Causes of presumed neonatal sepsis in Asia

Causes and incidence of community-acquired serious infections among young children in south Asia (ANISA): an observational cohort study
Saha SK, *et al*. Lancet 2018; 392: 145–59

ANISA is a large study which enrolled 84,971 mothers antenatally in Bangladesh, India, and Pakistan, and used community health-care workers to follow up neonates after birth, and identify "neonatal sepsis". It is an important study, because there are few population-based studies of community-acquired newborn sepsis in Asia.

1. **In the ANISA study what proportion of "neonatal sepsis" had a proven bacterial cause?**

   There were 6022 "possible serious bacterial infection" episodes in 63 114 babies, of which only 16% had a proven bacterial cause. However 3061 of the 63,000 babies (4%) died, most of these soon after birth and it is possible bacterial infections was the cause of many of these deaths. More than 90% of the infectious causes that were proven in those neonates who died were bacterial.

2. **What proportion of blood cultures were positive, and what were the common bacteria isolated?**

   Only 102 (2%) of 4859 blood cultures or bacterial molecular assays were positive for clinically significant pathogens. However not all babies had cultures done, especially those who died, so bacterial infections may be more represented in these newborn 3000 who died. E. coli and Ureaplasma were more commonly found in babies who died. The cause of the deaths was not fully established, but likely to be vertically transmitted bacterial infections, complications of prematurity and birth asphyxia (neonatal encephalopathy). The most common bacteria isolated were E coli, Klebsiella spp, Staphylococcus aureus, and group A streptococcus. 66 bacteria were Gram negative, and 36 were Gram positive.

   Some atypical bacteria were commonly identified from nasopharyngeal culture, particularly *Ureaplasma urealiticum*.

3. **What proportion of "neonatal sepsis" was proven to be caused by viruses, and what was the most common virus isolated?**

   RSV was the most commonly isolated virus. Virus infections were the cause of 12% of "presumed serious bacterial infections". RSV was found in 8% of symptomatic newborns, and was considered the cause of 6.5% of cases of neonatal sepsis, and RSV was found in 1% of healthy newborns. Other viruses were found as commonly in symptomatic and asymptomatic newborns, including Enterovirus or rhinovirus and

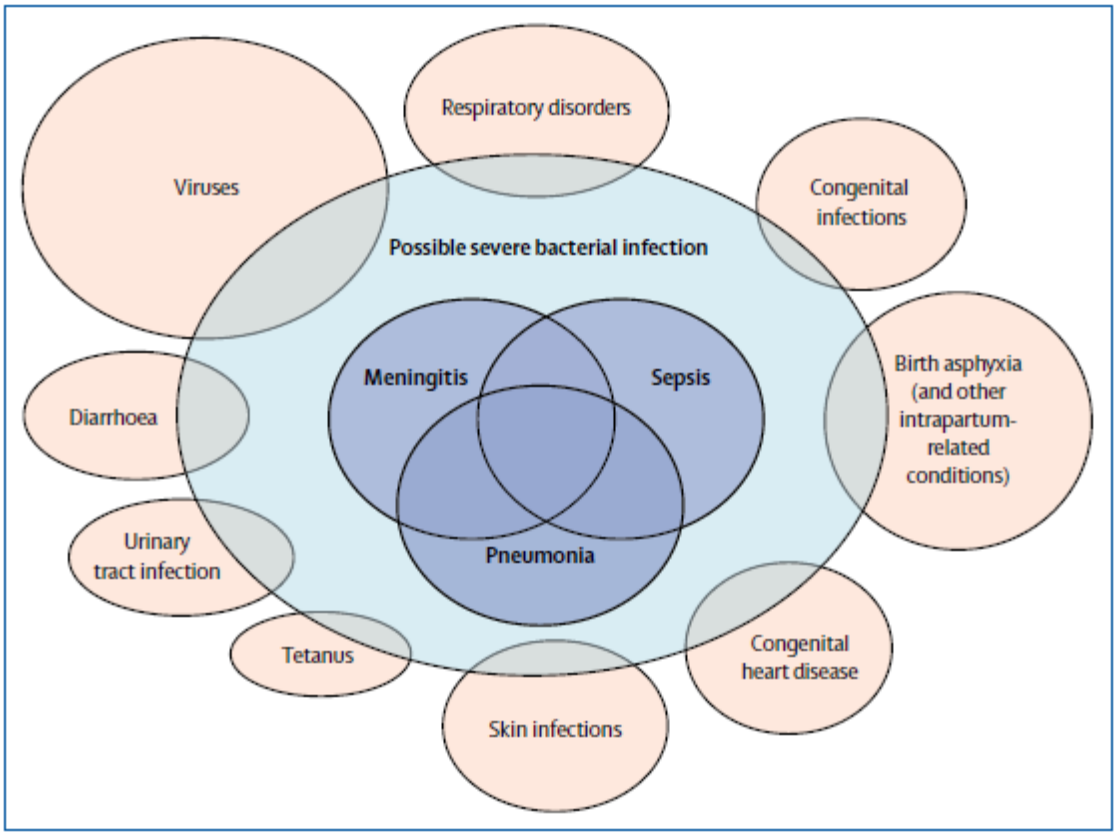
cytomegalovirus was found in 30% and 8% of newborns, both sick and healthy.

4. Were standard treatment antibiotics effective?

Most bacterial infections were susceptible to penicillin, ampicillin, gentamicin, or a combination of these drugs. Isolates were more susceptible to gentamicin (74%) than ampicillin or penicillin (41%). So this means that most community acquired neonatal bacterial infections can be successfully treated with ampicillin (or penicillin) plus gentamicin. It means broader-spectrum and more costly antibiotics such as third-generation cephalosporins (cefotaxime, ceftriaxone, ceftazidime), carbapenems (meropenem), fluoroquinolones (ciprofloxacin) and vancomycin can be kept for proven resistant infections or bacterial sepsis that is failing to respond to first-line therapy.

5. What is the main message of the study, regarding the causes of "presumed neonatal sepsis"?

There is much overlap between the signs of "possible serious bacterial infection" in neonates and other diagnoses. This is illustrated in the figure below, from the accompanying editorial. The signs of what we often diagnose as "neonatal sepsis" and presume is due to bacterial infection, may overlap with virus infections, congenital heart disease, congenital respiratory disorders, and complications of prematurity including hypoglycaemia, hypothermia, apnoea, and birth asphyxia. If a newborn is only mildly unwell, they are more likely to have another condition besides bacterial sepsis, but if a newborn has risk factors or is moderately or severely unwell, the probability of bacterial sepsis increases a lot.



Neonatal jaundice

Neonatal hyperbilirubinaemia: a global perspective
Olusanya, *et al*. Lancet Child Adolesc Health 2018 http://dx.doi.org/10.1016/S2352-4642(18)30139-1

A review of the epidemiology, causes, consequences and treatment of neonatal jaundice.

1. **What proportion of newborns become jaundiced, and what proportion have clinically significant jaundice?**

   Jaundice affects at least 60% of full-term and 80% of preterm neonates. . About one in ten newborn babies are likely to develop clinically significant jaundice and require close monitoring and treatment.

2. **What level of bilirubin is visibly detectable?**

   A total serum bilirubin level of 85-100 micromol/L is visibly detectable.

3. **Is a little bit of jaundice good for newborn babies? Explain.**

   Bilirubin is an antioxidant; a potent superoxide with peroxyl radical scavenger activity.

4. What are the manifestations of bilirubin encephalopathy.

Bilirubin is toxic to the basal ganglia and brainstem nuclei. The early features are poor feeding, lethargy, high-pitched cry, irritability, hypertonia, or when advanced deep stupor, apnoea, opisthotonos, and obtundation. Can lead to chronic bilirubin encephalopathy: choreoathetotic cerebral palsy (kernicterus), hearing loss. Even in people who are not obviously affected by cerebral palsy or deafness, poor school achievement, impulsivity, hyperactivity is more common among those exposed to severe hyperbilirubinaemia in the newborn period.

5. What are the risk factors for severe jaundice in the newborn period?

Sibling history of jaundice, family history of haemolytic disease, prematurity, haematomas (such as a cephalhaematoma), exaggerated weight loss in the first week of life (>10% weight loss).

6. How does phototherapy work, and when should it be started?

Phototherapy works by converting bilirubin to an isomer that can easily be excreted without conjugation by the liver. Photons interact with the predominant bilirubin IXα (Z-Z) isomer and change its structure, converting it to isomers that have increased polarity (photoisomers) that can be excreted in urine and bile without the need for liver conjugation. Therefore, the bilirubin products produced after phototherapy bypass the inadequate conjugation mechanisms in newborn infants thereby accelerating elimination. Effective phototherapy should produce blue-light wavelengths. If blue-light globes are not available, normal fluorescent globes can also be effective. There is some evidence that giving a single dose of clofibrate (a lipid lowering drug) at the beginning of giving phototherapy can reduce the need for phototherapy and lower the bilirubin level.

Where we cannot measure serum bilirubin, phototherapy should be started in a baby who has any jaundice on day 1 of life, deep jaundice involving palms and soles of the feet, prematurity and jaundice, and jaundice due to haemolysis (Hospital Care for Children page 65).

Rebound high levels of bilirubin can occur after stopping phototherapy, especially in preterm babies, so it is really important to monitor babies for 24-48 hours after ceasing phototherapy.

7. What are the indications for exchange transfusion, how does it work, and what are the complications?

Immediate exchange transfusion is indicated if phototherapy fails to effectively reduce the rate of bilirubin rise and the serum bilirubin is near or exceeding exchange concentrations, or if the infant has any signs of acute bilirubin encephalopathy. Exchange transfusion reduces the total serum bilirubin by removing circulating bilirubin, and it can also remove antibodies associated with Rh disease or other autoantibody haemolytic disease, and can also remove damaged red due to G6PD. Complications of

exchange transfusion if not done in a sterile and careful way can be sepsis, electrolyte imbalance (especially hypocalcaemia), portal vein thrombosis (if exchange is done via the umbilical vein), cardiac overload, thrombophlebitis, thrombocytopenia.

8. How can the complications of severe jaundice be prevented?

Teaching mothers and health workers to detect jaundice, and to seek timely and appropriate treatment is the first step in the prevention of potentially hazardous jaundice. Using a bilirubin treatment table (Hospital Care for Children, page 65), early phototherapy, adequate rehydration, checking for and treating malaria if present, and treatment of any bacterial infection.