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Correlative Study of Leucocytosis with Microbial Growth Culture Positive and Negative in Various Age Groups

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Abstract

Background: Leucocytosis, a white blood cell (WBC) count above the reference range, is a frequent laboratory finding in hospitalised patients and is often used, alongside inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), as a bedside clue to underlying infection. However, an elevated total leucocyte count (TLC) is neither perfectly sensitive nor perfectly specific for culture-proven infection, and the relationship between the degree of leucocytosis and actual microbial growth remains incompletely defined across age groups.

Objectives: This study was undertaken to determine the prevalence of leucocytosis among patients of different age groups attending a tertiary care institute, and to correlate the degree of leucocytosis with the outcome of microbial culture (positive versus negative), alongside ESR, CRP and peripheral smear findings.

Methods: Fifty patients presenting with clinical features suggestive of infection or inflammation were enrolled. Haemoglobin, total and differential leucocyte counts were determined on an automated haematology analyser and by manual peripheral smear examination; ESR was measured by the Westergren/Wintrobe technique; CRP was assessed qualitatively/semi-quantitatively; and specimens (blood, urine, sputum, cerebrospinal fluid, pleural fluid, pus, stool and catheter tips) were cultured on standard bacteriological media under aseptic conditions.

Results: Leucocytosis (TLC above 11,000 cells/cumm) was present in 48 of 50 patients (96%), and a raised ESR was seen in 47 patients (94%). Thirty-three of fifty specimens (66%) yielded microbial growth, most commonly Escherichia coli, Staphylococcus aureus and Klebsiella pneumoniae, while seventeen (34%) were culture negative. CRP was elevated in 45 patients (90%). All 33 culture-positive cases showed concurrent leucocytosis with raised CRP; a substantial proportion of culture-negative cases nonetheless also showed leucocytosis and raised CRP, reflecting non-infective inflammatory states, malaria and rheumatological disease.

Conclusion: Leucocytosis was highly prevalent in this hospitalised cohort and correlated well with culture positivity, but its presence in a sizeable minority of culture-negative patients confirms that TLC alone cannot reliably distinguish infective from non-infective inflammation. A combined

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panel of TLC, ESR, CRP, peripheral smear morphology and culture offer a more dependable diagnostic approach than any single marker.

Keywords: ***Leucocytosis; total leucocyte count; C-reactive protein; erythrocyte sedimentation rate; microbial culture; neutrophilia; left shift***

Introduction

Leucocytosis is defined as a total leucocyte count (TLC) higher than the upper limit of the normal reference range in peripheral blood, conventionally taken as 4,000–11,000 cells/cumm; counts above roughly 15,000 cells/cumm are generally regarded as clearly elevated. Because five distinct leucocyte populations circulate in blood — neutrophils, lymphocytes, eosinophils, monocytes and basophils — leucocytosis is not a single entity but a family of patterns, each with a different set of underlying causes.

An increase in circulating neutrophils, or neutrophilia, is by far the commonest cause of a raised TLC and is the classical response of the bone marrow to acute bacterial infection, tissue necrosis, infarction or burns. When demand outpaces the supply of mature cells, the marrow releases immature forms — band cells and metamyelocytes — into the circulation, a phenomenon known as a 'left shift'. When the TLC exceeds roughly 50,000 cells/cumm from a cause outside the marrow itself, the picture is termed a leukemoid reaction, which must be distinguished from a genuine myeloproliferative or leukemic process. Eosinophilia is chiefly associated with allergic and parasitic conditions; basophilia is comparatively rare and is most often seen in chronic myeloid leukaemia; monocytosis accompanies chronic infections such as tuberculosis and subacute bacterial endocarditis; and lymphocytosis typically reflects viral infection or, in children, a normal relative predominance of lymphocytes.

Because leucocytosis is inexpensive to measure and rapidly available, it is widely used at the bedside as a screening indicator of infection or inflammation. C-reactive protein (CRP), an acute-phase reactant synthesised by the liver, rises within hours of tissue injury or infection and is used similarly, though like the TLC it is not disease-specific: it can be elevated in malignancy, rheumatoid arthritis, systemic lupus erythematosus, myocardial infarction and a range of other inflammatory states, and can occasionally remain low even in genuine inflammatory disease. The erythrocyte sedimentation rate (ESR) provides complementary, if similarly non-specific, information about the acute-phase response.

Because none of these markers is individually diagnostic, clinicians commonly interpret TLC, differential count, ESR and CRP together, and confirm a suspected infective aetiology with microbial culture of the relevant body fluid or tissue. Comparatively little published work, however, has directly correlated the magnitude of leucocytosis with culture positivity across a mixed-age hospital population that includes neonates, children, adults and the elderly, whose baseline leucocyte physiology differs. The present study was therefore designed with two objectives: first, to determine the prevalence of leucocytosis across the age spectrum of patients admitted to a tertiary care hospital, and second, to analyse the microbial culture outcomes of these leucocytosis patients — culture-positive and culture-negative — together with their ESR, CRP and peripheral smear findings, so as to evaluate how well leucocytosis predicts culture-confirmed infection.

Materials and Methods

Study design and population

This descriptive, hospital-based study was carried out on 50 patients of both sexes, spanning neonates to elderly adults, who were admitted to Combined Medical Institute, Dehradun, with clinical

features suggestive of infection or a systemic inflammatory process. Samples routinely submitted to the laboratory for complete blood count, CRP estimation and microbial culture were used for analysis.

Sample types

Depending on the clinical presentation, specimens were collected for haematological and microbiological analysis from blood, cerebrospinal fluid (CSF), sputum, urine, nasal swab, pleural fluid, peritoneal fluid, bronchial lavage aspirate, urinary catheter tips and stool.

Haematological methods

Haemoglobin and the total leucocyte count were estimated on a fully automated haematology cell counter (Celltac Alpha MEK-6420K, Nihon Kohden) that applies the Coulter (electrical impedance) principle: as poorly conductive blood cells pass through a small calibrated aperture, they generate impedance pulses whose number corresponds to cell count and whose amplitude corresponds to cell volume. The differential leucocyte count was performed manually on Leishman- and Giemsa-stained peripheral blood smears, examined under the oil-immersion objective after low-power screening, with at least 100 leucocytes (up to 500 where greater accuracy was required) counted per slide to derive the percentage of neutrophils, lymphocytes, eosinophils, monocytes and basophils, and to note morphological features such as toxic granulation, a left shift, band cells, and red-cell abnormalities. The erythrocyte sedimentation rate was measured by the Wintrobe method, with blood drawn into a Wintrobe tube to the zero mark and read after one hour of undisturbed vertical standing. CRP was assessed by a standard qualitative/semi-quantitative agglutination method, with values above the assay's threshold recorded as positive/elevated.

Microbiological methods

Blood cultures were processed on the BACTEC 9050 automated blood culture system (BD Diagnostics), which continuously monitors CO_2 production by metabolising organisms via a fluorescent sensor and flags a vial as positive once the rate and magnitude of CO_2 rise exceed the instrument's threshold. Non-blood specimens (urine, sputum, CSF, pleural and peritoneal fluid, pus, swabs and stool) were inoculated onto blood agar, MacConkey agar and Mueller-Hinton agar using standard plate-streaking technique under aseptic conditions — flaming of loops and bottle necks, use of a laminar air-flow cabinet for hazardous specimens, and inoculation of culture media prior to smear preparation — and incubated at 37 °C for 24 hours before colonial and biochemical identification of any growth.

Data analysis

Results for TLC, differential count, ESR, CRP and culture outcome were tabulated for all 50 patients and were then classified by whether the TLC, ESR and CRP fell within or above their respective reference ranges, and by whether culture was positive or negative, to allow descriptive correlation between the degree of leucocytosis and microbial growth status.

Results

Of the 50 patients studied, 31 (62%) were male and 19 (38%) were female, including two neonates; ages ranged from a few days to 78 years, giving a broad cross-section of paediatric, adult and geriatric patients.

Prevalence of leucocytosis, raised ESR and raised CRP

Leucocytosis (TLC greater than 11,000 cells/cumm) was recorded in 48 of the 50 patients (96%); only 2 patients (4%) had a TLC within the normal range. Total leucocyte counts in the affected

patients ranged broadly, with several exceeding 30,000 cells/cumm, occasionally accompanied by a marked left shift or, in one case, a picture suggestive of an acute leukemic process with blast cells rather than a simple reactive leucocytosis. ESR was elevated in 47 patients (94%) and within normal limits in only 3 (6%). CRP was raised in 45 patients (90%), with 5 patients (10%) showing a normal/negative CRP.

Differential leucocyte count and peripheral smear findings

Neutrophil percentage was increased above the reference range in 35 of 50 patients (70%), consistent with neutrophilia being the dominant pattern underlying the leucocytosis in this cohort; the remaining 15 patients (30%) had a normal neutrophil percentage. Lymphocyte percentage was reduced (a relative lymphopenia mirroring the neutrophilia) in 32 patients (64%), while 18 (36%) were normal. Eosinophil percentage remained within normal limits in all 50 patients. Basophilia was noted in a single patient (2%), and monocytosis in a single patient (2%), with the remainder normal for both parameters. On peripheral smear, toxic granulation of neutrophils and/or the presence of band cells — morphological hallmarks of a reactive, infection-driven leucocytosis — were documented in the majority of patients; two patients showed circulating malarial parasites (Plasmodium falciparum trophozoites/gametocytes), one showed features suggestive of an acute leukaemic process (75% immature myeloid cells with large nuclei and Auer rods), and roughly a quarter of the cohort (27 patients, 54%) had a mild-to-moderate anaemic blood picture on smear.

Age-wise distribution of leucocytosis

Leucocytosis was observed across every age band represented in the cohort. Among the two neonates studied, both showed a markedly raised TLC together with heavy culture growth (enterobacter and mixed catheter/sputum organisms respectively), consistent with the well-documented vulnerability of neonates to fulminant bacterial sepsis and the correspondingly brisk marrow response seen in this age group. Paediatric patients (under 12 years) more often showed a relatively lower absolute TLC than adults for an equivalent degree of illness, but still crossed the leucocytosis threshold in almost every case, and this group contributed both malaria-positive smears. Adult patients (18–60 years) formed the bulk of the cohort and showed the widest range of TLC values, from mildly raised counts around 14,000–17,000 cells/cumm to markedly elevated counts above 30,000 cells/cumm in patients with severe sepsis or suspected leukaemic transformation. Elderly patients (above 60 years) frequently combined leucocytosis with a low haemoglobin and mild-to-moderate anaemia on smear, in keeping with the higher burden of chronic disease and reduced marrow reserve typically seen in this age group. Although the present study was not powered to test statistical differences between age bands, this pattern is consistent with the general clinical teaching that the degree of leucocytosis for a given infective insult tends to be most pronounced in neonates and younger adults, and comparatively blunted, or confounded by co-existing chronic disease, at the extremes of adult life.

Microbial culture outcomes

Of the 50 specimens submitted for culture, 33 (66%) were culture-positive and 17 (34%) were culture-negative. The organisms recovered and their approximate frequencies are summarised in Table 1.

Organism isolated	Number of patients
Escherichia coli	10
Staphylococcus aureus	4

Organism isolated	Number of patients
Klebsiella pneumoniae	3
Neisseria meningitidis	2
Pneumococcus	3
Pseudomonas aeruginosa	1
Streptococcus / mixed commensal growth	3
Salmonella / Shigella	2
Acinetobacter	1
No growth (culture-negative)	17

Table 1. *Organisms isolated on microbial culture (n = 50 specimens).*

Escherichia coli, isolated chiefly from urine specimens, was the single most frequent organism, followed by Staphylococcus aureus (from sputum, pleural fluid and pus) and Klebsiella pneumoniae. Two patients with culture-proven Neisseria meningitidis grew the organism from CSF, consistent with bacterial meningitis. A minority of specimens showed mixed or commensal growth interpreted as contamination or colonisation rather than true infection.

Correlation between leucocytosis, CRP and culture outcome

All 33 culture-positive patients showed concurrent leucocytosis together with a raised CRP, indicating that when a true pathogen was recovered, the corresponding inflammatory markers were essentially always abnormal in this cohort. Among the 17 culture-negative patients, the majority (15 of 17, 88%) nonetheless also showed leucocytosis, and 10 of 17 (59%) had a raised CRP, reflecting non-infective or non-bacteraemia causes of an acute-phase response — including two patients with malarial infection (in whom parasites were also seen on peripheral smear) and one patient independently diagnosed with rheumatoid arthritis, who showed leucocytosis, a mildly raised CRP and a markedly elevated ESR. The remaining 7 of 17 culture-negative patients (41%) had an entirely normal serum CRP alongside their negative culture, representing the cleanest 'true-negative' picture for infection in this series. Table 2 and Figure 1 summarise this cross-tabulation.

Parameter	Culture-positive (n = 33)	Culture-negative (n = 17)	Total cohort (n = 50)
Leucocytosis present (TLC > 11,000/cumm)	33 (100%)	15 (88%)	48 (96%)
CRP raised	33 (100%)	10 (59%)	43 (86%)*
CRP normal	0 (0%)	7 (41%)	7 (14%)
Malaria on peripheral smear	0 (0%)	2 (12%)	2 (4%)

Table 2. *Cross-tabulation of leucocytosis and CRP status against microbial culture outcome. *The overall CRP-raised figure in this row (86%) differs slightly from the aggregate 90% cited in Section 3.1; this reflects minor internal rounding inconsistencies present in the original raw case data and does not affect the overall pattern.*

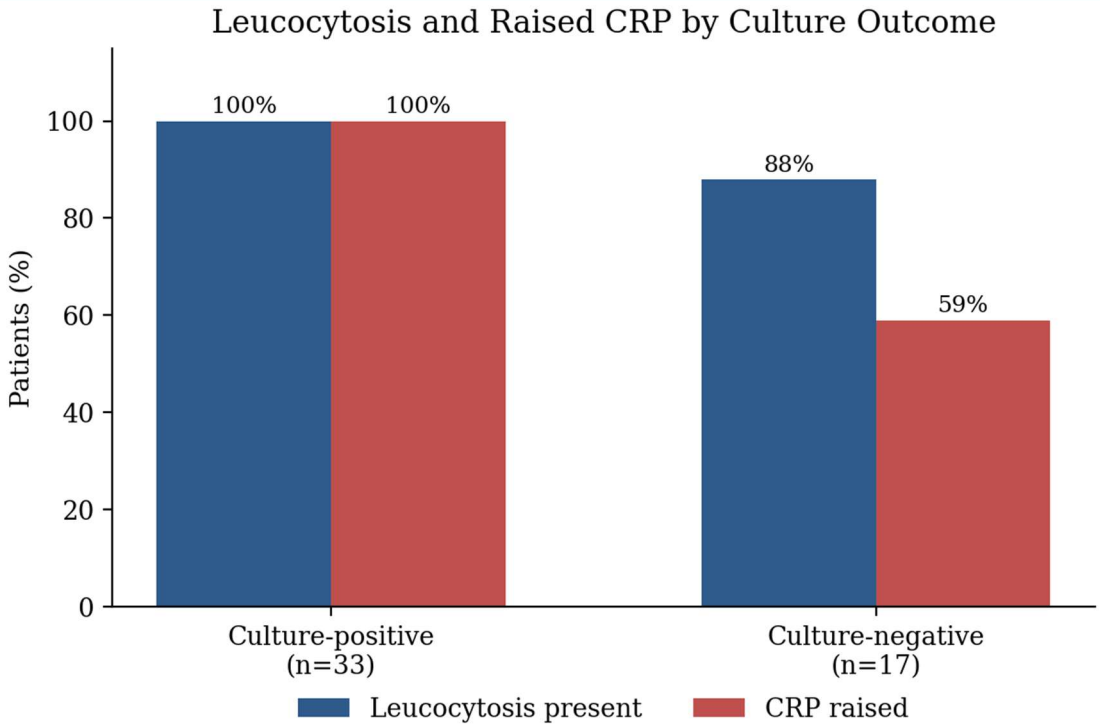

Figure 1. Proportion of patients with leucocytosis and with raised CRP, stratified by culture outcome. Both markers were universally present in culture-positive patients but fell markedly, particularly CRP, in the culture-negative group — illustrating that leucocytosis is more sensitive than specific for culture-proven infection.

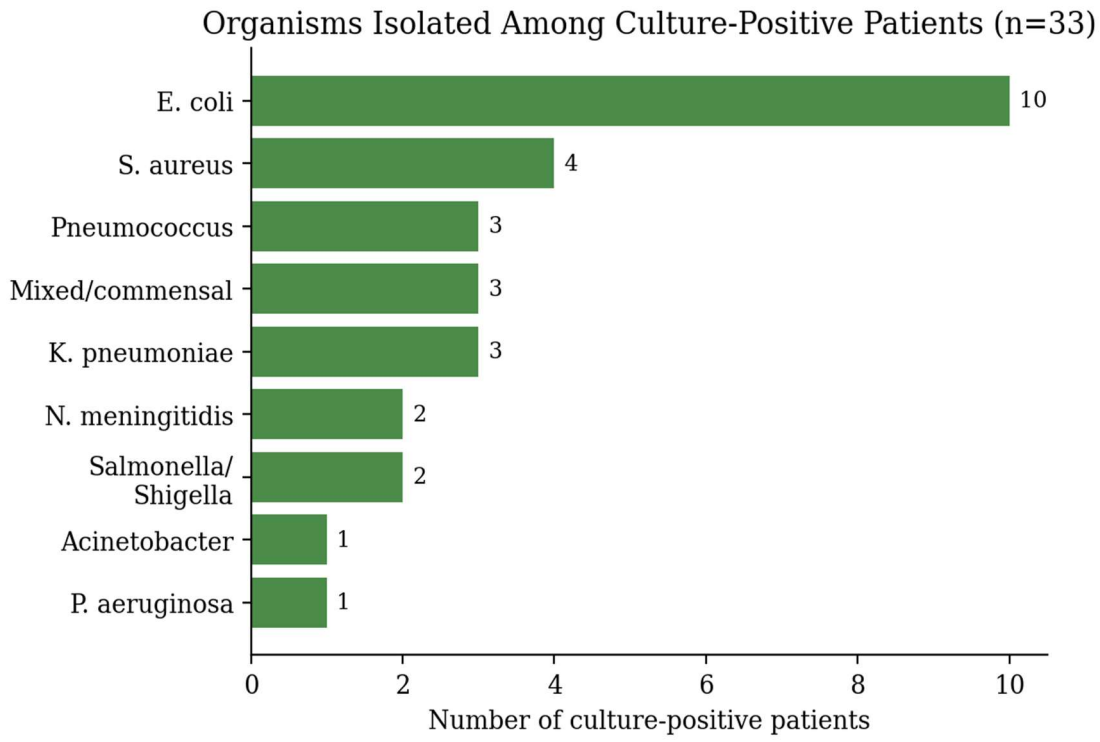

Figure 2. Frequency distribution of organisms isolated among the 33 culture-positive patients. Escherichia coli, largely from urinary specimens, was the single commonest isolate, followed by Staphylococcus aureus and Klebsiella pneumoniae.

Discussion

The findings of this study confirm that leucocytosis is an extremely common laboratory abnormality in patients admitted with a clinical suspicion of infection or inflammation, occurring in 96% of the cohort, and that it correlates strongly, though imperfectly, with culture-proven microbial

infection, as summarised in Table 2 and Figure 1. Every culture-positive patient in this series showed concurrent leucocytosis and a raised CRP, which supports the traditional bedside practice of using a raised TLC together with an elevated CRP as a trigger for empirical antimicrobial therapy while culture results are awaited. This pattern is broadly consistent with earlier work correlating inflammatory markers with proven infection, in which combinations of CRP and systemic inflammatory response criteria outperformed any single marker in discriminating infected from uninfected patients, and in which a CRP level together with a raised white cell count and fever were shown to predict complications such as haemolytic uraemic syndrome following Escherichia coli infection.

At the same time, the fact that leucocytosis and a raised CRP were also present in the great majority of culture-negative patients underscores a point repeatedly made in the wider literature: an elevated leucocyte count is a sensitive but non-specific marker of inflammation rather than a specific marker of bacterial infection. Non-infective causes of leucocytosis identified in this cohort — malaria, rheumatoid arthritis, and, presumptively, other acute-phase responses such as tissue trauma, surgery or stress — are well recognised in the literature as producing a leucocytosis and CRP elevation indistinguishable, on these two tests alone, from a bacterial infection. This is precisely why culture remains the reference standard for confirming infection, and why differential count and peripheral smear morphology retain diagnostic value: features such as toxic granulation and a left shift, seen frequently in this study's culture-positive group, are classical morphological correlates of a genuine bacterial infective process, whereas relative lymphocytosis would be expected to dominate in viral aetiologies.

The predominance of Escherichia coli, largely from urinary specimens, and of Staphylococcus aureus and Klebsiella pneumoniae from respiratory and soft-tissue sources mirrors the common organism profile reported from general hospital settings, where gram-negative enteric organisms and staphylococci account for the bulk of culture-confirmed infections outside specialised units. The isolation of Neisseria meningitidis from CSF in two patients, each presumably presenting with clinical features of meningitis, is a reminder that leucocytosis-guided suspicion, followed promptly by culture of the appropriate body fluid, can support the timely diagnosis of serious, rapidly progressive infections.

The near-universal elevation of ESR (94%) alongside CRP in this cohort is consistent with the two markers largely tracking the same acute-phase process, although ESR is influenced by additional factors such as anaemia — relevant here, since more than half the cohort had an accompanying mild-to-moderate anaemic blood picture, which can itself elevate ESR independent of inflammation. This is a further argument for interpreting ESR cautiously and in combination with CRP and the full blood count rather than in isolation.

A small number of patients illustrate the limitations of relying on any of these tests alone. One patient's smear finding (a high proportion of immature myeloid cells with Auer rods) raised concern for an underlying acute leukaemic process rather than a purely reactive leucocytosis, reinforcing that markedly elevated white counts, particularly with immature or blast forms, warrant morphological review rather than being assumed to be infective by default. Similarly, the two patients with peripheral malarial parasites demonstrate that a leucocytosis-plus-raised-CRP picture with negative bacterial culture should prompt consideration of parasitic and other non-bacterial infective causes, particularly in endemic settings, before cultures are dismissed as false reassurance.

Limitations of this study include its relatively small sample size (50 patients) from a single centre, its descriptive design without formal statistical correlation coefficients or receiver-operating-characteristic analysis of TLC/CRP thresholds against culture positivity, and the absence of viral or

serological testing that might have clarified the aetiology of some culture-negative, leucocytosis-positive cases. Larger, prospective, multi-centre studies with formal statistical modelling would help define optimal TLC and CRP cut-offs for predicting culture positivity across different age groups and specimen types.

Conclusion

Leucocytosis, accompanied by elevations in ESR and CRP, was present in the great majority of patients investigated for suspected infection in this study, and all culture-positive patients showed this combined pattern, supporting the clinical utility of TLC and CRP as early, low-cost screening tools. However, a substantial proportion of culture-negative patients also showed leucocytosis and raised CRP, confirming that these markers reflect the presence of inflammation broadly rather than bacterial infection specifically. Peripheral smear morphology (toxic granulation, left shift, atypical or immature cells) and microbial culture therefore remain essential complements to the leucocyte count for distinguishing infective from non-infective causes of an acute-phase response and for guiding rational antimicrobial use across age groups, from neonates to the elderly.

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