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DIAGNOSTIC EFFICACY OF HAEMATOLOGICAL MARKERS AND C-REACTIVE PROTEIN VALUE IN SUSPECTED PATIENTS OF SEPSIS

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Abstract:

Objective:*This study hopes to gauge the separate and combined diagnostic specificity and sensitivity of the different diagnostic modalities, in an attempt to draft a guideline for sepsis diagnosis.*

Methodology:*The cross-sectional analysis was conducted at the department of medicine, Liaquat university hospital, upon a total of 200 patients (100 with clinical features of sepsis and another 100 normal asymptomatic individuals) from January 2017 to July 2017. C.R.P (C - Reactive Protein), A.N.C (Absolute Neutrophil Count) and G.A.C (Gastric Aspirate Cytology) for platelets and polymorphs were used for sepsis diagnosis.*

Results:*CRP was positive in 86% of group-A (proven sepsis) and 81% of group-B (suspected sepsis) and consequently, the specificity was 95%. ANC test, was the runner-up with regards to sensitivity (Group A = 71% and Group-B = 64%). The resultant specificity was thus 88%. The sensitivity of GAC in group A for platelet count and polymorphs was 64% and 71%respectively.*

Conclusion:*All the aforementioned set of clinical investigations have proved largely sensitive on an individual basis and should be used for detection of culture negative cases of sepsis. Furthermore, when used in conjunction with other tests, the individual specificity and sensitivity of all the tests is heightened.*

Keywords: *Sepsis, Specificity, Diagnostic value, Screening, c - reactive protein, hematological markers, gastric aspirate cytology, absolute neutrophil count.*

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INTRODUCTION:

Sepsis is a grave disease with ironically subtle signs and symptoms which are unfortunately vague and un-specific. The tricky diagnosis and consequently delayed onset of treatment leads to a great many deaths and substantial suffering. Annually five million patients die battling infections, mostly in the developing world, twenty percent of whom are caused by sepsis. The occurrence of sepsis in the western world is 1-10/1000 whereas it is three times more in Pakistan [1] .

A clear diagnosis, whose basis lie on blood culture, analysis of CSF and analysis of urine is reached upon no sooner than two days. Thus, it is often recommended to initiate the process of administering antibiotics to patients with clinical signs of sepsis before the results of diagnostic investigations arrive. Antibiotic administration, prior to test result disclosure is also done in patients that match epidemiological correlates [2]. Attempts have been made repeatedly, to devise screening tests that may help identify individuals that are infected as early as possible[3].

Blood concentrations of many reactants (acute phase) hike in response to infection which may prove useful for the timely diagnosis of sepsis (of bacterial origin) including C-reactive protein (CRP), multiple leucocyte activation markers, IL 8, IL 6, TNF - alpha and pro-calcitonin in the diagnosis of sepsis [4-7]. Till date, no solid consensus has been reached at an international stage regarding screening of sepsis. CRP is a protein that hikes as a result of the inflammation. Sufficient proof validates the measurement of CRP values along with additional diagnostic tools, such as a total and differential leukocyte count (TLC and DLC) and blood culture to establish or exclude the diagnosis of sepsis [4]. Despite their limitations in sensitivity and specificity variations in TLC and DLC, an I/T ratio of 0.2 or greater suggests bacterial infection.

This study hopes to gauge the separate and combined diagnostic specificity and sensitivity of the different diagnostic modalities, in an attempt to draft a guideline for sepsis diagnosis.

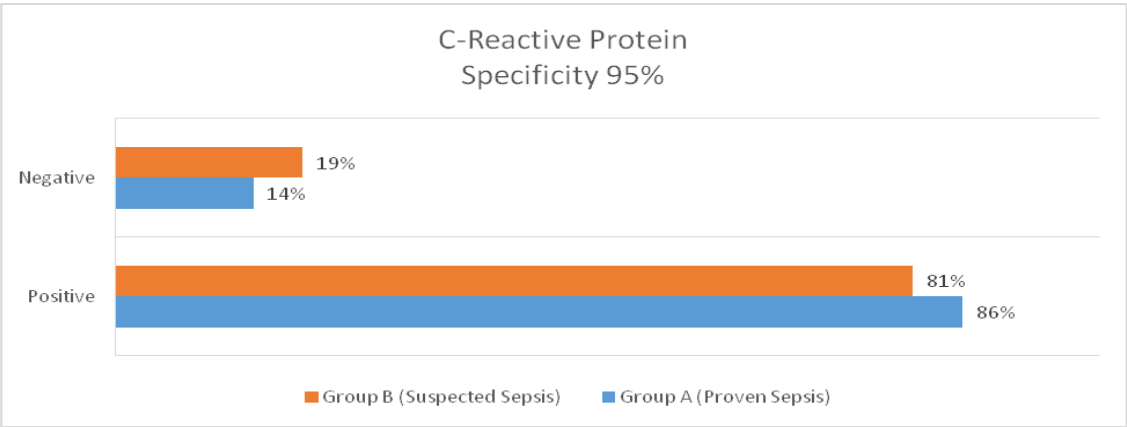
METHODOLOGY:

The cross-sectional analysis was conducted at the department of medicine, Liaquat university hospital, upon a total of 200 patients (100 with clinical features of sepsis and another 100 normal asymptomatic individuals) from January 2017 to July 2017. C.R.P (C - reactive protein), A.N.C (Absolute Neutrophil Count) and G.A.C (Gastric Aspirate Cytology) for platelets and polymorphs were used for sepsis diagnosis.

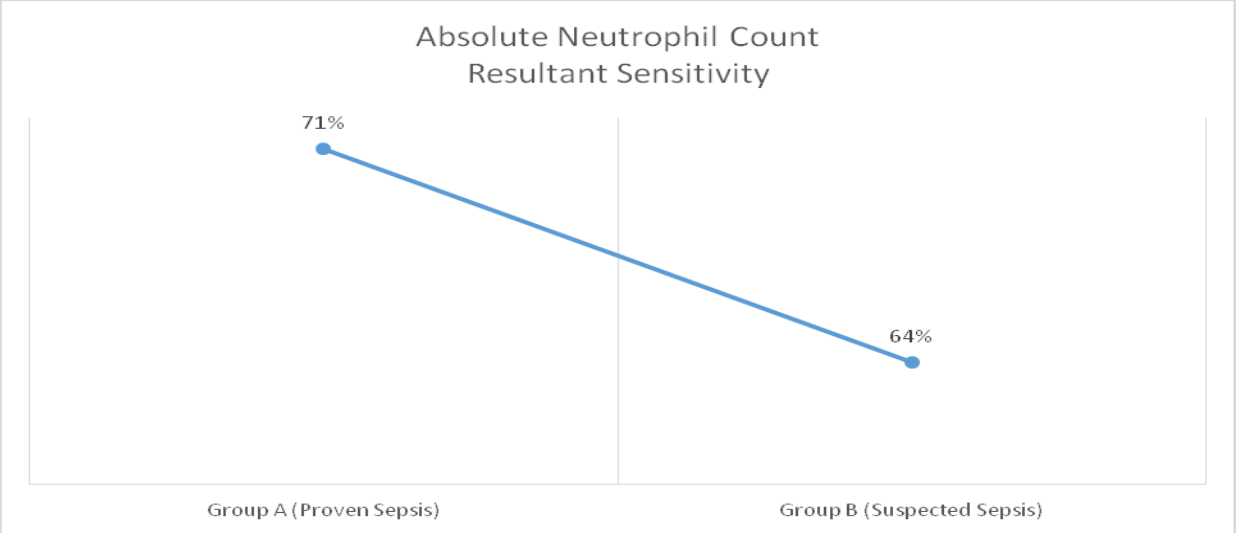
All patients were made to undergo a complete physical examination after a detailed history had been obtained and subject inclusion had been ascertained on set criteria. All relevant investigations (hematological, microbiological and radiological) to explore all possible sources of infection. Cerebrospinal fluid routine examination and culture was performed in selected cases, who had symptoms suggestive of meningitis. Every patient was administered intravenous antibiotics; generally a combination of an aminoglycoside (amikacin) and a 3rd generation cephalosporin (cefotaxime). Positive blood culture was taken as the gold standard for the diagnosis of sepsis and was performed on all 100 cases having clinical diagnosis of sepsis, whereas, the sepsis screening tests were performed on all 200 subjects including both sick and healthy individuals.

RESULTS:

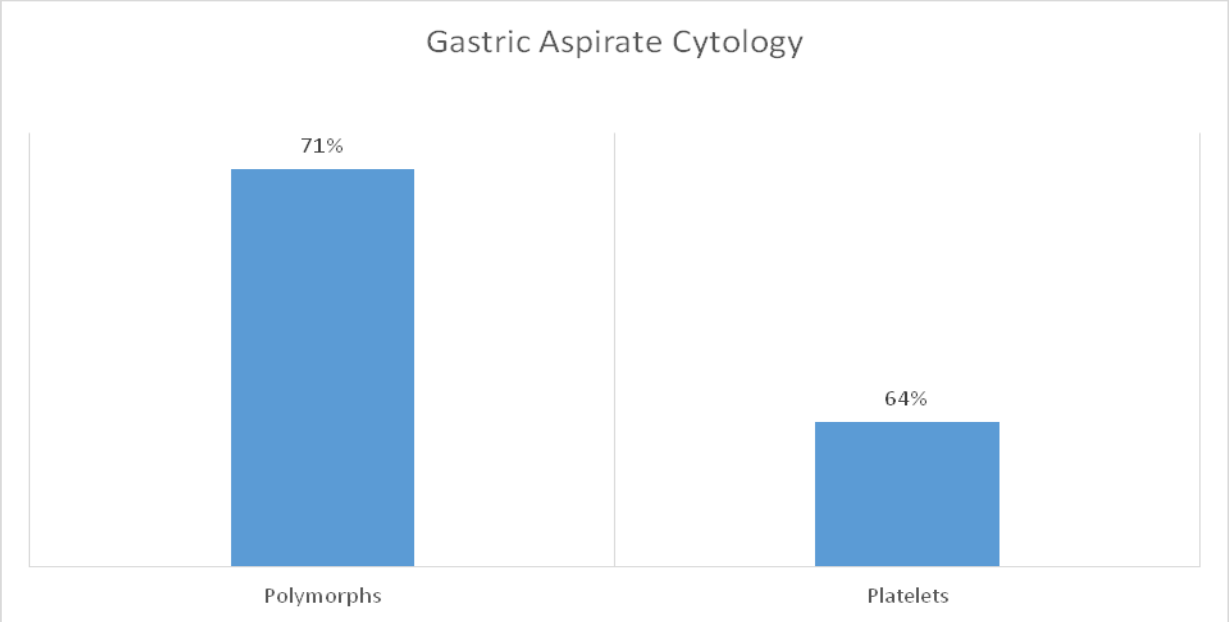
CRP was positive in 86% of group-A (proven sepsis) and 81% of group-B (suspected sepsis) and consequently, the specificity was 95%.



ANC test, was the runner-up with regards to sensitivity (Group A = 71% and Group-B = 64%).



The resultant specificity was thus 88%. The sensitivity of GAC in group A for platelet count and polymorphs was 64% and 71%, respectively.



DISCUSSION:

The present series has revalidated the utility of acute sepsis markers. An ideal screening test should have high sensitivity i.e. it should screen all infected cases. Another feature that makes the screening test more ideal, is a high negative predictive value that ensures easy exclusion of disease. [8] The loss in specificity is acceptable as the risks of over treatment with antibiotics are much less than the risks of missing a patient with a potentially life threatening condition. [9] Although essential for diagnosis and appropriate management, the results of blood culture are not obtained fast enough and their yield is low. In our study, 28% subjects tested positive for sepsis. Similarly, Arshad et al. [10] has reported that 25% cases of sepsis had positive blood cultures. However, Aurangzeb et al. [1] has reported 55.8% and Anwar et al. [11] have documented 42% blood culture positive cases of sepis.

C-reactive protein has the highest sensitivity, specificity and high negative and positive predictive values. High serum level of CRP is found in fifty to

ninety percent of patients suffering from sepsis. [11] CRP estimation has now an established value as a marker of sepsis and many workers have concurred upon its utility in diagnosis and monitoring of treatment of sepsis. [12-14]

Similarly Santana et al. [15] reported 80% sensitivity and 92% specificity for CRP whereas Australian studies have documented 67% sensitivity and 86% NPV of CRP in diagnosis of sepsis. [16, 17] Shabbir et al. [18] found that CRP had 74% sensitivity and 76% NPV. The discrepancy in the sensitivity of CRP in the works of various researchers may be because of variations in diagnostic criteria and varied CRP estimation protocols (latex agglutination method or quantitative radio-immunodiffusion technique).

Hematological findings including abnormal TLC, ANC, I/T ratio and pronounced neutrophil degeneration have been studied as screening tests for sepsis. [8, 11, 19] The present study documented a high specificity for TLC (92%), ANC (88%) and I/T ratio (91%). However, the sensitivity of these parameters was low in both group-A and B. TLC had low sensitivity 39.3% and 27.8% for group-A and B. Elevation in I/T ratio also had low sensitivity 25% and 20.8% for group-A and B respectively.

In the present study, nevertheless, ANC had the 2nd highest sensitivity yield in detection of sepsis. Its sensitivity was 71.4% in group-A and 63.9% in group-B. Anwer et al. [11] has reported almost comparable findings for these three parameters. He documented a high specificity for TLC (93.1%), I/T ratio (65.5%) and ANC (51.7%). The study also documented a low sensitivity 14.3% for TLC and 30.9% for I/T ratio. Similar to the present study the specificity of ANC was also good (61.9%). Contrary to this, a study from Switzerland reported good sensitivity and specificity of leukopenia (67% and 90%), neutropenia (78% and 80%) and I/T ratio (78% and 73%) and considers them good diagnostic parameters. [20] Likewise, Misra et al.found that I/T ratio > 0.2 was most sensitive index (92%) for sepsis. [21]

The tests combinations had much higher sensitivity and NPV than as individual tests. Similar enhancement in sensitivity of two or more tests combinations for detection of sepsis has been reported by other workers. [22-29]

CONCLUSION:

All the aforementioned tests and the C-reactive protein investigation are good screening tests for a neonate having a clinical diagnosis of sepsis. These tests are readily available, inexpensive, reliable and highly sensitive in detection of sepsis. Furthermore, when used in conjunction with other tests, the individual specificity, sensitivity and negative predictive value of all the tests is heightened to almost a 100 percent.

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