PARALLELL SESSION 3:

The septic road: step 1 defining the problem

Presenting Author: Ricky Dippenaar, Private Practice

INTRODUCTION: Neonatal susceptibility to sepsis is universal and the leading cause of mortality and morbidly. Environmental modification to reduce surface bioburden and the associated risk of nosocomial infections within the hospital settling represents a cost effective and proven strategy, however implementing measurable change should ideally only occur once the extend of the problem has been defined.

AIM: To evaluate late onset neonatal sepsis within a private tertiary neonatal intensive care unit (ICU) in South Africa.

METHOD: An unpublished preliminary retrospective analysis of all culture and infection marker data on all newborns admitted to Netcare Blaauwberg hospital since opening the neonatal ICU on 1 March 2007 until 31 May 2019. All central lines are routinely sent for culture following removal as surveillance control. Data regarding patient demographics, central line days and culture, all culture results and all positive infection markers were collated from the unit's Vermont Oxford Neonatal Network data, Bluebird antibiotic stewardship program, Netcare Blaauwberg hospital infection control database and Ampath laboratory reports and cross referenced against all admissions.

RESULTS: 1450 infant records were analysed creating a historical time line of culture positive and negative neonatal sepsis depicted relative to admission numbers and sub analysis into <35 preterm and >35 near term and term data. Furthermore key impact measure in infection control are also represented chronologically.

CONCLUSION: Preliminary data on the extend of the problem is evolving and highlights challenges in defining culture negative sepsis. Infective parameters need to be defined for preterm as compared to older infants . Environmental modification is measurable but long term studies are required.

Changes in prevalence and isolated organisms of sepsis in very-low-birth-weight (vlbw) neonates at johannesburg hospital, 2013-2017.

Presenting Author: Daynia Ballot, University of the Witwatersrand
Co-Authors: Charles Adjei Manful (University of the Witwatersrand), Tobias Chirwa (University of the Witwatersrand)

BACKGROUND: This study sought to explore changes in prevalence of sepsis. It further sought to identify and quantify factors influencing the changes in prevalence of sepsis in very-low-birth-weight (VLBW) neonates at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) between 1 January 2013 and 31 December 2017.

METHODS: The study included involved all VLBW neonates born or admitted to the neonatal unit at (CMJAH) between 1st January 2013 and 31st of December 2017 were involved in the analysis. Multivariate decomposition models were used to assess factors influencing the changes in prevalence of sepsis between two successive time points.

RESULTS: During the 5-year period, the overall prevalence almost doubled between 2013 (23%) and 2015 (40%) and later decreased to about 35% in 2017. Prevalence of late Onset Sepsis (LOS) was substantially higher compared with Early Onset Sepsis (EOS). The proportion of infections caused by gram negative bacteria l werewas between 46% and 53.4%. (similar trend was observed for both EOS and LOS).Difference in characteristics over time contributed significantly to the changes in prevalence of sepsis. There was an increase in prevalence of LOS by 8.7% between 2103 and 2014. The results from the decomposition model further show that, the difference in participant's characteristics significantly accounted for about two-thirds (66.3%) of the observed difference (increase) in the prevalence of LOS. The results from the decomposition models shows that increase in proportions of neonates who received blood transfusion significantly influenced the changes in prevalence of LOS by 38.8%.

CONCLUSION: Sepsis remains prevalent among VLBW neonates with remarkable variation over time. LOS is more prevalent and mostly caused by gram negative bacterial. Fungal sepsis is not prevalent in the study area but it is increasing over time. Differences in the proportion of neonates who received blood transfusions, proportion with NEC and proportion who received oxygen on day 28 are important in explaining the difference in prevalence of LOS over time.

Neurodevelopmental impairment at one-year of age in infants with invasive group b streptococcal sepsis

Presenting Author: Firdose Lambey Nakwa, Department of Paediatrics & Child Health, Faculty of Health Sciences, University of the Witwatersrand, South Africa
Co-Authors: Sanjay G. Lala (Department of Paediatrics & Child Health, Faculty of Health Sciences, University of the Witwatersrand, South Africa), Shabir Madhi (Medical Researc of Paediatrics & Child Health, Faculty of Health Sciences, University of the Witwatersrand, South Africa), Ziyaad Dangor (Department of Paediatrics & Child Health, Faculty of Health Sciences, University of the Witwatersrand, South Africa)

BACKGROUND: Invasive group B streptococcal (GBS) disease is associated significant morbidity and mortality in young infants. Approximately 18% of survivors of GBS meningitis have moderate to severe neurodevelopmental impairment, however, there is a paucity of data on neurological impairment following GBS sepsis.

METHODS: A case-control study was undertaken in infants at three secondary-tertiary hospitals in Johannesburg, South Africa. Neurodevelopmental assessment was done at one-year of age using the Denver Developmental screening tool.

RESULTS: Of 122 invasive GBS cases, 87 (71.3%) had sepsis and 35 (28.7%) meningitis. Among the invasive GBS cases, 22 (18%; including 17 of 87 with sepsis) demised during the course of

hospitalization for that episode, and a further two (1.6%; 1 sepsis) died by one-year of age. Five (1.1%) of 449 controls demised by one-year of age. Of the 50 invasive GBS sepsis cases and 160 matched controls followed through to one-year age, 12 (24%) cases (three with moderate to severe impairment) and 10 (6.3%) controls had an abnormal Denver score (aOR: 3.73; 95%CI: 1.33-10.49; p=0.012). Amongst GBS sepsis cases, premature infants had an 18-fold (95%CI: 3.2-105.4; p<0.001) increased odds of neurological impairment at one year of age.

CONCLUSION: Infant survivors of invasive GBS sepsis had a four-fold greater odds of moderate-severe neurological impairment by one year of age. This corroborates the need for strategies to prevent invasive GBS disease prevention in low-resourced settings.Keywords: GBS, sepsis, Neurodevelopmental impairment

Review of -multidrug-resistant enterobacteriaceae in a neonatal unit in johannesburg, south africa

Presenting Author: Daynia Ballot, University of the Witwatersrand
Co-Authors: Rossella Bandini (University of the Witwatersrand), Trusha Nana (National Health Laboratory Service), Noma Bosman (National Health Laboratory Service), Teeena Thomas (National Health Laboratory Service), Victor Davies (University of the Witwatersrand), Peter Cooper (University of the Witwatersrand), Mervyn Mer (University of the Witwatersrand), Jeff Lipman (University of Queensland)

BACKGROUND: Multi-drug resistant organisms are an increasingly important cause of neonatal sepsisAim:This study aimed to review neonatal sepsis caused by multi-drug resistant Enterobacteriaceae (MDRE) in neonates in Johannesburg, South Africa.

METHODS: This was a cross sectional retrospective review of MDRE in neonates admitted to a tertiary neonatal unit between 1 January 2013 and 31 December 2015.
RESULTS: There were 465 infections in 291 neonates. 68.6% were very low birth weight (< 1500 grams). The median age of infection was 14.0 days. Risk factors for MDRE included prematurity (p=0.01), lower birth weight (p=0.04), maternal HIV infection (p=0.02) and oxygen on day 28 (p<0.001).The most common isolate was Klebsiella pneumoniae (66.2%). Total MDRE isolates increased from 0.39 per 1000 neonatal admissions in 2013 to 1.4 per 1000 neonatal admissions in 2015 (p<0.001). There was an increase in carbapenem-resistant Enterobacteriaceae (CRE) from 2.6% in 2013 to 8.9% in 2015 (p=0.06). Most of the CRE were New Delhi metallo-beta-lactamase- (NDM) producers. The all-cause mortality rate was 33.3%. Birth weight (p=0.003), necrotising enterocolitis (p<0.001) and mechanical ventilation (p=0.007) were significantly associated with mortality. Serratia marcescens was isolated in 55.2% of neonates that died.

CONCLUSION:There was a significant increase in MDRE in neonatal sepsis during the study period, with the emergence of CRE. This confirms the urgent need to intensify antimicrobial stewardship efforts and address infection control and prevention in neonatal units in LMICs. Overuse of broad-spectrum antibiotics should be prevented.

Pharmacokinetics and safety of trimethoprim-sulfamethoxazole in hiv-exposed low birth weight infants

Presenting Author: Firdose L. Nakwa, Chris Hani Baragwanath Academic Hospital and the University of the Wiwatersrand
Co-Authors: Adrie Bekker (Family Infectious Diseases Clinical Research Unit (FAMCRU), Stellenbosch University, Cape Town, South Africa), Avy Violari (Perinatal HIV Research Unit, University of Witwatersrand (PHRU), Johannesburg, South Africa), Edmund Capparelli (University of California, San Diego, San Diego, CA, USA), Mark Cotton (Family Infectious Diseases Clinical Research Unit (FAMCRU), Stellenbosch University, Cape Town, South Africa), Mark Mirochnick (Boston University School of Medicine, Boston MA, USA), Mae Cabbasay (Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Heath, Boston, MA, USA), Jiajia Wang (Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Heath, Boston, MA, USA), Bobbie Graham (Frontier Science & Technology Research Foundation, Inc, Amherst, NY, USA), Jennifer Norman (Division of Clinical Pharmacology, University of Cape Town, Cape Town, South Africa,), Lubbe Wiesner (Division of Clinical Pharmacology, University of Cape Town, Cape Town, South Africa,), Katie McCarthy (FHI 360, Durham, USA), IMPAACT P1106 team (IMPAACT)

INTRODUCTION: Limited pharmacokinetic (PK) and safety data exist for low birth weight (LBW ;<2500g) infants receiving trimethoprim-sulfamethoxazole (TMP-SMX) to prevent opportunistic infections.

METHODS: IMPAACT P1106, a Phase IV study assessing PK and safety of antiretrovirals and related medicines including TMP-SMX in South African LBW infants. Analysis included HIV-exposed infants receiving TMP-SMX (20/100mg) from age 6 weeks. PK and safety evaluations were performed from enrollment (7-14 days of life) to week 24. Adverse events (AE) classification included expected (associated with prematurity) or unexpected. Plasma samples were assayed by LC MS/MS methods.

RESULTS:As of October 2018, 39 infants were included with median (range) birthweight 1650g (880-2424) and gestational age (GA) 32 (28-38) weeks. TMP-SMX was started at 5.5 (4.1 – 8.5) mg/kg/day at 39 (35-49) weeks corrected GA, and continued for 16 (3-21) weeks. Twenty-nine infants contributed 138 TMP-SMX concentrations; 38 (28%) observations below quantifiable levels for both TMP and SMX suggesting non-adherence were excluded. Median trough levels were TMP (0.22 mcg/ml) and SMX (7.35mcg/ml). Higher TMP troughs (0.62 vs 0.14 mcg/ml; p = 0.01 from t-test) were observed in infants born <1800g compared to >1800g (Figure 1). Seventeen (44%) had grade 3/4 expected AEs, with sepsis (n=5, 13%) the most common, only rare cases of anemia (n=2, 5%) and thrombocytopenia (n=1, 3%) and no neutropenia. Nine (23.1%) had grade 3/4 unexpected AEs, with pneumonia (n=5, 13%) the most common. Two infants died of SIDS.

CONCLUSION: TMP-SMX prophylaxis was well tolerated; grade 3/4 AEs were assessed as unrelated to TMP-SMX. Higher TMP troughs in infants with the lowest birth weight suggests immature clearance. Standard infant TMP-SMX prophylaxis was safely used in LBW infants from 35 weeks corrected GA.
Keywords: pharmacokinetics, TMP-SMX.