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EVALUATION OF C-RP LEVELS AS PROGNOSTIC INDICATORS OF OPPORTUNISTIC INFECTIONS IN AIDS PATIENTS & CORRELATION WITH CD4 COUNTS – A STUDY

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ABSTRACT

Determination of CD-4 counts being cost effective, Aimed at evaluating the role and utility of CRP as a diagnostic and prognostic indicator of opportunistic infection.The blood samples were collected from 50 patients, clinically diagnosed to be in stage 4 HIV disease for the estimation of CD4 counts and C - reactive protein levels at Microbiology lab. Cd4 counts was done by flow cytometry using BD FACS caliber. C-RP test carried out by semi qualitative slide latex agglutination test. Clinical conditions, C-RP levels and cd4 counts are correlated.The CD-4 count and the C-RP levels are tabulated. Patient with fever and T.B. have the CD-4 levels of50-128/ml and those with Candidiasis has 72-290, Diarrhoea 100-464, Genital infections has 40-140/ml .Patient with fever and T.B. have the C-RP level of 96 µ gm/ml and those with Candidiasis has 48, Diarrhoea 48, Genital infections24 µ gm/ml of CRP.The proposed study reveals that C-RP level serves as a good prognostic serological indicator in HIV or AIDS disease (stage 4 retro viral diseases). The test is cost effective, easily available, does not need elaborate equipment and technical skill. It may not replace the CD-4 count in diagnosis as a whole, but ads up more information on the state of the patient.

KEYWORDS: *C-reactive protein (C-RP), fluorescent isothiocyanate (FITC), phycoerythrin (PE).*

BACKGROUND

Acquired Immunodeficiency Syndrome a condition diagnosed when there are group of related symptoms that produce severe HIV infection caused by a retro virus[1, 2, 3].

Once HIV enters the body, it attaches itself to a white blood cell called CD_4 (T4 cell) and these cells are destroyed due to replication of virus[4]. As a result immune system is affected and CD_4 count is decreased giving rise to opportunistic infections, which result in acute inflammation and release C-reactive proteins [5,6]. C-reactive protein (C-RP) is an acute phase reactant found in concentrations up to 6 micro grams /ml in the serum of healthy persons. However, during an inflammatory response or infection, the levels of C-RP may increase by as much as 1000 fold. This increase in C-RP level may be detected as early as 5-10 hrs after tissue damage. The increase of C-RP levels in serum appears to be a non specific phenomenon but the change can be used to monitor the course of certain diseases and their treatment [7,8,9].The increased levels of C-RP are seen in cases of acute myocardial infection [10,11,12], rheumatoid arthritis [7,8] bacterial [7,8,13,14,15] and viral infections, acute

rheumatic fever with or without carditis and in several types of malignancies particularly those with metastasis. As HIV infection leads too many opportunistic infections, inflammation occurs generally which leads to increase in C-RP level and decrease in CD4 count. As CD4 count is not most cost effective, the study of C-RP in relation to opportunistic infections is aimed to evaluate the role of C-RP as a diagnostic and prognostic indicator of opportunistic infection.

METHOD

Institutional Ethics Committee clearance has been taken.

In this study blood samples were collected from 50 patients, clinically diagnosed to be in stage 4 HIV disease for the estimation of CD4 counts and C - reactive protein levels at Microbiology lab, Osmania General Hospital, Hyderabad for a period of 2 months.

- Cd4 counts was done by flow cytometry using BD FACS caliber.
- C-RP test carried out by semi qualitative slide latex agglutination test.

Clinical conditions, C-RP levels and cd4 counts are correlated.

CD4 TEST

INTRODUCTION

A CD4 count and a viral load test are ordered when a person is first diagnosed with HIV as part of a baseline measurement. Both tests should be repeated about two to eight weeks after starting or changing anti-HIV therapy. If treatment is maintained, CD4 count should be performed every three to six months thereafter. Normal CD4 counts in adults range from 500 to 1,500 cells per cubic millimetre of blood. Generally the CD4 count goes down as HIV disease progresses. Any single CD4 count value may differ from the last one even though the person's health status has not changed.If CD4 count declines over several months, the doctor may recommend beginning or changing anti-HIV treatment and/or starting preventive treatment for opportunistic infections like Pneumocystis carinii pneumonia (PCP) [16]. The CD4 count should increase or stabilize in response to effective combination anti-HIV therapy. According to public health guidelines, preventive therapy should be started when an HIV-positive person who has no symptoms registers a CD4 count under 200. Some physicians will opt to consider treatment earlier, at 350. The Centers for Disease Control and Prevention considers HIV-infected persons who have CD4 counts below 200 to have AIDS, regardless of whether they are sick or well.The CD4 count tends to be lower in the morning and higher in the evening. Acute illnesses, such as pneumonia, influenza, or herpes simplex virus infection, can cause the CD4 count to decline temporarily. Cancer chemotherapy can dramatically lower the CD4 count. Regardless, it can be used as an effective monitoring tool if the more sensitive HIV viral load test is not available. The CD4 count does not always reflect how someone with HIV disease feels and functions. For example, some people with higher counts are ill and have frequent complications, and some people with lower CD4 counts have few medical complications and function well.

C-RP TEST

This test is performed in acute inflammation of the body. It is also used to monitor wound healing and to monitor patients who have surgical cuts, organ transplantations, burns as an early detection system for possible infections.

C-RP level is usually less than 6ug/ml. in most infections and in inflammations the C-RP levels are 10ug/ml. This test is performed by latex slide and tube test by Beacon Company.

RESULTS

The CD-4 count and the C-RP levels of 50 samples are tabulated as below:-

Symptom	CD4 count	C-RP level (µ gm.)
1.Diarrhoea,candidiasis	146	48
2. Candidiasis	156	48
3. Candidiasis	72	12
4. Genital infection	140	12
5. Fever and T.B.	57	24
6. Candidiasis	290	12
7. Candidiasis	140	12
8. Diarrhoea	246	48
9. Diarrhoea	108	12
10. Candidiasis	143	12

11. Candidiasis	226	12
12. Candidiasis	187	12
13. T.B.	127	96
14. Diarrhoea	255	12
15. Diarrhoea	464	12
16. Diarrhoea	237	12
17. Candidiasis	145	12
18. Diarrhoea	118	12
19. Genital infection	44	24
20. Candidiasis	111	24
21. Diarrhoea	118	12
22. Diarrhoea	237	12
23. Diarrhoea	187	12
24. Genital infection	97	24
25. T.B.	128	12
26. Diarrhoea	212	48
27. Candidiasis	130	48
28. Candidiasis	150	24
29. Candidiasis	250	12
30. Candidiasis	200	24
31. Genital infection	130	12
32. Genital infection	40	24
33. Candidiasis	140	12
34. Candidiasis	230	24
35. Candidiasis	180	12
36. Genital infection	50	12
37. Diarrhoea	240	48
38. Diarrhoea	100	24
39. Diarrhoea	250	12
40. Diarrhoea	460	12
41. Genital infection	90	24
42. Genital infection	100	24
43. Diarrhoea	230	12
44. Fever and T.B.	50	24
45. Fever and T.B.	120	96
46. Fever and T.B.	122	24

47. Diarrhoea	115	12
48. Diarrhoea	110	12
49. Diarrhoea	235	24
50. Fever and T.B.	60	24

Symptom	No. of patients	CD4 (per ml)	C-RP (µ gm/ml)
Fever and T.B.	7	50-128	96
Candidiasis	17	72-290	48
Diarrhoea	18	100-464	48
Genital infection	8	40-140	24

DISCUSSION

CRP in addition to fibrinogen, serum amyloid A (SAA) are the acute phase proteins released during inflammatory response. Synthesis of these proteins by hepatocytes is regulated by cytokines especially interleukin-6 (for CRP and fibrinogen) and interleukin -1 or TNF (for SAA). *Role of C-RP:*C-RP during inflammatory response binds to microbial cell walls and acts as opsonin and fix complement.They also bind to chromatin, possibly aiding in the clearing of necrotic cell nuclei.That means C-RP helps to defend the infectious organisms i.e., more the C-RP more is the defense to the infection.A low C-RP with major infection indicates a fail in the defense mechanism. *"In AIDS, opportunistic an infection develops by which the C-RP level changes. The present study is on how this change can be related to the diagnosis of HIV."*

The following conclusions can be made from the results:-

Out of 50 patients

Patient with fever and T.B. have the C-RP level of 96 µ gm/ml. Those with Candidiasis, Diarrhoea, Genital infections have lesser levels of C-RP that means as the infection worsened even C-RP levels are lowered i.e., defence mechanism is failing. Hence any level of C-RP, either low or high will give us a broad view about the stage of an HIV patient.

NOURSADEGHIM, MILLER RF of PATRICK MANSON unit, University College London Hospitals Trust, London, U.K. [17] had measured C-RP in 109 HIV- 1 antibody positive patients. In 67 patients with intercurrent infection C-RP levels were 2.2 - 483.5µ gm./ml. and in 42 patients with alternative non-infection, diagnosed C-RP levels were 0.5 to 108.6 µgm./ml. whereas in those with infections the elevated C-RP levels were in response to specific therapy & the values remained abnormal in those with non-infection diagnosis. They concluded "The C-RP appears useful for diagnosis and monitoring of intercurrent infection in HIV-1 antibody positive patients.

CONCLUSION

The proposed study reveals that C-RP level serves as a good prognostic serological indicator in HIV or AIDS disease (stage 4 retro viral diseases). The test is cost effective, easily available, does not need elaborate equipment and technical skill. It may not replace the CD-4 count in diagnosis as a whole, but ads up more information on the state of the patient. The proposed study can be further extended by taking serum amyloid A, an acute phase protein into consideration and studying its role in diagnosis of HIV disease. The two tests i.e. C-RP & serum amyloid A estimation may altogether eliminate the need for CD4 counts.

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