The value of lumbar puncture in possible late onset sepsis

Ahmed A Khattab,and Dalia M El-Lahony

Pediatrics Department, Faculty of Medicine, Menoufiya University, Egypt.
dmlahony@yahoo.com

Abstract: Background: Bacterial sepsis and meningitis continue to be major causes of morbidity and mortality in newborns. However, it is still a question whether the lumbar puncture is a necessary procedure in neonatal sepsis or a risky one that neonates need not undergo. **Aim:** The aim of this work is to determine the significance of lumbar puncture in late onset sepsis. **Patients and methods:**The study included 92 neonates, their ages ranged between 7-28 days, all of them born without complication to a healthy mothers, also all were achieving the clinical sepsis score . All newborns were subjected to thorough clinical examination, complete blood count with diffrential, blood culture and cerebrospinal fluid analysis and culture. **Results**: The results showed that 39 out of the 92 newborns with possible late onset sepsis had positive cerebrospinal fluid culture, 4 out of the 39 with meningitis had negative blood culture. Using relative risk, bulging anterior fontanel (RR= 2.47), apnea (RR= 2.21), irritability (RR= 2.02) and seizures (RR= 2.00) increased the risk of acquiring meningitis. By comparing blood culture and cerebrospinal fluid culture, cerebrospinal fluid culture specificity is 87% in detecting sepsis and meningitis. **Conclusion**: Neonates with possible late onset sepsis should have lumbar puncture. In the presense of these risk factors lumbar puncture is warranted.
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1. Introduction

Neonatal sepsis is defined classically as a clinical syndrome characterized by systemic signs of infection frequently accompanied by bacteremia (Klein, 2001).Neonatal sepsis can be categorized as early and late onset sepsis (LOS) depending upon whether the onset of symptoms is before 72 hrs of life (early onset) or later (late onset) (Sanker *et al.,* 2008). The source of infection in LOS is either nosocomial or community acquired and neonates usually present with septicemia, pneumonia or meningitis(Tripathi and Malik, 2010).

The incidence of LOS is inversely related to birth weight. The risk of developing LOS associated with central cathers, parentral nutrition and mechanical ventilation are all increased with longer duration of these therapies(Stoll *et al.,*2002).

In Egypt, neonatal sepsis is considered a big problem as with lack of infection control meassures and inadequate nursing staff, the incidence range increases more than the documented incidence(Youssry *et al.,* 2008).

Positive blood culture confirm sepsis, and when the blood culture is negative, the condition is considered as clinical sepsis. It is almost impossible to distinguish sepsis from meningitis in the neonate clinically. However, cerebrospinal fluid (CSF) that is positive for pathogenic bacteria indicates meningitis(Klein, 2001).

Aim: The aim of this work is to determine the significance of lumbar puncture in late onset sepsis.

2. Patients and Methods:

Inclusion criteria: Any newborn delivered without complication to a healthy mother and developed signs of sepsis after 72 hours of labor and had clinical sepsis score more than 2 according to modified clinical sepsis score by Tollner, 1982 was enrolled in the study. Exclusion criteria:

- Diabetic mother or hypertension.
- Foul smelling and\ or meconium stained liquor amnii.
- Prolonged rupture of membrane more than 24 hours.
- Febrile illness in the mother within 2 weeks prior to delivery.
- Prolonged and difficult delivery with instrumentation.
- Drug abuse.
- Newborns with intracranial hemorrhage or congenital malformation.
- Newborns with congenital infection.
- Newborns with bleeding tendency.
- Newborns with perinatal asphyxia.
- Intra-uterin growth retardation.

Neonates of our study were subjected to full history taking: prenatal, natal and post natal and family history. Thorough clinical examination, application of clinical sepsis score (Tollner, 1982), complete blood picture with differential count, application of

hematological sepsis score (Roberts and Murray, 2003), blood culture and CSF analysis and culture.

Methods:

Two and half ml sample of blood collected from a fresh peripheral veni-puncture site using a clean technique, one and half ml added to tube contains EDTA (Ethylene Diamine Tetra Acetic acic) for complete blood picture with differential count and one ml added to a blood culture bottle containing 5-10 ml of culture media.

Lumbar puncture (LP) done under complete aseptic condition and we collect 3 ml of clear CSF by allowing the fluid to drip into the tubes. We send 3 tubes of CSF each contain 1 ml to laboratory in the following order:

Tube 1: for Gram stain, culture and sensitivity testing.

Tube 2: for glucose and protein levels. Tube 3 : for cell count and differential.

Table(1) Demographic, clinical and laboratory profile of newborns with LOS

Variables	Newborns with LOS n=92		Newborns with meningitis n=39	
	No	%	No	%
Age of their mothers:				
≤18y.	20	21.7	9	23
19-35 y.	50	54.3	21	53.8
>35y.	22	23.9	9	23
Parity of mother:				
1 child	20	21.7	11	28.2
2 child	9	9.7	4	10.2
3child	41	44.5	14	35.8
4 child	21	22.8	10	25.6
5 child	1	1	0	0
Maternal infection:				
Present	Zero	0	0	0
Non	92	100	39	100
Place of birth:				
Home	5	5.4	2	5.1
Hospital	87	94..5	37	94.8
Made of delivery:				
Vaginal	21	22.8	12	30.7
CS	71	77.1	27	69.2
Maturity:				
Preterm	29	31.5	15	38.4
full term	63	68.4	24	61.5
Sex:				
Male	61	66.3	25	64.1
Female	31	33.6	14	35.8
Hematological sepsis score:				
+ ve	85	92.3	39	100
- ve	7	7.6	0	0
Blood culture:				
+ ve	62	67.3	35	89.7
- ve	30	32.6	4	10.2
CSF culture:				
+ ve	39	42.3	39	100
- ve	53	57.6	0	0
Apnea: +	7	7.6	6	15.3
-	85	92.3	33	84.6
Tachypnea: +	18	19.5	11	28.2
-	74	80.4	28	71.7
RD: +	13	14.1	7	17.9
-	79	85.8	32	82
Bradycardia: +	2	2.1	1	2.5
-	90	97.8	38	97.4
Hypotonia: +	17	18.4	10	25.6
-	75	81.5	29	74.3
Seizures: +	12	13	9	23
-	80	86.9	30	76.9
Irritability: +	9	9.7	7	17.9
-	83	90.2	32	82
Lethargy: +	30	32.6	17	43.5
-	62	67.3	22	56.4
Moro reflex: +	83	90.2	32	82
-	9	9.7	7	17.9
Poor suckling: +	19	20.6	11	28.2
-	73	79.3	28	71.7
HSM: +	15	16.3	8	20.5
-	77	83.6	31	79.4
Hypothermia: +	3	3.2	2	5.1
-	39	96.7	37	94.8
Hyperthermia: +	2	2.1	1	2.5
-	90	97.8	38	97.4
Pulging anterior fontanel: +	3	3.2	3	7.6
-	89	96.7	36	92.3
Vomiting: +	3	3.2	1	2.5
-	89	96.7	38	97.4
Bleeding: +	6	6.5	4	10.2
-	86	93.4	35	89.7

+ ve: positive **- ve:** negative **+:** present **-:** absent **CS:** Cesarean Section

RD: Respiratory Distress HSM: hepatosplenomegaly

Table (2) Relative risk of the risk factors to the occurrence of meningitis.

Variables	CSF + ve n=53		CSF -ve N=39		Total		χ^2	*p*	Relative risk (CI 95%)
	No	%	No	%	No	%			
Age of mothers:							0.08	0.96	
≤ 18y.	9		11		20				
19-35 y.	21		29		50				
>35y.	9		13		22				
Party of mother:							3.43	0.48	
1 child	11	28.2	9	17	20	21.7			
2 child	4	10.3	5	9.4	9	8.9			
3child	14	35.9	27	50.9	41	44.6			
4 child	10	25.6	11	20.8	21	22.8			
5 child	0	0	1	1.9	1	1.1			
Place of birth:							0.01	0.91	
Home	2	5.1	3	5.7	5	5.4			
Hospital	37	94.9	50	94.3	92	84.5			
Made of delivery:							2.42	0.11	
Vaginel	12	30.8	9	17.0	21	22.8			
CS	27	69.2	44	83.0	71	77.1			
Maturity:									
Preterm	15	38.5	14	26.4	29	31.6	1.51	0.21	
full term	24	61.5	39	73.6	63	97.4			
Sex:									
Male	25	64.1	36	67.9	61	6.3	0.15	0.70	
Female	14	35.9	17	32.1	31	33.7			
Apnea :									2.21
+	6	15.4	1	1.9			5.82	0.01	(1.47;3.30)
-	33	84.6	52	98.1					
Tacchypnea :									
+	11	28.2	7	13.2			3.21	0.07	
-	28	71.8	46	86.8					
RD :									
+	7	18.0	6	11.3			0.81	0.36	
-	32	82.0	47	88.7					
Bradycardia :									
+	1	2.6	1	1.9			0.05	0.82	
-	38	97.4	52	98.1					
Hypotonia :									
+	10	25.6	7	13.2			2.31	0.12	
-	29	74.4	46	86.8					
Seizures :									2.00
+	9	23.1	3	5.7			6.01	0.01	(1.30;3.08)
-	30	76.9	50	94.3					
Irritability :									2.02
+	7	17.9	2	3.8			5.12	0.02	(1.30;3.14)
-	32	82.1	51	96.2					
Lethargy :									
+	17	43.6	13	24.5			2.19	0.13	
-	22	56.4	40	75.5					
Moro reflex :									
+	32	82.1	51	96.2			5.12	0.02	
-	7	17.9	2	3.8					
Poor suckling :									
+	11	28.2	9	17.0			1.66	0.19	
-	28	71.8	44	79.2					
HSM :									
+	8	20.5	9	17.0			0.19	0.66	
-	31	79.5	44	79.2					
Hypothermia :									
+	2	5.1	1	1.9			0.75	0.38	
-	37	94.9	52	98.1					
Hyperthermia:									
+	1	2.6		1.9			0.05	0.82	
-	38	97.4		98.1					
Pulging anterior fontanel :									2.47
+	3	7.7		0.0			4.21	0.04	(1.92;3.18)
-	36	92.3		100.0					
Vomiting :									
+	1	2.6		3.8			0.10	0.74	
-	38	97.4		96.2					
Bleeding :									
+	4	10.2		3.8			1.55	0.21	
-	35	89.8		96.2					

Table(3) Comparison between hematological sepsis score and CSF culture, its sensitivity, specificity, PPV, NPV and accuracy in studied newborns

	Hematological sepsis score +Ve	Hematological sepsis score –Ve	Total	χ^2	*P*
CSF culture +ve	**35**	**4**	**39**	**0.68**	**0.41**
CSF culture –ve	**50**	**3**	**53**		
Total	**85**	**7**	**92**		

Sensitivity: 41% Specificity: 43 % PPV (Positive Predictive Value): 90%
NPV(Negative Predictive Value): 6% Accuracy: 41% .

Table (4) Comparison between blood culture and CSF culture, its sensitivity, specificity, PPV, NPV and accuracy in studied newborns

	Blood culture +Ve	Blood culture –Ve	Total	χ^2	*P*
CSF culture +ve	**35**	**4**	**39**	**13.68**	**0.000**
CSF culture –ve	**27**	**26**	**53**		
Total	**62**	**30**	**92**		

Sensitivity: 56% Specificity: 87% NPP(Negative Predictive Value): 49 % PPV(Positive Predictive Value): 90% Accuracy :66%

4. Discussion:

In our study, we found 39 newborns out of 92 newborns with LOS had meningitis (42.3%), 4 of those had a positive CSF culture had both a negative hematological sepsis score and blood culture (10.25%).

Stool *et al.* (2002) reported that two-thirds of a cohort of 9000 infants had one or more blood cultures drawn after 72 hours of life; one-third had a lumbar puncture. Culture proven meningitis was diagnosed in 134 infants (5% of those on whom a LP was performed) and in 45 out of 134 cases, the coincident blood culture was negative. Emmalyn *et al.* (2005) found 5 out of the 44 full term baby with neonatal sepsis had meningitis.

Health *et al.* (2003) reported that as many as 25% of newborns who have sepsis have meningitis, and 15% to 55% of patients who have meningitis (positive CSF culture) have negative blood culture.

Garges *et al.,* 2006 found that between 92 newborns with meningitis, only 57 (62%) newborns had a concomitant positive blood culture. Also Smith *et al.,* 2008 found that 70% of their neonates with positive CSF

Nizet and Klein (2010) reported that there are studies focused on LP are invasive procedures and have been noted to be more difficult to perform in neonates than in other populations and to cause neonatal distress and complication such as bloody tap and contaminated specimens are common and therefore limiting a newborn,s exposure. On the other hand, some studies suggest that LPs performed only on newborns with signs of infection lead to missed diagnoses of meningitis and its associated morbidity. Still other studies have found discordance of cerebral spinal fluid and blood cultures in septic neonates, suggesting all newborns suspected of LOS should have LPS.

Using relative risk in our study, the presence of bulging anterior fontanel, apnea, irritability and seizures increase the incidence of acquiring memingitis.

Emmalyn *et al.* (2005) using relative risk, parity more than-1-child, maternal infection, duration of illness more than1 day, birth in a hospital, presence of seizure, poor activity, jaundice, diarrhea and dyspnea increased the risk of acquiring meningitis.

Stoll *et al.*(2002) underscores the importance of performing a LP in the evaluation of LOS in very low birth weight infants. Ideally cultures of urine and CSF should also be obtained before antibiotic therapy, both to guide empiric therapy and to ensure proper follow up.

Akin to Tripathi and Malik (2010) LP should be done in all infants prior to starting antibiotics.

Haque (2010) he routinely include CSF examination in LOS evaluation but he is selective in doing a lumbar puncture for early onset sepsis, a practice based on on-going surveillance data collected in his unit over last twenty years.

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