DISCUSSION

The primary aim of our study was to evaluate the levels of C-reactive protein in both superficial and deep infections of the newborns and to assess its superiority, if any, in the diagnosis of various neonatal infections. Further, the present venture was also directed to derive a correlation between the gestational age and birth weight of the newborn babies to the respective concentration of C-reactive protein (CRP) in the serum.

A total of 50 newborn babies were selected, of which 10 normal non-infected babies served as control, while the remaining 40 cases were of various neonatal infections. The study group of neonatal infections comprised of 22 cases of superficial infections, 14 cases of deep infections and 4 cases of combined infections.

A detailed clinical examination was done in each case and special emphasis was given to assess gestational age and birth weight of all the babies (Table 1 and 2). Besides evaluating CRP of both the control and study group of cases, other parameters of diagnosing infection viz. total leucocyte count, bacteriological profile, blood culture and sensitivity and/or X-ray chest was done in all the cases. Based on the observations depicted in tables 1 to 21, following inferences have been drawn and discussed under different headings.
It is evident from table 1 that amongst the study group of cases, the majority of cases (75%) were term babies, while in the control group of cases, there was an equitable distribution of cases according to gestational age. However, 67.5% of the infected cases, and 70% of the control group of cases had birth weight about 2.5 kg (Table 2). Table 3 clearly reveals, that majority of the infected cases (67.5%) and all the control groups of cases were below 10 days of age at the time of diagnosis and estimation of the concentration of CRP. 70% of all the cases were males in our study as is evident from table 4. The reason for predominance of male baby in our study can be ascribed to the fact that males are considered to be more precious than females.

Umpteen workers in the past have assessed the concentration of CRP in neonatal as well as in childhood infections, however only a few, viz. Philips et al (1983), Hindocha et al (1984) and Kalra et al (1985) have assessed the CRP in neonatal infections viz. 23 cases of neonatal meningitis, 41 cases of neonatal septicemia and 75 cases of mixed neonatal infections respectively. However, these authors, unlike us, have not elaborated on the gestational age, birth weight and sex of their case material, unabling us to do any comparative evaluation.
Obstetrical History:

Due emphasis was given to observe those factors in the antenatal and natal period which would have a bearing in the concentration of C-reactive protein. Accordingly, factors like leaking more than 12 hours, foetal distress, foetal asphyxia, aspiration and meconium staining were noted in each case. History of leaking for more than 12 hours was present in three cases and all of them suffered from septicemia.

Various workers viz., Kushner et al (1973) and Ambinder et al (1982) also studied different antenatal, natal and post-natal factors which cause an increase in susceptibility of infections and thereby a rise in the level of CRP in respective infections. Kushner et al (1973) identified maternal fever during labour, prolonged rupture of membrane (PROM), asphyxia and few other problems not resulting from infections, to be associated with elevated amounts of CRP in umbilical cord blood. Ambinder et al (1982) added shock, foetal distress and aspiration difficulties to the conditions in which serum CRP values were commonly high at birth and during the first few days of life. They also reported CRP values $\geq 2.0$ mg/dl in 11 infants of mothers who had prolong rupture of membrane.

Clinical Manifestations:

The fact that neonatal infections present with subtle clinical manifestations has been amply demonstrated
in our study, however, a broad group of manifestations as have been reported in table 5 clearly demonstrates that majority of the cases presented with umbilical discharge, refusal of feeds, fever, poor activity, discharge from eyes and jaundice. The cases of meningitis had evidence of altered sensorium and convulsions. Kalra et al (1985) was the only worker to have elaborated, like us, the clinical manifestations, viz. refusal of feeds (36.6%), listlessness (71.0%) and pyrexia (71.0%).

**Type of infection:**

As has been broadly classified earlier (Table 6), amongst the superficial infections, there were 17 cases of umbilical sepsis, 3 of conjunctivitis and 2 of furunculosis. While in deep infections, there were 6 cases of septicemia, 2 cases of septic meningitis, 4 cases of bronchopneumonia and 2 cases of septic arthritis. Kalra et al (1985) too, in their study had maximum number of cases of umbilical sepsis (25), septicemia (30) and pneumonia (7) for estimation of CRP.

**Bacteriological profile:**

In our study, we observed that in superficial infections the main organism, which was isolated, was staph aureus, while in deep infections especially in septicemia E. coli was grown in majority of cases, followed by staph epidermidis, streptococcus and klebsiella.
However, in cases of septic meningitis and broncho-
pneumonia, no organism was cultured, perhaps due to the
fact that these babies had received antibiotics prior to
the admission.

Philips et al (1983) observed that the main
organism in septic meningitis in their study, was group B
streptoccci. Clarke et al (1983), however reported
H. influenzae, N. meningitidis, L. pneumonise. E. coli and
group B streptococci in children suffering from meningitis.
Kalra et al (1985) in later study, reported staph-aureus
as the main organism grown in superficial infections,
bronchopneumonia and septicemia. E. coli was however,
found to be the main organism in cases of septic meningitis.
Khatua et al (1986), and Monga et al (1986) reported that
gram negative organisms (klesseilla) was found to be the
main pathogens in cases of neonatal septicemia. Mishra
and Rai (1986), and Sharma & Halder (1987), reported
E. coli to be the most predominant organism over others
in neonatal septicemia. Bhatia et al (1989) reported
that in septicemia, the main organism was staph-aureus,
while S. epidermidis, E. coli, klesseilla were reported
in less number of cases.

Haematological profile:

We observed in our study that bacterial culture
was more reliable indicator of infection than the total
leucocyte count in superficial infections, while it was
less reliable in deep infections. We found that total leucocyte count was more than 11,500 in 20, out of the 40 cases studied. Mean leucocyte count was 11,300 in superficial infections while it was 13,200 in deep infections. Values between the two being statistically significant (P value < 0.01).

However, various other workers, viz. Monroe et al (1979), Steigbigel et al (1974) and Desai (1984) reported leucopenia in cases of neonatal sepsisemia. Kalra et al (1985), like us, have reported leucocytosis in 68.4% cases of neonatal sepsis.

Detection of CRP and its concentration in neonatal infections:

It is evident from table 9 that CRP was not detected in serum in any of the control group of cases. In the study group, however, CRP was detectable in 70% of cases, while in rest 30%, CRP was undetectable. A significant finding of our study was, that though CRP was detectable in only 50% cases of superficial infections, it was detected in all (100%) cases of deep as well as combined infections. The mean concentration of CRP (ugm/ml) in superficial and deep infections in our study was 34.8 ± 19.5 and 69.6 ± 17.1 ugm/ml respectively, the values between the two being statistically significant (P value < 0.01).
Another important observation of our study was, that amongst the deep infections, septic meningitis was characterized by highest mean value of CRP (79.5 ug/ml) followed by septicemia (70.0 ug/ml), septic arthritis (64.0 ug/ml) and bronchopneumonia (63.5 ug/ml) (Table 10). We also tried to observe a correlation of the concentration of CRP to the gestational age and birth weight of all the cases (Table 11 and 12). It was observed that of the 10 pre-term babies in the study group, all (90%) but one case had detectable levels of CRP, while in the term infected babies, CRP was detectable in lesser number of cases (67%). Similar observation was also seen as regards the birth weight viz-a-viz, the CRP level, wherein, though in the babies weighing less than 2.5 kg, all cases (100%) had detectable CRP levels, only 68% of the babies weighing more than 2.5 kg had detectable CRP values. Further, it was seen that the mean value of CRP in deep infections (68.6 ± 17.1), irrespective of the period of gestation was highly significant than the values observed in the pre-term (33.6 ± 25.8) and term (35.8 ± 15.9) cases of superficial infections and combined infections (Tables 13, 15 and 17). However, no statistically significant difference was observed in the concentration of CRP between superficial and combined infections (Table 16).

An interesting observation of our study was that there was a significant difference of the CRP concentration between superficial and deep infections, as well as deep
and combined infections, when the values in low birth weight ($\leq 2.5$ kg) and normal weight ($\geq 2.5$ kg) babies were compared with each other (Tables 19, 20 and 41). However, no significant difference of the CRP concentration was observed amongst both superficial and deep infections viz-a-viz, birth weight ($p \geq 0.05$) (Table 18).

The CRP concentration has been evaluated in various neonatal infections by different workers from time to time. Kalra et al (1985), like us, has reported the CRP in 69.7% of cases, however, Mc Carthy et al (1978) and Pravastava et al (1984) detected CRP in fewer number of cases, viz. 54.1% and 41.4% respectively as compared to the detection (70%) of our study. Clarke and Cost (1983) and Wood et al (1984) were the only workers, who recorded 100% detection in cases of neonatal infections. The difference in percentage detection by various workers is because of the fact that, both Clarke (1983) and Wood (1984), who recorded a 100% detection, had taken the cases of deep infections, viz. neonatal meningitis and septicemia, while Kalra et al (1985), like us, had taken a conglomeration of both superficial and deep infections, hence their percentage of detection was more or less equal to us.

On comparison of the mean concentration of CRP observed by us, to that of other workers, it was seen that our values were much higher than that observed by various other workers in the field. Clarke and Cost (1983) reported a mean value of $17.2 \pm 2$ mg/dl in septic
meningitis and between 1.8 to 6.4 mg/dl in aseptic meningitis. Philip et al (1983) have not estimated the mean CRP concentration in cases of septic meningitis, but they found a maximum concentration of 17.7 mg/dl and a minimum concentration of 0.1 mg/dl. However, we found a much higher mean concentration of CRP (79.5 ugm/ml) in cases of septic meningitis. We also observed that mean concentration of CRP was raised in cases of pneumonia (63.5 ugm/ml), while Mc Carthy et al (1978) and Srivastava et al (1984) estimated that CRP was highly raised in cases of bacterial pneumonia as compared to viral pneumonia, but they have not estimated quantitatively the values of CRP concentration in either group of infections. Wood et al (1984) also estimated the maximum concentration of CRP which was 20 mg/dl and a minimum concentration of CRP 0.3 mg/dl in cases of neonatal septicemia, while we observed a mean concentration of 70.0 ugm/ml in these cases. We did not take any case of urinary tract infection in our study, however, Hallerstein et al (1982) reported the concentration of CRP between 67.23 ugm/ml in cases of acute pyelonephritis and more than 30 ugm/ml in lower urinary tract infections. Kalra et al (1985) were the only workers, who studied both superficial and deep neonatal infections and found a low percentage of detection of CRP in superficial infections as compared to high percentage of CRP in deep infections. Neither of the above mentioned workers have reported the
mean concentration of CRP in superficial infections, but we found a mean concentration of $34.8 \pm 19.5$ ug/m/l in superficial infections. Mean concentration of CRP in umbilical sepsis, furunculosis and conjunctivitis was found to be 41.6 ug/m/l, 33.3 ug/m/l and 16.8 ug/m/l respectively.

As already reported, an interesting observation of our study was that low birth weight babies (less than 2.5 kg.) and pre-term babies (less than 37 wks.) had higher percentage of detection of CRP values (100% and 90% respectively) than the values observed in cases of term and normal birth weight babies (67% and 68% respectively). In spite of our best efforts, none of the studies done so far have elaborated on the values of serum CRP vis-a-vis, gestational age and birth weight. The higher detection rate observed in low birth weight and pre-term babies can be attributed to the fact that both these groups of babies are immunocompromised and therefore are more prone to deeper infections.

In nutshell, our study amply demonstrates and collaborates the earlier findings, that the detection and the height of CRP concentration is directly correlated to the severity of infection, rate of detection and mean percentage being significantly higher in deeper infections as compared to superficial infections in the neonatal period. Clarke and Cost (1983) attributed the rise of
CRP to a greater extent in deeper infections to the fact that CRP production is a non-specific response to tissue damage, which is markedly more in deeper than superficial infections. The author also stated that bacterial infections produce greater tissue destruction than that caused by viral infections, so that values are much higher in cases of septic meningitis, septicemia, septic arthritis and bacterial pneumonias. Further, the greater CRP response in bacterial infections may be related to the extra-cellular life cycle of bacteria compared with the predominantly intra-cellular life cycle of viruses explaining low detection of CRP in cases of viral pneumonia. Similarly, Kaira et al (1985) in their study have also hypothesised that all superficial infections which are purely local and not systemic are unable to cause tissue destruction so as to induce the production of CRP.

We therefore conclude that CRP test is an important parameter to diagnose both superficial and deep infections and is more reliable indicator than total leucocyte count and bacterial culture specially in deeper infections.