Can Immature Granulocytes Predict Sepsis?

Amy Nixon
Associate Practitioner
Haematology
Russell's Hall Hospital,
Dudley, DY1 2HQ
Clinical lead: Dr Craig Taylor

Black Country Pathology Services
Supporting Dudley Group NHS Foundation Trust

Introduction

- Sepsis is a life-threatening condition caused by a dysregulated immune response to infection, resulting in a staggering 11 million deaths worldwide annually (1).
- Due to the systemic effect of sepsis there is not one biomarker that is sensitive or specific enough to give an ultimate diagnosis. Current practice relies upon a raised lactate level (2). Confirmation from blood culture is the current "gold standard" however, results take from 2-5 days (3).
- Immature granulocytes (IG) are an emerging potential early biomarker but are not yet routinely reported in clinical practice (4).
- The presence of acute infection increases proliferation of neutrophil precursors from the bone marrow, in the form of promyelocytes, myelocytes and metamyelocytes into peripheral blood (5).
- The Sysmex XN10 full blood count analyser provides a six-part differential white cell count (WBC). The analyser provides "flags" to the validator when an IG of >1.0 is present however, this is not currently reported (figure 1)(6).

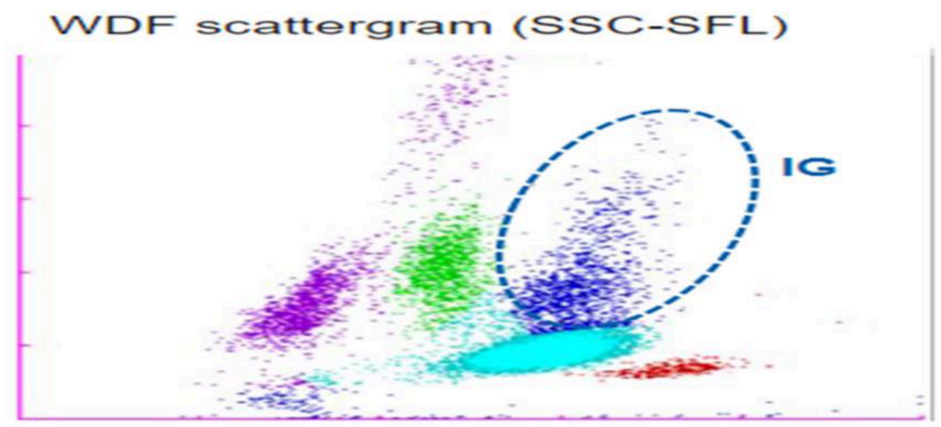


Figure 1. XN10 Analyser IG present scattergram. IG includes promyelocytes, myelocytes and metamyelocytes (circled in blue). The 'IG Present' IP message threshold is user-defined and programmable. The IG flag only appears when the IG%/# exceeds the threshold value (6).

Study Design

Retrospective analysis of 80 patients presenting with suspected sepsis at Russell's Hall Hospital Emergency Department from January to March 2025. Samples were analysed on the Sysmex XN10 analysers. This study did not require ethical approval

Objectives

The aim of this research was to assess IG as an early predictor of sepsis, comparing sensitivity and specificity with current biomarkers WBC, C-reactive protein (CRP), procalcitonin and lactate. To evaluate the effectiveness of IG# and IG% as early biomarkers for sepsis.

Methods

- Gold Standard: Blood culture (BC) results were used to confirm sepsis diagnosis.
- Negative BC of 40 patient's were analysed for IG 100% were <1.0 confirming the negative predictive value.
- Biomarkers Assessed: IG#, IG%, CRP, procalcitonin, lactate, and WBC.
- Statistical Analysis: receiver operating characteristic (ROC) curves and area under the curve (AUC) analysis. Youden's index (YI) was calculated using SPSS version 29.0.

Results

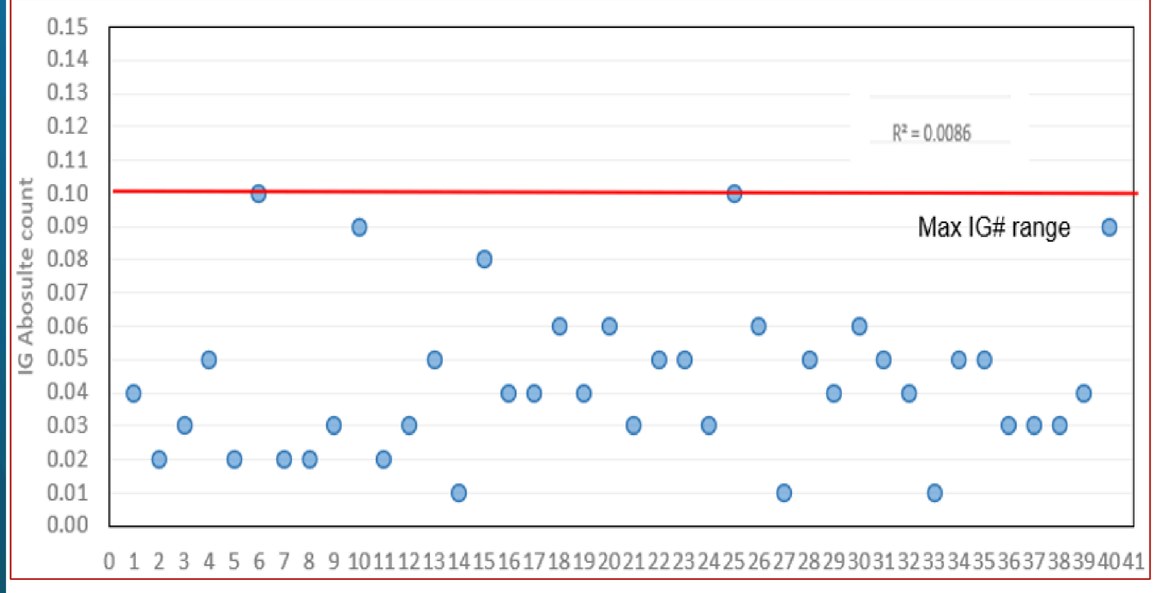
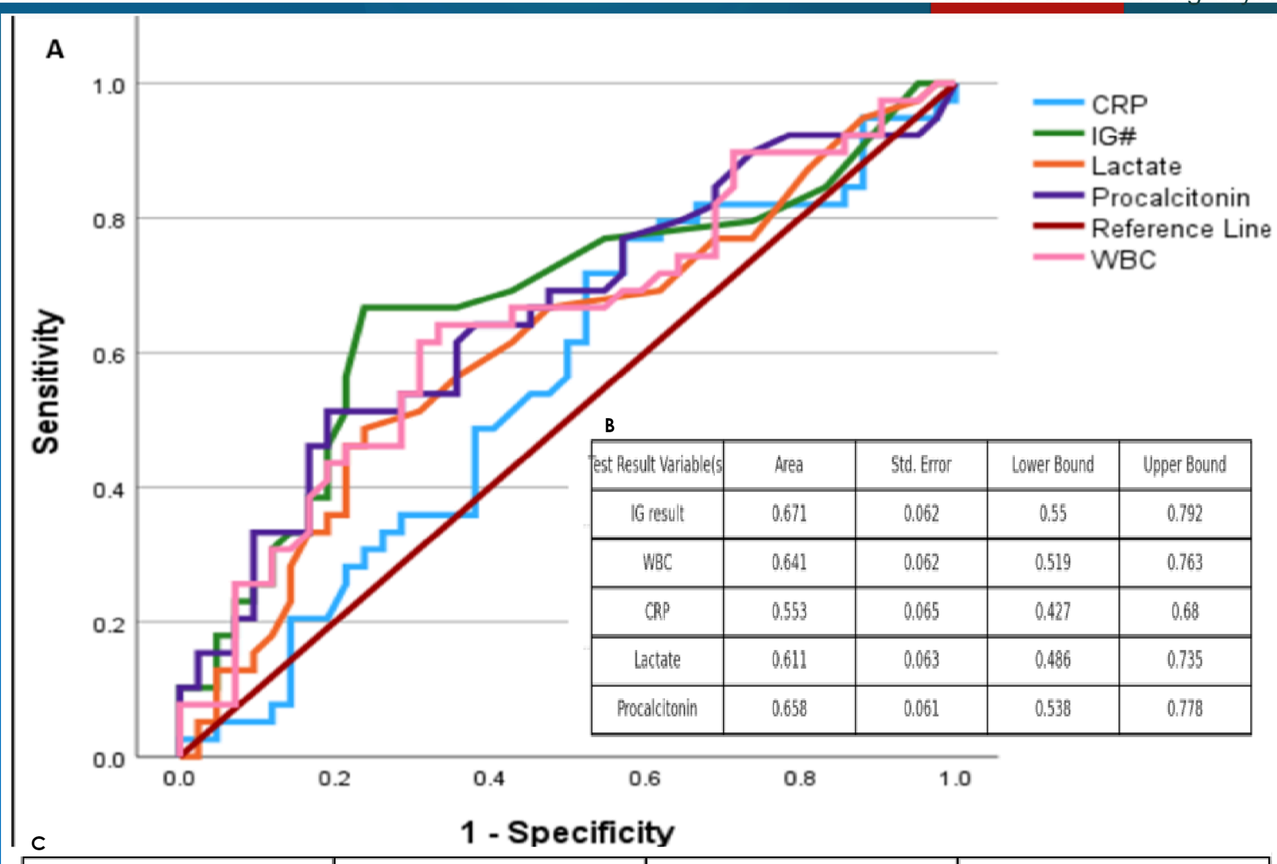


Figure 2. Patients with a negative BC and IG#. Patients with a negative BC and IG#. IG# Max (red) shows the bottom limit of detection for the analysers to produce an IG flag. 100% of results were ≤ 0.1 [10*3/µl] confirmed by negative BC. N=40 19 Females and 21 males Mean age of 77 years and range of 52 years.



B

Test Result Variable(s	Area	Std. Error	Lower Bound	Upper Bound
IG result	0.671	0.062	0.55	0.792
WBC	0.641	0.062	0.519	0.763
CRP	0.553	0.065	0.427	0.68
Lactate	0.611	0.063	0.486	0.735
Procalcitonin	0.658	0.061	0.538	0.778

C

Analyte	Sensitivity	Specificity	Youden's index
CRP	76.9%	42.9%	0.198
IG#	66.7%	76.2%	0.429
Lactate	48.7%	76.2%	0.249
Procalcitonin	51.3%	81%	0.322
WBC	64.1%	76.2%	0.308

Figure 3. ROC curves (A) and AUC (B) for all analytes. ROC and AUC were analysed to compare the ability of CRP (light blue), IG# (green), lactate (orange), procalcitonin (purple) and WBC (pink) to predict sepsis compared the gold standard BC (reference line). ROC curves are plotted and corresponding AUC values. YI was used to calculate the specificity and sensitivity values for each analyte (C). YI cut-off < 0.6. N=80, 38 Females and 42 males with a mean age 69 and a range of 92 years.

- Sensitivity & Specificity: IG# had a sensitivity of 66.7% and specificity of 76.2%, comparable to procalcitonin and superior to lactate and WBC.
- CRP Performance: CRP showed the highest sensitivity (76.9%) but the lowest specificity (42.9%).
- IG% Correlation: IG% >2% correlated strongly with positive BC results, reinforcing its potential as an early indicator of sepsis.

Discussion

- IG# demonstrated moderate sensitivity, specificity and excellent negative predictive value, making it a valuable early biomarker.
- IG measurements are readily available on automated haematology analysers but are not yet routinely reported to clinicians providing these results would come at a minimal cost.
- Results demonstrated that lactate has the lowest sensitivity.
- Integrating IG into routine sepsis screening may enhance early detection and guide clinical decisions, ultimately improving patient outcomes.

Conclusion & Recommendations

- IG# and IG% are promising early biomarkers for sepsis, measurement incurs no additional diagnostic cost and can be integrated into existing screening protocols.
- Further prospective studies are needed to refine IG cut-off values and validate their clinical utility.
- IG% percentage could be utilised when WBC counts are low in cases of neutropenic sepsis
- Despite these promising results, IG alone is not sufficiently sensitive or specific to serve as a standalone diagnostic tool for sepsis. However, integrating IG measurement into routine use, could enhance early detection, aid clinical decision-making, and reduce unnecessary antibiotic use. Sepsis requires a bio-marker panel, that includes both pro-inflammatory and anti-inflammatory. Significant work remains to identify the right combination.

Key Takeaways

- **IG# demonstrated similar performance to procalcitonin in the detection of sepsis.**
- **CRP remains a highly sensitive but non-specific biomarker.**
- **IG% >2% strongly correlates with positive BC results.**
- **Routine IG reporting could improve early sepsis diagnosis, patient management and save lives.**

1, Rudd, K. E., Johnson, S. C., Agesa, K. M., Shackelford, K. A., Tsoi, D., Kievlan, D. R., Colombara, D. V., Ikuta, K. S., Kissoon, N., Finfer, S., Fleischmann-Struzek, C., Machado, F. R., Reinhart, K. K., Rowan, K., Seymour, C. W., Watson, R. S., West, T. E., Marinho, F., Hay, S. I., Lozano, R., and Naghavi, M. (2020). Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet (London, England). 395(10219), 200–211. Available at: https://doi.org/10.1016/S0140-6736(19)32989-7. (Accessed 27 January 2025). 2, Arora, J., Mendelson, A., and Fox-Robichaud. A. (2023). Sepsis: network pathophysiology and implications for early diagnosis. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 2023 324:5, R613-R624. Available at: https://doi.org/10.1152/ajpregu.00003.2023. (Accessed 27th January 2025). 3, Martínez, M. L., Plata-Menchaca, E. P., Ruiz-Rodríguez, J. C., and Ferrer, R. (2020). An approach to antibiotic treatment in patients with sepsis. Journal of thoracic disease, 12(3), page 1007–1021. Available at: https://doi.org/10.21037/jtd.2020.01.47. (Accessed 22 February 2025). 4. Farkas, J. D. (2020). The complete blood count to diagnose septic shock. Journal of thoracic disease, 12 (Suppl 1), S16–S21. Available at: https://doi.org/10.21037/jtd.2019.12.63. (Accessed 1 March 2025). 5, Lakshmipriya, V., Kavitha, K., Yogalakshmi, E., and Shredevi, M. (2024). The clinical utility of automated Immature granulocyte measurement in the early diagnosis of bacteremia. Cureus. Available at: https://doi.org/10.7759/cureus.53660. (Accessed 23 February 2025). 7, Sysmex. (2022). XN-Series Flagging Interpretation Guide. SYSMEX CORPORATION. Software Version: 2. Available at: https://studylib.net/doc/26083889/xn-series-flagging-interpretation-guide-v2.0 (Accessed 23 February 2025).

Scan QR code for full paper

sysmex

Staffordshire UNIVERSITY