# Neonatal Sepsis in Derna, Libya

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**Abstract:**

**Background:** Neonatal sepsis is a common clinical syndrome. It occurs in approximately 1% of live births worldwide.

**Objectives:** To measure serum lipids profile and blood count indices as predictors of neonatal sepsis.

**Methodology:** This study was conducted on forty cases with neonatal sepsis admitted to the neonatal intensive care unit of Al Wahda Hospital, Derna, Libya, during the year 2006, in which they all conformed to the Tollner classification of sepsis. In addition, an apparently healthy forty neonates matched in age and sex were chosen as a control group. Risk factors, apgar score, gestational age, birth weight and the clinically apparent signs or complications of sepsis, complete blood picture, blood culture and total cholesterol, triglycerides, high density lipoprotein and low density lipoprotein were assessed.

**Results:** Hemoglobin level, Red blood cells, white blood cells and platelets count indices were significantly lower in septic cases (12.2±3.8 gm/dl, 3.6±1.02/$10^6$/ul, 4.9±5.2x$10^3$ ul and 166.7±133.5/$10^3$/ul) than the control group (14.3±2.4 gm/dl, 4.3±3.2/$10^6$ /ul, 7.4±3.8x$10^3$/ul and 201±121.4x$10^3$ /ul, respectively). I/T ratio (Imature/ Total neutrophils) was significantly higher in cases (0.24 ±0.43) than the control group (0.1 ±0.76). The mean values of the serum triglycerides (159.5±49.9 mg/dl), cholesterol (201±11.9 mg/dl) and LDL (185±38.9 mg/dl) in infants with sepsis were significantly higher than the controls (82±26.9 mg/dl, 147±39.2 mg/dl and 86.6±2.9 mg/dl, respectively). Whereas serum HDL (28.1±10.2 mg/dl) in the septic group was significantly, lower than the controls (86.6±2.9 mg/dl). Premature rupture of membrane, respiratory distress syndrome, ventilation and convulsions were significantly higher in neonates of sepsis than the controls. Klebsielia pneumonie was the predominant cultured pathogens in this study.

**Conclusion:** Lipid profile is disturbed among cases with neonatal sepsis compared to controls.

**Introduction:**

Neonatal sepsis is a clinical syndrome characterized by signs of infection and accompanied by bacteremia in the first 28 days of life.[1]

Group B streptococci and E. coli continue to be the most common responsible organisms for early neonatal sepsis, so blood culture is the gold standard for the isolation of organisms.[2]

A relation between the serum lipid and cytokines (the key mediators of acute phase reactants) might mediate the endotoxine-induced alterations in lipid metabolism. They induce hypertriglyceridemia, stimulate hepatic fatty acids synthesis, induce lipolysis and increase very low-density lipoprotein production.[3]

Martin et al. (1992)[4] postulated that the clearance rate of endogenous and exogenous circulating lipids during the septic or inflammatory state remains a controversial subject.

**Objectives:**

The study aims to measure serum lipid profile and blood count indices as predictors of neonatal sepsis and to describe its relationship with the dominating spectrum of pathogens in the first 28 days of life.

**Subjects:**

Reviewing the neonatal intensive care unit at Al Wahda Hospital, Derna, Libya for the year 2005, 359 neonates were admitted, septicemia or pneumonia represented 8% of cases for each.[5]

The present study was conducted on 40 infants admitted to the neonatal intensive care unit of Al Wahda Hospital, Derna, Libya, during the year 2006. In addition, 40 apparently healthy neonates matching in age and sex were chosen as a control group.

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All the studied cases were clinically typical of sepsis and conformed to the criteria of Tollner classification **(**1988**)** of neonatal sepsis. Twenty five (60%) were males and 15 (40%) were females, with a male to female ratio of 1.5:1. The age range was 1 to 28 days. An informed parental consent for entering the study was obtained for each subject prior to enrollment.

**Methods:**

Each case, in the experimental and control group, was subjected to the following:

1- **Full Medical History:** Including the mode of delivery, parity, history of premature rupture of membrane, perinatal asphyxia, toxemia of pregnancy, congenital infection and gestational age.

2- **Meticulous Medical Examination:** Including the apgar score at 1 and 5 minutes respectively, weight, associated distress syndrome, symptoms or signs of neonatal sepsis (lethargy, convulsions, apnea, intraventricular hemorrhage or DIC).

3- **Sepsis scoring:** According to Tollner staging of neonatal sepsis in 1988.

4- **Complete Blood Picture.**

5- **Blood Culture Incubation:** According to (Hoffman and Haris, 1996).[2]

6- **Estimation of Serum Lipid:** A 4 ml of venous blood was drawn from each subject by venipuncture, centrifuged and the serum was separated and analyzed for the estimation of serum cholesterol and triglycerides by enzymatic method. Estimation of serum lipoproteins was performed using electrophoresis procedure.

**Results:**

Regarding the mode of delivery, vaginal delivery was the most common mode of delivery (70%) in our study [including normal vaginal (60%) and breach delivery (10%)], followed by the cesarean section (30%).

Table **(**1**)** shows that gestational age was significantly lower in cases of neonatal sepsis (32±1.5 weeks) than the control group (36±2.3 weeks), denoting that sepsis is more common among preterm infants.

The birth weight was significantly lower in cases (2.1±0.4 Kg.) than the control group (3±3.3 Kg.), indicating a higher risk of sepsis neotorum among low birth weight infants.

Regarding apgar score, the first and 5th minutes mean of the control group were 6.3±1.1 and 8.1±2.3 respectively, while that of the septic group were 3.4±2.3 and 5.7±0.8 respectively.

**Table (1): Mean values of the gestational age, weight and Apgar score in septic cases as compared to the controls .**

| Variable | Controls | Septic | t-value | P-value |
|---|---|---|---|---|
| **Gestional age /week** | 36 ± 2.3 | 32 ±1.5 | 14.7 | **< 0.001*** |
| **Weight/Kg.** | 3.0 ±3.3 | 2.1±0.43 | 2.7 | **< 0.01*** |
| **Apgar score** | 6.3 ± 1.1 | 3.4±2.4 | 4.1 | **<0.001*** |

*** Significant as P< 0.05**

Table (2) shows that hemoglobin level, RBCs, WBCs and platelets count indices were significantly lower in septic cases (12.2±3.8 gm/dl, 3.6±1.02x$10^6$ul, 4.9±5.2x$10^3$ul and 166.7±133.5x$10^3$ul) than the control group (14.3±2.4 gm/dl, 4.3±3.2x$10^6$ul, 7.4±3.8x$10^3$ul and 201±121.4x$10^3$ul, respectively).

I/T ratio (Imature/ Total neutrophils) was significantly higher in the cases (0.24 ±0.43) than the control group (0.1 ±0.76). Cases with a ratio <0.2 were 42.5%, while those with a ratio > 0.2 were 57.7%. However, those with a score of more than 10 in the applied sepsis score were 57.7% while those with a score range between 5 – 10 were 32.5%.

**Table (2): Comparison of hematological indices between cases and the control group.**

| Variable | Controls | Cases | t-value | P-value |
|---|---|---|---|---|
| **Hb gm/dl** | 14.3±2.4 | 12.2±3.8 | 13.4 | **<0.001*** |
| **RBCs countx$10^6$ul** | 4.3±3.2 | 3.6±1.02 | 4.1 | **<0.001*** |
| **WBCs countx$10^3$ul** | 7.4±3.8 | 4.9±5.2 | 5.4 | **<0.001*** |
| **PLTs countx$10^3$ul** | 201±121.4 | 166.7±133.5 | 18.6 | **<0.001*** |

*** Significant as P< 0.05**

Table (3) shows that the mean values of the serum triglycerides (159.5±49.9 mg/dl), cholesterol (201±11.9 mg/dl) and LDL (185±38.9 mg/dl) in the infants with sepsis were significantly higher than the control group (82±26.9, 147±39.2, 86.6±2.9 mg/dl respectively). Whereas serum HDL (28.1±10.2 mg/dl) in the septic group was significantly lower than the control group (86.6±2.9 mg/dl).

**Table (3): Comparison of serum lipid profile between septic cases and the control group.**

| Variable | Control | Septic | t-value | P-value |
|---|---|---|---|---|
| **Triglycerides** mg/dl | 82±26.9 | 159.5±49.9 | 16.7 | **<0.001*** |
| **Cholesterol** mg/dl | 147±39.2 | 201±11.9 | 7.7 | **<0.001*** |
| **HDL-cholesterol** mg/dl | 44.7±5.8 | 28.1±10.2 | 6.4 | **<0.001*** |
| **LDL-cholesterol** mg/dl | 86.6±2.9 | 185±38.9 | 13.9 | **<0.001*** |

*** Significant as P< 0.05**

Table (4) shows that premature rupture of membrane (PROM), RDS, ventilation and convulsions were significantly higher in cases of sepsis neonates than the controls.

A positive correlation was revealed between gestational age and serum cholesterol, HDL and LDL, while a negative correlation with serum triglycerides was noted.

A positive correlation between triglycerides and both sepsis score and I/T ratio, also between cholesterol and both sepsis score and I/T ratio were revealed.

Regarding the pathogens, Klebsiela pneumonie was the predominant organism and was cultured from 22.5% of cases, while E-coli and staphylococci were found in 5% of cases for each. Also pseudomonous and proteus were detected in 15% and 7.5% of cases respectively, whereas anaerobes were cultured from 7.5% of cases.

**Table (4): Comparison of some risk factors between septic cases and controls**

| Risk factors | | Cases | Controls | $X^2$ | P-value |
|---|---|---|---|---|---|
| Premature rupture | **Negative** | 28 | 39 | 9.2 | **0.003*** |
| | **Positive** | 12 | 1 | | |
| Toxemia | **Negative** | 35 | 37 | 0.14 | **0.7** |
| | **Positive** | 5 | 3 | | |
| Congenital | **Negative** | 39 | 40 | 0.0 | **1.0** |
| | **Positive** | 1 | 0 | | |
| R.D.S | **Negative** | 15 | 39 | 30 | **0.001*** |
| | **Positive** | 25 | 1 | | |
| Ventilation | **Negative** | 20 | 40 | 24.1 | **0.001*** |
| | **Positive** | 20 | 0 | | |
| Convulsions | **Negative** | 19 | 38 | 19.7 | **0.001*** |
| | **Positive** | 21 | 2 | | |
| Apnea | **Negative** | 25 | 38 | 10.7 | **0.001*** |
| | **Positive** | 15 | 2 | | |

*** Significant as P< 0.05**

**Discussion:**

Neonatal sepsis is a common clinical syndrome. Radestsky **(**1996**)**[6] reported that neonatal infections occur in approximately 1% of live births worldwide, whereas Hervas et al. (1993)[7] stated that the incidence varies from less than 1 to 8.1 cases / 1000 live births.

The relation between serum lipid and immune system signifies the dearrangement of the lipid profile among septic cases compared to the normals. Cytokines (the key mediators of acute phase reactants) might mediate endotoxin induced alterations in lipid metabolism; they induce hypertriglyceridaemia, stimulate hepatic fatty acid synthesis, induce lipolysis and increase VLDL production.[3]

Furthermore, Feingold et al. (1994)[8] found that a number of cytokines inhibit lipoprotein lipase activity. Whereas Hardardottir et al. (1994)[9] postulated that TNF and IL-1 might be important mediators of the effect of endotoxin

on cholesterol metabolism. They both increase serum cholesterol, hepatic cholesterol synthesis and HMG-CoA reductase mRNA.

In the present study, gestational age was significantly lower in cases of neonatal sepsis (32±1.5 weeks) than the control group (36±2.3 weeks). This denotes that sepsis is more common among preterm infants than other groups of age. This was in agreement with Klein and Marcy (1995)[1] who documented that preterm infants are more prone to sepsis than others. This could be either due to the state of immune deficiency encountered in preterms or to the frequent use of invasive maneuvers in the neonatal intensive care units.

The demonstrated lower birth weight among cases in the present study (2.1± 0.43 kg) than the control group (3±3.3 kg) was indicative of higher risk of sepsis neonatorum among LBW infants and was confirmed by the significant negative correlation revealed between birth weight and septic score ($P < 0.001$). These results are in agreement with Guerina et al. (1991)**[10]** who documented an increase in the incidence of sepsis among very low birth weight infants (< 1500 gms) in whom it may exceed 300/1000 live births. Also, Radestsky (1996)[6] reported the increased incidence of sepsis in low and very low birth weight neonates.

Vaginal delivery was the most common mode of delivery, (70% of cases) in this study compared to the 30% delivered by cesarean section. These results were not in agreement with Roberton (1993)[11] who reported instrumental intervention in delivery as one of major sources of neonatal sepsis.

The incidence of premature rupture of membranes (PROM) for more than 12 hours in cases was 22.5%, compared to the control ($P < 0.001$).This was in agreement with the study done by Hoffman and Haris (1996)**.[2]**

Apgar scores at the first and fifth minutes were significantly lower in cases (3.4±2.3 and 5.7±0.8) than the control group (6.3±1.1 and 8.1±2.3). This denotes a state of ante-and /or perinatal hypoxia among cases of neonatal sepsis. Apgar score was found to be negatively correlated with sepsis score ($P <0.001$). In fact Tollner **(**1988**)** considered apgar score as an item in scoring of neonatal sepsis.

Regarding perinatal asphyxia as a risk factor for neonatal sepsis, 17.5% of cases had a history of perinatal asphyxia. Also, a significant relationship ($P <0.001$) was revealed between history of asphyxia and septic score. The same conclusion was reported by Johanson et al. **(**1992**)**.[12] Also, Hebra and Ross **(**1996**)**[13], reported that hypoxic-ischemic reperfusion injury played a major part in the pathogenesis of sepsis.

Regarding hyaline membrane disease (RDS), it was reported very common among cases (62.5%) compared to the control. There was a significant association between the syndrome and septic score. Guerina et al. (1991)[10] reported that RDS was the most common symptom occurring in up to 90% of infants with sepsis.

The I/T ratio was significantly higher in septic cases (0.24±0.43) than the control (0.1±0.76). Considering a value of 0.2 as a predictive parameter for sepsis, it was found that 57.5% of cases were above it compared to the control group. Furthermore, I/T ratio was related to the severity of sepsis.These results were in agreement with the study of Rodwell et al. (1993)[14] who reported that neutrophil count less than 500/mm$^3$ together with either hematologic score more than 3, or I/T ratio more than 0.2 provided a more valuable diagnostic and prognostic information. Moreover, Gendrel et al. (1996)[15] had approved that the best approach for the diagnosis of neonatal infection was to combine a number of hematological tests as the number of the immature cells. The I/T ratio was included in both Edwards et al. (1997)[16] and Rodwell et al. (1988)[17] scoring criteria.

Platelet count was significantly lower in septic cases (166.7 ± 133.5 x $10^3$/ul) than the control (201±121.4 x $10^3$/ul). These results are in agreement with the study of Gendrel et al. (1996).[15]

Regarding triglycerides, serum levels were significantly higher among neonatal sepsis group than the control group ($P < 0.001$). Moreover a positive correlation was found between triglycerides and septic score ($r = 0.121$) and between triglycerides and I/T ratio ($r = 0.146$).

Lopez and Williams (1994)[18] and Gouni et al. (1993)[19] found an increase in the triglyceride serum level in cases of neonatal gram negative sepsis. They postulated that the increased triacylglycerol levels were accounted for by an increase in very-low-dose-density lipoproteins [VLDL]. According to Nonogaki et al. (1995)[3], cytokines might mediate the endotoxin-induced alterations in lipid metabolism, they induce hypertriglyceri-daemia, stimulate hepatic fatty acid synthesis, induce lipolysis and increase VLDL production.

Serum total cholesterol was significantly higher in septic group than the control group (P< 0.001) with the strongly positive correlation with septic score (r = 0.487).

Hardardottir et al. (1994)[9] reported that there was an increase in the serum cholesterol level, hepatic cholesterol synthesis and HMGCoA reductase mRNA in cases of sepsis, whereas the above results were in disagreement with Abarcia and Garcia (1993)[20] who documented the decrease in the serum cholesterol level in septic humans and other primates. Also Sammel et al. (1988**)** found that total cholesterol level decreased in infectious states.

The mean value of serum HDL in the septic group (28.1 ±10.2 mg/dl) was significantly lower than the control group (44.70 ±5.8 mg /dl, P< 0.001). Hardardottir et al. (1994**)**[9] found that decrease in cholesterol ester was mainly responsible for the decreased HDL, whereas Ly et al. (1995)[21] found that endotoxin decreased the activity of lecithin: cholesterol acyltransferase (LCAT), which was responsible for esterifying free cholesterol in HDL.

Serum LDL was significantly higher in cases with neonatal sepsis (185 ±38.9 mg/dl) than the control group (86.6±28.9 mg / dl, P< 0.001). Fiengold et al. (1995)[22] reported an increase in the LDL serum level in cases with sepsis, denoting that endotoxin had minimal or no effects on LDL receptor protein or mRNA levels in the liver, the organ primarily responsible for LDL clearance, whereas Sammel et al. (1988) found that both LDL and HDL-C were reduced during acute infections due to the decrease in cholesterol, phospholipids and protein contents of both LDL and HDL-C. Merainhi et al. (1991)[4] postulated that the clearance rate of endogenous and exogenous circulating lipids during septic or inflammatory state remain a controversial subject.

Regarding pathogens, Klebsiela pneumonie was the predominant organism and was cultured from 22.5% of cases, while E-coli and staphylococci were found in 5% of cases for each. Also pseudomonous and proteus were detected in 15% and 7.5% of cases respectively, whereas anaerobes were cultured from 7.5% of cases. These findings show that fecal transmitted organisms (E.coli and others) seem to be the most hazardous pathogens compared to the droplet transmitted organisms.

**Conclusion:**

Lipid profile is disturbed among cases with neonatal sepsis compared to controls.

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