Neonatal Sepsis

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Introduction

- Every year 2.6million neonates die; three-fourths of these deaths occur in the first week of life; and almost all (99%) in low- and middle-income countries (1)

- Neonatal sepsis is the third leading cause of neonatal mortality, only behind prematurity and intrapartum-related complications (or birth asphyxia) (2)

Terminology

- Neonatal Sepsis is clinical Syndrome in an infant 28 days of life or younger, manifested by systemic signs of infection and isolation of bacterial pathogen from the bloodstream.

- Early-onset sepsis is defined by symptoms before 7days of age. some expert limit the definition to infection occur 72hs and late-onset sepsis is generally as the onset symptom at>/ 7days of age.

Incidence of neonatal sepsis in 1000 live births

- 7,1 to 38 Asia
- 6,5 to 23 Africa
- 3,5 to 8,9 South America
- 1 to 8,1 Europe USA and Australia

S Vergnano Neonatal sepsis: an international perspective
Arch Dis Child Fetal Neonatal Ed 2005;90:F220-FF224

Risks of early onset neonatal sepsis

- Group B Streptococcus infection
- Chorioamnionitis (intraamniotic infection)
- Intrapartum maternal fever
- Maternal GBS colonization
- Preterm delivery
- Prolonged rupture of the membranes.

Risk of late onset neonatal sepsis

- Preterm birth and newborns with prolonged hospitalizations, use of central line, parenteral feeding and mechanical ventilation.

Bacterial pathogens in neonatal sepsis

Early Onset	Common pathogens	Less common pathogen
Term and late preterm infants (GA≥34WG	• Group B Streptococcus • E coli	Enterobacter, Enterococcus, Klebsiella,Listeria ,H influenzea, other enteric gram-negative bacilli,S aureus….
Preterm infants GA≤34WG	• E-coli • GBS	Enterobacter, Klebsiella, listeria, listeria, gram negative bacilli Streptococcus aureus.

Bacterial pathogens in neonatal sepsis

Late Onset	Common pathogens	Less common pathogen
Term and late preterm infants (GA≥34WG	• E coli • GBS • Additional pathogen seen in NICU setting. S aureus	Enterobacter, Enterococcus, Klebsiella,Listeria ,N menigitis, other non enteric gram-negative bacilli,S pneumonia , salmonella, additional pathogens in NICU,
Preterm infants GA≤34WG	• CoNS • S aureus • E Coli • Klebsiella • GBS	Enterobacter, enterococcus Listeria, other non enteric gram-negative bacilli, pseudomonas , seratia

Clinical findings in neonatal sepsis

Finding	Frequency
Tachycardia	+++
Lethargy / Bradycardia	+++
Apnea	+++
Poor perfusion/Hypotension	+++
Cyanosis	++
Respiratory Distress	+++
Jaundice	++
Hyperthermia/ Hypothermia	+++
Irritability	+

Realize studies in three hospitals

- **Ours Objectives:**
  1. Estimate the prevalence of bacterial neonatal sepsis based on pregnancy risk factors.
  2. Define the characteristics of the risk factors, signs and investigations in neonatal sepsis.
  3. Identify the pathogens causing in neonatal sepsis.

Materials and Methods

- **Study design:** Multi-hospital based retrospective study, conducted from Jan 2020 to Dec 2020 at Calmette Hospital in Phnom Penh capital, Kompongcham Referral Hospital in Kompongcham province and Angkor Hospital for Children in Siem Reap province, which are the tertiary hospitals of Cambodia.

- **Inclusion criterias:** All neonates admitted to Neonatal Intensive Care Unit of the 3 Referral Hospitals during the study period, who are treated as suspected of infection in the first week of life.

- **Exclusion criterias:**
  - complex congenital malformation,
  - discharged before laboratory evaluation

- **Data analysis:** Data were entered into EPI-INFO version 7.2.4 . In all analysis, a p-value < 0.05 was considered significant.

Results

- Among 1477 admitted and treated as neonatal infection, we found 241 cases (16.3%) are infected.
- Most of admission is before 3 days of life (> 90%), considered as suspected of early-onset neonatal sepsis

Results

- Among of admission:
  - ❖ Preterm infants : 41,6%
  - ❖Deliveries Site :
    - Public hospital : 86,23%
    - Health center : 5,56%
    - Private clinic : 8,21%
  - ❖Mode of deliveries:
    - Vaginal deliveries : 59,91%
    - C-Section :40,09%,

Results

- Infection was considered highly probable based on clinical and laboratory signs.
  - Confirmed infection 40 cases (2,7%)
  - Infection highly probable cases (13,6%)
  - Infection not Confirmed 1236 cases (83,7 %)

Results

- Among infected neonates were admitted as:
  - Early Onset Neonatal Sepsis : 216 cases (85.62%)
  - Late Onset Neonatal Sepsis : 25 cases (10.38%)
- If we regroupe these 2 categories : the Pecentage of infected newborns were 241 cases (16.3%).

Infected	Frequency	Percentage
Yes	241	16,3%
No	1236	83,7%
Total	1477	100,00%

Results

- Depends on the risk factors, we noticed that :
  - Some of them are not significant related to infection : CRP/WBC maternal, culture positive, UTI, maternal fever (lack of samples or detection?), antibiotics in the mother and ANC
  - Premature, SGA and PROM > 18h, are significant related to infection but do not increase the risk of infection.
  - but *meconium stained liquor* and *perinatal asphyxia* increase significantly the infection.

Characteristics of risk factors related to infection

Risk Factors	Frequency	Percent (%)	Infected (241)	Not infected (1236)	Odds ratio	P value
Premature	615	41.5	77 (31.9%)	538 (43.5%)	0.6	0.0004
SGA	310	21	41 (17%)	269 (21.8%)	0.7	0.0049
PROM>18h	283	19.1	30 (12.5%)	253 (20.5%)	0.5	0.002
Meconium Strain	358	24.2	72 (30%)	286 (23.1%)	1.4	0.015
Low apgar score	295	20	66 (27.4%)	229 (18.5%)	2.1	0.0005
UTI	3	0.2	1 (0.5%)	2 (0.1%)	-	N/A
Increased CRP/WBC	35	2.4	8 (3.9%)	27 (2.1%)	-	N/A
Maternal fever	112	7.6	18 (10.9%)	94 (7.6%)	-	N/A
Culture positive	8	0.5	2 (3%)	6 (0.5%)	-	N/A
Empiric ATB in mother	341	23.6	56 (37.8%)	285 (23%)	-	N/A
ANC : < 4 **≥ 4**	355 1122	24 76	63 (26.1%) 176 (73%)	292 (23.6%) 945 (76.5%)	-	N/A

Results

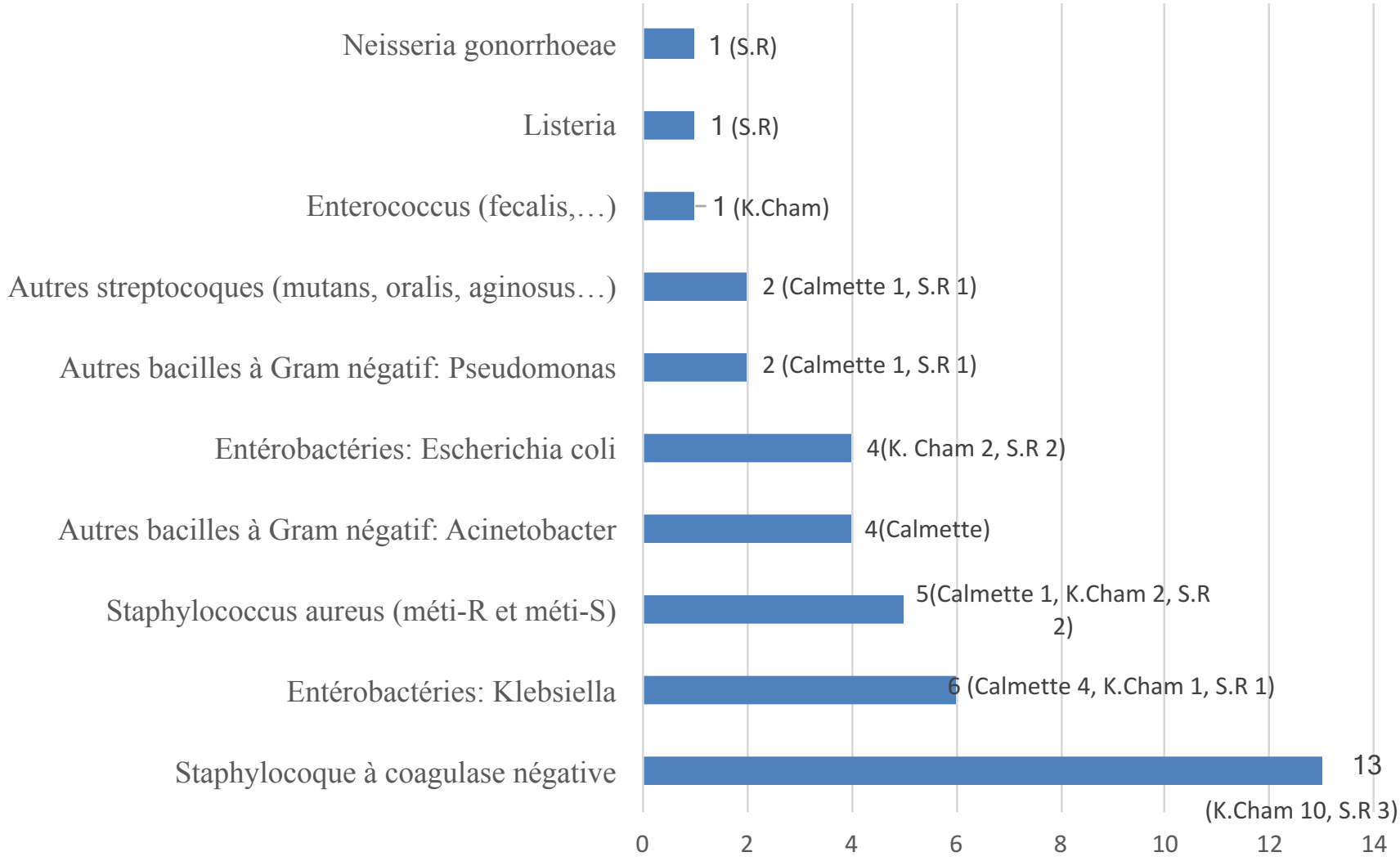
- Clinical signs as *airway failure, abnormal glycaemia, feeding difficulty and neurological signs* are very significant related to and increased the infection.

- The change in *WBC, increase CRP* are very strong correlation with infection as *blood culture* is very sensitive for confirmation. But there are significant statistic that confirmed infection cases (culture+) have normal CRP or WBC.

- Our pathogens isolated are more likely of hospital pathogens.

=> Is it likely that highly unclean delivery practices lead to infectious with nosocomial agents very early in life?? Or is it the community acquired infection??

Cocci gram (+) represented > 50% of bacterias



Characteristics of clinical signs related to infection

Admission clinical signs	Frequency	Percent (%)	Infected (241)	Not infected (1236)	Odd ratio	P value
Hypo/Hyperthermia	441	29.8	76 (31.5%)	365 (29.5%)	-	N/A
Airway failure	512	34.6	83 (34.4%)	429 (34.7%)	1.6	0.0134
Shock	112	7.6	22 (9.1%)	90 (7.3%)	-	N/A
Hypo/Hyperglycemia	687	46.5	133 (55.2%)	554 (44.8%	1.5	0.0019
Seizure/Floppiness	96	6.5	28 (11.6%)	68 (5.5%)	2.2	0.0007
Feeding difficulty	238	16.1	59 (24.5%)	179 (14.5%)	1.9	0.00014
Brady/Tachycardia	36	2.4	10 (4.1%)	26 (2.1%)	-	N/A

Results

- Statistically, among 40 cases of confirmed infection (Culture +), we notified that CRP elevated only 35% vs 65% of normal CRP (P<0.000).

- The same as WBC, which increase 17.5% and decreased 10% of confirmed infection vs 72.5% that found as normal (P<0.000).

- 95% (38/40) are blood culture (different practice of each hospital : systematic for K. Cham and Siem Reap while 20.8% for Calmette).

Outcomes

- 32 death (2.2%) and 17 complications (1.1%)
- Complications and death occurred mostly in infected newborn than not infected (p=0.000).
  - *Mortality rate* is 7.05% of infected newborn vs 1.21% of not infected newborn.
  - And *complications rate* is 3.32% of infected newborn vs 0.73% of not infected newborn.

- Statistically, there is a link between death and prematurity at Calmette Hospital. Among 27 deaths of Calmette Hospital, 25 (92.6%) are premature. (p=00008).

- This statistical link between death and prematurity exists whether the newborn infected or not.
  - Infected newborn (p=0.00003), multiple risk by 10.8
  - Not infected newborn (p=0.0055), multiple risk by 5

  ⇒Infection increase the risk of death of premature.

Results

- Infected neonates have increased the mortality rate and complications in newborn admitted.

- All the babies admitted got experience with empiric treatment by mono-, bi- or tri-therapy of antibiotics depend on different guidelines of the each hospital.

Conclusion

- 1 year study period among 3 hospitals, we found 241 (16.3%) infection cases, included 216 cases (85.62%) of EONS and 25 cases (10.38%) of LONS.

- The study show that all risk factors during pregnancy are not always the risk for the sepsis outcome in neonate. Only meconium stain liquor and low Apgar score at birth are significant increased the risk of neonatal sepsis. But the origin of those risk factors are very important to identify.

Conclusion

- Beside the risk factors, clinical signs in neonatal periods are also very important for us to identify the sepsis case.

- Pathogens founded are positive gram cocci (more than 50%) and followed by negative gram bacillus in our confirmed study cases.

Recommendation

- The study found both maternal factors and neonatal signs as possible risk of neonatal sepsis.

=> Antenatal services might help identify the risk factors and possible interventions to minimize the risk factors of adverse birth outcomes including neonatal sepsis.

=> Healthcare personnel improving the care to mothers by a strong detection (blood culture, Urine examination, Vaginal swab sample for Streto B…) to identify pathogens ASAP that guides to the on-time management of antenatal infections. Also creating an infection-control policy could be a key factor in reducing neonatal sepsis.

Recommendation

- Clinicians are usually compelled to empirically administer antibiotics to infants with risk factors and/or signs of suspected sepsis.

- Using broad-spectrum of antibiotics could increase antimicrobial resistance rate.

  => Review the guideline of diagnosis (clinical + blood tests: CRP, CBC, Culture for all suspected cases) and treatment of neonatal sepsis is one the most important interventions.

Challenges

- Difficulty of multicenter studies which only work well if the same protocol is applied everywhere.

Thank you for your attention!