I. INTRODUCTION

Typhoid fever continues to be a global health problem, with an estimated 12 to 33 million cases occurring worldwide each year. Incidence of typhoid fever has been estimated approximately 17 million cases with 6,00,000 associated deaths occurring annually. (Gerald T. Mandell et al. 2002).

Typhoid fever was so called because it resembled Typhus. The first detailed description of ‘Typhoid’ was given by William Jenner in 1850. The term "enteric fever" was introduced in 1869. *Salmonella typhi* was discovered by Eberth in 1880 and was first cultured by Gaffky 1884 (Wilson J.C. 1881).

Typhoid fever occurs in all parts of the world where water suppliers and sanitation are substandard. The disease is now uncommon in the developed countries, where most of the cases that occur are either acquired abroad or imported by immigrants. Typhoid fever is endemic in India. A limited study in an urban slum showed 1% of children up to 17 years of age suffer from Typhoid fever every year (Park K. 2001). Annual incidence rates of 980 per lakh in India (Sinha S. 1999).

Typhoid fever invariably comes from another human source - a patient with active disease, a convalescing patient or a carrier. The ultimate sources of infection invariably the patient or carrier. Chronic carriers are generally over 50 years old more commonly women (Gerald T Keusch, 1992). Typhoid usually comes by ingestion of food or water contaminated by fecal or urinary carriers with excreting *Salmonella enterica serotype typhi*. In endemic areas, identified risk factors for disease includes eating food prepared outside the home, ice cream or flavoured cool drinks from street vendors (Black R.E 1985 and Luby S.P., 1998),
drinking contaminated water (Mermim J.H., 1999), having close contact or relative with recent typhoid fever (Black R.E., 1985 and Luxemburg C., 2001), poor housing with inadequate facilities for personal hygiene (Gasem M.H., 2001), and use of inappropriate antimicrobial drugs (Luby S.P., 1998).

The high mortality rates which continue to be reported from some endemic countries like ours are undoubtedly related to delayed diagnosis and or inappropriate use of antibiotics. In the pro-antibiotic era, the mortality rate for typhoid fever was as high as 15%. The introduction of Chloramphenicol in 1948 greatly altered the disease course, decreasing mortality to less than 1% and the duration of fever from 14-28 days to 3-5 days. As a result Chloramphenicol remained the standard treatment for typhoid fever for more than three decades (Chogle A.R., 2002). Subsequently several reports confirmed the emergence of multidrug resistance (MDR) in *Salmonella typhi* (Agarwal S., 1991 and Mukkerjee P. 1991). Outbreaks occurred in Mexico, Vietnam, Thailand, Korea, Peru and India (Mirja S.H., 1996). The MDR strains of *Salmonella enterica serotype typhi* are increasingly being reported from India and World wide (Ackers M.L., 2000 and Madhulika U., 2004). Isolates of *Salmonella typhi* with reduced susceptibility to Fluoroquinolones have now appeared in Indian subcontinent and other regions (Wain J., 1997 and Kapil A., 2002).

Ciprofloxacin sensitive strains have increased minimum inhibitory concentrations (MIC) for Ciprofloxacin (Crump J.A., 2004) and therapeutic failure of Ciprofloxacin have been reported in these cases of typhoid fever (Crump J.A., 2003: Thresfall E.J., 1999 and Nguyen T.C., 1997). However, reemergence of Chloramphenicol susceptible strains have also been reported during recent years (Mandal S., 2004 and Chandel D.S., 2000). Hence in our research work the efforts have been focused on 'current status of *Salmonella typhi* by the
study of extended pattern of antimicrobial susceptibilities, MIC, Serotyping, Biotyping and Phagetyping.

The early diagnosis of bacterimia is critical and depends on alertness of the clinicians. However, bacteriological data unfortunately are not available for 24 hours therapy is delayed or instituted with expensive potentially toxic or marginally effective antimicrobials. In India where typhoid fever is endemic and there are few microbiological laboratories to provide diagnosis by culture. So we also focused on non-culture techniques for rapid diagnosis of typhoid fever 'with special references to immunological functions’. An investigation that has acquired a parallel and perhaps greater diagnostic and prognostic significance is CRP and Buffycoat smear study.

Interrelated in the light of immunological background, CRP values can provide extremely useful diagnostic information. C-reactive protein (CRP) is an abnormal β-globulin produced by liver during any inflammatory process, bacterial infections, and malignancies and even in tissue destruction by the liver as a result of stimulation by interleukin. CRP level takes atleast 6-8 hours to rise after the onset of infection and are therefore helpful in early diagnosis at the onset of the disease. But after 24 hours CRP value is very helpful and this test also has prognostic value as the levels strongly fall when patient is responding to treatment (Roitt, 1998). Many authors reported the importance of CRP in early diagnosis of septicemia (Gerdas T.S., 1998, Krishna B.V.S. 2000, Choo K.E. et al 2001 and Ahamed Z. et al 2005).
In our study, the rapid diagnosis of typhoid fever is also focussed on buffycoat smear study, an another immunological reaction. It is a simple method in which smears were prepared from buffycoat and stained with Methylene blue or Acridine orange. Many authors reported the importance of Buffycoat smear examination (Anuradha D.E., 1998 and Parikh M., 1995).

India is an endemic country; sera of particular healthy individuals contain antibodies capable of reacting to a variable titre in Widal test due to previous stimuli (Punia J.N., 2003). It is therefore, important to establish the antibody level in the normal population by “Widal baseline titre” in a particular locality, in order to determine a threshold above which the antibody titre is considered significant (Pang T., 1989). Therefore Widal baseline titre for anti-O and anti-H for *Salmonella typhi* are important. In India most patients present late to the hospital and require immediate diagnosis and specific treatment and often a single serum sample is relayed upon instead of paired serum samples. In these case high titre of anti-O and anti-H should be considered presumptive diagnosis for typhoid fever (Punia J.N., 2000).

Thus effort have been made to survey the epidemiological studies by ‘current status of *Salmonella typhi* with special references to immunological functions’.