Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

Paediatrics

Value of Serial Measurement of C - reactive protein in Assessment of Clinically Suspected Neonatal Sepsis

Dr. Md. Homayun Shikdar[1*], Dr. Anjana Basak[2], Dr. Sharmin Afrozy[3]
[1]Junior Consultant (Paediatrics), MBBS, FCPS, Upazila Health Complex, Dhunat, Bogura, Bangladesh
[2]Junior Consultant (Paediatrics), MBBS, FCPS, Upazila Health Complex, Adamdighi, Bogura, Bangladesh
[3]Resident Physician, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh

Original Research Article

***Corresponding author**
Dr. Md. Homayun Shikdar

Article History
Received: 01.12.2018
Accepted: 10.12.2018
Published: 30.12.2018

DOI:
10.36347/sjams.2018.v06i12.031

Abstract: A prospective cohort study was conducted at Neonatal care unit of Department of Paediatrics, Sahaeed Ziaur Rahman Medical College Hospital. From July 2012 to December 2012 to determine value of serial measurement of C - reactive protein in assessment of clinically suspect neonatal sepsis. Total 100 patients were assessed. Fifty new born were included as cases (Group-A) & fifty were included as control (Group-B). Among total 100 patients, 55 were male baby and 45 were female baby. In group-A, 28 neonate were male and 22 were female. In group-B, 27 were male and 23 were female. In this study, there is male preponderance among the suspected cases of neonatal sepsis. Male and female ratio is 14:11. Most of the parents were from Bogura (68%) and rest was from Gybandha, Sirajgonj and Naogaon. Economic status was mostly slightly sufficient (72%). About 33% parents were illiterate, 56% parents were literate, 09% parents were educated and 02% of the parents were highly educated. All neonates selected as control were delivered by doctors posted in Gynea and Obstetric department of this hospital. 32% of neonates in group-A were given intrapartum antibiotic prophylaxis whereas 58% of those in group-B were given so. In group-A, 68% were delivered by naturals, 26% by cesarean section and 6% were delivered by assistance. In group-B, 60% were delivered by naturals, 36% by cesarean section and 4% were delivered by assistance. 74% of cases in group-A, sterile or clean instruments were used to cut cord whereas that was done in 100% of the control. On admission or during enrollment in study 74% of the cases in group-A had positive CRP and 30% of the control in group-B had positive CRP. There was significant difference between two groups. All the demographic features, clinical records and laboratory data were compared between case (Group-A) and controls (Group-B). Distribution of the newborn pair in group-A and group-B was analyzed with chi square test. Among four serial measurement of CRP, first three serum samples show significant difference of positive CRP level between cases and controls. There is no significant difference of positive CRP level in last sample taken before discharge between cases and controls .It can be concluded that positive CRP level can be considered as a useful indicator alternative to blood culture to diagnose sepsis in neonate in our setup when it is correlated with clinical data and easily available laboratory findings i.e thrombocytopenia, total leucocyte count etc. Serial measurement of CRP can be considered as a valuable indicator to see the prognosis of neonatal sepsis.

Keywords: Risk factors, Socio-economic conditions, Socio-demographic conditions, Sepsis.

INTRODUCTION

Neonatal sepsis is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life [1]. Globally 8.8 million children a year die before their 5th birthday, more than 50% of them during their 1st four weeks of life [2]. Perinatal and neonatal mortality and morbidity rate are the reflection of obstetric and neonatal services of a country, which again is determined by various complex interrelated medical, socio-economic, cultural and infrastructural factors [3]. The under-five mortality rate in Bangladesh (per thousand live birth) is 67 [4] and the infant mortality rate (per thousand live birth) is 39 [5]. Although childhood and infant mortality in South Asia has reduced substantially during the last decade, the rate of neonatal mortality is still high [6]. The high level of

neonatal death in Bangladesh is a matter of great concern among all health professionals and health policy makers. Though the rate of neonatal death has fallen from 78 to 42/1000 live birth during last 25 years, it still remains unacceptably and alarmingly high [7].The major causes of neonatal death in hospitalized babies are severe perinatal asphyxia, preterm LBW and septicaemia [8]. Sepsis remains significant cause of neonatal morbidity and mortality. Till now infection contribute to approximately 30-40% of neonatal deaths in the low income countries [9]. Neonatal sepsis is best defined by Khan and Rahman as a systemic inflammatory response syndrome (SIRS) resulting from a suspected or proven infection in the first month of life [10]. Babies usually emerge from a sterile intrauterine environment to the world of microorganism. Our body defends itself against infection in three ways - physical, cellular and humoral. Neonates are deficient in all three of these defenses [11]. So a newborn contains higher risk of infection and sepsis. The comparative immunodeficiency of the neonate not only predisposes him to infection, but also means that when infection occurs it may disseminate very rapidly with septicaemia, shock and death. This dissemination has two major implications: 1) Early diagnosis is essential. Even very trivial clinical findings that suggest infection demand full laboratory evaluation. 2) Initial therapy must be started on the basis of clinical suspicion. There is no time to wait for the laboratory result to come back 24-48 hours later [11]. A quick decision should be made about whether or not the baby will treat with antibiotics. The clinical manifestations of sepsis vary from being specific to subtle. Subtle and nonspecific symptoms and signs of sepsis may delay in recognition and treatment of such cases where a few hours of delay of therapy may change the prognosis [12]. Most definite evidence is positive culture, but it could be positive only in 30-40% of the patient [13]. To diagnose sepsis in neonate by doing blood culture in the developing countries like Bangladesh is difficult due to lack facilities and cost and is only available in a few only tertiary level hospitals [14]. However, it increases the difficulty for those clinicians caring for newborn infants, because positive blood culture results are even more difficult to obtain, so a definitive diagnosis of sepsis cannot be made. In addition, false-positive blood cultures secondary to contamination may be encountered. These may be distinguished by determining serial CRP levels [15]. The yeld of blood cultures may depend on such things as skin disinfection technique, sample volume and the number of cultures taken as well as technical factors: the dilution of blood to culture medium and the blood culture system used [16].This has prompted the evaluation of surrogate markers of inflammation as the possible tools for early diagnosis of bacterial sepsis. Estimation of cytokines and CRP levels are potentially useful in this respect [17]. Also hematological parameters including thrombocytopenia, total leukocyte count, total neutrophil count, immature/mature neutrophil ratio, band form count are good predictor of sepsis in newborn [18]. IL-6 is one of the markers on infection which appear earlier and remain elevated in the 1st 14 hours after which it declines. This initiates the formation of CRP which is elevated 24 to 48 hours after the onset of infection and persists up to the time until the infection is not resolved [19]. CRP was described initially in 1930 by Tillet and associates as a non- type-specific somatic polysaccharide fraction extracted from *Strptococcuspneumonae.* The assaysdeveloped to measure CRP values during infection or inflammationhave lower detection limits of 3 mg/L. High-sensitivity CRP methods are now available that can measure CRP values less than1 mg/L and are used for cardiovascular risk assessment [20].Factors that can influence CRP values are [20]. Mode of delivery, Gestational age, Types of organism causing sepsis, Granulocytopenia Surgery, Immunizations, Severe viral infections etc. In Bangladesh there are some published reports on neonatal sepsis. A study of 54 cases done by Chowdhury MAKA in special care baby unit in Dhaka Shishu (Child) Hospital raveled that poor socioeconomic condition, maternal infection, inappropriate management of labor and lack care of the umbilical stump appear to be principle factors for the development of umbilical sepsis. Reluctant to feed, lethargy, apneic spell, jaundice, temperature instability, umbilical discharge were main presenting features. *E. coli* was found in 30% cases, *Staph. aureus* in 20.73%, *Psudomonas* in 14.8% and others in 25% cases [21].To achieve the Millennium Development Goal 4 which aims at reducing under five child mortality by two thirds by the year 2015, serious efforts needs to be given by professionals & policy makers [22].Reducing the morbidity & mortality due to neonatal infection may help to achieve the goal of MDG-4. Perinatal asphyxia and prematurity with LBW are preventable conditions but neonatal sepsis is a treatable condition. So the neonatologists and pediatricians can do many things for this patients.Use of serial measurement of CRP level may be helpful to asses suspected sepsis of newborn as well as helpful to see the prognosis of this condition. The value of CRP also can help us to determine various risk factors associated with its raised level. So it is desired to design a prospective study to correlate the serial measurement of CRP value with the clinical features of neonatal sepsis and / or easily available laboratory data which may be a valuable tool to assess suspected neonatal sepsis and its prognosis in our set up.

OBJECTIVES

General objective

- To evaluate the serial measurement of C-reactive protein (CRP) in a neonate when bacterial infection is being considered which is helpful for prompt management, reducing cost of care and hospital staying.

Specific objectives

- To determine the value of serial measurement of CRP as a prognostic marker of neonatal sepsis.
- To evaluate the risk factors associated with raised CPP in neonatal sepsis.

MATERIALS AND METHODS

A prospective cohort study was conducted at Neonatal care unit of Department of Paediatrics, Sahaeed Ziaur Rahman Medical College Hospital from July 2012 to December 2012. After taking informed written consent from mother/father of newborn and permission from concerned authorities, a total 100 neonates were selected by convenience sampling where 50 neonates were taken as cases (Group-A) and another 50 neonates as control (Group-B). A structured data collection sheet was used to record the clinical data and laboratory results of the newborn babies included in the study. The parents were at large on taking decision whether to participate or not. They were assured that their voluntary withdrawal from the study at any point would not interrupt the treatment of their child. Data was collected on a pre designed, pre tested data collection sheet in English. It had been used to collect primary data regarding demographic information of patient & mother, obstetric history, clinical history and findings & results of the laboratory tests. On admission 1st CRP level, total leucocyte count and thrombocyte count were done. Next two serum samples to measure CRP level were taken after 24 and 72 hours of admission and last sample was taken before discharge. Distribution of the newborn pair in group-A and group-B was analyzed with chi square test. P value reached from chi square test at a significance level of 0.05.

RESULTS

This study was a hospital based prospective study conducted at the Neonatal Care Unit of department of Pediatrics, Saheed Ziaur Rahman Medical College Hospital (SZMCH), Bogura. Total 100 patients were assessed. 50 newborn were included as cases (Group-A) and another 50 were included as control (Group- B).

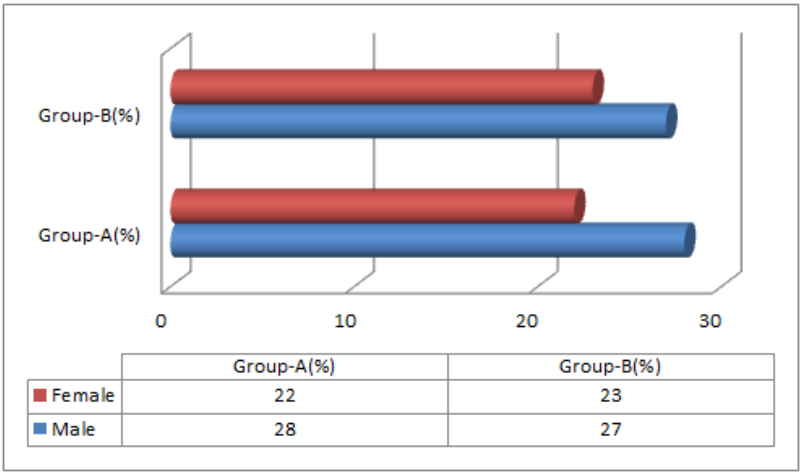

Fig-1: Sex distribution of neonates (n=100)

Among total 100 patients, 55 were male baby and 45 were female baby. In group-A, 28 neonate were male and 22 were female. In group-B, 27 were male and 23 were female. In this study, there is male preponderance among the suspected cases of neonatal sepsis. Male and female ratio in group-A is 14: 11.

Table-I: Economic status and educational status of the parents of study participants (n=100)

Socio-demographic characteristic	Group-A & Group-B	
Economic Class		
	Frequency	Percentage
Insufficient	16	16
Slightly Sufficient	71	71
Sufficient	10	10
Sufficient and Save	3	3
Educational Status		
	Frequency	Percentage
Illiterate	33	33
Literate	56	56
Educated	9	9

Highly Educated	2	2

Economic status was mostly slightly sufficient (72%). About 33% parents were illiterate, 56% parents were literate, 09% parents were educated and 02% of the parents were highly educated.

Table-II: Distribution of newborn pair of group A and group B by maternal and antenatal features (n=100)

Maternal and antenatal features	Group A (n=50)		Group B (n=50)		*P* value
	n	%	n	%	
Maternal age					
< 20 years	11	22	13	26	>0.10 ^{ns}
20years-24years	16	32	15	30	
25 years-29 years	12	24	11	22	
30years-34 years	07	14	06	12	
35 years or more	04	08	05	10	
Maternal weight					
50 Kg or less	17	34	15	30	
51Kg - 60 Kg	22	44	21	42	>0.10 ^{ns}
> 60 Kg	11	22	14	28	
Maternal height					
<5 Fit or 152.4 cm	29	58	27	54	>0.10 ^{ns}
>5 Fit or 152.4 cm	21	42	23	46	
Mothers previous medical illness					
Significant medical illness	06	12	09	18	>0.10 ^{ns}
No significant medical illness	44	88	41	82	
Mothers illness during pregnancy					
Maternal infection	21	42	08	16	
APH	02	04	04	08	<0.01 ^{s}
PET	03	06	06	12	
PROM	23	46	11	22	
Fits	01	02	07	14	
Tetanus toxoid given					
Yes	36	72	38	76	>0.10 ^{ns}
No	14	28	12	24	

Table II shows age of 32% of mother of cases and 30% of control is in between 20 to 24 years and maternal age is below 20 years in 22% cases and 26% of control respectively. There is no significant difference between case and control. The weight of 44% and 42% of the mothers of group A and group B respectively was in between 50 to 60 kg with no significant difference. The height of the most of the mothers in both groups is < 5 fit. Most of the mothers in both groups have no history of previous significant medical illness. 42% of the mothers of group A had maternal infection during pregnancy whereas that of 16% in group B. 46% of the mother in group A and 22% of the mother in group B had history of PROM. So there is significant difference between both groups in relation with maternal illness during pregnancy. 72% and 76% of the mothers in group A and group B respectively had taken Tetanus Toxoid with no significant difference in both groups.

56% of the newborn in group-A were born at home, 32% of those were in hospitals and rest 12% were born at different clinics. Among them 36% were delivered by doctors, 24% by relatives, 18% by traditional dai, 14% by skilled birth attendant and only 8% were delivered by nurses or midwives. All neonates selected as control were delivered by doctors posted in Gynea and Obstetric department of this hospital. 32% of neonates in group-A were given intrapartum antibiotic prophylaxis whereas 58% of those in group-B were given so. In group-A, 68% were delivered by naturals, 26% by cesarean section and 6% were delivered by assistance. In group-B, 60% were delivered by naturals, 36% by cesarean section and 4% were delivered by assistance. 74% of cases in group-A, sterile or clean instruments were used to cut cord whereas that was done in 100% of the control.

Table-III: Distribution of newborn pair of group A and group B by delivery records (n=100)

Maternal and antenatal features factors	Group A (n=50)		Group B (n=50)		*P* value
	n	%	n	%	
Place of delivery					
Home	28	56	00	00	<0.001[s]
Hospital	16	32	50	100	
Clinic	06	12	00	00	
Delivered by					
Doctor	18	36	50	100	
Nurse/ Midwife	04	08	00	00	
Trained birth attendant	07	14	00	00	<0.001[s]
Dai	09	18	00	00	
Relative	12	24	00	00	
Intrapartum antibiotic prophylaxis					
Yes	16	32	29	58	
No	34	68	21	42	<0.01[s]
Mode of delivery					
Vaginal delivery	34	68	30	60	
Cesarean section	13	26	18	36	>0.10 [ns]
Assisted delivery	03	06	02	04	
Cord cut by					
Sterile or clean instrument	37	74	50	100	<0.001[s]
Unclean instrument	13	26	00	00	

First feed was given within one hour of birth in 36% of neonate in group-A, whereas 84% in group B and the difference is statistically significant. First feed was colostrum given to 28% of the newborn in group-A and 94% in group-B. The difference is statistically significant (Table-V).

Table-IV: Distribution of newborn pair of group A and group B by risk factors of neonatal sepsis (n=100)

Evaluated risk factors	Group A (n=50)		Group B (n=50)		*P* value
	n	%	n	%	
Maternal infection					
Yes	21	42	08	16	<0.01[s]
No	29	68	42	84	
PROM or leaking membrane					
Yes	23	46	11	22	
No	27	54	39	78	<0.05[s]
Prolonged labour					
Yes	19	38	10	20	<0.05[s]
No	31	62	40	80	
Assisted delivery					
Yes	03	06	02	04	>0.10 [ns]
No	47	94	48	96	
Unhealthy umbilical stump					
Yes	14	28	06	12	
No	36	72	44	88	<0.05[s]
Abnormal liquor					
Yes	09	18	04	08	>0.10 [ns]
No	41	82	46	92	
Repeated or unsterile vaginal examination					
Yes	25	50	07	14	<0.001[s]
No	25	50	43	86	

Table-V: Distribution of newborn pair of group A and group B by their feeding status (n=100)

Characteristics	Group A (n=50)		Group B (n=50)		*P* value
	n	%	n	%	
First feed given at					
Within 1 hour of birth	18	36	42	84	<0.001[s]
After 1 hour of birth	32	64	08	16	
First feed was					
Colostrum	14	28	47	94	<0.001[s]
Other than colostrum	36	72	03	06	

Table-VI: Distribution of newborn pair of group A and group B by clinical features (n=100)

Clinical features	Group I (n=50)		Group II (n=50)		*P* value
	n	%	n	%	
Temperature instability					
Yes	34	68	00	00	<0.001[s]
No	16	32	50	100	
Feeding problem					
Yes	42	84	00	00	<0.001[s]
No	08	16	50	100	
Lethargy or excessive sleepiness					
Yes	45	90	00	00	
No	05	10	50	100	<0.001[s]
Gastrointestinal problem					
Yes	11	22	02	04	
No	39	78	48	96	<0.01[s]
Apnea					
Yes	21	42	00	00	<0.001[s]
No	29	58	50	100	
Difficulty in respiration					
Yes	22	44	04	08	<0.001[s]
No	28	56	46	92	
Convulsion					
Yes	12	24	03	06	
No	38	76	47	94	<0.001[s]
Poor perfusion					
Yes	20	40	00	00	<0.001[s]
No	30	60	50	100	
Hypotonia					
Yes	18	36	01	02	<0.001[s]
No	32	64	49	98	
Abnormal primitive reflexes					
Yes	42	84	02	04	
No	08	16	48	96	<0.001[s]
Bradycardia					<0.10[ns]
Yes	09	18	10	20	
No	41	82	40	80	
Tachycardia					
Yes	33	66	24	48	<0.05[s]
No	17	34	26	52	
Sclerema					
Yes	06	12	00	00	<0.01[s]
No	44	88	50	100	

History of the maternal infection was present in 42% and 8% of the mother in group-A and group-B respectively. 46% of the mother of newborn in group-A and 22% of that of group-B had the history of **PROM** or leaking membrane. 38% and 20% of the mothers of newborn of the group-A and group-B respectively had

the history prolonged labor. 6% of the cases and 4% off the control were born by assisted delivery. 28% of the cases and 12% of the control had unhealthy umbilical stump. 18% and 8% of the mothers of the newborn of group-A and group-B respectively had the history of abnormal liquor. 50% of the mothers of cases had the history of repeated or unsterile vaginal examination which was present only 14% of the mothers of the control. There is significant deference between newborn pair of group A and group B by all the risk factors of neonatal sepsis except assisted delivery and abnormal liquor.

Table VI showed the distribution of newborn pair of group A and group B by clinical features. 68% of the cases had temperature instability, 84% had feeding problem, 90% had lethargy or excessive sleepiness, 42% had apnea, 40% had poor perfusion, 12% had sclerema but no control had the above mentioned clinical features. 22% of the cases had gastrointestinal problem where as 4% of the control had that feature. 44% of the cases and 8% of the control had difficulty in respiration. 24% of the cases and 6% of the control had convulsion. 36% and 2% of the cases and control had hypotonia respectively. 84% of the cases had abnormal primitive reflexes whereas only 4% had that problem. 18% of the cases had bradycardia and 20% of the control had that which was not significantly different from the cases. 66% of the cases and 48% of the control had tachycardia.

Table-VII: Distribution of newborn pair of group A and group B by leukocyte count (n=100)

WBC status	Group-A (n=50)		Group- B (n=50)		*P* value
	n	%	n	%	
Normal count (5000-25000/ mm³)	44	88	43	86	
Leucopenia (<5000/mm³)	4	08	00	00	0.001^{s}
Leucocytosis (>25000/ mm³)	2	04	07	14	

Table VII shows that only 08% of the sick newborns in group-A have leucopenia but none of the group-B has leucopenia. On the other hand 04 % of the cases have leucocytosis but 14% of the controls also have the same blood picture.

Table-VIII: Distribution of newborn pair of group A and group B by presence of diagnostic markers (n=100)

Diagnostic markers	Group – A (n=50)		Group – B (n=50)		*P* value
	n	%	n	%	
Thrombocytopenia	35	70	09	18	
Positive CRP (1st sample)	37	74	15	30	
Both thrombocytopenia & positive CRP	32	64	02	04	0.001^{s}

Table VIII shows that 70% of the cases have thrombocytopenia but 09% of the controls have that. The 1st serum sample of 74% of cases and 30% of controls show positive CRP. 64% of cases have both thrombocytopenia & positive CRP whereas only 04% of controls have both thrombocytopenia & positive CRP. The difference between blood pictures of cases and controls is statistically significant.

Table-IX: Distribution of newborn pair of group A and group B by serial measurement of CRP level (n=100)

Serial measurement of CRP level	Group-A (Case)		Group-B (Control)		*P* value
	n	%	n	%	
On admission or during enrollment in study	50		50		$<0.001^{s}$
Positive	37	74	15	30.0	
Negative	13	26	35	70.0	
After 24 hours of enrollment of study	46		50		
Positive	38	82.60	21	42.0	$<0.001^{s}$
Negative	08	17.40	29	58.0	
After 72 hours of enrollment of study	39		50		
Positive	26	66.67	14	28.0	$<0.001^{s}$
Negative	13	33.33	36	72.0	
Before discharge	37		50		
Positive	07	18.92	07	14.0	$<0.10^{ns}$
Negative	30	81.08	43	86.0	

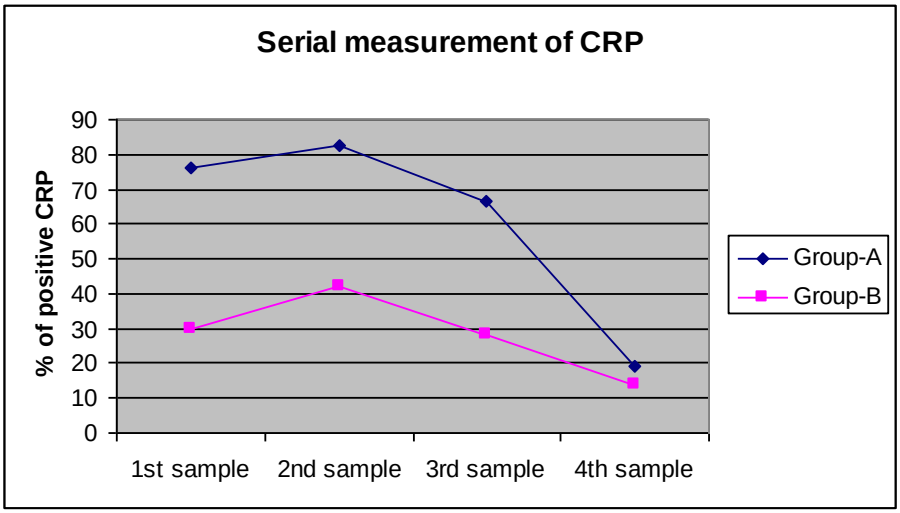

Fig-2: Serial measurment of CRP

Above Table and figure shows that the distribution of newborn pair of group A and group B by serial measurement of CRP level. On admission or during enrollment in study 74% of the cases in group-A had positive CRP and 30% of the control in group-B had positive CRP. There was significant difference between two groups. In next 24 hours 4 cases in group-A were expired. After 24 hours of enrollment of study, among the 46 cases 38 (82.60%) had positive CRP level and 21(42%) of control in group-B had positive CRP level. The difference is significant. In next 48 hours, 7 cases in group-A were expired. After 72 hours of enrollment of study, out of 39 cases in group-A 26(66.67%) cases had positive CRP level and 14(28%) of the control in group-B had positive CRP level. Out of 50 cases in group-A, 34 cases were discharged with clinical improvement and 3 cases were discharged with referral to institute with NICU facilities. Before discharge 7(18.92%) of cases had positive CRP level and 7(14%) control had positive CRP level that showed no significant difference between case and control.

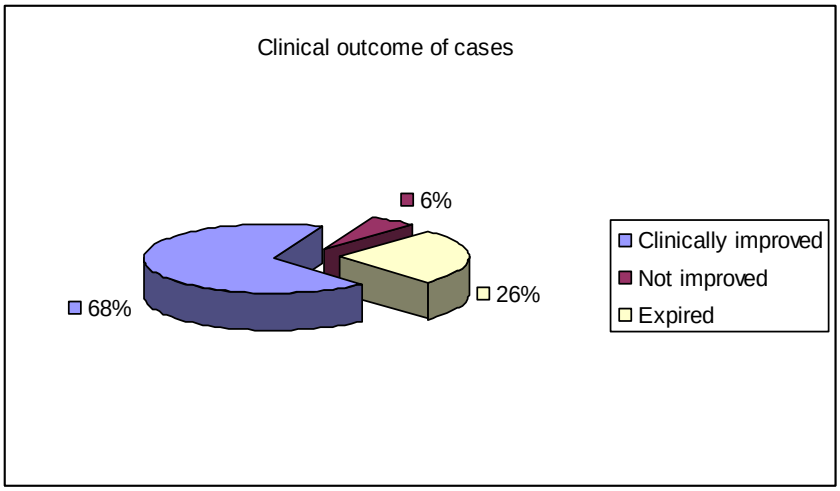

Fig-3: Clinical outcome of suspected cases(n=100)

Of the 50 cases of suspected sepsis, 68% of cases were improved clinically by getting antibiotics and discharged, 6% of cases were not improved and discharged with referral and 26% cases were expired. Among 37 cases that were discharged, 30 cases had normal CRP level before discharged.

DISCUSSION

Intrapartum antibiotic prophylaxis was given to mothers of 32% of newborn in group–A and 58% of newborn in group- B. There is significant difference between both groups. Mode of delivery has no statistically different role in both group-A and group-B. Sterile or clean instruments were used to cut cord in 74% of cases in group-A, whereas that was done in 100% of the control. So using unsterile instrument to cut cord is a risk factor of neonatal sepsis. History of maternal infection, PROM or leaking membrane, prolonged labor, unhealthy umbilical stump, repeated or unsterile vaginal examination make a significant

deference between newborn pair of group A and group B but not assisted delivery and abnormal liquor. So the present study shows the positive correlation between these risk factors and suspected sepsis as well as raised CRP. 46% of mothers in group A and 22% of mothers in group B have history of PROM. So there is significant difference between both groups in relation with PROM or leaking membrane. Another Table shows the distribution of newborn pair of group A and group B by clinical features. Temperature instability, reluctant to feed, lethargy or excessive sleepiness, apnea, poor perfusion, sclerema, gastrointestinal problem, difficulty in respiration, convulsion, hypotonia and abnormal primitive reflexes are the clinical features that are present in newborn babies of group-A and make significant difference in between cases and control. Bradycardia makes no significant difference in both groups. Usually newborn baby with sepsis is associated with hypothermia. But fever whenever developed should be considered to be ominous sign of sepsis being other cause of hyperthermia should be excluded. The temperature of the infant with sepsis may also be normal. Phagocytes of infant born after normal labor are able to produce sufficient concentration of leukocytic pyrogens whereas those born after caesarian section have markedly suppressed ability to produce leukocytic pyrogens [23]. In our study 68% of septic newborn developed temperature instability and normal body temperature was found in 32% cases. Our present study shows that only 08% of the newborns in group-A have leucopenia but none of the group-B has leucopenia. On the other hand 04 % of the cases have leucocytosis but 14% of the controls also have the same blood picture. We also find that 70% of the cases and 18% of the controls have thrombocytopenia. The 1st serum sample of 74% of cases and 30% of controls show positive CRP. 64% of cases have both thrombocytopenia & positive CRP whereas only 04% of controls has both thrombocytopenia & positive CRP. Table IX showes the distribution of newborn pair of group A and group B by serial measurement of CRP level. Among four serial measurement of CRP, first three serum samples shows significant difference of positive CRP level between cases and controls. There is no significant difference of positive CRP level in last sample taken before discharge between cases and controls. After completing antibiotic treatment 81.08% of the cases in group- A were CRP negative. So our present study shows that serial measurement of serum CRP levels have significant role to understand the clinical course of neonatal sepsis. As well as it may be a clinical guide to see the prognosis of neonatal sepsis.

CONCLUSION AND RECOMMENDATIONS

History of maternal infection, PROM or leaking membrane, prolonged labor, unhealthy umbilical stump, repeated or unsterile vaginal examination are found to be associated risk factors with raised CRP in neonatal sepsis. Positive CRP level can be considered as an useful indicator alternative to blood culture to diagnose sepsis in neonate in our setup when it is correlated with clinical data and easily available laboratory findings i.e thrombocytopenia, total leucocyte count etc. Serial measurement of CRP can be considered as a valuable indicator to see the prognosis of neonatal sepsis. In neonatal care unit of tertiary level hospitals like ours, there is massive patient load and huge economic strain of the family of the patient. Here we usually apply empirical and prolonged use of antibiotic in suspected sepsis in fear of missing life threatening infections. Serial CRP level may help us to understand the natural course of neonatal sepsis, to initiate its prompt management, reducing cost of care and hospital staying. Following recommendations can be suggested from the result of this study for future action to combat challenges to the caring physician of the septicnewborn: Larger study should be carried out to determine the value of easily available laboratory support such as serial CRP. Huge patient load may be reduced in tertiary care hospitals by establishing neonatal care unit in district hospitals. A national guideline should be adopted on the basis of clinical data, CRP and haematological profile for the management of neonatal sepsis. Policy should be taken to improve community based obstetric care to reduce the incidence of neonatal Sepsis.

REFERENCES

1. Murray RK, Granner DK, Mayes P, Rodwell V. Harper's Illustrated Biochemistry. 28. New York: McGraw-Hill; 2009.
2. World Health Organization, Unicef. Countdown to 2015 decade report (2000-2010) with country profiles: taking stock of maternal, newborn and child survival.
3. Bangladesh Neonatal Forum. Essential Newborn Care. Dhaka: Bangladesh Neonatal Forum. Department of Paediatrics, Dhaka Medical College. 2002.
4. Bangladesh Bureau of Statistics. Millennium Development Goal: Bangladesh Progress at a Glance, Bangladesh. 2009.
5. Bangladesh Bureau of Statistics. Monthly Statistical Bulletin, Bangladesh. 2011.
6. UNICEF. What works for children in South Asia: Newborn care an overview. Kathmandu, Nepal: UNICEF Regional Office for South Asia. 2004.
7. Hossain MM, Amin, MR, Akbar MS. Mortality determination among critically ill newborn treated in intensive care unit. *D S (child) H J*. 2000; 16, 1-9.
8. Chowdhury MA, Banu K, Rahman M, Rahman M. Birth asphyxia-a prospective study in Dhaka Shishu Hospital. DS (Child) HJ. 1996;12:18-22.
9. WHO Young Infants Study Group. Bacterial etiology of serious infections in young infants in developing countries: results of a multicenter study. The Pediatric infectious disease journal. 1999 Oct 1;18(10):S17-22.

10. Khan MR, Rahman ME. Essence of Pediatrics, New Delhi, Elsevier. 2011.
11. Rennie IM, Roberton NCR. Manual of Neonatal Intensive Care. 4th ed. London, Arnold. 2002.
12. Kumary S, Pruthi PK, Mera R, Guzral VV. Infection screening in early neonatal infection. Indian J Pediatr.1993; 50, 177-81.
13. Joshi SG, Ghole VS, Niphadkar KB. Neonatal gram-negative bacteremia. The Indian Journal of Pediatrics. 2000 Jan 1;67(1):27-32.
14. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, Lemons JA, Donovan EF, Stark AR, Tyson JE, Oh W. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. Pediatrics. 2002 Aug 1;110(2):285-91.
15. Philip AG, Mills PC. Use of C-reactive protein in minimizing antibiotic exposure: experience with infants initially admitted to a well-baby nursery. Pediatrics. 2000 Jul 1;106(1):e4-.
16. McI Niosh N, Helms PJ, Smyth, RL, Logan S, eds. Forfar & Arneil's Textbook of Pediatrics. 7th ed. London, Elsevier. 2008.
17. Chies C, Pellegrim G, Panero A, Osbom JF, Singore F, Asumma HJ. C-reactive protein, interlukin-6 and procalcitonin in immediate postnatal period: influence of illness severity, risk status, antenatal and perinatal complications and infection. Clin Chem. 2003; 49. 60-68.
18. Ottolini MC, Lundgren K, Mirkinson LJ, Cason S, Ottolini MG. Utility of complete blood count and blood culture screening to diagnose neonatal sepsis in the asymptomatic at risk newborn. The Pediatric infectious disease journal. 2003 May 1;22(5):430-4.
19. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics. 1998 Oct 1;102(4):e41-.
20. Weitkamp JH, Aschner JL. Diagnostic use of C-reactive protein (CRP) in assessment of neonatal sepsis. NeoReviews. 2005 Nov 1;6(11):e508-15.
21. Chowdhury AK, Rahman MM, Karim AQ. Characteristics of septicaemia in newborns in Dhaka Shishu Hospital. ORION. 1998 Sep;1.
22. Nahar N. Hand Book on Essential Newborn Care for Doctors & Nurses. Dhaka: Bangladesh Neonatal Forum. 2009.
23. Harris MC, Polms RA. Neonatal Septicemia. Ped Clin North Am. 1983; 30, 243-258.