Original Article

C - reactive protein as an Indicator of Bacterial Infection- A Prospective Institutional Based Survey

Gurveer Singh Raien

M.B.B.S. DMCH Ludhiana, Punjab, India

ABSTRACT:
Background: Majority of subjects reporting to the primary Healthcare suffer from self-limiting infectious diseases. Few of the infections amongst them progress to the development of serious infections that need an antibiotic coverage or hospital admission.The common test for diagnosis isestimation of Salmonella typhi in blood cultures but they are time-consuming, affected by antibiotic treatment and can provide clueless results for various days. The aim of the present study was to evaluate the levels of CRP amongst enteric fever subjects. **Materials and Methods:** The patients were divided into three categories. In group I, patients with positive blood culture for S. typhi were included, in group II subjects with negative blood culture for S. typhi but showing clinical features of enteric fever were included. Group III included patients with symptoms of infection but not necessarily enteric fever. Blood samples were obtained from the subjects and freshly separated serum was used for the estimation of the level of C-reactive protein. All the data thus obtained was arranged in a tabulated form and analyzed using SPSS software. **Results:** The mean age of group I subjects was 18.3+/- 2.3 years, group II subjects had mean age of 19.1+/- 1.6 and mean age of group III subjects was 16.9+/- 2.7 years. There was a significant difference between the groups. The mean duration of fever was 4.5-13.2 days in group I, 6.2-15.5 days in group II and 2.5-9.7 days. **Conclusion:** From the present study, we can conclude that CRP is elevated amongst subjects with bacterial infection and it can be used to differentiate subjects with bacterial and viral infections.
Key Words: Enteric, Salmonella, serological, widal.

Corresponding author: Dr. Suni Gurveer Singh Raien, M.B.B.S. DMCH Ludhiana, Punjab, India

INTRODUCTION
Majority of subjects reporting to the primary Healthcare suffer from self-limiting infectious diseases. Few of the infections amongst them progress to the development of serious infections that need an antibiotic coverage or hospital admission.[1,2] Alarming signs are frequently seen amongst febrile subjects, and few of them are very common and are difficult to differentiate between subjects at high or low risk of serious infections. Therefore, they are responsible for large burden to the society and heath care service providers. Simple laboratory investigationswith good discriminative skillscan help the triage at the level of general practitioner more effective and prevent redundantantibiotic prescriptions.[3] C-reactive protein is an acute-phase protein that is increased in blood during infections.[4]An increased level of CRP concentration has useful value in pneumonia amongst elderly and children presenting to primary carehospitals[5–7] and also has a significant role amongst febrile children staying at emergency department.[5,6]Enteric fever is endemic amongst different developing nations. The common test for diagnosis isestimation of Salmonella typhiin blood cultures but they are time-consuming, affected by antibiotic treatment andcan provide clueless results for various days. Thediagnosis of enteric fever is dependenton the clinical presentation and laboratory investigations likeWidal test, and Typhidotserological tests.[8,9] Even with good specificity and sensitivity of these tests, the results of serologicalare notimmediately available and they are difficult to interpret inthe borderline cases, especially in theprone area. Estimation of serum C-reactive protein is robust, widely available and inexpensive. The aim of the present study was to evaluate the levels of CRP amongst enteric fever subjects.

MATERIALS AND METHODS
The study was performed in the medicine department for a period of one year. The study was approved by the institutional ethical board and all the subjects were informed about the study and a written consent was obtained from

them in their vernacular language. The patients were divided into three categories. In group I, patients with positive blood culture for S. typhi were included, in group II subjects with negative blood culture for S. typhi but showing clinical features of enteric fever were included. Group III included patients with symptoms of infection but not necessarily enteric fever. A complete and detailed history of all the subjects weretaken along with detailed physical examination and serological testing. Patient's blood and stool samples were examined for S. typhi. Every patient was ensured to be appropriately rehydrated either by using intravenous or oral fluids depending on their physical condition. First line of therapy advised to the subjects was that of chloramphenicol. Blood samples were obtained from the subjects and freshly separated serum was used for the estimation of the level of C-reactive protein. Fluorescence polarization immunoassay was used as a method of estimation of CRP. All the subjects were made aware about good hygienic practices and regular usage of antimicrobial medicaments. All the data thus obtained was arranged in a tabulated form and analyzed using SPSS software. Student t test was used for statistical analysis. Probability value of less than 0.05 was regarded as significant.

RESULTS

The study was divided into three groups. Group I included 50 subjects, Group II had 30 and Group III had 30 subjects. The mean age of group I subjects was 18.3+/- 2.3 years, group II subjects had mean age of 19.1+/- 1.6 and mean age of group III subjects was 16.9+/- 2.7 years. There was a significant difference in the age group between the groups. The range of CRP in group I, group II and group III were 14-181 mg/dl, 10-91 mg/dl and 8-99 mg/dl respectively. There was a significant difference between the groups. The mean duration of fever was 4.5-13.2 days in group I, 6.2-15.5 days in group II and 2.5-9.7 days. There was a significant difference in the duration of fever between the groups. The rate of widal O+ in group I, group II and group III were 92%(n=46), 83.3%(n=25) and 20%(n=6). The rate of widal H+ in group I, group II and group III were 88%(n=44), 73.3%(n=22) and 16.7%(n=5). (table 1, graph 1)

Table 1: Baseline characteristics of children

Variable	Group I	Group II	Group III	P value
Number	50	30	30	
Age	18.3+/- 2.3	19.1+/- 1.6	16.9+/- 2.7	<0.05
M (%)	50%(n=25)	60%(n=18)	50%(n=15)	
Serum CRP (mg/dl)	14-181	10-91	8-99	<0.05
Duration of fever	4.5-13.2	6.2-15.5	2.5-9.7	<0.05
Widal O+	92%(n=46)	83.3%(n=25)	20%(n=6)	
Widal H+	88%(n=44)	73.3%(n=22)	16.7%(n=5)	

Graph 1: Mean level of CRP amongst various groups
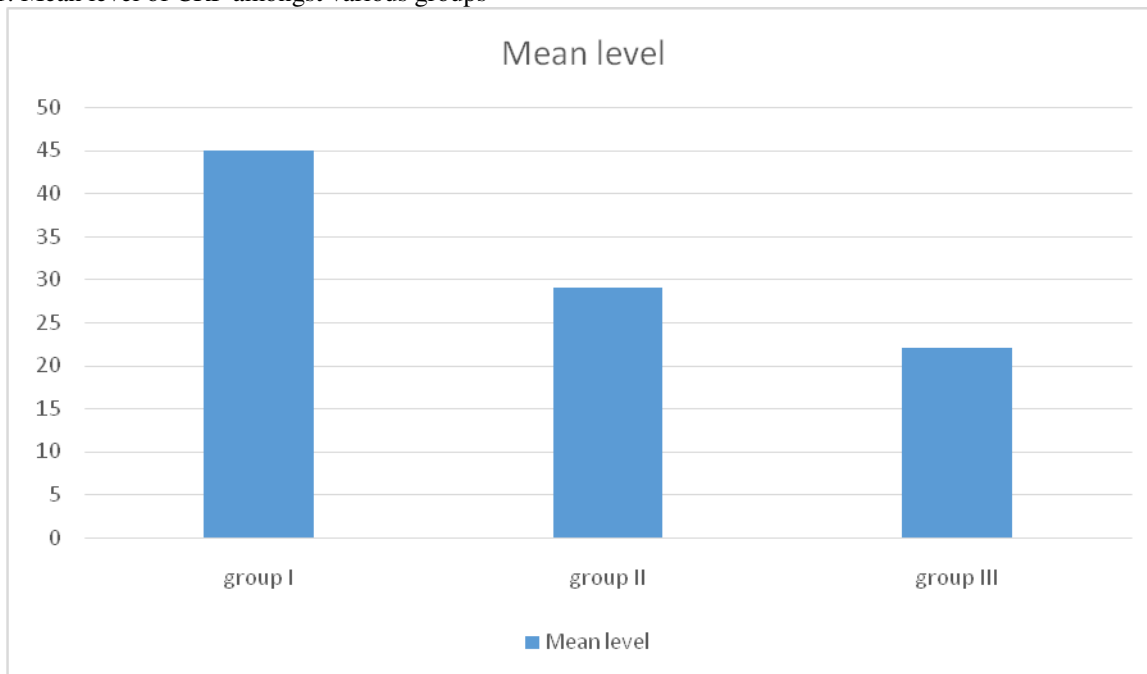
DISCUSSION

Different diseases of viral, bacterial, and immune origin are indicated by the presence of fever. Recent investigations have shown that endogenous pyrogen,are indirectly responsible forcausation of fever and are a byproduct of monocytes.[10]These mediators are known as interleukin-1 (IL-1) and have varied functional properties.[11] Investigations have proven that macrophages can be induced by different stimuli to produce interleukin-1. The stimuli can be endotoxins, lymphokines,and particulate ingestions.[12,13]Interleukin are also responsible for liver synthesis of different serum proteins.The most common amongst them is acute phase reactant known asC-reactive protein.[14] Since fever is the commonest occurrence in both viral and bacterial infections, to differentiate between both, CRP acts as a marker. CRP is rarely raised in viral infections. [15]The present study was done to determine the level of CRP in enteric fever subjects. As per the present study, the mean age of group I subjects was 18.3+/- 2.3 years, group II subjects had mean age of 19.1+/- 1.6 and mean age of group III subjects was 16.9+/- 2.7 years. There was a significant difference in the age group between the groups. The range of CRP in group I, group II and group III were 14-181 mg/dl, 10-91 mg/dl and 8-99 mg/dl respectively. There was a significant difference between the groups. The mean duration of fever was 4.5-13.2 days in group I, 6.2-15.5 days in group II and 2.5-9.7 days. There was a significant difference in the duration of fever between the groups. The rate of widal O+ in group I, group II and group III were 92%(n=46), 83.3%(n=25) and 20%(n=6). The rate of widal H+ in group I, group II and group III were 88%(n=44), 73.3%(n=22) and 16.7%(n=5).A physician should not only rely on the clinical symptoms of the conditionsbut promptly ask for the laboratory investigationsto make an appropriate inference of diagnosis at the time of admission to the hospital in areas prone to enteric fever. A study amongstchildren with gastroenteritis the agents used ROC analysis, and found that serum C-reactive proteinis a valuable tool for predictingthe source of infection asviral or bacterial.[16] CRP should be regularly used amongst subjects but should not be the sole criteria affecting the decision strategy.[17]The cut off levels of CRP varies amongst different subjects and amongst different diseases.[6] As per the recent investigation, the level of C reactive protein iselevated amongst the subjects that are infected with multi strains compared with single strain of S typhi.[18]

CONCLUSION

S. typhi infection in endemic areas is difficult to detect. Detection of typhoid infection using widal test can be cumbersome. CRP is a useful indicator for S.typhi detection in endemic areas. From the present study, we can conclude that CRP is elevated amongst subjects with bacterial infection and it can be used to differentiate subjects with bacterial and viral infections.

REFRENCES

1. Van den Bruel A, Bartholomeeusen S, Aertgeerts B, Truyers C, Buntinx F. Serious infections in children: an incidence study in family practice. BMC Fam Pract2006;7:23.
2. Kool M. Serious infections and healthcare use in children with fever presenting at a general practice out-of-hours service. In: Febrile children at a general practice out-of-hours service [thesis]. Rotterdam: Erasmus University; 2015.
3. Cals JW, Butler CC, Hopstaken RM, Hood K, Dinant GJ. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomized trial. BMC 2009;338:b1374.
4. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest 2003;111:1805–12.
5. Sanders S, Barnett A, Correa-Velez, Coulthard M, Doust J. Systematic review of the diagnostic accuracy of C-reactive protein to detect bacterial infection in nonhospitalized infants and children with fever. J Pediatr2008;153:570–4.
6. Van den Bruel A, Thompson MJ, Hai-Hassan T, et al. Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review. BMJ 2011;342:d3082.
7. Sanders S, Barnett A, Correa-Velez, Coulthard M, Doust J. Systematic review of the diagnostic accuracy of C-reactive protein to detect bacterial infection in
8. Choo KE, Razif A, Ariffin WA, Sepiah M, Gururaj A. Typhoid fever in hospitalized children in Kelantan, Malaysia. Ann Trop Paediatr 1988; 8: 207–12.
9. Choo KE, Oppenheimer SJ, Ismail AB, Ong KH. Rapid sero-diagnosis of typhoid fever by dot enzyme immunoassay in an endemic area. Clin Infect Dis 1994; 19: 172–76.
10. Hanson, D. F., P. A. Murphy, and B. E. Windk. 1980. Failure of rabbit neutrophils to secrete endogenous pyrogen when stimulated with staphylococci. J. Exp. Med. 151:1360-1371.
11. Mizel, S. B., and J. J. Farrar. 1979. Letter to the editor: revised nomenclature for antigen-nonspecific T cell proliferation and helper factors. Cell. Immunol. 48:433-436.
12. Atdns, E., L. Francis, and H. A. Bernheim. 1978. Pathogenesis of fever in delayed hypersensitivity: role of monocytes.Infect. Immun. 21:813-820.
13. Unanue, E. R., J.-M. KIely, and J. Calderon. 1976. The modulation of lymphocyte functions by molecules secreted by macrophages. II. Conditions leading to increased secretion. J. Exp. Med. 144:155-166.
14. Pepys, M. B. 1981. C-reactive protein fifty years on.Lancet i:653-656,
15. Pdtola, H. 0. 1982. C-reactive protein for rapid monitoring of infections of the central nervous system. Lancet 1:980-983.
16. Borgnole G, Barbone F, Guidobaldi G, Olivio G. C-reactive protein in viral and bacterial gastroenteritis in children. Acta Paediatr 1996; 85: 670–74.
17. Nabulsi M, Hani A, Karam M. Impact of C-reactive protein test results on evidence-based decision-making in cases of bacterial infection. BMC Pediatr2012;12:140.
18. Bhutta ZA. Cytokine profile in typhoid fever: correlation with clinical features and sensitivity patterns (Abstract Cp-5). Proceedings of the Third Asia-Pacific Symposium on Typhoid Fever and Other Salmonelloses, Bali, Indonesia, 1997; 92