

Microbiology of Postoperative Sepsis: Pharmacotherapy, Antibiotic Resistance and Associated Mortality

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ABSTRACT

Postoperative sepsis (POS) is a condition characterized by infection occurring after surgery, often caused by microbial contamination, with potential severe consequences including widespread inflammation and organ failure. This comprehensive review delves into the intricate landscape of postoperative sepsis, causative microorganisms, global incidence, mortality rates, and diverse treatment approaches across different surgical procedures. Microbial factors, ranging from contaminated instruments to the host's skin flora, can contribute to POS. The prevalence of resistant microorganisms in healthcare settings amplifies the complexity of treatment and underscores its critical impact on postoperative outcomes. Effective pharmacotherapy forms the basis of treating POS, where timely initiation of broad-spectrum antibiotics is significant. Antibiotic choices are tailored according to local resistance patterns, where drugs such as carbapenems, vancomycin, and linezolid are commonly employed for the treatment of multi drug resistant organisms. The multifactorial nature of POS, influenced by host immunity, antibiotic usage, anaesthesia types, and surgical duration, is dissected to highlight areas for targeted intervention. The review culminates in a discussion of potential avenues for research and improvement in the management of postoperative sepsis on a global scale.

KEYWORDS postoperative sepsis, surgical infections, microbial contamination, antimicrobial resistance, mortality rates, antibiotic therapy, global incidence

INTRODUCTION

Nearly 40.0% of postoperative complications are attributed to postoperative sepsis (POS). Worldwide, POS accounts for about 20.0% of all healthcare-associated diseases. POS is an infection that may be acquired within 30 days of surgery or, in case of an implant, after a year. It is common in rural hospitals due to the lack of adequate hygienic infrastructure to perform surgeries and is also prevalent in developing and developed countries. The source of infection could

be from contamination of surgical equipment or from the patient's microflora. POS has multiple risk factors, including both procedural and patient-related variables, with high body mass index (BMI) being a significant concern, with obesity (BMI ≥ 30 kg/m²) associated with increased surgical site infections (SSI) due to poor wound healing and immune dysregulation. Additionally, the host's immunity, use of antibiotics, the type of anaesthesia and duration of the surgery are also considerations (1). Risk factors can also be associated

with race, age, and sex of the patient as well as the proportion of untrained hospital professionals. POS is frequent after abdominal and thoracic surgery.

POS can be visualized as an infected region of the surgical site, but immune components also play a major role in this process (2). Neutrophil and monocyte activation coincides with the incidence of POS. Monocyte activation impairment may lead to defective antigen presenting ability of the cells, eventually leading to POS. Immunosuppression resulting from postoperative anergy is the major concern among causes of POS (3).

Pharmacotherapy can help prevent and manage POS, covering both prophylactic and therapeutic aspects. Antibiotics administered prior to surgery as part of preoperative antibiotic prophylaxis, can lower the risk of postoperative infections (4). Research indicates that administering antibiotics preoperatively can lower the incidence of wound infection by more than 80.0% when compared to patients who do not receive prophylactic treatment. This is especially crucial for procedures involving bone grafting, artificial implants, major dissections, or significant blood loss. Preoperative systemic prophylactic antibiotics should be administered at least half an hour before the skin incision. A number of considerations, including cost, safety, convenience of administration, pharmacokinetic profile, and bactericidal activity, are taken into consideration

in choosing antibiotics. For surgical prophylaxis, cefazolin is often prescribed for individuals who have never experienced Methicillin-Resistant *Staphylococcus aureus* (MRSA) infection or β -lactam allergy. Patients with severe cefazolin allergies are frequently medicated with substitutes such as clindamycin or vancomycin. For individuals who need more defence against microbes, other antibiotics including cefazolin plus metronidazole, cefoxitin, or ertapenem may be required (5). Significant therapy with agents like carbapenems, are effective against ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*, and vancomycin or linezolid for early intervention are very important. Further targeted therapy with antimicrobial agents can be guided by susceptibility testing, making the determination of the intervention more precise, e.g., combining regimens of ceftriaxone with metronidazole for polymicrobial infections (6).

Microorganisms that cause POS are numerous and difficult to control as all of them are resistant to a wide range of antibiotics. The fact that microorganisms that cause POS are widespread in hospital settings is an underlying cause of their antimicrobial resistance. For this reason, the microorganisms must be widely known and development of further understanding of their specific resistance is warranted to help fight against POS. The global incidence of POS associated with different surgical conditions, is depicted in Figure 1.

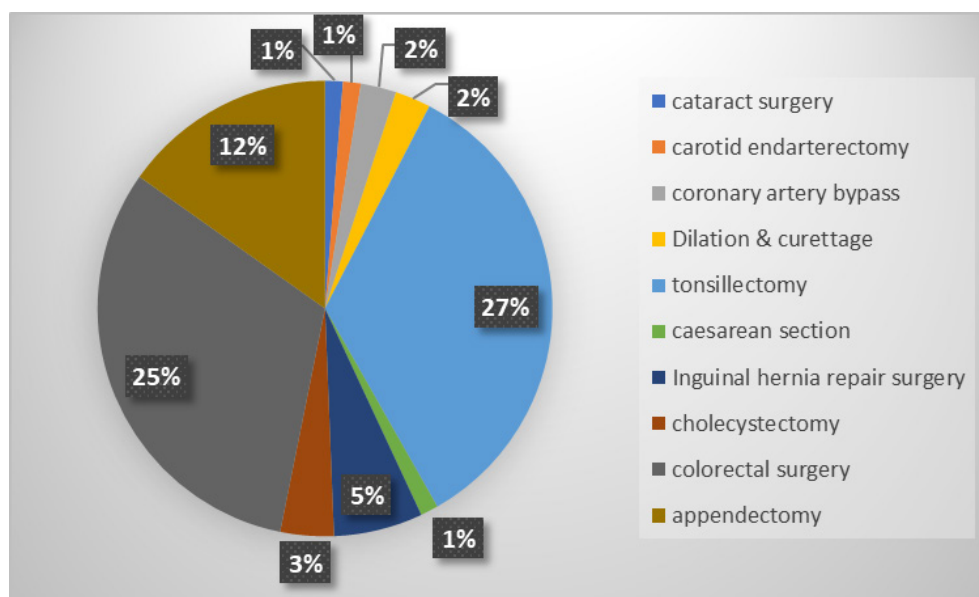


Figure 1. Global occurrence of POS associated with the surgical conditions studied

CATARACT SURGERY

Cataract surgery is a common procedure in which a cataract (opaque) lens is extracted in order to restore vision by replacement with a new artificial lens. The indications for cataract surgery include obscured vision, double vision, impaired night vision, hypersensitivity to the glare of the sun and increased size of the cataract as diagnosed by clinician. An atypical yet severe post-operative septic condition subsequent to this surgical intervention is endophthalmitis (7). This condition is represented by purulent discharge because of infection but has a surprisingly low mortality rate (8).

A number of co-morbid factors have been identified that could potentially increase the risk and occurrence of post-cataract endophthalmitis. Preoperative risk factors include age ≥ 85 years, diabetes mellitus, immunosuppression and the use of contact lenses in addition to co-existing ophthalmic conditions like uveitis, retinal detachment, ocular prosthesis, blockage of lacrimal duct, blepharitis, canaliculitis, glaucoma, conjunctivitis and several other eye abnormalities (8).

Certain surgical incisions, such as clear corneal incision and scleral tunnel incision, are employed for cataract surgery of which the former is associated with an increased risk for the manifestation of endophthalmitis. A frequent complication in this surgery is the risk of rupture of the posterior lens capsule which can pave the way for this septic condition. Furthermore, the material of the artificial lens used for the replacement following removal of a cataract influences likelihood of acquiring sepsis. For instance, a lens made of silicon optics enhances the chances for sepsis in contrast to a lens made of acrylic optics (9).

Sepsis resulting from a galactosaemic cataract is typically triggered by bacterial infections including *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Beta Streptococcus* spp. and *Streptococcus faecalis* (10). On the other hand, MRSA (11), *Stenotrophomonas maltophilia*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Candida albicans*, *Corynebacterium* spp. (8), *Pseudomonas aeruginosa* (9) and *Propionibacterium acnes* (12) are predominantly responsible for endophthalmitis with coagulase-negative *Streptococci* accounting for the majority of cases (70.0%).

Pharmacotherapy for post-cataract septic conditions varies with respect to antibiotic sensitivity of the bacterial strains and grouping of sepsis. *E. coli*-induced sepsis in galactosaemic cataracts is treated with Cefotaxime, Ceftriaxone, piperacillin, gentamycin, ampicillin and amikacin (10). In general, Cefuroxime (9) is commonly prescribed for reducing the possibility of post-cataract endophthalmitis. Gentamycin and Vancomycin (11) are administered for endophthalmitis caused by MRSA owing to the resistance exhibited by certain strains of MRSA to Fluoroquinolones (12).

Drug resistant strains are targeted by suitable and specific antibiotics. For example: (i) a combination of Cefotaxime (inhibition of penicillin-binding proteins causing cell death) and Mecillinam (inhibition of penicillin-binding protein) (2) for multidrug resistant *E. coli* strains (13), (ii) Doripenem (inhibition of penicillin-binding proteins causing cell death) and Ceftobiprole to treat *P. aeruginosa* infections and (iii) Levonadifloxacin WCK 771 (specific binding to DNA gyrase thus terminating DNA replication) (14) to treat Fluoroquinolone resistant MRSA have demonstrated promising results.

CAROTID ENDARTERECTOMY

Carotid endarterectomy (CEA) is a surgical procedure that involves the removal of plaque from the carotid arteries in order to minimize the risk of stroke arising from carotid artery stenosis. This surgery is indicated in symptomatic cases presenting with stroke or transient ischemic attack (TIA) as well as in asymptomatic cases (15). A study reported a very low incidence of POS, about <1%, following CEA (16).

Risk factors for CEA include age ≥ 80 years, congestive cardiac failure (CCF), coronary artery disease (CAD), need for open heart surgery, angina pectoris, recent heart attack, chronic obstructive pulmonary disease (COPD), renal disease and prior radical neck surgery or radiation therapy.

The causative organisms responsible for POS encompass MRSA, *S. epidermidis*, *S. aureus*, *Enterobacter aerogenes*, methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus epidermidis* (MRSE), *Streptococcus agalactiae*, *Bacteroides fragilis*, *Streptococcus viridans*, *Proteus mirabilis*, *P. aeruginosa* (15-18)

Staphylococcus hominis and *Streptococcus pyogenes*. Pharmacotherapy for post-op CEA sepsis is crucial for successful recovery of affected people. Vancomycin and cefazolin (inhibition of cell wall synthesis) have been prescribed for preoperative antibiotic regimens (18). MRSA infection is treated with cefuroxime (inhibition of cell wall synthesis) and vancomycin, linezolid (inhibition of protein synthesis) (17). Rocephin (inhibition of cell wall synthesis) is administered for MSSA, *S. agalactiae* and *E. aerogenes* infections. Doxycycline (inhibition of protein synthesis), a broad-spectrum antibiotic, is employed for MRSE infection. Zosyn is recommended for *S. hominis* infection. Other suggested antibiotics include levofloxacin, trovafloxacin, amoxicillin/clavulanate (β -lactamase inhibition), ceftriaxone, ceftazidime and oxacillin (18). Specific strains of *S. hominis* have exhibited multidrug resistance towards penicillin, oxacillin, methicillin, kanamycin, gentamycin, streptomycin, tetracycline, erythromycin, clindamycin, chloramphenicol, cotrimoxazole and ciprofloxacin (inhibition of cell wall synthesis) for which limited alternatives exist (19).

CORONARY ARTERY BYPASS

Coronary artery bypass (CAB) is a medical procedure that re-establishes blood circulation to the heart by removing any obstruction in the coronary artery, which plays a vital role in supplying blood to heart. Reasons that demand the surgery include angina, prominent left main coronary artery stenosis, left main equivalent disease, triple vessel disease, double coronary vessel disease, stenosis involving single or multiple vessels, disabling angina, abnormal left ventricular activity, unsuccessful percutaneous transluminal coronary angioplasty (PTCA), as well as immediately after myocardial infarction (MI), arrhythmias and occlusion of grafts from previous CABs.

Postoperative septic manifestation has been recognised as a perpetuating factor contributing to increased mortality. Some of the co-morbid factors for the POS following CAB include the age factor (generally above 80 years), poor pre-operative functional management (20), chronic diseases like diabetes mellitus, congestive heart failure, chronic kidney disease, obesity (high BMI ≥ 30 kg/m²), smoking (21), ill health, malnutrition, immunosuppressive effects of extracor-

poreal bypass, prolonged intubation and use of indwelling appliances (drains) (22). Other considerations could include infections such as pneumonia, mediastinitis, urinary tract infections, endocarditis or infected prosthetic materials, airway colonization with nosocomial bacteria (23), systemic arterial hypertension, dyslipidaemia, family history of CAD, haemodialysis and cardiogenic shock in the pre-operative period and treatment with immunosuppressive agents as in the case of an extracorporeal bypass (24).

A wide variety of microorganisms were found to be involved in sepsis development. Lineaweaver et al. (1992) observed *E. coli*, *Klebsiella* spp. and *Enterobacter* spp. Ford et al. (1991) reported *Haemophilus* spp. and *Candida* spp. De Oliveira et al. (2010) isolated *P. mirabilis*, *S. maltophilia*, *E. aerogenes*, *S. aureus*, *Enterobacter cloacae*, *Acinetobacter calcoaceticus*, *Candida glabrata*, *S. maltophilia*, *S. viridans*, *Staphylococcus coagulase*, *Flavobacterium*, *S. faecalis*, *Neisseria* spp. and yeast. *S. epidermidis* and *C. albicans* were identified as the two common pathogens in various works including those of De Oliveira et al. (2010) and Michalopoulos et al. (2003). Ceftriaxone, meropenem, cefepime, teicoplanin, clindamycin and ceftazidime were the antibiotics used in those cases (20). *S. epidermidis* infection can be treated with a broad range of antibiotics including gentamycin, vancomycin, imipenem, cephapirin, clindamycin and trimethoprim-sulfamethoxazole. *Pseudomonas* MDR was noted to be resistant but treatable with ceftazidime, cefepime and polymyxin. Colistin (Polymyxin E), an effective drug, adheres to the lipopolysaccharides on the cell membrane, causing lysis of the cell (Table 1) (25, 26).

DILATION AND CURETTAGE

Dilation and curettage (D&C) is a gynaecological procedure which involves the dilation of the cervix and excision tissue from the uterine lining by scraping or scooping techniques using a curette. This surgery is recommended by clinicians in cases such as abnormal uterine bleeding, cervical polyps (27), vaginal bleeding, detection of cancerous cells (28), caesarean scar pregnancy (CSP) (29), molar pregnancy (30), abortion and miscarriage (31). Precipitating factors for POS include molar pregnancy, hypertension, intercourse, use of

Table 1. Drug resistance associated with postoperative sepsis

Surgery	Drug resistant microbes	Details of drug resistance	Mechanism of antibiotic resistance
Cataract surgery	Methicillin-Resistant <i>Staphylococcus aureus</i> (MRSA), <i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i> , <i>Candida albicans</i> , Coagulase-negative <i>Staphylococci</i>	Penicillin, cephalosporins, carbapenems, fluoroquinolones, azoles	Altered penicillin-binding proteins (PBPs), β -lactamase production, efflux pumps, enzymatic degradation of antifungals, cell wall synthesis inhibition resistance
Carotid endarterectomy, patch angioplasty	<i>P. aeruginosa</i> , Methicillin-Resistant <i>Staphylococcus epidermidis</i> (MRSE), Methicillin-susceptible <i>Staphylococcus aureus</i> (MSSA), <i>Enterobacter aerogenes</i> , <i>Serratia marcescens</i>	Carbapenems, cephalosporins, aminoglycosides, penicillin	Efflux pump overexpression, carbapenemase enzyme production, β -lactamase production, porin loss
Coronary artery bypass	<i>Klebsiella pneumoniae</i> (ESBL-producing), Multidrug-Resistant <i>Pseudomonas</i> spp., <i>Enterobacter cloacae</i> , <i>Acinetobacter calcoaceticus</i> , <i>Candida glabrata</i> , <i>S. epidermidis</i>	Penicillin, cephalosporins, azoles, aminoglycosides	Hydrolysis of β -lactam antibiotics by ESBLs, efflux pumps, β -lactamase enzyme activity, resistance to azoles by ergosterol binding alteration, multidrug efflux pumps
Dilation & curettage	ESBL-producing <i>Escherichia coli</i> , <i>Streptococcus agalactiae</i> , <i>Clostridium perfringens</i> , <i>Gardnerella vaginalis</i> , Group B <i>Streptococcus</i>	Cephalosporins (3 rd gen), aminoglycosides, vancomycin, penicillin	Plasmid-mediated ESBL gene resistance, β -lactamase production, enzymatic inactivation of antimicrobials, altered protein binding
Tonsillectomy	Macrolide-Resistant <i>Streptococcus pyogenes</i> , <i>Haemophilus influenzae</i> , β -lactamase-producing <i>Bacteroides</i> spp.	Macrolides, penicillin, β -lactams	Methylation of 23S rRNA (blocking macrolide binding), β -lactamase enzyme activity, porin modifications, altered nitro-reductase enzyme for drug activation
Caesarean section	Vancomycin-resistant <i>Enterococcus faecium</i> (VRE), Carbapenem-Resistant <i>E. coli</i> , <i>K. pneumoniae</i> , MRSA, MSSA	Vancomycin, carbapenems, penicillin, cephalosporins	VanA/VanB operons modifying D-Ala-D-Ala terminal, carbapenemase enzyme production, β -lactamase activity, altered PBPs
Inguinal hernia repair surgery	Multidrug-resistant <i>Acinetobacter baumannii</i> , Azole-Resistant <i>Aspergillus fumigatus</i> , <i>S. epidermidis</i> , <i>Corynebacterium</i> spp., Coagulase-negative <i>Staphylococci</i>	Azoles, β -lactams, aminoglycosides	Efflux pumps, β -lactamase enzymes, outer membrane protein loss, ergosterol binding alteration, enzymatic degradation of cell wall inhibitors
Cholecystectomy	Carbapenem-Resistant <i>E. coli</i> , <i>Clostridium perfringens</i> , <i>P. aeruginosa</i> , <i>Enterococcus</i> spp.	Carbapenems, vancomycin, aminoglycosides, cephalosporins	Carbapenemase enzyme activity, altered cell wall synthesis pathways, efflux pumps, β -lactamase production
Colorectal surgery	Metronidazole-resistant <i>Bacteroides fragilis</i> , ESBL-producing <i>E. coli</i> , <i>K. pneumoniae</i> , <i>Candida albicans</i> , Carbapenem-resistant <i>A. baumannii</i>	Metronidazole, carbapenems, β -lactamase, azoles	Altered nitro-reductase enzyme, hydrolysis of β -lactamase antibiotics, efflux pumps, azole resistance via ergosterol modification
Appendectomy	AmpC β -lactamase-producing <i>Enterobacter cloacae</i> , ESBL-producing <i>E. coli</i> and <i>Klebsiella</i> spp., <i>Enterobacter</i> spp., <i>Bacteroides fragilis</i> , Multi-drug-Resistant Gram-Negative Rods (GNRs)	Cephalosporins, β -lactamase, carbapenems, metronidazole	Inducible AmpC genemediated cephalosporin hydrolysis, β -lactamase enzyme production, altered nitro-reductase enzyme, efflux pumps, carbapenemase activity

tampons, douching, diabetes, cancer, alcoholism, pelvic inflammatory disease (PID), liver cirrhosis, neurological impairment (32) and placenta accreta (33).

Organisms involved in the occurrence of sepsis can cause a wide variety of manifestations ranging from fever and abdominal pain to life-threatening conditions like haemolysis, coagulopathy, uterine haemorrhage, and endocarditis. Potential pathogenic organisms cited include *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (32), *Clostridium perfringens*, *Clostridium sordelli* (34), *S. viridans*, *E. coli*, Group A *Streptococcus* (33), Group B *Streptococcus* (32), *Lactobacillus jensenii* (35), *Gardnerella vaginalis* (36) and *E. faecalis* (37).

Antibiotic therapy treatment is comprised of the combination of one or more drugs for an effective recovery. Intravenous ceftriaxone, gentamycin, doxycycline, penicillin, vancomycin (32), IV piperacillin/tazobactam, metronidazole (33, 38), cefmetazole, cefepime, cephalexin, cefuroxime, erythromycin, trimethoprim/sulfamethoxazole, ertapenem and metronidazole, ertapenem and clindamycin (33) levofloxacin and ciprofloxacin (38) are some of the suggested drugs. The mode of action of these antibiotics includes inhibition of nucleic acid synthesis and protein synthesis inhibition. In recent years, due to increased demand for these drugs employed as a remedy, several microbes have acquired resistance to antibiotics, making counter treatment a challenging task.

TONSILLECTOMY

Tonsillectomy is a surgical intervention that involves the excision of both the palatine tonsils. The common cues that indicate surgery is necessary include frequent infection instigating tonsillitis, difficulty in breathing and swallowing due to obstruction caused by swollen tonsils, obstructive sleep apnea (OSA), atypical tonsils, cancer of either/both tonsils (squamous cell carcinoma and lymphoma), haemorrhage in tonsils' blood vessels, adenoiditis, peritonsillar abscess, tonsillitis as a complication arising from immunoglobulin A nephropathy (IgAN) (39), guttate psoriasis, chronic plaque psoriasis (40), periodic fever aphthous stomatitis pharyngitis adenitis (PFAPA) syndrome (41) and paediatric autoimmune neuropsychiatric

disorders associated with streptococcal infection syndrome (PANDAS) (42).

Since children represent the majority of patients referred for tonsillectomy, certain standards need to be met in order to minimize any postoperative consequences. The prime points of the paradise criteria for tonsillectomy include individuals affected at a frequency greater than or equal to seven episodes in the past year, five episodes per year for the last two years and three episodes per year for the last three years. In addition to this, vigorousness of the episodes also influences the final decision. Distributed sepsis is a quite rare phenomenon post-tonsillectomy. Young children are more susceptible to acquiring infections, tachycardia, hypotension (43), bleeding disorders (anaemia), local infection, allergic conditions and hyperthermia are among the risk factors.

Microorganisms associated with post-tonsillectomy septic infection include Aerobes – *E. coli*, Group A β Hemolytic *Streptococci* (GABHS), *Enterobacter* spp., *Haemophilus influenza*, Group C β Hemolytic *Streptococci* (GCBHS), *S. aureus*, Group F β Hemolytic *Streptococci* (GFBHS), *S. pneumoniae*, *S. viridans*, *Strep. pyogenes*; anaerobes–*Fusobacterium necrophorum* (obligate), *Bacteroides melanigenicus* gram-negative coccobacilli and gram-positive cocci. Interestingly, normal flora and unclassified *Streptococci* (44) have also been identified.

In order to reduce the possibility of developing sepsis, only a few, yet effective, antibiotics are prescribed. The administration of antibiotics reduces the intensity of infection but not the obstruction. Hence, the latter remains a primary indicator for tonsillectomy surgery. Cefazolin for the preoperative period, ampicillin and amoxicillin for *S. pyogenes* (45), amoxicillin and clavulanate potassium (Augmentin) for β -lactamase producing bacteria, ticarcillin disodium and clavulanate potassium (inhibition of beta lactamase) and Timentin (46) for the perioperative period have been prescribed. However, the use of antibiotics following surgery is not recommended unless it is necessary since evidence suggests that worsening of an already existing condition is possible, e.g., oral antibiotics might exaggerate the postoperative consequences (bleeding) (47).

CAESAREAN SECTION

Caesarean section or C-section (CS) is an obstetrical procedure wherein an incision is created in the mother's abdomen and/or uterus for parturition. This surgery may be opted for in cases of earlier CS, post term dates, cephalopelvic disproportion, labour dystocia, foetal distress, unfavourable cervix, rhesus incompatibility, failed induction, antepartum haemorrhage, oligohydramnios, placenta praevia, HIV infection, narrowed pelvis, breech presentation (48) fear of vaginal childbirth, to avoid episiotomy, older age and the number of previous abortions.

Associated factors that increase the prevalence of sepsis include gestational age, Cesarean section, mechanical ventilation, patent ductus arteriosus, necrotizing enterocolitis, bronchopulmonary dysplasia, duration of labour, frequency of preoperative vaginal examinations and membrane ruptures prior to delivery. Other factors may include postoperative anaemia (49), obesity, use of intrauterine devices, avoidance of the use of plastic draping, re-disinfection, diabetes mellitus, gestational diabetes and chronic hypertension (50).

Microbial species that play a pivotal role in the development of sepsis include Beta Hemolytic *Streptococci*, *E. coli*, *S. aureus*, *Actinomyces neuui*, *S. epidermidis*, *Micrococcus* spp., *Bacillus* spp., *Propionibacterium* spp., group A and group B *Streptococci* (49, 51). A few more factors that can be added to the list include being coagulase negative for *Staphylococci*, *Klebsiella* spp., gram positive and negative organisms, *Candida* spp., *Acinetobacter* spp., *P. aeruginosa*, *S. pneumoniae*, *Enterococcus* spp., *K. pneumoniae*, *Neisseria* and *C. freundii* (52).

Medications prescribed for treatment of POS include intravenous cefuroxime, first- or second-generation cephalosporins for *S. aureus*, second-generation cephalosporins for *E. coli*, ceftazidime, metronidazole, G-penicillin, erythromycin, gentamicin, penicillin and cephalexin (51). Tumhamye et al. (2020) mentioned some other drugs such as vancomycin, ampicillin, netilmicin, tetracycline, trimethoprim/sulfamethoxazole, chloramphenicol, amoxicillin/clavulanic acid, ceftriaxone and imipenem which inhibit cell wall and protein synthesis (52).

Microbes carrying resistance to antibiotics include metronidazole-resistant *Actinomyces neuui* which can be countered with cefuroxime which possess bactericidal activity, blocking the interconnection of peptidoglycan and thus inhibiting bacterial cell wall synthesis. They also induce production of autolysins that leads to cell death. Another resistant organism is *Morganella morganii* that is insensitive to first and second-generation cephalosporin (51).

INGUINAL HERNIA REPAIR SURGERY

Hernia is a swelling that occurs in the abdominal wall that loosens and causes spillage of abdominal components into the inguinal canal which can be rectified by inguinal hernia repair (IHR) surgery. Unilateral or bilateral inguinal hernia, hindrance of day-to-day tasks and excruciating pain are some of the common indications for the surgery (53-55).

Diabetes mellitus, smoking (56), obesity, co-existing infection, altered immune response, increased age (>60 years), nutritional status, HIV status and gender (53) are significant influencing factors for POS. Certain other factors include complicated hernia repair, type of mesh used, history of prior mesh infection (56), operative contamination (57), ischemic heart disease, COPD (58), hypertension, liver or renal impairment, respiratory conditions, MI and peptic ulcer (59, 60).

Microorganisms involved in sepsis manifestation include *S. aureus*, coagulase negative *Staphylococci* (56, 57, 61), *E. faecalis*, Group G *Streptococcus*, *Anaerobic coccus*, *Corynebacterium*, *Hemolytic Streptococcus*, *Aspergillus fumigatus* (53), gram negative cocci, *S. epidermidis* and gram-negative bacteria (62, 63).

Chemotherapy advised for the treatment of a septic condition includes cefuroxime (53), vancomycin, cephalosporins, cefazolin (56), amoxicillin and clavulanic acid (57), ampicillin and sulbactam. Teicoplanin, oxacillin, nafcillin, piperacillin, penicillin g, imipenem, gentamycin, streptomycin, ceftriaxone, cefotaxime, arbekacin, ofloxacin, daptomycin, ceftobiprole and ceftaroline (62) are also commonly prescribed. Among the listed organisms, *A. fumigatus* was found to be resistant to azoles (63, 64) which can be mitigated by amphotericin B (disrupts the cell membrane) (65). The drug binds to ergosterol, a lipid component

of the cell wall, leading to perforation, oozing of intracellular contents and fungal cell death.

CHOLECYSTECTOMY

Cholecystectomy is a surgical intervention involving removal of the gall bladder. Conditions for which surgery is recommended include acute or chronic cholecystitis, pancreatitis, obstructive jaundice, gallstone disease (66) and cholelithiasis (67).

Older age, decreased preoperative albumin, prolonged operation time, female gender (68), chronic kidney disease, connective tissue disease, cirrhosis, complicated and uncomplicated diabetes, obesity, gallbladder perforation, antibiotic treatment (67) open or laparoscopic surgery (66), development of bile leakage, intra-abdominal abscess and pneumonia after laparoscopic cholecystectomy, degree of contamination (68), neoplasm, pre-operative razor shaving (67) are regarded as risk factors for SSI.

Organisms associated with postoperative infection include *E. coli*, *Klebsiella* spp., *Streptococcus* spp. (69), *S. aureus* (70), *Enterobacter* spp, *Enterococcus* spp. (68), *E. faecium*, *K. pneumonia*, *C. albicans*, *P. aeruginosa*, *M. morganii*, *P. mirabilis* (67), *C. perfringens* (71), (72) and *E. cloacae* (73).

Amoxicillin-clavulanic acid (73), gentamycin (67), ciprofloxacin + metronidazole (74) cefazolin (75-77) cefotaxime (78, 79) and cefuroxime (80, 81) are prescribed for infection. Resistance to metronidazole, ceftriaxone, imipenem, clindamycin, penicillin G, chloramphenicol (82), and vancomycin has been demonstrated in certain strains, including *Clostridium perfringens*. These infections may be effectively treated with alternatives such as amoxicillin, cephadrine, fosfomycin (which inhibits nucleic acid synthesis), and florfenicol (83). Thus, understanding the patterns of antibiotic resistance among important infections can be crucial for developing therapeutic approaches (Table 2).

COLORECTAL SURGERY

Colorectal surgery is a surgical procedure done to treat disorders arising from the rectum, colon or anus. Indications for surgery include abdominal adhesions, volvulus, ulcerative colitis, diverticulitis, colorectal cancer, Crohn's disease and familial adenomatous polyposis (FAP) (84).

Factors associated with this surgery include age, race, sex, diabetes, obesity, smoking, immunosuppression, steroid use, malnutrition, postoperative hypothermia, Hartmann's procedure, hypoalbuminemia, postoperative hypotension, BMI ≥ 30 kg/m² (85), chronic liver disease, metastatic neoplasm cardiovascular disease and chronic renal disease. Antibiotic prophylaxis, bowel preparation, fluid management, oxygen supply and skin disinfection also influence the occurrence.

E. coli, *E. cloacae*, *Aeromonas sobria*, *P. aeruginosa*, *K. pneumonia* (85, 86), *E. faecalis*, *M. morganii*, *E. faecium*, *Candida albicans* (87), *Acinetobacter baumannii*, *S. epidermidis*, *S. aureus* and *P. mirabilis* (88) are some of the microorganisms identified as causing SSI.

Aminoglycoside, ampicillin, metronidazole (89, 90) piperacillin-tazobactam, Amikacin, Amoxicillin-clavulanate, Ciprofloxacin, Co-trimoxazole, gentamicin, cefotaxime, nitrofurantoin, ceftazidime, carbapenems, ampicillin-sulbactam, linezolid, vancomycin (83), clindamycin, cephalosporins (89), neomycin, erythromycin, tobramycin and colistin sulphate (disrupts the cell membrane) (90, 91) are widely employed in the treatment of infection. Extended-spectrum β -lactamase (ESBL) producing pathogens are resistant to β -lactam antibiotics such as amoxicillin-clavulanate (92), but can be managed by administration of Mero-penem, Imipenem and other carbapenems (93).

APPENDECTOMY

Appendectomy is a surgery that involves removal of the appendix in order to cure appendicitis (94, 95). Acute cholecystitis, simple and suppurative acute appendicitis, gangrenous and perforated acute appendicitis (96, 97) and lesion in the appendix are some of the conditions that necessitate the procedure. Co-morbidities for POS include age ≥ 60 years, African American race, morbid obesity, acute renal failure or dialysis, disseminated malignancy, open appendectomy (98), diabetes, greater incisional length, faecal contamination, and longer operative time (99).

Sepsis following surgery may involve one or more microorganisms such as *B. fragilis* and *E. coli* (97, 100). Beta *Streptococcus*, *S. aureus* (100), *P. aeruginosa*, and other gram-negative rods including *Enterococcus* and other anaerobes (96),

Bacteroides, Klebsiella/Enterobacter spp., S. faecalis and anaerobic Streptococci (100) may also play a role.

Sepsis can be prevented by administration of antibiotics. Cephalosporin, cefamandole, netilmicin, gentamicin (96), penicillin, streptomycin, chlorotetracycline, oxytetracycline, tetracycline, chloramphenicol and erythromycin (94), sulbactam and ampicillin (sa), metronidazole and cefotaxime (101) are widely used in chemotherapy.

The prevalence and mortality rates associated with the postoperative sepsis conditions are summarised in Table 2 (102-108).

CONCLUSION

POS remains a significant challenge across various surgical conditions encompassing complications that extend beyond the immediate postoperative period. Microbial pathogens play a crucial role in the development and progression of sepsis, highlighting the importance of effective infection prevention strategies and targeted antimicrobial therapy. Pharmacotherapy plays an essential role in minimizing the load of POS, especially with increasing multidrug-resistant pathogens. Targeted therapies, including linezolid for vancomycin-resistant *E. faecium* and ceftazidime-avibactam for β -lactamase-producing organisms,

Table 2. List of surgical conditions, their prevalence and mortality rates due to postoperative sepsis (POS)

Surgery	Surgical prevalence	POS	Risk factors for POS	Mortality rate due to POS
Cataract surgery	7.75% (6.38% in males and 9.01% in females)	Postoperative endophthalmitis	Older age, preexisting ocular inflammation	4.60% in duration of 30 days
Carotid endarterectomy, patch angioplasty	67.20%	Rare complication of infection	Diabetes mellitus (type 2, HbA1c $\geq$ 6.50%), poor surgical hygiene	3.00%
Coronary artery bypass	150,000 surgeries done annually	Airway colonisation, UTI	Prolonged ICU stay, obesity (BMI $\geq$ 35), diabetes (type 2, un-controlled HbA1c $>$ 8.00%), smoking	32.00-79.00%
Dilation & curettage	30.00% in females	Uterine infection, bleeding (haemolysis)	Incomplete abortion, anaemia (Hb $<$ 9 g/dL)	0.6 per 100,000 legally performed induced abortions
Tonsillectomy	13.60%	Pneumonia, superficial site infection and urinary tract infection	Immune suppression, inadequate postoperative care	7 per 100,000 operations
Caesarean section	10.00-15.00%	Post-caesarean section peritonitis, surgical site infection	Obesity, diabetes (Gestational or type 2), prolonged labor	Up to 3.00%
Inguinal hernia repair surgery	7.20% in males and 2.60% in females	Deep groin infection, surgical site infection (SSIs)	Poor surgical site preparation, immune suppression	4.00-5.00%
Cholecystectomy	8.36 to 13.81%	Intra-abdominal abscess and pneumonia	Older age, obesity, biliary tract infections	0.10-0.70%
Colorectal surgery	65.40%	Surgical site infection (SSIs)	Bowel perforation, malnutrition, prolonged surgery	13.00%
Appendectomy	12.00% in males and 23.10% in females	Intra-abdominal abscess	Delay in diagnosis, perforated appendix	17 of 311 patients (5.47%) with post-operative sepsis die within 30 days

which have had success, indicate the possibilities of such new approaches. Additionally, advances in diagnostic techniques, such as rapid pathogen identification and antimicrobial susceptibility testing, hold promise for optimizing treatment regimens and improving patient outcomes. Future research should focus on elucidating the complex interplay between host factors, microbial virulence, and surgical strategies in order to enhance personalized interventions aimed at reducing the complications of POS and its associated morbidity and mortality.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ADDITIONAL INFORMATION

Compliance with ethical standards

This manuscript does not contain studies involving animals or human participants.

Author contributions

V.H. and Y.R.: designed the review and wrote the manuscript; L.M.: contributed to final editing of the manuscript; L.V.: supervised and approved the design.

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