

HIGHLIGHTS ISSAD 2023

OPENING SESSION

- **Dr Lucia Teixeira and Dr Tatiana Pinto, co-leads of ISSAD**

The ISSAD co-leads welcomed all attendees to ISSAD 2023 in Rio de Janeiro, Brazil, and thanked the members of the Local and Scientific Organizing Committees for their commitment to help build up a scientific program of excellence. The co-leads also acknowledged the support provided by the London School of Hygiene and Tropical Medicine and the Bill and Melinda Gates Foundation.

- **Dr Keith Klugman - The road to Gates Foundation Support of a GBS conjugate vaccine delivered through maternal immunization**

Dr Klugman talked about the efforts that have been done over the years on the development of a GBS vaccine, covering the most important aspects in history on the GBS epidemiology. Dr Klugman also highlighted the work the Bill and Melinda Gates Foundation have done to foster the development of a maternal GBS vaccine and to make it affordable in low-and-middle income countries.

PARENT VOICE

In this session, the voices of parents and patients were heard as they shared their histories with GBS disease and the impacts caused in their lives. The Parent Voice session was led by Jane Plumb, Chief Executive and Founder of the Group B Strep Support (<https://gbss.org.uk/>), Marti Perhach, co-founder and CEO of the Group B Strep International (<https://www.groupbstrepinternational.org/>). They are both mothers who lost their babies to GBS in the past and dedicate their lives to raise awareness of GBS disease among the lay public and provide support to affected families. At the beginning of all sessions, a video of parents that suffered from GBS was displayed and their experiences were shared with the audience.

- **Jane Plumb and Marti Perhach - Focus on Families and Partnering with Parents**

Despite all the suffering, Jane and Marti managed to turn the pain of losing their children into meaningful charity work that has informed people across the world and has provided support to many affected families. They advocate for parents' and patients' voices and experiences to be at the center of all efforts to tackle GBS disease, and their goal is to stop group B Strep infection in babies so no family has to endure the pain of suffering from GBS anymore.

WHO MENINGITIS SYMPOSIUM

The WHO Director-General, Dr Tedros Adhanom Ghebreyesus, and Dr Marie Pierre Preziosi talked about meningitis severity and its impacts on the global public health and the economy, affecting people from across the globe. Dr Tedros and Dr Marie Pierre introduced the Defeating Meningitis Global Roadmap launched by the WHO in 2020 and highlighted the achievements made so far, as well as the next steps towards a world free of meningitis.

- **Dr Ruth Lynfield - The increasing importance of group B *Streptococcus* as a cause of bacterial meningitis — United States**

Surveillance data on bacterial meningitis in the US (2008-2021) showed that the disease incidence decreased over the years, driven by a decrease of *S. pneumoniae*, *H. influenzae*, and *N. meningitidis* meningitis, but no significant change was observed for GBS meningitis. However, the relative etiologic contribution of GBS has increased and GBS is the leading etiology among infants aged 0–2m, which is the group with the highest incidence of bacterial meningitis.

- **Dr Margareth IP - Defeating Meningitis 2030: Asian Perspective**

In this presentation, Dr Margareth IP talked about the burden of GBS disease in Asia over the years, the current challenges and the goals to be achieved in next years, including focus on prevention (IAP and vaccination), early management of meningitis, and improved surveillance of meningitis and sepsis.

- **Dr Soufiane Sanou - Pilot surveillance of GBS can inform the development of national plans for defeating meningitis: the Burkina Faso experience**

A study to determine the GBS carriage prevalence in a cohort of pregnant women and the serotype distribution was conducted in Burkina Faso in 2022. The ultimate goal of this study is to foster the development of a national surveillance system for GBS screening.

- **Dr Felipe Neves - Current panorama of bacterial meningitis in Brazil**

Bacterial meningitis reporting is mandatory in Brazil, but a high number of cases don't have information regarding the causative agent and there's no specific data on GBS meningitis in the national database (SINAN). In Brazil, there isn't a public policy for GBS surveillance, which leads to the underreporting of GBS meningitis cases in the national system.

LABORATORY & MICROBIOLOGY

This track aimed to discuss diagnostic methods for detecting GBS, bringing updates on aspects of resistance and distribution of serotypes. Furthermore, data obtained from WGS analyzes were exposed.

Plenary Section Laboratory & Microbiology:

- **Dr Hans-Christian Slotved - Decoding *Streptococcus agalactiae*: Phenotyping vs. Genotyping for Diagnostic Purposes**

Phenotypic methodologies for characterizing GBS, whether for determining serotypes or determining the antimicrobial susceptibility profile, remain important, although methodologies based on genome sequencing have allowed the accumulation of extensive information about GBS.

- **Dr Lesley McGee - Invasive Group B *Streptococcus* Strain Features: A US Active Bacterial Core Surveillance Perspective**

Genomic analysis allows a higher level of strain discrimination to include more detailed identification of major lineages, sub-lineages, genetic determinants of antimicrobial resistance, and vaccine candidate surface proteins. Macrolide, especially clindamycin and erythromycin resistance is common and continues to increase, while isolates resistant to vancomycin remain rare.

- **Dr Uzma Basit Khan - Genomic Mechanisms of Antimicrobial Resistance in global GBS Population**

While still at a very low prevalence, pbp2x mutations associated with reduced beta-lactam resistance have been identified but require careful phenotypic testing and are important to monitor. The genomic data can provide a greater understanding of population structure of GBS and adaptive evolutionary changes, coupled with detailed patient demographic and clinical information.

Oral Abstracts Laboratory & Microbiology:

- **GBS detection among pregnant women from rural western Kenya using an alternative method**

qPCR showed good performance when compared to culture. The DNA extraction step proved to be crucial to the success of the proposed methodology.

- **GBS Serotype IV – a new kid on the block?**

Serotype IV has become more prevalent in recent years, and is associated with higher tetracycline and macrolide resistance, requiring ongoing surveillance.

- **Group B *Streptococcus* prophages: Colonising the colonisers**

Bacteriophages can collaborate in gene transfer and contribute to the colonization or virulence of GBS. Understanding the roles phages play in GBS is an important step to understanding their contribution to health and disease

- **Detection and characterization of aminoglycoside resistance genes associated with mobile genetic elements in Argentinean *Streptococcus agalactiae* isolates**

Integrative and conjugative elements were found to be associated with the presence of the high-level gentamicin resistance gene “acc(6’)-aph(2’)”, as well as macrolides resistance genes and other AMR genes. It is important to take these elements into account since they can lead to the dissemination of antibiotic resistance determinants, the development of multiresistant strains and, consequently, therapeutic failure.

- **Genomic characterisation of virulence factors of *Streptococcus agalactiae* from healthy Indian women**

The virulence genes are more often carried on pathogenicity islands and are seen as clusters of genes. Presence of the pathogenicity islands in commensal GBS is concerning and further studies are needed to understand the role of different pathogenicity islands on diseases caused in neonates.

CLINICS

This session showcased the advancements in GBS research related to clinical settings. The first speaker, Shabir Madhi, emphasized the use of genome data in conjunction with clinical data to gain deeper insights into early onset GBS diseases (EOD). The second speaker, Tara Randis, explored alternative options apart from Intrapartum Antibiotic Prophylaxis (IAP) to reduce maternal colonization.

Plenary Section Clinics:

- **Dr Shabir Madhi - Exploring association of Group B streptococcus genome diversity and early onset disease**

GBS whole genome sequencing studies can inform the burden of GBS invasive disease and evaluate the vaccine impacts on population genome, and geographic differences at serotype, CC, and ST levels should be considered to evaluate EOD and maternal GBS colonization prevalence. Differences in naturally acquired serotype-specific antibodies (IgG) may contribute to differences in the risk of invasive disease and prevalence of maternal colonization.

- **Dr Tara Randis - The Search for Non-pharmacologic Interventions to Reduce Maternal GBS Colonization**

Treatment with probiotics may reduce GBS burden in the vaginal tract, although there's scientific evidence to support its effectiveness in reducing GBS invasive disease. Intrapartum Antibiotic Prophylaxis (IAP) remains as the only effective intervention to reduce the risk of invasive disease in colonized pregnant women but there are promising studies indicating the potential of pre/probiotics to the development of non-antibiotic based interventions.

CAROL BAKER LECTURE

Prof Joy E. Lawn - Group B *Streptococcus*: a myth busting journey

Prof Carol Baker introduced Prof Joy Lawn, who was nominated by the ISSAD Scientific Committee to be honored with the Carol Baker Lecture Award in recognition of her outstanding contribution to GBS research. Prof Joy Lawn talked about GBS “myths” that have slowed priority and progress over the last 3 decades, and the solutions to refute these myths based on interdisciplinary science, global public health measures, policy framing, vaccine development, and public awareness of GBS.

EPIDEMIOLOGY & BURDEN

This track focused on data collection and analysis of the global incidence of GBS disease and outcomes. Talks ranged from multicountry projects such as JUNO and CHAMPS which aim to fill gaps in data on GBS genotyping and outcomes for infants, to location specific projects in Kenya, Denmark, and England. These more specific talks focus on smaller projects detailing the effects of vaginal washing on GBS colonization, effects of GBS infection on mental disorders later in life, and tracking fatal outcomes of GBS disease. Many presenters stressed the need for more data collection to further our understanding of the global burden of GBS disease.

Plenary section Epidemiology & Burden:

- **Dr Dorota Jamrozy - Global genomic epidemiology of Group B *Streptococcus***

The JUNO project aims to define global genomic diversity of GBS to support vaccine development and implementation. Currently, 8,600 GBS genomes were sequenced and data is being analyzed regarding the distribution of vaccine targets and global GBS population structure. The estimated coverage for the GBS6 vaccine is 96%, with regional variability, and 97% for Minervax antigen (alpha-like surface proteins).

- **Dr Konstantionos Karampatas - Late-onset disease transmission and dynamics**
IAP can sometimes lower but not suppress anovaginal colonization, leading to vertical transmission and increasing the risk of late-onset disease. Parent-to-infant transmission post delivery accounts for a large proportion of late-onset disease but is not driven by breastfeeding. Antenatal and postnatal colonization is a dynamic process.

Oral abstracts Epidemiology & Burden:

- **Association between vaginal washing and GBS colonization in women seeking pregnancy**

A research that showed vaginal washing with water and soap and water was associated with four-fold higher detection of GBS and cessation or modification of washing practices could decrease GBS colonization.

- **Long-term risk of mental disorders following iGBS - a population-based study from Denmark**

A talk about a research that investigated if there's a link between iGBS and neurodevelopmental outcomes. The study showed an increased incidence of psychiatric disorders among iGBS exposed children. iGBS meningitis and sepsis were associated with a higher incidence of psychiatric disorders later in childhood.

- **Predictors of fatal outcome in infants diagnosed with invasive GBS infection, England**

A research that used national datasets to assess factors associated with EOD and LOD in England. An increased trend of deaths in infants with LOD was observed in 2022, indicating the need for further data collection to understand this recent phenomenon. Understanding the factors behind infant mortality is essential to improve outcomes.

- **The Global Burden of Group B *Streptococcus* and Implications for Public Health**

A talk about the global panorama of GBS burden in terms of antimicrobial resistance, mortality, and GBS meningitis. In 2019, GBS accounted for nearly 320,000 deaths and is listed among the top 10 bacterial pathogens causing deaths worldwide. GBS is the main bacterial agent of neonatal meningitis and about 50% of cases are caused by antibiotic resistant strains of GBS.

- **Role of Group B *Streptococcus* invasive disease as a cause of stillbirths and neonatal deaths in Africa**

The Child Health and Mortality Prevention Surveillance (CHAMPS) investigates causes of stillbirths and childhood death. Invasive GBS is potentially underestimated as the cause of stillbirths in some lower- and middle-income countries. Better prevention measures, including vaccines, are needed during pregnancy and neonatal period in high-mortality settings.

IMMUNITY & SEROEPIDEMIOLOGY

The Immunity and Seroepidemiology track aims to discuss the role of GBS virulence antigens in inducing immunity and the GBS seroepidemiology to investigate if protein-based and/or CPS-based GBS vaccines would elicit a protective immune response.

Plenary Section Immunity & Seroepidemiology:

- **Dr Gaurav Kwatra- Role of sero-epidemiology in the GBS vaccine development**

A talk about the importance of sero-epidemiology in GBS vaccine development, highlighting the diverse IgG response between different populations around the globe and sharing the findings that transplacental transfer gets better with age in gestation.

- **Dr Lakshmi Rajagopal- Adaptive immunity to GBS hemolysin**

Research on GBS hemolysin highlights that the granadaene lipid is responsible for its activity and that vaccinating against this lipid antigens leads to protection and reduced GBS infection burden.

Oral abstracts Immunity & Seroepidemiology:

- **Development of a standardized opsonophagocytic killing assay (OPkA) to quantify functional serotype-specific anti-capsular polysaccharide (CPS) antibody against Group B *Streptococcus***

A study to develop and optimize the OPkA protocol considering different conditions such as incubation temperature, incubation time, exogenous complement sources and batch pooling between complement, where the finalized protocol was found to be highly sensitive.

- **The U.S. CDC-led study to establish immunologic endpoints associated with protection against infant GBS disease**

In 2018 the US FDA launched a study to aid licensure decision making towards a maternal GBS vaccine focused on serotypes Ia and III, and results showed that more EOD cases are above the minimum antibody level than LOD cases.

- **Impact of HIV status on GBS colonization and antibody responses in serum and vaginal mucosa**

A GBS screening of non-pregnant women in Uganda, a country with high HIV prevalence, found that antibody levels in serum and vaginal secretions are lower in women living with HIV and constant over time despite transient colonization.

- **Anti-gbs2106 protein IgG in serum of newborns and risk reduction of invasive infant GBS disease**

The study focuses on the GBS 2106 gene, a highly conserved gene around the world, and found that an anti-gbs2106 antibody is efficiently transferred from mother to infants.

- **Opsonophagocytosis and molecular epidemiology of GBS strains from carriage and disease in Brazil**

The study comprised isolates with high diversity in serotypes, clonal complexes and surface proteins and all isolates tested were susceptible to killing by serotype-specific serum.

Flash-talks Immunity & Seroepidemiology:

- Impact of surface immunogenic protein deletion on vaginal colonization and cellular interactions in Group B *Streptococcus*
- Maternal GBS serotype-specific antibody prevalence and placental transfer ratios
- Serum-equivalency comparison, detection, & quantification of GBS antibodies from dried blood spots
- Using Dried Blood Spots for a Sero-surveillance Study of Maternally Derived Antibody against GBS
- The Group B Streptococcal serine protease HtrA is a pleiotropic virulence regulator

- GBS hyaluronidase B (hylB) is a potent immunosuppressive virulence factor that promotes adverse pregnancy outcomes in animal models

VACCINES & CONFIDENCE

The Vaccines and Confidence track aims to discuss the distinct formulations of vaccines against GBS in development and the vaccine confidence to support GBS vaccine policy and advocacy.

Plenary Section Vaccines & Confidence:

- **Dr Anna Seale - GBS vaccines**

Dr Anna Seale presented a summary of the current GBS vaccine approaches in clinical studies addressing the importance of GBS vaccine development and considerations for country engagement and global policy to enable maternal immunization at a global level.

- **Dr Jadhav Percio - Vaccination of pregnant women: challenges and lessons learned in Brazil**

In this talk, Dr. Percio from the Brazilian Immunization Program presented the context of prenatal care, the coverage of vaccination for pregnant women, the reasons for pregnant women acceptability to vaccination and what can be done to improve this vaccination coverage among this population in Brazil.

Oral abstracts Vaccines & Confidence:

- **Two doses of the Group B *Streptococcus* vaccine GBS-NN/NN2 induce an immune response in pregnant women living with HIV or not, and their infants, and show an acceptable safety profile**

Results from a phase 2 trial addressing safety for babies over the first 12 months after birth, comparison of transfer rate of vaccine-specific IgG concentrations from mother to baby at birth in women with HIV and without HIV, and functional activity of vaccine-specific antibodies from cord blood in OPkA.

- **Potential efficacy of a maternal GBS vaccine to prevent invasive GBS disease in infants**

The study focuses on the use of correlates of protection to facilitate earlier licensure and access to GBS6 vaccine from Pfizer, showing that based on natural history studies, GBS6 has a predicted efficacy of >80% in South African newborns. Stage 3 is continuing in the US, UK and South Africa.

- **GBS maternal immunisation: A global analysis of health impact and cost-effectiveness**

Results have shown that an effective GBS maternal immunization is likely to be cost-effective and globally reduce GBS burden in children and that, at a regional and country level, cost-effectiveness is sensitive to vaccine prices and to choices policymakers may use to value benefits in improved health.

- **An Improved Multivalent GBS Polysaccharide Conjugate Vaccine with 100% Sialic Acid Retention**

This work reports the use of bioconjugation to improve conjugate vaccines, showing the possibility of producing GBS polysaccharides with a 100% retention of sialic acid residues, leading to an increased control of vaccine design.

- **Future GBS vaccines: Perspectives from pregnant and lactating people, health workers, community members, and policymakers in Kenya**

Although GBS knowledge and awareness are low among pregnant women and community members in Kenya, people would be willing to take a safe and effective vaccine, making this an opportune moment to increase demand for future maternal GBS vaccines through community sensitization, engagement with healthcare providers and advocacy with policymakers.

Flash-talks Vaccines & Confidence:

- A vaccine against GBS based on *L.lactis*: A novel alternative with low value of production
- Assessing GBS Vaccine Acceptance Among Pregnant Women In Rio De Janeiro, Brazil
- Evaluating a Multivalent Group B *Streptococcus* Vaccine in Pregnant Women and Their Infants
- The alpha-like protein vaccine GBS-NN, promotes memory B cell formation in non-pregnant healthy women
- Phase 2b Trial Evaluating the Safety and Immunogenicity of GBS6 Administered Concomitantly with Tdap.

ONE HEALTH SYMPOSIUM

The One Health Symposium's comprehensive approach to addressing GBS illustrated the interconnected nature of global health ecosystems and the imperative for collaborative solutions that span human, animal, and environmental health sectors.

Plenary One Health Symposium:

- **Dr Tim Barkham - Foodborne invasive GBS**

Insightful discussion on the emergence of foodborne GBS highlighted the importance of integrated approaches combining food safety and public health.

- **Dr Carlos Leal - GBS in aquatic species and vaccination of tilapia**

Research on GBS infections in tilapia underscored the relevance of vaccination in aquaculture, linking animal health directly to food security.

- **Dr Chiara Crestani - Unveiling the Dynamics of Host Adaptation in Group B *Streptococcus*: a Key Trio of Accessory Genomic Elements**

Presentations delved into the genomic intricacies that enable GBS to infect a variety of hosts, offering perspectives for targeted prevention strategies.

Oral Abstracts One Health Symposium:

- **Whole-genome analysis of human and animal *Streptococcus agalactiae* identified in Hong Kong SAR:**

This study shows genomic evidence that multiple hosts can share similar ST types with similar antimicrobial resistance gene profiles, shedding light on its potential for zoonotic transmission.

- **Phylogenetic Analysis Reveals Ancestral Host Association of Clonal Group 103/314 in Humans and Cattle**

Results have shown that using phylogenetic analysis can trace ancestral host associations. This research provided insights into the pathogen's history and potential patterns of cross-species transmission, which is vital for predicting and preventing future outbreaks.

Flash-talks One Health Symposium:

- Prevalence and Antibiotic Susceptibility of *S. agalactiae* in Macaca mulatta Vaginal Secretions
- Antimicrobial resistance in GBS and *S. aureus* from bovine mastitis in Brazil over 35 years
- Group B *Streptococcus* ST103 is a host-generalist lineage in Brazil able to infect humans and cattle
- *Streptococcus agalactiae* genetic diversity from human and cattle microbiota in Paraíba state, northeast Brazil
- Comparative genomic analysis of serotype III/ST17 GBS strains from human and animal sources

GBS DISEASE IN ADULTS

This track focused on discussing GBS infections in non-pregnant adults that are challenging to diagnose and report due to non-specific symptoms, low awareness among healthcare providers, and limitations in diagnostic testing. There is no routine screening for GBS in non-pregnant adults, and the variability in how these infections present makes it difficult to recognize a common pattern. Data collection also faces challenges, resulting in potential underreporting and incomplete information about the incidence of GBS infections in this population.

Oral Abstracts GBS disease in adults:

- **Molecular epidemiology of Group B *Streptococcus* infection in Thailand shows hypervirulent clone ST28**

This study highlights the importance of incorporating GBS genomic data from broader demographic groups, other than just maternal or infant groups, in order to inform the development of a GBS vaccine that will provide protection across age groups and geographical settings.

- ***Streptococcus agalactiae* isolated from semen samples in Brazil**

This study brought data on isolates from semen samples whose data are scarce in literature. The actual impact of these findings is not yet known, reinforcing the need for additional studies.

- **Population heterogeneity and antimicrobial resistance of Serotype V Group B *Streptococci* in India**

The study reveals the existence of a diverse population pool of Serotype V among the Indian circulating strains of GBS harboring a unique convergence of resistome and virulome. The population is different from other parts of the world. Vaccine formulations could aid in combating and diversity of circulating population in India has to be considered while formulating vaccines.

- **Invasive *Streptococcus agalactiae* causing disseminated infection in a non-pregnant adult**

This is a case study. PCR was negative for GBS, but blood culture showed positive for GBS. The patient had complications due to the infection and died after 7 days. In recent years, GBS has been shown the potential to cause invasive disseminated infection in adults with chronic comorbidities.

HOT TOPICS YOUNG ISSAD

The Hot Topics Young ISSAD track features the most recent, innovative and cutting-edge science that have been done by early-career scientists.

- **Dr Elita Jauneikaite - Genomic advancements in understanding Group B *Streptococcus* disease**

In this talk, Dr Jauneikaite highlighted the significant progress made so far to unravel and contain Group B *Streptococcus* (GBS) globally and the role genomics played in such advancement. Genomics is useful to understand GBS co-colonization. The talk was concluded with the following reflection: how (and if) multiple colonization in mother or babies affect the baby's chance of getting infection? How antimicrobial resistance and mobile genetic elements drive GBS evolution?

Oral Abstracts Hot Topics Young ISSAD:

- **Pangenome analysis of group B *Streptococcus* (GBS) reveals the emergence of hypermutators recovered after intrapartum antibiotic prophylaxis (IAP) that impact colonization**

This study presented on the pangenome analysis of GBS and emergence of hypermutation after intrapartum antibiotic prophylaxis. Variation between persistent isolates with the same serotype after intrapartum antibiotic prophylaxis, besides that evidence of microevolution in GBS recovered after IAP that promote persistent colonization were also observed.

- **Estimating incidence of group B *Streptococcus* early onset disease in Africa and Asia**

This study presented a modeling study to predict the risk of GBS EOS using characteristics of GBS colonized mothers and their infants in Africa and Asia. Results showed that reasonable estimates to predict incidence of EOD can be obtained through clinical, demographic and immunological features.

- **CRISPR1-RFLP typing of serotype III Group B *Streptococcus* from human, bovine and fish hosts**

This study assessed the use of CRISPR-RFLP typing methods for detection of GBS strains infecting multiple hosts in Brazil and demonstrated that the combination of these methods can be suitable for GBS surveillance in resource-constrained settings.

- **Burden, antimicrobial sensitivity and seroepidemiology of Group B *Streptococcus* in Uganda**

This study described the epidemiology of maternal colonization and iGBS in Uganda.

- **TLR4 agonist vaccine adjuvant based on SIP from GBS promotes cross-presentation by Dendritic Cells**

This study presented on the biological function of the surface immunogenic protein (sip) from GBS to act as vaccine adjuvant.

- **Unraveling the characteristics of Group B Streptococci isolated from Indian Hospitals over Six Years**

This study presented results from a 6-year study on characteristics of GBS isolates from Indian hospitals.

FAREWELL LUNCH AND CLOSING SESSION

In the closing session, prof Sérgio Fracalanza and prof Lucia Teixeira (Federal University of Rio de Janeiro) received a tribute from the Young ISSAD Committee for their outstanding contribution to GBS research, especially in Brazil. Prof Tatiana Pinto announced the name of ISSAD 2023 mascot, “Açaí”, and the winners of the Best Presentation Award of each track. Lastly, Prof Tatiana Pinto thanked all participants, speakers, and committee members for attending ISSAD 2023, in Rio de Janeiro, Brazil.

This document was produced by the Young ISSAD Committee.

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