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Summary of the doctoral thesis “GLOBAL EVALUATION OF MATERNAL SEPSIS”

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Sepsis represents a medical emergency that is well-known to be one of the preventable causes of death, being defined as a life-threatening organ dysfunction that is the result of the dysregulated host response to infection. When evaluating maternal sepsis worldwide, sepsis remains one of the leading causes of maternal mortality and morbidity, despite the decrease in global maternal mortality; most of these cases are reported in low- and middle-income countries. Infection is still an important and life-threatening complication of pregnancy and childbirth. Unfortunately, normal physiological changes during pregnancy might significantly alter diagnosis criteria and the treatment response in case of maternal sepsis.

Recognizing the lack of focus and research in the area, in 2016 the WHO created a consensus definition, based on international expert consultation and a systematic review: “Maternal sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or post-partum period”. The next step was GLOSS (Global Maternal Sepsis Study).

GLOSS was a prospective, one-week inception study that took place in 52 countries from different WHO regions across the world. From November 28, 2017 until December 4, 2017 all women admitted to 713 facilities from countries included in the study, with suspected or confirmed infection, during any stage of pregnancy, including postpartum and post-abortion, up to the 42nd day after the end of pregnancy were enrolled in the study.

The first study evaluated 1456 women with a single source of pregnancy-related infection included in the GLOSS study regarding the method of diagnosis, causative pathogens and antibiotics used to treat the source of infection. Urinary and genital tract infections were the most common pregnancy-related infections among pregnant or recently pregnant women. The commonest uropathogen was *Escherichia coli* and for skin/soft tissue infection the most frequent causative pathogen was *Staphylococcus aureus*. Cephalosporin was the commonest antibiotic class prescribed for urinary tract infection and metronidazole for other sources of infection.

The second study described rates of infection in 502 hospitals included in the GLOSS study, evaluated facility- and area-level factors that could influence the variation in rates between facilities and assessed the association between severity of infection and the rate of infection. The majority of hospitals were public (77%) and 44% were university facilities. Most of the hospitals were located in an urban area, 37% being a tertiary level hospital and 22% a primary level hospital. Facilities with



a high rate of infection were more likely to be university facilities and with a higher volume of births. Facilities with a high rate of infection are more likely to be a part of an endemic area.

The third study assessed the adherence to WHO recommendations regarding the management of direct obstetric risk conditions and explored other factors associated with severity amongst women with pregnancy-related infections. From the total of 1195 pregnant and recently pregnant women 198 suffered an infection-related severe maternal outcome. Most of those women (57%) were postpartum when the infection was suspected or confirmed. Data regarding usage of prophylactic antibiotics showed that coverage varies within countries, the presence of certain risk factors making women more likely to receive such intervention. Was found a significant number of women for whom the WHO recommendations for prevention of peripartum infection such as pre-operative vaginal cleansing for women who undergo caesarean section were not followed. It was also noted missing data on the use of preventative measures, which is a concern and highlights the importance for this information to be included in medical charts.

The fourth study described prevalence of infection and characteristics of pregnant, postpartum, post abortion women with infection included in the GLOSS study in Europe and evaluated differences between Eastern and Western Europe regarding characteristics of women, diagnosis and management of maternal infections. The country with the lowest prevalence of maternal infection/ 1000 livebirths was Belgium with 14.55/1000 livebirths and the highest ratio was recorded in Moldova, with a ratio of 118.86/ 1000 livebirths. Several differences between Eastern and Western Europe were identified such as antibiotics used to treat the source of infection. Women from Western Europe received penicillin more often and lincosamides as treatment. For women with infection from Eastern Europe cephalosporins and metronidazole were more often used as treatment. Among women from Western Europe, about 40% received antibiotics in the “golden hour” and 19% before meeting the WHO criteria of suspected or confirm infection.

The fifth study evaluated frequency and maternal risk factors associated with adverse perinatal outcomes among women with suspected or confirmed infection during pregnancy from low- and middle-income countries. 276 infants born alive were suspected of having a neonatal infection, among those 199 neonatal near-miss and 20 perinatal deaths. The perinatal death's rate was 108.5 per 1000 livebirths and 40.0% of stillbirths were fresh. Any condition that affects the mother's health during pregnancy or immediately after birth can result in a worse perinatal outcome.

The sixth study evaluated the risk of death among patients with healthcare-associated infections (HAIs) admitted in Intensive Care Unit (ICU), hospitalized for cardiovascular diseases. . For patients acquiring a HAI during their stay in ICU, the risk of death is significantly higher than those with similar cardiovascular pathologies, with a longer hospitalization and a consequent rise in costs for the healthcare system.

Assessing the burden of maternal infections, as well as management across the world, raising awareness about maternal sepsis for women, policy-makers and healthcare workers, and creating strategies for prevention, early identification and prompt management will ensure the reduction of maternal morbidity and mortality related to sepsis.