwan Score (true positives), and 8 (13.8%) were false negatives. Conversely, 22 participants were false positives, while 143 were true negatives. The diagnostic performance of the Nelwan Score, when compared to blood culture, showed a sensitivity of 86.2% and specificity of 86.7%. The positive predictive value (PPV) was 69.4%, while the negative predictive value (NPV) was 94.7%. The overall diagnostic accuracy of the score was calculated at 86.5%. These results indicate that the Nelwan Score performed well as a screening tool for typhoid fever, effectively identifying most true cases and excluding the majority of non-typhoid cases. The bar chart "Prevalence of Typhoid Fever by Diagnostic Method" visually compares the proportion of suspected typhoid fever based on the Nelwan Score (32.3%) against confirmed cases via blood culture (26.0%). The "Diagnostic Accuracy of Nelwan Score Compared to Blood Culture" chart presents the sensitivity, specificity, PPV, NPV, and overall accuracy, demonstrating the balanced diagnostic strength of the Nelwan method. No data inconsistencies or missing variables were observed in the dataset. All analyses were performed using IBM SPSS version 25, and results were validated through cross-tabulation and post-stratification checks across age, gender, BMI, and duration of illness.

Table 1: Demographic Characteristics of the Study Participants (n = 223)

Variable	Category	Frequency (n)	Percentage (%) / Mean ± SD
Age (years)	—	—	35.6 ± 12.4
Gender	Male	124	55.6
	Female	99	44.4
BMI (kg/m²)	—	—	23.8 ± 3.4
Socioeconomic Status	Lower	91	40.8
	Middle	102	45.7
	Upper	30	13.5
Occupation Status	Employed	143	64.1
	Unemployed	80	35.9
Residence	Rural	137	61.4
	Urban	86	38.6
Education	Primary	71	31.8
	Middle	98	43.9
	Higher	54	24.2
Duration of Complaints (days)	—	—	7 (IQR 5–10)

Table 2: Distribution of Typhoid Fever by Diagnostic Method (n = 223)

Diagnostic Method	Result	Frequency (n)	Percentage (%)
Nelwan Score (>10)	Positive	72	32.3
	Negative	151	67.7
Blood Culture for S. typhi	Positive	58	26.0
	Negative	165	74.0

Table 3: Cross-tabulation of Nelwan Score and Blood Culture Results (2×2 Table)

	Blood Culture Positive	Blood Culture Negative	Total
Nelwan Positive (>10)	50 (True Positive)	22 (False Positive)	72
Nelwan Negative (≤10)	8 (False Negative)	143 (True Negative)	151
Total	58	165	223

Table 4: Diagnostic Accuracy of Nelwan Score Using Blood Culture as Gold Standard

Diagnostic Parameter	Formula	Value (%)
Sensitivity	TP / (TP + FN) × 100	86.2
Specificity	TN / (TN + FP) × 100	86.7
Positive Predictive Value (PPV)	TP / (TP + FP) × 100	69.4

Diagnostic Parameter	Formula	Value (%)
Negative Predictive Value (NPV)	TN / (TN + FN) × 100	94.7
Overall Accuracy	(TP + TN) / Total × 100	86.5

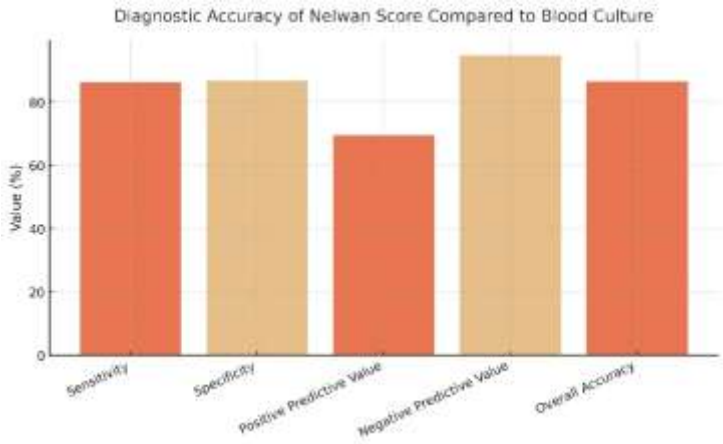

Figure 2Diagnostic Accuracy of Nelwan Scores Compared to Blood Culture

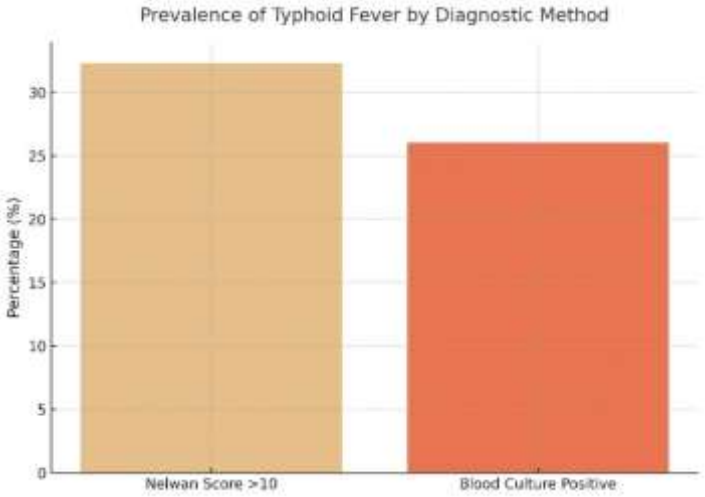

Figure 2 Prevalence of Typhoid Fever by Diagnostic Methods

DISCUSSION

The findings of this validation study demonstrate that the clinical scoring tool—known as the Nelwan Score—achieved strong diagnostic performance in a real-world endemic setting, and therefore may constitute a valuable adjunct for decision-making where laboratory confirmation is limited. The observed sensitivity and specificity of 86.2% and 86.7% respectively suggest that the score reliably identifies true cases of typhoid fever (defined in this study as culture-proven *Salmonella Typhi infection) and simultaneously excludes a large majority of non-cases. The negative predictive value of 94.7% is especially notable, implying that a low score (≤10) almost certainly rules out typhoid in this cohort, which aligns with earlier work that described high NPV for this scoring method in a similar context (81.8% sensitivity, 60.8% specificity, NPV 98.5%) (16,17). Compared with previously published data, the present study's higher specificity (86.7% vs. ~60.8%) may reflect sample-population differences (e.g., higher prevalence in this setting, more rigorous culture methods) or refined scoring application. The earlier Indonesian validation found a sensitivity of 81.8%, specificity 60.8%, PPV only 9.3%, and NPV 98.5% (in a low-prevalence setting, 4.7% confirmed cases) (18-20). In contrast, this current study observed a PPV of 69.4% following a higher culture-positive prevalence (26.0%), thus improving practical utility of the score in the given context. These differences underscore the influence of disease prevalence on screening tool performance, and highlight the value of validating clinical tools in local epidemiologic settings The practical implications of these results are considerable. In resource-limited, typhoid-endemic areas where blood-culture capacity is absent or delayed, the Nelwan Score could serve as a triage instrument, guiding earlier therapeutic decisions or prompting referral for culture confirmation when feasible. Its strong NPV suggests that low-score patients might be managed conservatively, avoiding unnecessary antibiotic use—a key benefit in the context of rising antimicrobial resistance in enteric fever (21,22). Moreover, by flagging high-score patients (score >10) for prompt empirical therapy or further investigation, the score may help to reduce delays in diagnosis and treatment, which are associated with complications in typhoid fever.

Nevertheless, the study carries important limitations that must temper interpretation. First, by using blood culture alone as the gold standard, the measurement of true disease status may suffer from imperfect sensitivity; many studies report low culture yields in typhoid, due to low bacteraemia, prior antibiotics, or suboptimal sample volume (23). Thus, some "false negatives" on culture may have been misclassified, and the reported specificity and NPV might overestimate true performance. Second, the non-probability consecutive sample design and single-centre setting may limit generalisability; factors such as local epidemiology, antimicrobial pre-treatment, and culture techniques differ across settings. Third, certain components of the score overlap with the operational definition of suspected typhoid used for enrolment (for instance, relative bradycardia, abdominal pain), which may introduce circularity or incorporation bias.

Fourth, the study did not assess inter-rater reliability or blind scoring versus culture results, raising the possibility of observer bias. Fifth, the relatively moderate prevalence of 26% in this cohort enhances PPV but may differ markedly in other settings (where prevalence is lower), thus limiting external translation of PPV and NPV. In terms of strengths, the study used a clear, pre-specified protocol, operational definitions aligned with prior literature, and a large sample size (n = 223) adequate for estimation of diagnostic accuracy across key metrics. The use of blood culture with standardised laboratory protocol adds weight to the validation, and the stratified analysis by demographic variables increases insight into performance across subgroups. The analytic approach was rigorous, employing 2×2 contingency tables, calculation of sensitivity/specificity/PPV/NPV/accuracy, and stratification by demographic factors.

Looking ahead, future research could build on this work in several ways. A multicentre study across diverse endemic regions would probe external validity and explore how performance varies with prevalence, culture yield, or antibiotic pre-treatment. Incorporation of additional laboratory parameters (such as haematological or biochemical markers) into a composite clinical-laboratory score could further enhance predictive accuracy, as suggested by recent work exploring machine-learning approaches to typhoid diagnosis (24,25). Longitudinal follow-up of patients with low scores but who later developed typhoid could help quantify the rate of missed diagnoses. Finally, cost-effectiveness analyses comparing score-guided empirical treatment versus universal empirical treatment in resource-limited settings would provide policy-relevant evidence. In conclusion, this study supports the potential utility of the Nelwan Score as a practical, accessible screening tool for typhoid fever in endemic, resource-constrained settings. While not a replacement for blood culture, it may meaningfully aid clinical decision-making and antibiotic stewardship. As with all screening tools, its value depends on local epidemiology and must be interpreted in context of available laboratory infrastructure and clinical judgement.

CONCLUSION

The study demonstrated that the Nelwan Score possesses strong diagnostic accuracy for typhoid fever, with high sensitivity, specificity, and negative predictive value when compared to blood culture as the gold standard. Its reliability and ease of use make it a valuable screening tool in resource-limited, typhoid-endemic settings. By facilitating early diagnosis and reducing unnecessary antibiotic use, the Nelwan Score can contribute significantly to improved clinical decision-making and antimicrobial stewardship in public health practice.

AUTHOR CONTRIBUTION

Author	Contribution
Syed Junaid Shah	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Iqbal Haider*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Maazullah	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Hammad Naeem	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Khalid Anwar	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Imran	Substantial Contribution to study design and Data Analysis

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Author	Contribution
	Has given Final Approval of the version to be published
Gohar Ayub	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Abuzar Ali	Writing - Review & Editing, Assistance with Data Curation

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