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How to prevent sepsis in Mozambican primary health care: a literature review

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Abstract

Introduction

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection and is worldwide one of the leading causes of infant mortality and the third most frequent direct cause of maternal mortality. Organised and systematic assessment is crucial to identify sepsis early, when signs and symptoms may still be very subtle, as this is when there are most opportunities for interventions. But the World Health Organization has already found that antimicrobial resistance of pathogens responsible for common infections is extremely high.

Objective

To identify strategies and interventions to reduce the occurrence of sepsis in primary health care.

Method

Bibliographic review of references available at the Family and Community Medicine Resource Centre of the Medical Residencies Committee of the Faculty of Health Sciences of Lúrio University. Two keywords were used (septicaemia, sepsis) and 5 books and 62 articles were selected, 17 were excluded and 45 articles and 5 books were referred to.

Results

The 50 reviewed publications show a long list of conditions and procedures at the origin of sepsis. Likewise, its signs, symptoms and complications are multiple and diverse, also depending on its cause. Reducing the occurrence of this pathology can be achieved with general, public health recommendations as well as specific measures aimed at controlling the different risk factors.

Conclusion

The incidence of sepsis has decreased, but it remains a major cause of maternal and neonatal death. There are effective public health measures to reduce its occurrence, which should be implemented by the National Health Service. Strict aseptic rules, a thorough and targeted anamnesis in risk groups, as well as a high level of quaternary

prevention and health education for patients and families are recommended for the doctor.

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Introduction

Sepsis is defined as a set of pathological manifestations due to the invasion, by blood, of the organism by pathogenic germs from an infectious focus.^[1]

It corresponds to the most serious stage of infectious disease in which the spread of pathogens extends to the whole organism: a general infection due to high and repeated discharges of pathogenic bacteria into the blood. Originating in a septic focus, this continuous migration of germs causes serious general signs due to microbial embolisms, the action of toxins and the harmful effects of cell disintegration products, symptoms which leave the initial infectious focus in the background.^[2]

Septicaemia should be defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection (systemic inflammatory syndrome of response to infection, called 'cytokine storm').^{[3][4]}

In 2017, there was an estimated global incidence of 48.9 million cases of sepsis with a mortality of 19.7%. From 1990 to 2017 mortality decreased by 52.8%. In improving prognosis, early recognition and stratification of severity and therapeutic approach in the first hour are critical.^[5]

Worldwide, sepsis is one of the leading causes of infant mortality. Its prevalence in children and adolescents varies from 1.4 to 8.9% according to different studies and mortality from 5.6 to 24%.^[6]

A study conducted in Nampula Central Hospital (NCH) neonatal unit (2011), with 2,540 newborns admitted, found 20% with a principal diagnosis of sepsis. The lethality rate was 47% and the hospital-specific mortality rate for sepsis was 30%. About 35% were late hospital sepsis cases related to prematurity (25%) and severe asphyxia cases (10%); 40% were community late sepsis cases and the remaining 25% were early sepsis cases.^[7]

In 2013, the Ministry of Health of the Republic of Mozambique presented in the Health Sector Strategic Plan PESS 2014-

2019 neonatal and puerperal sepsis mortality rates of 17%.^[8]

A study conducted in the neonatal unit of NCH in 2016 and 2017 pointed to sepsis as the second leading cause of hospitalization (24%), occupying the third position in the causes of death (25%).^[9]

Maternal sepsis, although its incidence has been decreasing over the last 30 years, remains the third most frequent direct cause of maternal mortality. It is currently defined as a life-threatening condition resulting from organ dysfunction caused by an infection during pregnancy, delivery, after abortion or during the puerperium.^[10]

It is estimated that the mortality rate of postabortion or puerperal septicaemia, due to *Clostridium perfringens* and when associated with intense haemolysis, reaches between 40 and 70% of patients.

According to the International Classification of Diseases, in 2007 in Brazil, sepsis was the second cause of maternal mortality (10%).^[11]

A study conducted in NCH found puerperal septicaemia rates between 1.17 and 2.1% with a maternal mortality rate of 21.9%.^[12] Another study conducted in Southern Mozambique between 2015 and 2017 found a prevalence of 3.9% of obstetric sepsis.^[13]

There are various screening and scoring systems for sepsis, incorporating vital signs and state of consciousness. NEWS checks six parameters: temperature, respiratory rate, pulse, oxygen saturation, systolic blood pressure and state of consciousness. The MEWS includes temperature, heart rate, blood pressure, respiratory rate, mental status, and urine output.

An organised and systematic assessment is crucial to identify sepsis early, when signs and symptoms may still be very subtle, as this is when there are more opportunities for intervention. By the time shock becomes clearly recognisable, organ dysfunction may have already occurred, or the effectiveness of interventions may be severely limited.

The World Health Organization (WHO) has identified a new challenge, finding that antimicrobial resistance of pathogens responsible for common infections is extremely high: in the Middle East, 90% of new-borns hospitalised with sepsis had antibiotic-resistant bacteria; the same was true in 66% of new-borns in sub-Saharan Africa.^[14]

The diagnosis and treatment of this pathology are the domain of hospital medicine, in the subspecialties of internal medicine, infectious diseases and intensive care. For family and community medicine, taking care of 95% of the population's health problems in primary health care and focusing on health education activities, including disease prevention, is particularly important to intervene to prevent this disease with a high mortality rate.

Objective

To identify strategies and interventions in primary health care to reduce the occurrence of sepsis.

Method

Literature review, conducted in September 2022, using the physical and digital references available at the Family and Community Medicine Resource Centre (CREMEFAC) of the Medical Residencies Committee (MRC) of the Faculty of Health Sciences (FHS) of the Lúrio University (LU) in Nampula.

Two keywords were used for the literature search (septicaemia, sepsis) and 62 articles and 5 books were selected; 11 articles were excluded after reading the abstract; 51 were analysed in detail and 6 were excluded. The results presented stem from the analysis of 45 articles and 5 books.

The results were presented and discussed by colleagues at the “First Sepsis Symposium” on the LU campus at Marrere, Nampula in October 2022.

Results

Etiopathogenesis

A 1988 study showed that adopted children had a 5.81-fold increased risk of dying from infection if their birth parents had died from sepsis. There are genetic links to the body's ability to recognise invading microbes, produce certain cell lines or manufacture cytokines, increasing the risk of death from sepsis.

We can consider as risk factors for sepsis the PIRO concept: P - predisposition (pre-existing comorbidities), I - infection (some organisms are more lethal than others), R - response to the infectious challenge, O - organ dysfunction and failure of the coagulation system.

It is estimated that 50% of septicaemia due to gram-negative bacteria originate in the genital-urinary tract, resulting from pyelonephritis, septic catheterisation, bladder interventions, female genital tract, and biliary tract infections. Sepsis due to Gram-positive bacteria most often comes from cutaneous infections.^[15]

Thus, we must consider three determining dimensions of this disease: 1) genetic predisposition; 2) pre-existing clinical conditions; 3) pathogen(s). Without indicating the order of prevalence, we will present the most frequent ones.

Pre-existing clinical conditions

a) In obstetrics

- Incomplete, unsafe abortion.^[16]
- Spontaneous abortion.
- Anaemia in pregnant women.^[17]
- Pregnant woman's delay in arriving at the maternity hospital.
- Complication of labour (3rd stage of vaginal delivery: uterine atony, genital tract trauma, retained placenta, uterine

inversion).^[18]

- Poor personal hygiene of the pregnant woman and infection prevention techniques during delivery.
- Uterine artery embolization.^[19]
- Endometritis
- Ectopic or molar pregnancy.^[20]
- Ascending infection of the woman's genital tract.
- Intrauterine infection of the pregnant woman.
- Female genital mutilation.
- Prolonged labour at term.
- Burning of the skin (in pregnant women >20%).
- Retained placenta.
- Premature rupture of membranes preterm (<37 weeks gestation).

b) In the area of child health

- Severe asphyxia of the new-born.
- Intranasal foreign body in the child.^[21]
- Postpartum umbilical cord infection.
- Neonatal intensive care admission.^[22]
- Prematurity of the new-born.
- Very low birth weight newborn.^[23]
- Invasive mechanical ventilation in children.^[24]
- Intravenous route in the new-born.

c) Adverse drug reactions (ADR)

- ADR from the treatment of resistant tuberculosis (with Linezolid or Bedaquiline).^[25]
- Treatment with Clozapine (treatment of resistant schizophrenia).^[26]
- Treatment with Tocilizumab (monoclonal anti-interleukin 6 - IL-6 antibody - used in the treatment of rheumatoid arthritis and giant cell arteritis).^[27]

d) General

- Peri pharyngeal space abscess (post-angina).
- Agranulocytosis.
- Aplastic anaemia
- Sickle-cell anaemia.^[28]
- Septic arthritis.^[29]
- Postoperative complication.^[30]
- Diabetes.

- Acute haemorrhagic diarrhoea.
- Chronic liver disease.
- Chronic pulmonary disease.
- Ritual scarification by the traditional health practitioner.
- Exsanguinous transfusion.
- Injecting drugs dependence.
- Lack of up-to-date immunisations.
- Necrotising fasciitis.^[31]
- Cystic fibrosis.
- Septic foci (boils, anthrax, urinary infection, thrombophlebitis, empyema of the gall bladder).
- Impaired heart function.
- Major surgery.^[32]
- Acute hepatitis.
- Immunotherapy.
- HIV infection.^[33]
- Advanced neoplasia (leukaemia, lymphoma, metastases from solid tumours).
- Chemotherapy.
- Radiotherapy.
- Systemic inflammatory response syndrome (SIRS): non-specific response of the host to different infectious or other aggressions (traumatic, toxic, burns).
- Prolonged length of stay in intensive care.

Pathogens

- Infection with *Bacillus anthracis* (Anthrax).
- Infection by gram-negative bacteria (*Yersinia pseudotuberculosis*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*).^[34]
- Infection with *Clostridium*, *Bacteroides*, *Chlamydia*, *Mycoplasma*, *Listeria monocytogenes*.
- Infection with endotoxin-producing enterobacteria (*Escherichia coli*, *Enterobacter cloacae*).^[35]
- Infection with group A beta-haemolytic streptococcus, *Staphylococcus aureus*, *Pseudomonas (Pseudomonas pseudo mallei*, Gram-negative bacillus which causes the disease Melioidosis).
- Fungal infection.
- Gonococcal infection.
- Meningococcal infection: produced by *Neisseria meningitidis* (gram-negative diplococcus) constitutes more than 90% of cases of neonatal septicaemia worldwide. It is caused by three sera groups: sera group A, the main cause in underdeveloped countries, and sera groups B and C, which constitute most cases in industrialised countries.^{[36][37]}
- SARS-CoV-2 infection.^{[38][39][40]}
- Malaria.
- Syphilis.

- Monkeypox.^[41]

Clinical

Septicaemia can evolve in different ways, depending on the subject, clinical condition, and pathogen responsible. One may encounter various signs, symptoms, and complications.

Signs and symptoms

- Acidosis.
- Cardiac arrhythmia.^[42]
- Cyanosis.
- Confusion or disorientation.
- Convulsions.
- Diarrhoea, nausea, vomiting.
- Dyspnoea.
- Extreme pain or discomfort.
- Hemoglobinemia.
- Haemoglobinuria.
- Unconjugated or conjugated hyperbilirubinaemia.
- Hyperthermia (shivering or feeling very cold).
- Neonatal hypoglycaemia.^[43]
- Hypothermia.
- Hypotension.
- Hypovolaemia.
- Jaundice.
- Damp or clammy skin.
- Polypnea.
- Pus, secretions.
- Flu-like symptoms.
- Tachycardia.

Syndromes

- Septic shock.
- Disseminated intravascular coagulation.^[44]
- Neonatal cardiovascular collapse.
- Sudden and unexpected postnatal collapse.^[45]
- Cardiovascular dysfunction.

- Diaphragmatic dysfunction.
- Pulmonary oedema.
- Encephalopathy.
- Endocarditis.
- Empyema.
- Open wound.
- Metastatic septic foci (lung abscess, kidney, prostate, parotid, bone marrow).
- Massive intravascular haemolysis.
- Upper digestive haemorrhage (newborn infant).
- Haemorrhage of the adrenal glands (adrenal "apoplexy").
- Infection of the urinary tract.
- Respiratory infection.
- Infertility.^[46]
- Heart failure.
- Acute liver failure.
- Acute renal failure.
- Respiratory failure.
- Lymphangitis.^[47]
- Death.
- Cardiac arrest.
- Cytomegalovirus reactivation in intensive care patients.^[48]
- Emetic syndrome.
- Haemolytic uraemic syndrome (acute kidney injury, thrombocytopenia and microangiopathic haemolytic anaemia).^[49]

Prevention

The most affected groups by this pathology are pregnant women, parturient and puerperal women, children under one year of age and especially new-borns, immuno-compromised (HIV, Nutritional Acquired Immunodeficiency Syndrome - NAIDS, chemotherapy, radiotherapy, immunotherapy), elderly and intensive care patients, patients treated with corticosteroid anti-inflammatory drugs.

As preventive measures, we can consider general recommendations and specific guidelines for each risk factor.

General guidelines

- Expanded vaccination of populations (rate varies according to vaccine type, up to 95%).
- In Mozambique, annual HIV testing and early initiation of ART when positive.
- Personal hygiene of health professionals, availability of personal protection equipment.

- Asepsis of infrastructure, equipment and consumables in health units and control of the movement of people.
- Directed anamnesis.
- Quaternary prevention: adjust and reduce diagnostic manoeuvres and therapeutic procedures.

Specific guidelines

Table 1. prevention of the most frequent risk factors for sepsis in Mozambique.

Risk factor	Prevention
Unsafe abortion	<p>Family planning / contraception</p> <p>Voluntary interruption of pregnancy in hospital with qualified professional.</p>
Pregnancy	<p>Nutrition education of women of reproductive age.</p> <p>Prenatal consultation.</p> <p>Anaemia screening.</p> <p>Early identification of severe infection.</p>
Infection	<p>Asepsis of health professionals, facilities (drinking water and sanitation),^[50] equipment and consumables.</p>
Patients and families	<p>Educate about the early symptoms of severe infection and sepsis and when to seek care for an infection, especially for those at the highest risk.</p> <p>Remind patients that caring for chronic illnesses helps prevent infections.</p> <p>Encourage infection prevention measures such as hand hygiene and vaccination.</p>
Delivery	<p>Asepsis (health care workers, facility, equipment, and supplies).</p> <p>Use of chlorhexidine in umbilical cord care.</p>
Low weight / pre-term newborn	<p>Family planning.</p> <p>Dietary education for women.</p> <p>Prenatal consultation.</p> <p>Improve access to essential new-born care, including neonatal resuscitation and follow-up, with emphasis on the first week of life.</p> <p>Expand the number of health units offering new-born care.</p>
Antimicrobial resistance	<p>Correct diagnosis.</p> <p>Targeted antibiotic therapy (culture, antibiogram).</p>
Nutritional acquired immunodeficiency syndrome	<p>Nutrition education for women.</p> <p>Consultation of the child at risk.</p> <p>Food supplements.</p>
HIV	<p>Antiretroviral treatment.</p>

Conclusion

The incidence of sepsis has decreased over the last three decades but remains a leading cause of maternal and neonatal death with multiple causes, exacerbated in the last two years due to the SARS-CoV-2 pandemic. There are effective

public health measures to reduce the occurrence of this acute disease, which should be implemented by the National Health Service (family planning, vaccination programme, asepsis of health facilities and equipment). Strict asepsis rules, a complete directed anamnesis in risk groups, as well as a high level of quaternary prevention and health education of patients and families are recommended for the family doctor.

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