Human Neutrophil Lipocalin As An Early Marker Of Neonatal Sepsis

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Abstract:

Objective was to evaluate the potential usefulness of measuring serum human neutrophil lipocalin (HNL) as an early predictor of neonatal sepsis.

Methodology:

The study was done on thirty six neonates admitted with clinical signs of infection in NICU of EL- Galaa teaching Hospital duringthe period from February 2009 to August 2010. Complete blood count, C reactive protein and NHL concentration by ELISA were assessed on day 1& 3 and 5. Neonates were subdivided in to: proven sepsis group, (GI:18) (with positive blood culture) and non proven sepsis group (G2: 18) (with clinical feature of sepsis but negative blood culture). Additionally, fifteen healthy neonates were recruited at age of (1- 5) days as control group.

Results:

Serum of HNL was significantly higher in proven sepsis group than non proven sepsis group and control group in the first day of life and also on days 3- 5 ($p < 0.003$). Moreover, A significant decline of HNL levels was observed in survivors on day 3- 5. There was no statistical significant difference between proven sepsis group and non proven sepsis group regarding total leucocytic count, absolute neutrophil count, I/T ratio, platelet count and CRP on day 1. There is a positive significant correlation between HNL and CRP from day 1 of life ($r= 0.566$, $p < 0.001$).

Conclusion:

Human neutrophile lipocalin level increases in the first day of life, in early onset sepsis. serum, HNL was found to distinguish between proven infected and non-proven infected newborns. The HNL values correlated with CRP, the correlation being strongest between CRP and HNL in the first day of life.

Keywords:

Human neutrophil lipocalin, neonatal sepsis, newborn infants, early marker.

Introduction:

Neonatal sepsis is defined as a clinical syndrome of bacteremia with signs and symptoms of infection in the first four weeks of life. When pathogenic bacteria gain access into the blood stream, they may cause overwhelming infection without much localization termed as septicemia or may get predominantly localized to the lungs resulting in pneumonia, or the meninges causing meningitis. Early onset and late onset sepsis are defined on the basis of presentation within 72 hours or after 72 hours of life respectively (Khinchi et al., 2010).

Currently initial diagnosis is based upon clinical suspicion accompanied by nonspecific clinical signs and is confirmed upon positive microbiologic culture results several days after institution of empiric therapy. There exists a significant need for rapid, objective, in vitro tests for diagnosis of infection in neonates who are experiencing clinical instability (Kita et al., 2006). Neonatal sepsis has a high mortality and morbidity. Timely detection and treatment will help in decreasing mortality and morbidity (Himayun et al., 2010).

Human neutrophil lipocalin (HNL) is a newly discovered protein from human neutrophil secondary granules. It is regarded as a specific marker of neutrophil activity. It is located in bone marrow cells as well as lung, bronchial and colonic epithelial cells (Carlson et al., 2002).

Increased concentrations of HNL have been demonstrated in the sera of patients with acute bacterial infections, and HNL appears to be more specific and sensitive in the distinction between viral and bacterial infections (Fjaertoft et al., 2005).

The release of HNL is not increased in healthy term newborns at birth, but that neutrophils from newborns, even premature infants, are capable of rapidly releasing HNL upon bacterial or fungal stimulation in vivo. (Bjorkqvist et al., 2004).

The aim of the present study was to investigate whether neonatal sepsis was associated with early elevation of serum HNL, which would help in early and accurate diagnosis of neonatal sepsis.

Subjects And Methods:

This prospective case control study done on thirty six neonates aging from day one of life admitted with suspected infection during the period from February 2009 to August 2010, 15 healthy neonates as a control group; signed approval consents were taken from parents. The sample is simple random sample; cases were classified into three groups:

- Group I: proven sepsis group included 18 cases with clinical picture of sepsis and a positive blood culture.
- Group II: non proven sepsis group included 18 cases of neonates with clinical features of sepsis and non specific laboratory markers of sepsis.
- Group III: control group included 15 healthy newborns with absence of any clinical picture of sepsis.

All cases were subjected to the following:

1. Careful history taking: personal., antenatal., natal and postnatal.
2. Full clinical examination: for early detection of neonatal sepsis.
3. Laboratory Investigation:
   a. Sample Collection: From each neonate of the present study, three milliliters of blood were collected on the first day of life (day 1) and repeated on day 3- 5 postnatally. Each sample was divided in two tubes; the first tube was EDTA tube for complete blood count. The second tube was a plain tube into which blood was left to clot and serum was separated and divided into two parts, one was used for CRP determination, while

the other was stored at 20°C till assay of serum human neutrophile lipocalin.

For blood culture another 3 ml of venous blood was taken from patient group not control group which requested at the age of (0- 24) hours.

b. Analytical Method:

- Complete blood count: The blood count was performed using automated blood counter (Cell- DYN 1700). The differential leucocytic counts were performed manually from blood film and expressed in absolute count values (Metrov and Crain, 2005).
- Semiquantitative C- reactive protein (CRP): Using latex agglutination test, CRP kit Teco Diagnostics, 1268N Lakeview Ave. Anaheim, USA. It was considered positive when the titer was >6mg/dl (Philip, 2000).
- Blood Cultures: Using neonatal bottles supplied and subculture on blood agar plate (Decamp et al., 2009).
- Serum Human Neutrophil Lipocalin: Was performed using Quantikine ELIZA kit (R& D systems; Winneapdis, MN) (Björkqvist etal, 2004).

Statistical Methods:

All studied statistical methods were performed using SPSS 17 soft ware package (Statistical Package of Social Science).All numeric variables were expressed as Mean± SD. Comparison of different variables in various groups was done using student t test. Analysis of variance (ANOVA) test was applied for comparison of paired observation. Statistical significant was set at P>0.05. The relation between the various numerical parameters was studied by Person correlation coefficient (r) test. The diagnostic performance of measured markers was analyzed using (ROC).

Moreover, chi square test was used to analyze qualitative variables. Using (SPSS ver.17) software package.

Results:

Table (1) shows that there is a non significant statistical difference between group I and group II as regarding demographic& fetal risk factors.

Table (1): Clinical characteristics and fetal risk factors of the studied groups

Variables	Group I no=18	Group II no=18	P-Value	S
Multiple Gestation:				
Single No (%)	14 (77.78%)	17 (94.44%)	0.269	NS
Twin No (%)	2 (11.11%)	1 (5.56%)		
Triplet No (%)	2 (11.11%)	0 (0.00%)		
Gestational Age				
Range (Wks)	(30- 39)	(32- 40)	0.99	NS
Mean ± Sd	35±2.058	35.556±2.479		
Apgar 1ts Min				
Range	(2.0- 6.0)	(2.0- 5.0)	0.739	NS
Mean ±Sd	3.611±1.145	3.500 ±0.786		
Apgar 5 Min				
Range	(5.0- 10.0)	(6.0- 9.0)	0.660	NS
Mean ±Sd	7.444±1.199	7.611±1.092		
Birth Weight				
Range (Kg)	(1.1- 3.7)	(1.3- 3.5)	0.967	NS
Mean±Sd	2.378±0.708	2.368±0.761		
Length				
Range (Cm)	(45.0- 50.0)	(43.0- 50.0)	0.648	NS
Mean±SD	47.333±1.455	47.056±2.100		
Head Circumference				
Range (Cm)	(30.0- 35.0)	(30.0- 35.0)	0.616	NS
Mean±SD	33±1.372	32.778±1.263		
Sex:				
Males No (%)	12 (66.67%)	11 (61.11%)	0.729	NS
Females No (%)	6 (33.33%)	7 (38.89%)		
Maturity:				
Preterm No (%)	15 (83.33%)	11 (61.11%)	0.137	N S
Full Term No(%)	3 (16.67%)	7 (38.89%)		
ETT No (%)	9 (50%)	7 (38.89%)	0.411	NS

NS= non significant S= significant HS= highly significant

Table (2): It shows a statistical significant difference regarding PROM≥ 18 hrs and intrapartum use of antibiotics between group I, group II while other parameters are not significant.

Table (2): Comparative statistics of maternal risk factors for neonatal sepsis in the studied groups

Maternal History	Group I No=18	Group II No=18	P Value	S
PROM≥18hs no (%)	13 (72.22%)	6 (33.33%)	0.045	S
Intrapartum Fever no(%)	4 (22.22%)	5 (27.78%)	0.70	NS
Chorioamnionitis no(%)	4 (22.22%)	5 (27.78%)	0.70	NS
Intrapartum Antibiotics no(%)	17 (94.44%)	14 (77.78%)	0.015	S
Prenatal Steroids no (%)	5 (27.78%)	5 (27.78%)	1.000	NS
Hypertension/pre-eclampsia no (%)	0 (0.00%)	2 (11.11%)	0.146	NS
Other disease Gestational DM no (%)	2 (11.11%)	6 (33.33%)	0.109	NS
MSAF no (%)	1 (5.56%)	2 (11.11%)	0.546	NS
Maternal Age				
Range (Yrs)	(18.0- 36.0)	(19.0- 37.0)	0.891	NS
Mean ± Sd	28.0±4.982	27.722±5.004		
Parity				
Multiparity no (%)	9 (5o%)	10 (55.56%)	0.738	NS
Primiparous no (%)	9 (50%)	8 (44.44%)		
Socioeconomic Factors				
Low no (%)	15 (83.33%)	13 (72.22%)	0.423	NS
Mod no (%)	3 (16.67%)	5 (27.78%)		
Delivery:				
SVD no (%)	5 (27.78%)	6 (33.33%)	0.717	NS
LSCS no (%)	13 (72.22%)	12 (66.67%)		

NS= non significant S= significant HS= highly significant
N.B. PROM: Premature rupture of membranes. MSAF: Meconium stained amniotic fluid.

Table (3):shows the most common organism is klebsiella followed by E.coli, Staph. aureus and the least common is Pseudomonas.

Table (3): Organisms involved in neonatal sepsis:

Organisms	Number	%
Klebsiella	11	61.11
E.Coli	4	22.22
Staph. Aureus	2	11.11
Pseudomonas	1	5.55

Table (4): there is significant decrease in platelets counts in the group I and group II less than control group and significant increase in I/T ratio in group II and group I more than control group. On the contrary, there is a non statistical significant difference between studied groups as regarding other parameters.

Table (4): Comparative hematological indices of the studied neonates on day 1

Variables	Group I No=18	Group II No=18	Control No=15	P-Value	S
WBC ($\times 10^9$/L)					
(Range)	4.4- 35.5	5.2- 28.3	7.9- 10.2	0.996	N S
Mean±SD	14.22±10.00	14.44±7.45	14.35±3.47		
Neutrophil Count ($\times 10^9$/L)					
(Range)	1.0- 16.5	1.5- 19.7	3.5- 8.7	0.650	NS
Mean±SD	7.10±6.04	8.14±5.49	6.59±1.38		
HB (Gm/Dl)					
(Range)	10.7- 20.9	10.2- 19.4	12.6- 18.3	0.832	NS
Mean±SD	15.50±3.20	15.06±2.77	14.98 ±1.85		
I/T Ratio					
Range	0.2- 0.5	0.2- 0.6	0.2- 0.2	0.000	HS
Mean±Sd	0.33±0.09	0.27±0.09	0.20±0.0		
Platelets ($\times 10^9$/L)					
Range	32.0- 315.0	80.0- 350.0	160.0- 400.0	0.001	HS
Mean± SD	141.78± 68.20	192.83± 84.05	251.27± 84.10		

Table (5): there is highly statistical significant difference as regarding I/T ratio, platelets counts, CRP and HNL between group I & control group. Also, there is statistical significant difference as regarding I/T ratio, and CRP between group II & control group. On the other hand, comparative statistics between group I and group II revealed a highly significant difference only as regard HNL.

Table (5): Comparison between studied groups as regarding I/T ratio, Platelets, CRP and HNL on day 1

Variables / Groups	I/T ratio (mean±SD)	P	S	Platelets×10^9 (mean ±SD)	P	S	CRP(mg/dl) (mean ±SD)	P	S	HNL(ng/ml) (mean ±SD)	P	S
Control Vs	0.20±0.00	0.000	HS	251.27±84.10	0.001	HS	6.00±0.00	0.001	HS	85.60±68.11	0.002	HS
Group I	0.33±0.91			141.78±68.11			19.00±12.56			532.89±582.32		
Control Vs	0.20±0.00	0.020	HS	251.27±84.10	0.096	NS	6.00±0.00	0.022	S	85.60±68.11	0.645	NS
Group II	0.27±0.88			192.83±84.05			15.33±10.34			196.11±89.91		
Group I Vs	0.33±0.09	0.070	NS	141.79±68.11	0.138	NS	19.00±12.56	0.497	NS	532.89±582.32	0.017	HS
Group II	0.27±0.09			192.83±84.05			15.33±10.34			196.11±89.91		

Table (6): there is significant decrease in HB% and platelet counts on days 3- 5 between the group I and group II less than control group. Also, there is significant increase in I/T ratio between the group I& group II more than control group.

Table (6): Hematological indices of the studied neonates on days 3- 5

Variables	Group I No=18	Group II No=18	Control No=15	P-Value	S
WBC (×10^9/L)					
(Range)	3.9- 40.8	4.8- 28.6	7.9- 20.2	0.675	NS
Mean ±SD	13.34±10.32	12.01± 6.81	14.35± 3.47		
Absolute Neutrophil count (×10^9/L)					
(Range)	1.1- 25.9	1.4- 16.9	3.5- 8.7	0.935	NS
Mean ±SD	7.23±7.01	7.11± 5.07	6.59± 1.38		
HB% (Gm/Dl)					
(Range)	7.5- 15.3	9.5- 15.6	12.6- 18.3	0.000	HS
Mean ±SD	12.25±2.39	12.13± 1.82	14.98± 1.85		
I/T Ratio					
(Range)	0.2- 0.6	0.2- 0.3	0.2- 0.2	0.000	HS
Mean ± Sd	0.32±0.08	0.25±0.04	0.20±0.00		
Platelets Count (×10^9/L)					
(Range)	46.0- 185.0	64.0- 265	160.0- 400.0	0.000	HS
Mean ±SD	111.28± 47.29	142.39± 53.82	251.27± 84.10		

Table (7): there is highly statistical significant difference between group I & control group as regarding I/T ratio, platelets count, CRP and HNL, also, there is statistical significant difference between group II & control group as regarding platelets count, CRP and non statistical significant difference regarding HNL & I/T ratio. Regarding, group I & group II, there is statistical significant difference in I/T ratio and HNL in days 3- 5.

Fig. (1): There is highly positive significant correlation between HNL and CRP in day1.

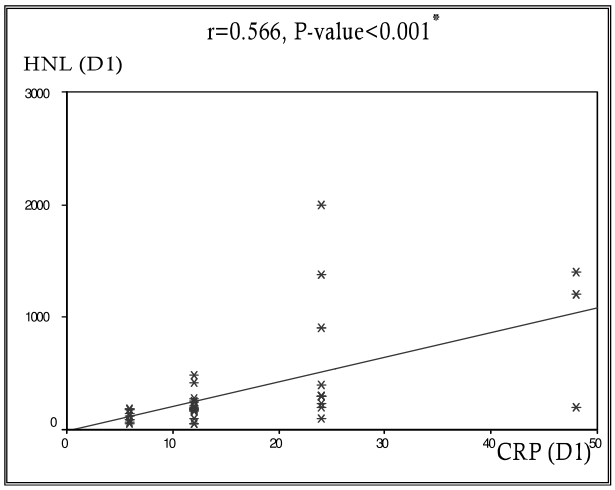

Table (7): Comparison between studied groups as regarding I/T ratio, Platelets, CRP and HNL on days 3- 5:

Variables / Groups	I/T ratio (mean±SD)	P	S	Platelets ×10^9 (mean ±SD)	P	S	CRP(mg/dl) (mean ±SD)	P	S	HNL(ng/ml) (mean ±SD)	P	S
Control Vs	0.20±0.00	0.000	HS	251.27±84.10	0.000	HS	6.00±0.00	0.000	HS	85.60±68.11	0.001	HS
Group I	0.32±0.08			111.28±47.29			45.33±30.40			205.28±259.91		
Control Vs	0.20±0.00	0.054	NS	251.27±84.10	0.000	HS	6.00±0.00	0.000	HS	85.60±68.11	0.185	NS
Group II	0.25±0.03			142.39±53.82			36.67±15.11			90.78±57.23		
Group I Vs	0.32±0.08	0.001	HS	111.28±47.29	0.301	NS	45.23±30.40	0.409	NS	205.28±259.91	0.001	HS
Group II	0.25±0.04			142.39±53.82			36.67±15.11			90.78±57.23		

Table (8): Shows that there is statistical significant difference between survivors & non

Survivors cases in group I as regarding serum HNL concentration on day 3- 5 but not on day 1.

Table (8): Comparative statistics of serum HNL concentration between survivors & non survivors among patients of group I:

Variables / Groups	Survivors (Mean ±SD) ng/ml	Non Survivors (Mean ±SD) ng/ml	P	S
Hnl (Day 1)	320.00±432.00	520.30 ± 483.40	0.267	NS
HNL (Day3- 5)	113.10± 127.50	270.12± 322.90	0.042	S
P.Value	0.003	0.091		
S	S	NS		

Fig: (2)

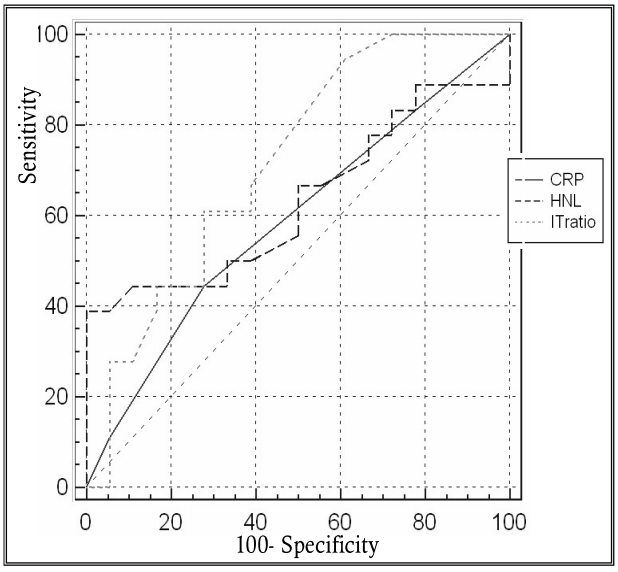

Table (9): Diagnostic performance of CRP, HNL & I/T ratio on day 1:

	CRP (mg/dl)	HNL (ng/ml)	I/T Ratio
Best Cut Off	>12	>184	>0.27
Sensitivity	44.4	66.6	61.1
Specificity	72.2	50.0	72.2
PPV	61.5	57.7	68.7
NPV	56.5	60.0	65.0

Discussion:

Newborns are uniquely susceptible to overwhelming bacterial infections. The incidence of early- onset bacterial infections ranges from (1- 10) per 1000 live births and the related mortality ranges between 15% and 30%. The morbidity among the survivors is also high. Furthermore, newborns that develop sepsis often deteriorate rapidly (Ramesh and Amitha, 2010).

Neonatal sepsis is the single most important cause of neonatal deaths in the community, accounting for half of them. If diagnosed early and treated aggressively with antibiotics and good supportive care, it may be possible to save most cases of neonatal sepsis. Surviving infants can have significant neurological sequelae as a consequence of CNS involvement, septic shock or hypoxemia secondary to severe parenchyma lung disease (Khinchi et al., 2010).

Clinical characteristics of our study population revealed that PROM≥18 hours was the most significant risk factor in proven sepsis group while other parameters such as gestational age, sex, birth weight, mode of delivery, parity, Apgar score at 1st and 5 minutes were not significant.

In the current study, different organisms causing septicemia for proven sepsis cases with positive blood culture were that; the most frequently cultured organism was Klebsiella (61.11%) followed by E. coli (22.22%) followed by Staphylococcal aureus (11.11%) and only (5.55%) for Pseudomonas.

Isolation of pathogenic microorganisms from the blood is usually considered to be the most specific method of diagnosing neonatal sepsis (Fos et al., 2010). On the other hand, several observations suggest that the sensitivity of this diagnostic criterion may be low when the test is applied to neonates (Schelonka et al., 1996). Moreover, Polin, (2003) found that blood culture which is unreliable when intrapartum antibiotics have been administered. Even when intrapartum antibiotics are not used, postnatal blood cultures fail to detect bacteremia in an appreciable number of cases. This is because bacteremia is transient or intermittent, an insufficient amount of blood has been obtained for culture and processing of specimens is suboptimal.

Infective parameters routinely used for sepsis screen utilized in our studied neonates, on the first

day of life, revealed that the I/T ratio, total leucocytic counts, absolute neutrophil counts, platelets count and CRP were unable to differentiate between proven and non proven sepsis group.

Serum concentrations of CRP increase several hundredfold in response to bacterial infection, making it an attractive diagnostic test for neonatal sepsis. Several hours are needed for CRP levels to increase in serum (including activation of neutrophils, elaboration of interleukin- 6, and induction of hepatic synthesis of CRP) therefore limiting the sensitivity of this test in diagnosing neonatal sepsis. CRP levels are consistently elevated 24 to 48 hours after the onset of infection; therefore serial normal levels may be useful for identification of infants who do not have bacterial infection (Himayun et al., 2010).

Quantitative serial CRP levels, obtained 24 hours after the onset of signs and symptoms of infections, with serial measurements 12 to 24 hours apart, offer the most sensitive and reliable information. At least 2 CRP levels, obtained 24 hours apart, with levels ≤10mg/L are needed to identify infants unlikely to be infected. The use of CRP to exclude infection may allow clinicians to discontinue antibiotics at 48 hours in selected infants, limiting extended unnecessary antibiotic exposure (Joan et al., 2003).

The specificity for CRP in this study between proven sepsis group and non proven sepsis group on day 1 was 72.2% and its sensitivity was 44.4% .It means that it has modest specificity and low sensitivity. This is agree with McKenney, 2001 since the concentration of CRP increases rather slowly in the initial phase, its sensitivity at the time of sepsis evaluation is only 60%. Serial quantities measurements at 24 and 48 hours after the onset of sepsis considerably improve the sensitivity about 82% and 84% respectively. Thus, CRP can be considered as a specific but late marker of neonatal infection.

On repeating the infective parameters routinely used for sepsis screen on days 3- 5 of life, the results revealed that the I/T ratio was only significant parameter while total leucocytic counts, absolute neutrophil counts, platelets count and CRP were unable to differentiate between proven and non proven sepsis group. The increase in I/T ratio on days 3- 5 due to migration of neutrophils out of the capillaries into the infected site, where they ingest and destroy the pathogens causing the infection. When the demand for the neutrophils exceeds the supply in circulation, immature neutrophils are released into the blood to help fight off the infection. This is labeled a "left shift" and indicates that an infection may be present. As the infection diminishes and neutrophils are replenished, a "shift to the right" occurs, indicating that everything is back to normal (Benuck and David, 2003).

Serum HNL level on the first day of life among patients with proven sepsis group ranged between (500- 2000) ng/ml with mean value of (532.889± 582.318) ng/ml, while in non proven sepsis group it ranged between (60.0- 400.0) ng/ml with mean of 196.111±89.914ng/ml. On the other hand, serum HNL in proven sepsis group in days 3- 5 ranged between (20.0- 1040.0) ng/ml with a mean value of (205.278± 259.912) ng/ml and in non proven sepsis group HNL ranged between (16.0- 200.0) ng/ml with a mean value of 90.778±57.231.

The results of our study indicated that in neonates with early onset sepsis HNL levels were higher on the first day of life, than corresponding levels in non proven group, suggesting that HNL may be an early inflammatory marker for infection. Despite a subsequent decline in HNL levels that was demonstrated among all studied groups on day 3- 5, the significant difference between the proven and

non proven sepsis group persisted.

These findings agree with Björkqvist et al. (2004) who found that HNL level in serum distinguish between proven sepsis patients and non proven sepsis patients. Also, the increased HNL level both in proven sepsis patients and non proven sepsis patients included≤ 24hr of age verify that neonatal neutrophiles are capable of releasing HNL even during the first day of life. Medical conditions other than invasive infection causing neutrophils release of HNL in lower levels in patients belonging to the non proven sepsis group might be another explanation for the released HNL level in these newborns. Respiratory disturbances such as RDS and TTN were found in 40% of the children classified as non proven infection included <24hr of age. In these children HNL levels was still elevated at 3- 5 days but at much lower levels.

Björkqvist et al. (2004) found that in symptomatic patients of ages≥ 24hours, HNL to be a useful tool for identifying infected patients since CRP level was included in the criteria for infection, they found that HNL peaked at inclusions in the study, indicating that HNL is an earlier inflammatory marker than CRP, since HNL levels probably more correctly reflect ongoing bacterial infection. Also his study showed that the release of HNL was not increased in healthy term newborns at birth, but that neutrophiles from newborns even premature infants are capable of rapidly releasing HNL upon bacterial or fungal stimulation in vivo.

Our results have shown that serum HNL levels in proven sepsis group demonstrated much lower levels in survivors as compared to non survivors, moreover, a significant decline of HNL level was observed in survivors on day 3- 5. Xu and Venge (2000) found that HNL is a better marker for monitoring antibacterial treatment with a decrease in serum HNL levels and elevated only when an active bacterial infection is at hand. However, Wheeler et al. (2009) concluded that serum HNL was not significantly different between survivors and non-survivors in his study on pediatric age group.

In the current study, a highly positive significant correlation was found between HNL and CRP in day 1 (r =0.566, P=0.001). These findings agrees with Björkqvist et al. (2004) who found that CRP peaked 1 day later than HNL and the difference in mean HNL was highly statistically significant at all measurement points (HNL days: 0- 3). Moreover, the HNL values correlated with CRP, the correlation being strongest between CRP1 and HNL1 (r=0.697, P=0.0001) but there is no significant correlation between HNL and other laboratory parameters.

In this study, gender and mode of delivery showed no influence on HNL levels in the studied groups. Huynh et al. (2009) reported that variation in sex, gestational age and postnatal age, although present, are probably clinically unimportant in the level of urinary HNL.

In this study HNL shows a sensitivity of 66.7% and specificity of 50.0% for HNL at a cut- off value of> 184ng/mL on day 1, Björkqvist et al. (2004) who found HNL sensitivity for infection of 76% and a specificity of 64% on day 1 at a cut- off value of 275 ng/ml. The positive predictive value was 46% and the negative predictive value was 87%.

Gustav et al. (2005) concluded that HNL seems to reflect the present and ongoing infection, whereas CRP also reflects past infection with a lag of several days. Also, the initial kinetics of HNL and CRP are different with HNL having an elimination rate (t½) of (10- 20) min (Axelsson et al., 1995) and CRP a turn over 19h (Vigushin et al., 1993). Thus, markers such as HNL should be the most useful tools in the therapy monitoring of acute infection.

In patients admitted very early with bacterial infections, CRP levels may be low because of the

delay in production as response to cytokines such as IL- 6, whereas the levels of HNL are raised at an early stage. HNL is a product of blood neutrophiles and is therefore expected to correlate to the number of circulating neutrophiles (Xu et al., 1994).

Xu and Venge, (2000) found that HNL concentration in cord blood from term healthy neonates was similar to the reported HNL level in sera from healthy adults. There was no difference in HNL level between healthy term neonates at birth and at 3- 5 days of age. This is remarkable, since the cord blood neutrophiles are expected to be activated as a result of labour stress (Ambruso et al., 1987). On the contrary, Björkqvist et al. (2004) suggested that activation of neutrophils during delivery is limited in absence of inflammatory stimulus.

Conclusion:

Human neutrophile lipocalin level increases in the first day of life, in early onset sepsis. serum, HNL was found to distinguish between proven infected and non proven infected newborns. The HNL values correlated with CRP, the correlation being strongest between CRP and HNL in the first day of life.

References:

1. Ambruso DR, Bentwood B, Henson BM, Johnston RB: Oxidative metabolism of cord blood neutrophils: relationship to content and degranulation of cytoplasmic granules. **Pediatr Res**, 1987; 18:1148- 1153.
2. Axelsson L, Bergenfeldt M, Ohlsson K. Studies of the release and turnover of a human neutrophil lipocalin. **Scand J. Clin Lab Invest** 1995; 55:577- 88.
3. Benuck L and David RJ: Sensitivity of published neutrophil indices in identifying newborn infants with sepsis. **J. pediatr**: 2003; 103:961- 963.
4. Björkqvist M, Kallman J., Fjaertoft G, Xu S, Venge P., SchollinJ. Human neutrophil lipocalin: normal levels and use as a marker for invasive infection in the newborn. **Acta Paediatr** 2004; 934:534- 9.
5. Fos N, Gomis R, Gomis C, Rubio J., Justich P, Valera J., ChicanoFand Borrajo E: Blood Culture From The Umbilical Vein In The Diagnosis Of Neonatal Sepsis. The Internet **Journal of Pediatrics and Neonatology**: 2010 Volume 12 Number 1.
6. Gustav F, Tony F, Shengyuan XU and Venge P: Human neutrophil lipocalin as a diagnostic tool in children with acute infections: A study of kinetics. **Acta Paediatr**: 2005; 94:661- 666
7. Himayun M, Ahmad S, and Rasool A: Role Of C- Reactive Protein In Early Onset Neonatal sepsis. The Internet **Journal of Pediatrics and Neonatology**. 2010 Volume 11 Number 2.
8. Huynh TK, Bateman DA, Parravicini E, et al.: Reference values of urinary neutrophil gelatinase associated lipocalin in very low birth weight infants. **Pediatr Res**: 2009; 669:528- 532.
9. Joan M, Hengst, RNC, MSN, ARNP: The role of C- reactive protein in the Evaluation and Management of Infants with Suspected Sepsis. Advances in Neonatal Care Official **Journal of the National Association of Neonatal Nurses**, e Medicine: 2003.
10. Khinchi YR, Anit Kumar and Satish Yadav: Profile of Neonatal sepsis. **Journal of college of Medical Sciences- Nepal**: 2010; Vol.6, No.2, 1- 6.
11. Mc Kenney WM: Understanding the neonatal immune system: High risk for infection.**Crit Care Nurse**: 2001; 21(6):35- 47.
12. Nupponen I, Venge P, Pohjavuori M, Lassus Pand Andersson S: Phagocyte activation in preterm infants following premature rupture of the membranes or 23- chorioamnionitis. **Acta**

Paediatr: 2000; 89:1207- 12.

13. Polin R: The "Ins and Outs" of neonatal sepsis. **J. Pediatr**: 2003; 143: 3- 4.
14. Ramsh Bhat Y and Amitha: The performance of hematological screening parameters and CRP in early onset neonatal infections. **Journal of Clinical and Diagnostic Research** (2010): December; Vol: 4, Issue 6: 33331- 33336.
15. Schelonka RL, Chai MK, Yoder BA, Hensley D, Brockett RM, Ascher DP: Volume of blood required to detect common neonatal pathogens. **J. Pediatr**, 1996; 129:275- 278.
16. Vigushin DM, Pepys MB, Hawkins PN. Metabolic and scintigraphic studies of radioiodinated human C- reactive protein in health and disease. **J. Clin Invest** 1993; 914:1351- 7.
17. Wheeler DS, Devarajan P, Ma Q, et al.: Serum NGAL as a marker of AKI in critically ill children with septic shock. **Crit Care Med**, 2009; 36: 1297- 1303.
18. Xu SY and Venge P: Lipocalin as biochemical marker of disease. **Biochem Biophys Acta**, 2000; 18; 1482 (1- 2): 298- 307.
19. Xu SY, Pauksen K, and Venge P. Serum measurements of human neutrophil lipocalin [HNL] discriminate between acute bacterial and viral infections. **Scand J. Clin Lab Invest** 1994; 55:125- 31.

الملخص

دراسة ليبوكالين البشرى فى الخلايا متعددة الأنوية كإحدى الدلائل المبكرة فى تشخيص التسمم الدموى فى الأطفال حديثى الولادة

إن التسمم الدموى يمثل تهديداً خطيراً للحياة فى الأربعة أسابيع الأولى من العمر، وهو السبب الرئيسى للمضاعفات والوفاة فى الأطفال حديثى الولادة بالرغم من استخدام المضادات الحيوية.

يتم حاليا التشخيص المبكر اعتمادا على الاشتباه الطبى مصحوبا بعلامات طبية غير محددة ويتم تأكيده بمزرعة ايجابية للكائنات الدقيقة والتى تظهر نتيجتها بعد عدة ايام من بدء العلاج التجريبى.

يعتبر النيوتروفيل ليبوكالين الآدمى بروتين مكتشف حديثا من الحويصلات الثانوية للنيوتروفيل الادمى وهو يعمل مكملاً للاكتوفرين كعامل قوى للدفاع ضد البكتريا عن طريق تقليل الحديد بالجهاز المناعي.

الهدف من الدراسة:

تهدف هذة الدراسة الى قياس مستوى بروتين النيوتروفيل ليبوكالين كعامل توقع مبكر لحدوث تلوث ميكروبى بالدم فى الاطفال حديثى الولادة مما يساعد على التشخيص واختيار العلاج المناسب.

منهجية البحث:

شملت الدراسة ست وثلاثون طفل حديثي الولادة مكتملى وناقصى الوزن ويتراوح عمرهم الجنينى بين ٣٢ إلى٤١ أسبوع. وكذلك تم دراسة خمسة عشر طفل حديثي الولادة مكتملى وناقصى الوزن من الاصحاء كمجموعة ضابطة. هؤلاء الأطفال هم من الموجدين بوحدة الرعاية المركزة للأطفال حديثى الولادة فى مستشفى الجلاء التعليمى للنساء والولادة والأطفال فى الفترة بين فبراير ٢٠٠٩ حتى اغسطس ٢٠١٠.

ولجميع الأطفال تم عمل الاتى:

١. دراسة تاريخية كاملة للأم
٢. دراسة تاريخية كاملة للطفل
٣. فحص أكلينيكى شامل
٤. التحاليل الأتية فى اليوم الأول من العمر وفى اليوم الثالث الى اليوم الخامس:
   - صورة دم كاملة وتفصيلية.
   - قياس نسبة البروتين التفاعلى "سى" فى الدم.
   - عمل مزرعة دم.
   - اشعة عادية على الصدر.
   - قياس نسبة بروتين النيوتروفيل ليبوكالين فى الدم.

نتائج الدراسة:

من خلال الدراسة وجد أن مستوى بروتين نيوتروفيل الليبوكالين فى الدم عند الاطفال حديثى الولاده المصابين بالتسمم الدموى اعلى من مستواه فى الاطفال الاكثر عرضه للاصابه بالتسمم الدموى اعلى من ذلك فى الاطفال الغير مصابين بالتسمم الدموى من اليوم الاول من الولادة مع ظهور مزرعة دم ايجابية فى اليوم الثالث الى اليوم الخامس مما يساعد على التشخيص المبكر لمرض تسمم الدم الجرثومى للاطفال حديثى الولادة .وكذلك يوجد علاقة بين بروتين النيوتروفيل ليبوكالين والبروتين التفاعلى "سى" من اليوم الأول من الولادة.

مجلة دراسات الطفولة

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Counseling Intervention for Parents Caring for Children with Autism

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Abstract

This study is an experimental research aimed to assess the effect of counseling intervention for parents caring for chilren with autism to help parents to provide there children with skills necessary or successful caring, enhance parents practice and coping patterns. This study was conducted at special needs care center affiliated to institute of post graduate childhood studenties and out patient clinic for children psychiatric treatment at elabassia mental health hospital. The sample consisted of 60 parents providing care for their children suffering from autism.

Data were collected through interview questionnaire sheet to assess child and parent sociodemographic charachteristics and parents practices.

Results:

1. The main results revealed that the majority of children were completely dependant on their parents on dailly living activity.
2. Counseling intervention has a positive effect on parents' care providing patterns and their stress from child dependancy.

Recommendations:

1. The study recommended necessary of continuous free health education and counseling programs for parents to improve their care.
2. Increase community awareness about childrens with autism and their rights.

Key words:

Children with autism, Parents, Practices, Counseling intervention.

Introduction

Autism is a complex developmental disability; it is a neurological based developmental disorder. It is characterized by varying degrees of impairment in communication skills, social interactions and the presence of repetitive and stereotyped behaviors, (Elbahnasawy & Girgis 2011). Onset occurs before