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TO STUDY THE DIFFERENT CLINICAL PRESENTATIONS OF NEONATAL SEPSIS AND THE RISK FACTORS IN BABIES PRESENTING WITH NEONATAL SEPSIS

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ABSTRACT

Background: Neonatal septicemia or sepsis neonatorum refers to systemic infection of the new born. It is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life. Prompt recognition, appropriate antimicrobial therapy and judicious supportive care are the key determinants of positive outcome in this serious pediatric emergency. Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30% - 50% of the neonatal deaths each year in developing countries. The reported incidence of neonatal sepsis is 38 per 1000 live births in Asia. The incidence is lower in western countries. According to Neonatal Perinatal Database (NNPD) last reported data collected in 2002-2003 from 18 various parts of India, the incidence of neonatal sepsis has been reported to be 29 per 1000 live births. According to WHO estimates, there were about 5 million deaths in 1995, 98% of them occurred in developing countries**. Aim:** To study the different clinical presentations of neonatal sepsis and the risk factors in babies presenting with neonatal sepsis **Methods:** This study was a prospective observational study in neonatology section of Post Graduate Department of Pediatrics at GB Panth hospital, an associated tertiary care pediatric hospital of Government Medical College Srinagar, Northern India, from1st April 2018 to May 30 2019. **Results:** A total of 5128 neonates were admitted in our neonatology during this study period. Out of these a total of 414 neonates presenting with a wide spectrum of clinical signs and symptoms were diagnosed with neonatal

septicemia. Among these 414 neonatal septicemia cases 265 neonates were inflicted with community acquired sepsis and 149 neonates developed Nosocomial sepsis. In our study the commonest presenting feature was lethargy/ refusal of feeds observed in 66.18% (274 cases) followed by hypothermia 44.20% (183), tachypnoea 40.09% (166 cases), grunting 32.12% (133 cases), delayed CRT 29.95% (128 cases), feeding intolerance 29.95% (124), prolonged jaundice 14.97% (62), Oliguria 11.83% (49), irritability 9.90% (41), seizures 9.17% (38), diarrhea 7% (29), vomiting 4.83% (20), abscesses 3.38% (14), umbilical discharge 1.93% (8) and pustulosis. 96% (4) respectively. In our study low birth weight (wt<2.5 kg) was found as the leading risk factor in 68.35% babies of neonatal septicemia, followed by preterm gestation (37 weeks) in 40.57%, PROM>18hours in mother in 31.88%, delivery at home in 22.22 %, positive pressure ventilation in 20.29%,Perinatal asphyxia in 13.77%, maternal fever during labour in 10.62%,multiple intrapartum vaginal examinations (>3) in mother in 4.59%,Chorioamnionitis in 3.62%,central venous arterial catheterization in 3.14% and purulent foul smelling vaginal discharge in 2.89%. **Conclusions:** Clinical assessment using a combination of symptoms and signs are useful guides to provisional diagnosis of neonatal sepsis. Prevalence of sepsis is inversely related to birth weight and gestational age. High degree of culture positivity is noted in neonatal sepsis.

INTRODUCTION

Neonatal septicemia or sepsis neonatorum refers to systemic infection of the new born. It is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life. Prompt recognition, appropriate antimicrobial therapy and judicious supportive care are the key determinants of positive outcome in this serious pediatric emergency.[1] Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30% - 50% of the neonatal deaths each year in developing countries.[1,2] The reported incidence of neonatal sepsis is 38 per 1000 live births in Asia. The incidence is lower in western countries.[3] According to Neonatal Perinatal Database (NNPD) last reported data collected in 2002-2003 from 18 various parts of India, the incidence of neonatal sepsis has been reported to be 29 per 1000 live births.[4] According to WHO estimates, there were about 5 million deaths in 1995, 98% of them occurred in developing countries. The number of deaths decreased to 4 million in 2005, but among them 98% still occurred in developing countries.[5] In developing countries neonatal mortality from all the causes are about 34 per 1000 live births, most of the deaths occurring in the first week of life and most of them on the first day. In contrast in the developed world it is only five per 1000 live births.[3]

Classification of sepsis

Early onset sepsis usually presents within first 72 hours of life. In severe cases, the neonate may be symptomatic in utero (fetal tachycardia, poor beat to beat variability) or within a few hours after birth.[1] It is associated with acquisition of microorganism from the mother, transplacental infection or an ascending infection from the cervix caused by organisms that colonize in the mother's genitourinary tract.[1,2,6,7] Late onset sepsis usually presents after 72 hours of age.[1] It is acquired from the environment. The infant's skin, respiratory tract, conjunctiva, gastrointestinal tract and umbilicus may become colonized from environment, leading to possibility of late onset sepsis from invasive microorganisms. Vectors for colonization include vascular or urinary catheter, indwelling lines or contact from care givers with bacterial colonization.[1,2,6,7]

AIMS AND OBJECTIVES

To study the different clinical presentations of neonatal sepsis and the risk factors in babies presenting with neonatal sepsis.

The study was done over a period of one year from 1st April 2018 to 30th May 2019 in neonatology section of post graduate department of pediatrics at GB panth hospital an associated tertiary care pediatric hospital of government medical college Srinagar. Our neonatology section is a exclusively out born facility where all neonates admitted are born outside. Nosocomial or hospital acquired infections include any infection that are not present or incubated at the moment of hospital admission and, thus, are acquired during hospitalization or upto 72 hours after discharge. The centers for disease control and prevention (CDC) defines a Nosocomial infection as infection arising after admission to NICU, that was not transplacentally acquired.

MATERIAL AND METHODS

This study was a prospective observational study in neonatology section of Post Graduate Department of Pediatrics at GB Panth hospital, an associated tertiary care pediatric hospital of Government Medical College Srinagar, Northern India, from1st April 2018 to May 30 2019. Our neonatology section is a exclusively out born facility where all neonates admitted are born outside. The study population consisted of all neonates fulfilling the inclusion criterias and whose legal guardians/parents consented for the study with signs and symptoms suggestive of infection along with any antenatal risk factors for neonatal sepsis if any, admitted in this unit within the study period.

Patient selection

- **Inclusion criteria**

Infants < 28 days clinically suspected as a case of neonatal septicemia.

- **Exclusion criteria**
- Age more than 28 days
- Patients who had already received IV antibiotics for more than 3 days at the time of admission

Patient selection

All the neonates, with at least one of the following clinical criteria:

Clinical criteria

General: - Alteration in behavior and change in established feeding pattern is an early sign. Lethargy, refusal to feed, feed intolerance, failure to gain weight, temperature instability (Hypothermia/ Fever).

Circulatory system: - Pallor, cyanosis, cold clammy skin, bradycardia / tachycardia, poor capillary filling and hypotension.

Respiratory system: - Apnea, dyspnea, tachypnea with chest retraction, cyanosis, grunting and flaring.

Central nervous system: - Lethargy. Irritability, high pitched cry, vacant stare, hypotonia, abnormal reflexes, seizures, tremors and bulging anterior fontanel.

Gastrointestinal tract: - Vomiting, diarrhea, abdominal distension hepatomegaly and splenomegaly.

Renal system: - Oliguria.

Hematological system: - Jaundice, Pallor, Splenomegaly, Petechiae, Purpura and Mucosal bleeding.

Skin changes: - Multiple pustules, Abscesses, Sclerema, Mottling, Umbilical redness and Discharge.

Patients admitted as suspected cases of neonatal septicemia were evaluated for presence or absence of following risk factors

- Unexplained prematurity with gestational age ≤37 weeks
- Birth weight <2500grams
- Prolonged rupture of membranes (≥18 hours).
- Meconium stained or purulent amniotic fluid.

- Chorioamnionitis (presence of fever more than 100.4^0 F (38^0 C) with one or more of the following findings, i.e. maternal tachycardia, fetal tachycardia, uterine tenderness, foul vaginal discharge or maternal leukocytosis.
- Untreated recurrent urogenital infections in the last trimester of pregnancy.
- Delivery at home.

Once the patients were admitted as suspected neonatal septicemia, evaluation was done as Samples for complete blood count (CBC),total leukocyte count (TLC), absolute neutrophil count(ANC), Platelet count, C-reactive protein (CRP), urine, blood and cerebrospinal fluid (CSF) cultures were taken and sent to the laboratory. Chest x-rays were done in those who presented with respiratory symptoms. Once samples were taken, the neonates with strong clinical suspicion of sepsis were placed on appropriate antibiotic therapy. In those with positive cultures, antibiotic therapy was re-adjusted according to sensitivity results. A positive sepsis screen was defined as two or more abnormal test results.[8,9,10,11,12,13]

Sample collection

An area of approximately 5 cm over the venipuncture site was disinfected with 70% alcohol rubbing vigorously and allowed to dry. This was followed by application of povidine Iodine in concentric circles over the site and allowed to dry for atleast 1minute. About 1 ml of the blood sample was inoculated aseptically into a blood culture bottle.

Samples for CBC, CRP, urine examination and CSF were collected from appropirite sites under all aseptic conditions.

Blood culture: 1 ml of venous blood was withdrawn under all aseptic conditions and inoculated into the available BacT/ALERT® PF vials and culture done by automated blood culture system known as BacT/ALERT-3D System

Antibiotic susceptibility testing

Antibiotic susceptibility testing was done by automated VITEK-3-compact system antibiotic sensitivity testing.

Statistical analysis

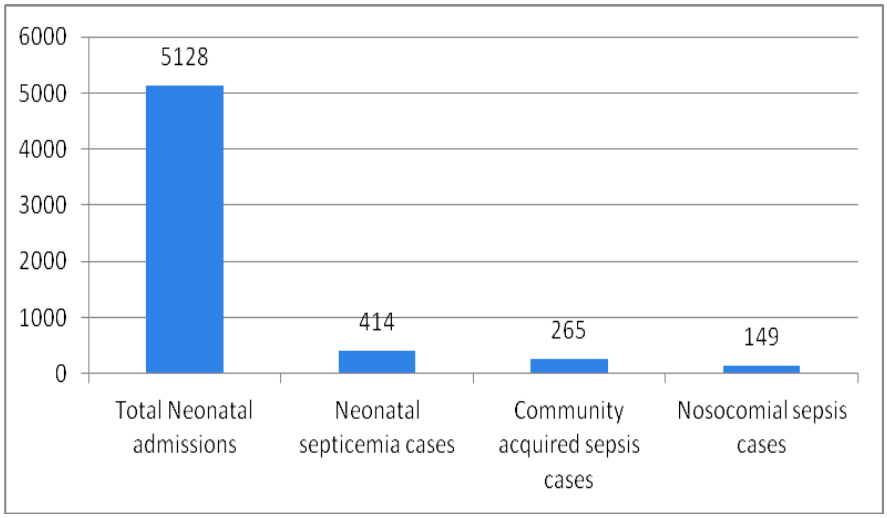
Data was analyzed as per standard statistical analysis. Data was entered in a Microsoft excel spreadsheet. Continuous variables were summarized as mean and standard deviation. Categorical variables were summarized as percentage.

OBSERVATIONS AND RESULTS

A total of 5128 neonates were admitted in our neonatology during this study period. Out of these a total of 414 neonates presenting with a wide spectrum of clinical signs and symptoms were diagnosed with neonatal septicemia. Among these 414 neonatal septicemia cases 265 neonates were inflicted with community acquired sepsis and 149 neonates developed Nosocomial sepsis (table1 and bar chart 1).

Table 1: Showing the spectrum of community Acquired and Nosocomial sepsis.

Total Neonatal admissions	5128
Neonatal septicemia cases	0414
Community acquired sepsis cases	0265
Nosocomial sepsis cases	0149



Bar chart 1: Showing the spectrum of community Acquired and Nosocomial sepsis.

Clinical features profile

In our study the commonest presenting feature was lethargy/ refusal of feeds observed in 66.18% (274 cases) followed by hypothermia 44.20% (183), tachypnoea 40.09% (166 cases), grunting 32.12% (133 cases), delayed CRT 29.95% (128 cases), feeding intolerance 29.95% (124), prolonged jaundice 14.97% (62),Oliguria 11.83% (49), irritability 9.90% (41), seizures 9.17% (38), diarrhea 7% (29), vomiting 4.83% (20), abscesses 3.38% (14), umbilical discharge 1.93% (8) and pustulosis. 96% (4) respectively.(table 2).

Table 2: Showing the spectrum of presenting clinical features of neonatal sepsis.

Presenting feature	Number of patients	Percentage (%)
Lethargy /Refusal of feed	274	66.18
Feeding intolerance	124	29.95
Tachypnea	166	40.09
Hypothermia	183	44.20
Fever	082	19.80
Grunting	133	32.12
Delayed CRT	124	29.95
Prolonged jaundice	062	14.97
Seizures	038	09.17
Irritability	041	09.90
Diarrhea	029	07.00
Oliguria	049	11.83
Umbilical discharge	008	01.93
Abscess	014	03.38
Pustulosis	004	00.96

Clinical features profile of community acquired sepsis

In our study the commonest presenting feature in community acquired sepsis was lethargy/ refusal of feeds observed in 67.14% (179 cases) followed by hypothermia 57.73% (153), grunting 45.66% (121), delayed CRT 40.75% (108), tachypnoea 36.98% (98), prolonged jaundice 23.39% (62), Oliguria 18.49% (49), irritability 06.79% (18), seizures 11.69% (31), diarrhea 10.94% (29), feeding intolerance 07.92% (21), abscesses 05.28% (14), umbilical discharge 03.01% (8) and pustulosis 01.50% (4) respectively. (table 3)

Table 3: Showing the spectrum of presenting clinical features of community acquired neonatal sepsis.

Presenting feature	Number of patients	Percentage (%)
Lethargy /Refusal of feed	179	67.54
Tachypnea	098	36.98
Hypothermia	153	57.73
Fever	077	29.05
Grunting	121	45.66
Delayed CRT	108	40.75
Prolonged jaundice	062	23.39
Feeding intolerance	021	07.92
Seizures	031	11.69
Irritability	018	06.79
Diarrhea	029	10.94
Oliguria	049	18.49
Umbilical discharge	008	03.01
Abscess	014	05.28
Pustulosis	004	01.50

Clinical features profile of nosocomial sepsis

In our study the commonest presenting feature in Nosocomial sepsis was feeding intolerance observed in 69.12% (103 cases) followed by Tachypnea in 45.63% (cases), lethargy/hypotonia in 34.89% (52), refusal of feeds 28.85% (430), hypothermia 20.13 5 (30), irritability 15.43% (23), apnea 12.08% (18), delayed CRT/mottling 10.73% (16), new onset grunt 8.05% (12), seizures 4.69% (07), encephalopathy and fever 3.35% (05) respectively. (Table 4).

Table 4: Showing the spectrum of presenting clinical features in nosocomial neonatal sepsis.

Clinical feature	No of patients	Percentage (%)
Feeding intolerance	103	69.12
Lethargy /Hypotonia	52	34.89
Refusal of feeds	43	28.85
Tachypnea	68	45.63
New onset Grunt	12	08.05
Seizures	07	04.69
Irritability	23	15.43
Encephalopathy	05	03.35
Apnea	18	12.08
Delayed CRT /Mottling	16	10.73
Hypothermia	30	20.13
Fever	05	03.35

Risk factor profile

In our study low birth weight (wt<2.5 kg) was found as the leading risk factor in 68.35% babies of neonatal septicemia, followed by preterm gestation (37 weeks) in 40.57%, PROM>18hours in mother in 31.88%, delivery at home in 22.22 %, positive pressure ventilation in 20.29%, Perinatal asphyxia in 13.77%, maternal fever during labour in 10.62%, multiple intrapartum vaginal examinations (>3) in mother in 4.59%, Chorioamnionitis in 3.62%, central venous arterial catheterization in 3.14% and purulent foul smelling vaginal discharge in 2.89%.(Table 5)

Table 5: Showing the spectrum of risk factors in babies presenting with neonatal sepsis.

Risk factors	No of patients	Percentage (%)
Low birth weight	283	68.35
Preterm	168	40.57
PROM>18hrs	132	31.88
Delivery at home	92	22.22
Purulent/foul smelling vaginal discharge	12	02.89

Chorioamnionitis	15	03.62
Maternal fever during labour	44	10.62
Multiple intrapartum PV examinations	19	04.59
Perinatal asphyxia	57	13.77
Positive pressure ventilation	84	20.29
Central venous/arterial catherization	13	03.14

Risk factor profile of community acquired sepsis

In our study low birth weight (wt<2.5 kg) was found as the leading risk factor in 43.47% babies of Nosocomial neonatal septicemia, followed by PROM>18hours in mother in 31.88%, delivery at home in 22.22 %, preterm gestation (37 weeks) in 17.87%, Perinatal asphyxia in 13.77%, maternal fever during labour in 10.62%,multiple intrapartum vaginal examinations (>3) in mother in 4.59%,Chorioamnionitis in 3.62% and purulent foul smelling vaginal discharge in 2.89% respectively. (Table 6)

Table 6: Showing spectrum of risk factors in community acquired neonatal sepsis.

Risk factors	No of patients	Percentage (%)
Low birth weight	180	43.47
Preterm	74	17.87
PROM>18hrs	132	31.88
Delivery at home	92	22.22
Purulent/foul smelling vaginal discharge	12	02.89
Chorioamnionitis	15	03.62
Maternal fever during labour	44	10.62
Multiple intrapartum PV examinations	19	04.59
Perinatal asphyxia	57	13.77

Risk factor profile of nosocomial sepsis

In our study low birth weight (wt<2.5 kg) was found as the leading risk factor in Nosocomial sepsis observed in 24.87% (103) babies of neonatal septicemia, followed by preterm gestation (37 weeks) in 22.70%, invasive and non invasive positive pressure ventilation in 20.28% and central venous/arterial catheterization in 3.14% neonates. (Table 7)

Table 7: Showing the spectrum of risk factors in nosocomial sepsis.

Risk factors	No of patients	Percentage (%)
Low birth weight	103	24.87
Preterm	094	22.70
Positive pressure ventilation	084	20.28
Central venous/arterial catheterization	013	03.14

DISCUSSION

Neonatal sepsis with its high mortality rate still remains a diagnostic and treatment challenge for neonatal health care providers, developing countries having the highest incidence and mortality rates. Early diagnosis of neonatal septicemia helps the clinician in instituting antibiotics therapy at the earliest thereby reducing mortality in neonates. Early identification of an infected neonate also helps in avoiding unnecessary treatment of a non infected neonate.

The study was conducted in the Neonatology Unit of Postgraduate Department of Pediatrics, in G B Pant hospital, an associated hospital of Government Medical College Srinagar. It was a hospital based prospective observational study conducted from 1st April 2018 to 31st March 2019.

All neonates admitted in Neonatology Unit fulfilling the inclusion criteria of the study from 1/4/2018 to 31/3/2019 were prospectively studied observed and recorded.

In the present study an attempt has been made to document the varied clinical presentations, risk factors both in the mother and baby attributing to neonatal sepsis.

Clinical presentation

In our study the commonest presenting feature was lethargy/ refusal of feeds, which was observed in 66.18% (274) cases, followed by hypothermia in 44.20% (183) cases, tachypnoea 40.09 %(166) cases, grunting 32.12%(133) cases, delayed CRT 29.95% (128), prolonged jaundice 14.97% (62),Oliguria 11.83% (49),feeding intolerance 10.14% (42),irritability 9.90% (41), seizures 9.17% (38),diarrhea 7% (29),vomiting 4.83% (20), abscesses 3.38% (14),umbilical discharge 1.93% (8) and pustulosis 0.96% (4) respectively. Our results were comparable with the studies done by R.Nandana Reddy Jonnala et al,[14] Y R Khinchi et al[16] and A S M Nawhad et al.[15] R. Nandana Reddy Jonnala et al[14] in their study observed that the commonest presenting feature was lethargy and refusal of feeds, observed in 59.5% cases followed by Tachypnea in 35.7%, apnea in 34.5%, jaundice and delayed CRT seen in 26.2% each, grunting 21.4% and fever 9.5%. Y R Khinchi et al[16] in their study observed that refusal to feeds was present in 74%, Tachypnea or respiratory distress in 75%, fever in 69%, jaundice in 41%, apnea in 15%. The study done by A S M Nawhad et al[15] observed that poor feeding was presenting feature in 26.7%, respiratory distress in 46.7%, fever in 36.3%, apnea in 20%, jaundice in 50% and abdominal distension in 20%.

Risk factor profile

In our study low birth weight (wt<2.5kg) was found as the leading risk factor in 68.35% babies of neonatal septicemia, followed by preterm gestation (<37 weeks) in 40.57%,PROM>18 hours in mother in 31.88%, delivery at home in 22.22%,positive pressure ventilation in 20.29%, Perinatal asphyxia in 13.77%, maternal fever during labour in 10.62%, chorioamnionitis in 3.62%,central venous /arterial catheterization in 3.14%, purulent foul smelling vaginal discharge in 2.89% and multiple intrapartum vaginal examinations in mother (>3) in 4.59%. The results of our study were comparable with the studies done by R.Nandana Reddy Jonnala et al.[14] who observed low birth weight as leading risk factor in 67.8%, preterm in 70.23%. The results observed by A S M Nawhad et al[15] were low birth weight in 50%, Preterm gestation 51%, PROM>18 hours in mother in 21%, delivery at home in 3.17%, Perinatal asphyxia in 7.33%, maternal fever during labour in 5.4%,multiple intrapartum vaginal examinations in mother in 3.2%, purulent foul smelling discharge in 3.5% and chorioamnionitis in 3.2%. The results observed by R Amru et al[17] were low birth weight in 70%, preterm gestation in 58%, PROM>18 Hours in mother in 13%, delivery at home in 11%, Perinatal asphyxia in 12%, multiple intrapartum vaginal examinations in mother in 7.56%, chorioamnionitis in 2.4%, purulent foul smelling vaginal discharge in 5.3%, maternal fever during labour in 2.1%. Furthermore comparable results were observed by Sinha et al[18] low birth weight in 61%, preterm gestation in 44% and Bhakoo et al [19] (low birth weight-52%, preterm gestation-49%).

The reason for some higher and varied results observed in our study regarding the risk factors of neonatal sepsis could be that our institution is the main tertiary care hospital and referral centre in Kashmir division with NICU set up and ventilator support. Furthermore due to poor antenatal and obstetric setup in our peripheral areas there are a lot of preterm and home deliveries and most of these preterm babies are referred to our institution from across the state of Jammu and Kashmir.

CONCLUSION

Clinical assessment using a combination of symptoms and signs are useful guides to provisional diagnosis of neonatal sepsis. Prevalence of sepsis is inversely related to birth weight and gestational age. High degree of culture positivity is noted in neonatal sepsis. Time has come where a multifaceted approach needs to be put in action for reducing the incidence of community acquired and Nosocomial sepsis.

Following suggestions are highly recommended.

- Prevention of preterm birth is potentially the most effective strategy to decrease the risk of community acquired and Nosocomial sepsis by reducing the size of the most susceptible population.
- Maternal and child healthcare in the peripheral areas needs to be upgraded for better outcome.
- Elimination of overcrowding and understaffing.
- Personnel should remove rings, watches, and bracelets before entering nursery or obstetric areas.
- Fingernails should be trimmed short and no artificial fingernails or nail polish should be permitted. This applies to all the handlers whether at home or neonatology nursery
- A 10-second wash is recommended before and after handling each infant both at hospital and home.
- No alteration of hyper alimentation solutions after preparation.
- Initiation of enteral feedings as early as possible.
- Reduced exposure to intravenous lipids and hyper alimentation.
- Promotion of the use of human milk, ensuring proper collection and storage.
- Initiation of a skin care protocol for all neonates weighing <1,000 g, the goals of which are to promote skin maturation and to prevent skin breakdown.
- Reduced laboratory testing that requires venipuncture or heel stick.
- Development of a systematic approach to intravenous therapy that reduces
- The frequency and number of skin punctures for placement of an intravenous catheter.
- Establishment of a minimum sample size for a blood culture that is 1 ml per aerobic culture bottle.
- Preference for two samples of 1 mL each in two aerobic culture bottles.
- Development of a method to distinguish true infection from a contaminated Culture.
- Minimization of intubation days.
- Minimization of the interruption of the ventilator-endotracheal tube circuit.
- Minimization of the use of central lines, and when used, minimization of the Frequency of daily entries and the duration of use.
- Prospective placement of central lines when intravenous therapy will be of long duration.
- Establishment of sound policies and procedures for line care and access and regular monitoring of compliance.ure
- Promotion of developmentally supportive care, with an emphasis on minimal handling.

- Development and maintenance of a culture of cooperation and teamwork that supports and encourages all team members to feel responsible for outcomes.

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