Combating Sepsis: How to Overcome the Challenges

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University of Medicine 2

Our Team

18.1.18

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Intervention may be life-saving!

- 80 years old
- High fever 2 days,
- Confusion 1 day with constipation

- E Beta Thalassaemia
- DM
- Hypertension
- Parkinsonism
- 2 times surgery for renal stone

- Drugs for hypertension, memory, parkinsonism, prostate treatment with Dabegatrin 150mg OD for portal vein thrombosis after abd sepsis 6 months ago

Intervention may be life-saving!

Physical examination

- T-99.8F GCS – 9/15
- BP-140/90mmHg,PR-90/min, RR 36/minute
- Pallor+, Tinge of Jaundice+
- Ht-1st+2nd +0
- Lung-VBS+0
- Abdomen- Distended, reduce bowel sound

Intervention may be life-saving!

Investigation

	2/10	4/10	7/10	8/10	10/10	12/10	13/10	14/10	
Hb	10.6			9.1			8.7	9.1	
WBC	24.87			16.37			10.5	9.34	
PLT	233			340			365	394	
ESR	80						70		
Urea			32					14	
Na+	132	137	141		142	140		140	
K+	3.1	3.3	3.38		3.3	3.39		3.4	
Cl-	98	104	109		110	108		107	
HCO3-	26	27	25		29	25		31	
Cr-	65	55	43			37		42	

Intervention may be life-saving!

Investigation

- APTT -38.4
- PT-13.1
- INR-1.09
- AST/SGOT-45
- Total bilirubin-0.9
- ALP-100
- ALT-7
- HbA1C-5.7
- **CRP>120**
- **USG(abd)- calculous cholecystitis, bilateral renal stone with hydronephrosis**
- **Blood C and S- sterile**
- Urine culture sterile

Intervention may be life-saving!

Investigation

- CT(abd &pelvis)

1.Calculous cholecystitis

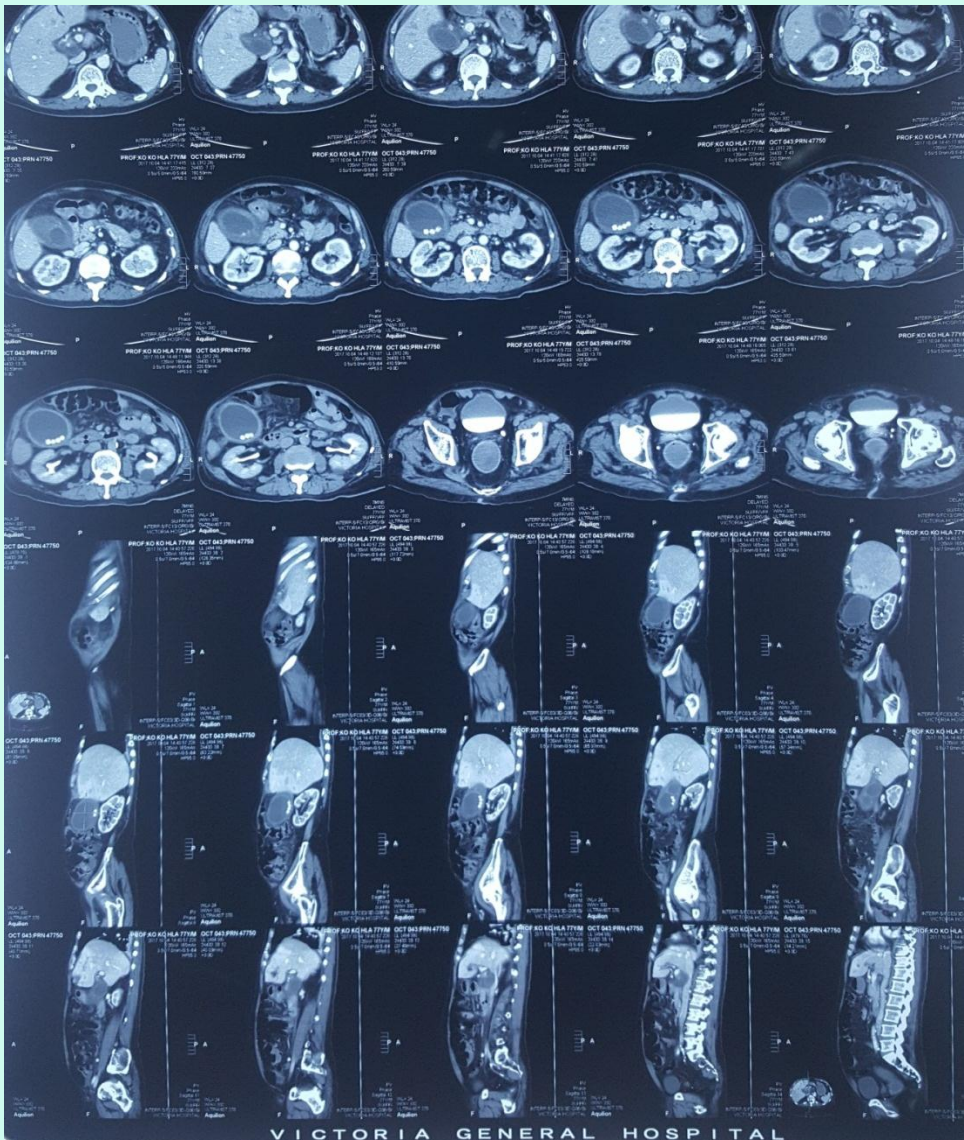
2.bilateral renal stones,no hydronephrosis,

3.A small left renal cyst

4.small right inguinal hernia.

There is no bowel dilatation or intussusception.

Left portal vein thrombosis is improving



Intervention may be life-saving!

Investigations

Echo

- EF - 63%, no pericardial effusion

USG Recheck

- Empyaema gall bladder
- Pericholecystic abscess

Intervention may be life-saving!

Treatment

- IV Antibiotics
- Operation - successful

- Complicated by aspiration pneumonia
- Sputum- Heavy growth of Pseudomonus – Aerugenosa
- Resistant to all antibiotics except gentamycin and amikacin

Intervention may be life-saving!

Treatment

- IV Antibiotics
- Operation - successful

- Complicated by aspiration pneumonia
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Definitions are changing

Sepsis-3 Definitions

- ***Sepsis***: Life-threatening organ dysfunction caused by dysregulated host response to infection
- ***Septic Shock***: Subset of sepsis with circulatory and cellular/metabolic dysfunction associated with higher risk of mortality

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Definitions

qSOFA score

- Hypotension: SBP ≤100mmHg
- Altered mental status (any GCS <15)
- Tachypnoea: Respiratory rate ≥22

SOFA score

Baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.

SOFA variables

- PaO_2/FiO_2 ratio
- Glasgow Coma Scale Score
- Platelets
- Bilirubin
- Mean Arterial Pressure
- Creatinine
- Urine Output(ml/d)

Definitions

Bloodstream Infection

Bloodstream infections (BSI) are infectious diseases defined by the presence of viable bacterial or fungal microorganisms in the bloodstream (later demonstrated by the positivity of one or more blood cultures) that elicit or have elicited an inflammatory response characterized by the alteration of clinical, laboratory and hemodynamic parameters.

Bacteraemia

- The transient presence of organisms in the blood.

Ref: Claudio Viscoli (2016) Bloodstream Infections: The peak of the iceberg, Virulence, 7:3, 248-251, DOI: 10.1080/21505594.2016.1152440

Causes and Risk Factors

Causes of Sepsis

- Bacteria
- Fungi
- Parasites

May be the result of

- Primary infection (e.g., pneumonia)
- Clinical interventions for other conditions (e.g., immunosupressive drugs, chemotherapy, invaseve lines)

Common Causes of Sepsis

In a previously healthy adult

Site of origin	**Usual pathogen(s)**
Skin	Staphylococcus aureus and other Gram-positive cocci
Urinary tract	Escherichia coli and other aerobic Gram-negative rods
Respiratory tract	Streptococcus pneumoniae
Gall bladder or bowel	Enterococcus faecalis, E. coli and other Gram-negative rods, Bacteroides fragilis
Pelvic organs	Neisseria gonorrhoeae, anaerobes

Common Causes of Sepsis

In hospitalized patients

Clinical problem	**Usual pathogen(s)**
Urinary catheter	Escherichia coli, Klebsiella spp., Proteus spp., Serratia spp., Pseudomonas spp.
Invasive catheter	Staphylococcus aureus, Staph. epidermidis, Klebsiella spp., Pseudomonas spp., Candida albicans
Post-surgery Wound infection Deep infection	 *Staph. Aurues*, *E. coli*, anerobes (depending on the site) Depends on anatomical location
Burns	Gram-positive cocci, Pseudomonas spp., Candida albicans
Immunocompromised patients	Any of the above

Risk Factors for Sepsis

- DM
- Immunodeficiency
- Trauma
- Burns
- Alcohol and substance abuse
- Chronic disease
- Haematological disorders
- Recent surgery/ Invasive procedure
- Invasive lines (Intravenous, intraarterial, urinary, nasogastric)

The incidence of sepsis is increasing

- Growing elderly population
- Greater number of immunocompromised patients
- Increased use of invasive surgery
- Higher bacterial resistance

Risk Factors for Sepsis

- DM
- Immunodeficiency
- Trauma
- Burns
- Alcohol and substance abuse
- Chronic disease
- Haematological disorders
- Recent surgery/ Invasive procedure
- Invasive lines (Intravenous, intraarterial, urinary, nasogastric)

Clinical Characteristics of Blood Stream Infections in IGH

Kyi Le Yee Lin, Ne Myo Aung, Mar Mar Kyi, Myo Lwin Nyein

Method – Hospital based cross sectional descriptive study from January, 2017 to May,2017

DMR presentation 12.1.18

Clinical Characteristics of Blood Stream Infections in IGH

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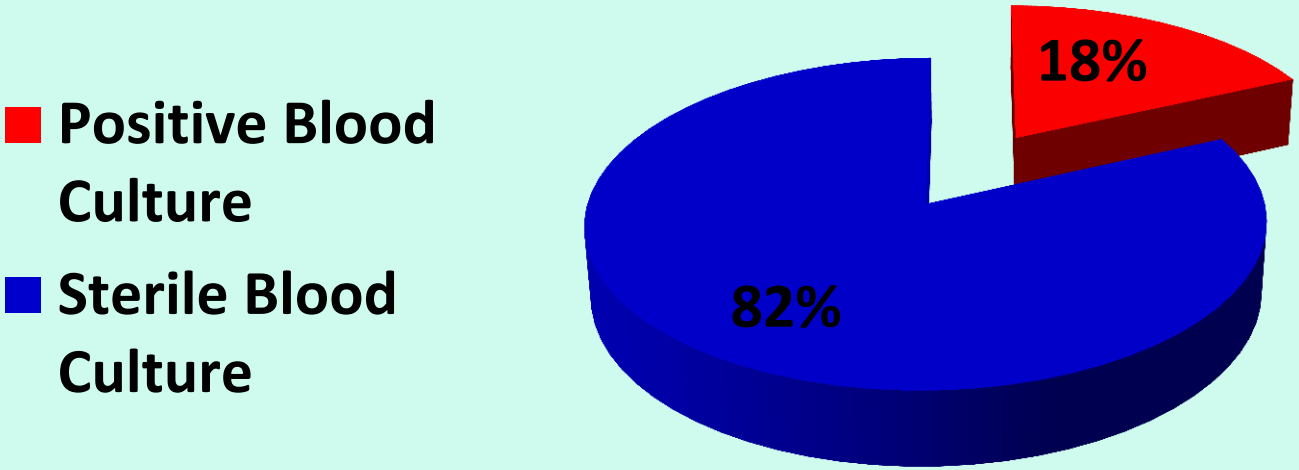
Results

- In the study, 143 cases with possible sepsis were recruited.
- Among them 26 cases (**18.2 percent**) were identified as blood stream infection (BSI).



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Results

- The mean age of patients was 51 (range 21-85).
- Female to male ratio was 3.6 with an excess of females.
- **None of the cases with BSI had HIV infection, active cancer, intensive chemotherapy or end stage organ failures**.
- Among them, 73 percent were previously apparently healthy prior to admission.
- The **co-morbid conditions** (in 27% of cases) were mainly non-communicable diseases like **asthma, diabetes, peptic ulcer and hypertension**.

Clinical Characteristics of Blood Stream Infections in IGH

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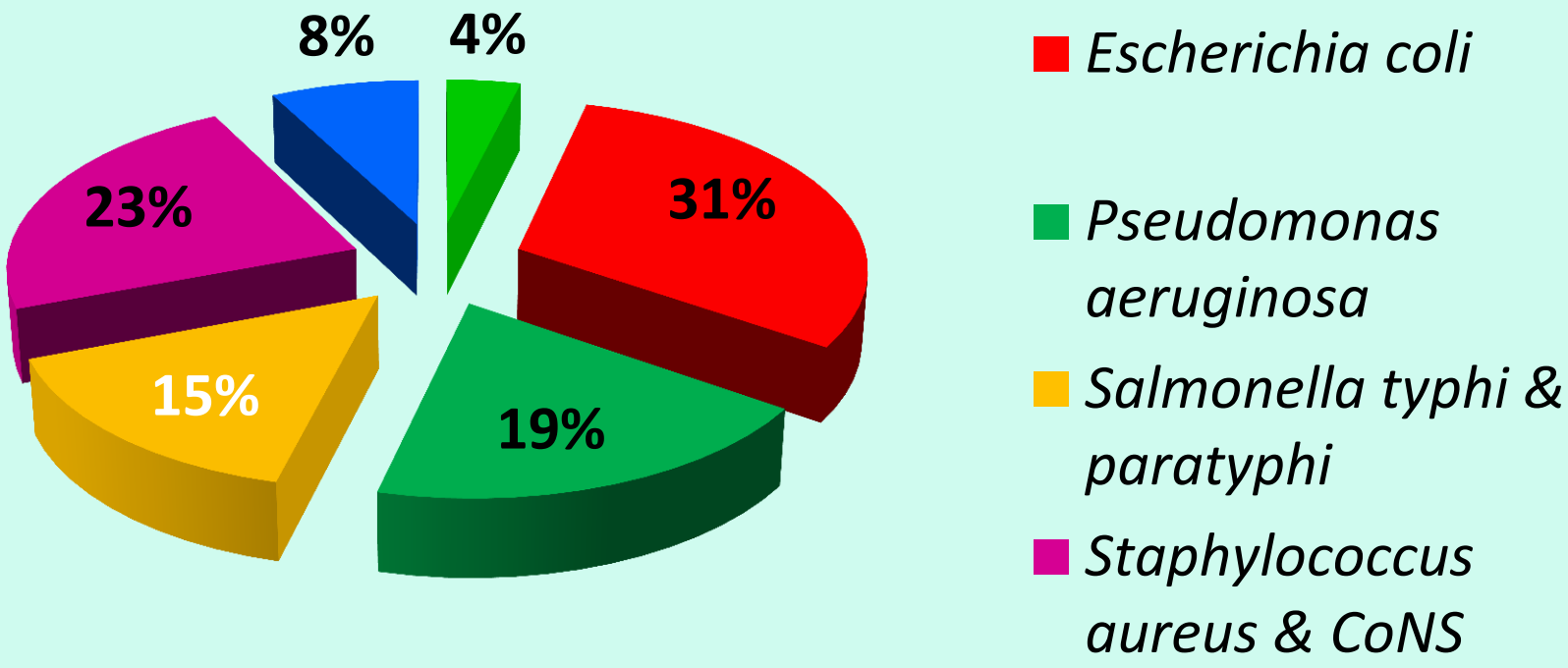
Results

- **Organisms**



Clinical Characteristics of Blood Stream Infections in IGH

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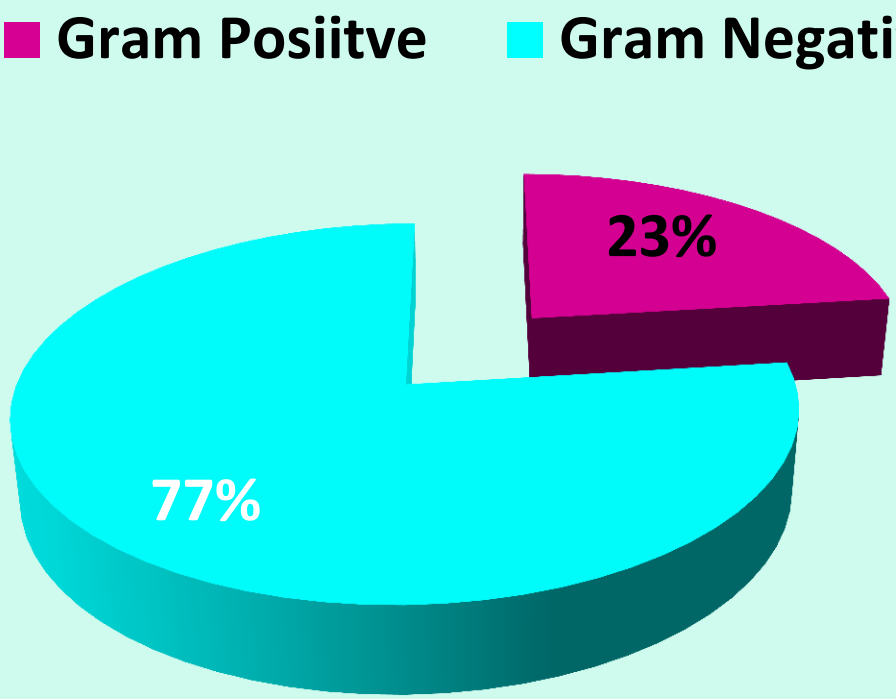
Results

- **Organisms on gram staining**



Clinical Characteristics of Blood Stream Infections in IGH

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Results

- The occurrence of clinical symptoms were

- ✓ **rigor (34.6 percent),**
- ✓ headache (15.4 percent),
- ✓ convulsion (0 percent),
- ✓ **cough (46 percent),**
- ✓ purulent sputum (11.5 percent),
- ✓ **dyspnea (42.3 percent),**
- ✓ chest pain (11.5 percent),
- ✓ **abdominal pain (38.5 percent),**
- ✓ **diarrhea (23 percent),**
- ✓ back pain (3.8 percent),
- ✓ joint pain (3.8 percent),
- ✓ muscle pain (7.7 percent),
- ✓ sore throat (0 percent),
- ✓ dysuria (15.4 percent).

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Results

- The occurrence of clinical signs were
  - ✓ jaundice (7.7 percent),
  - ✓ cellulitis (7.7 percent),
  - ✓ skin rash (11.5 percent),
  - ✓ weight loss (3.8 percent),
  - ✓ **crackles on auscultation (50 percent),**
  - ✓ cachexia (3.8 percent),
  - ✓ neck stiffness (7.7 percent),
  - ✓ murmur (0 percent),
  - ✓ **hepatomegaly (11.5 percent),**
  - ✓ splenomegaly (0 percent),
  - ✓ **loin tenderness (23 percent)** and
  - ✓ joint swelling (0 percent).

Clinical Characteristics of Blood Stream Infections in IGH

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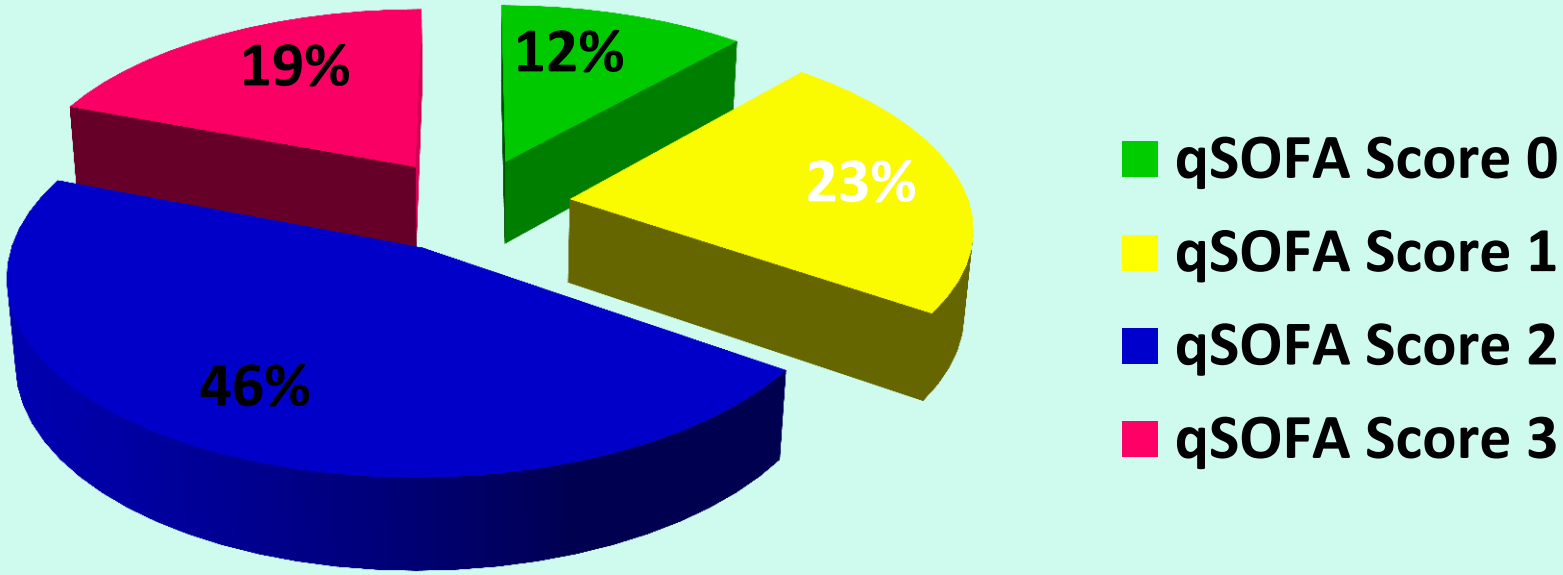
Results

The quick Sequential Organ Failure Assessment (**qSOFA**) Scores of BSI patients



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Results

- The occurrence of organ dysfunction were compared;

qSOFA	BSI	Non BSI	p value
altered mental state	46%	25%	0.003
respiratory rate > 21	85%	78%	0.2
systolic blood pressure < 100	35%	31%	0.54

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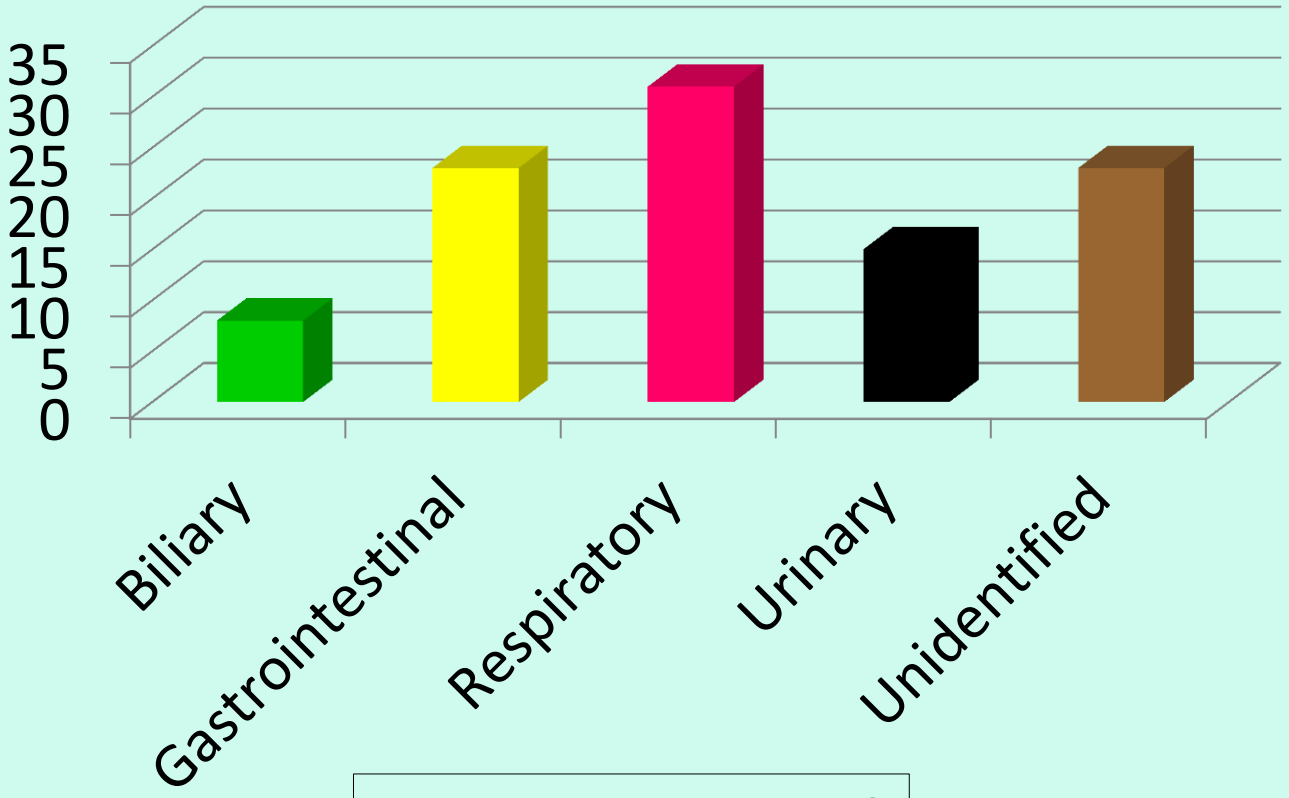
Results

- The sources of sepsis origin were identified as



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RESULTS – Rule of pathogen estimation

- BSI with unidentified source were mainly caused by coagulase negative staphylococci (68%).
- BSI with sepsis source from urinary, hepatobiliary and gastrointestinal were all caused by Gram negative organisms.
- **BSI with sepsis source from respiratory tract were caused mainly by Gram negative organisms (75%).**

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RESULTS - OUTCOME

- **Case fatality rate** for BSI was **46 percent**.
- Case fatality rate of non-BSI was 20.5 percent.
- Among the death, **58 percent of death occurred within 24 hours** after admission.

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RESULTS - OUTCOME

❖ Those with BSI were

- more likely to **die** (**odd ratio of 3.2** (95% CI 1.7 to 5.9; p = 0.0002)
- more likely to **develop shock** (**odd ratio of 13.2**; 95% CI 4.9 to 35.4, p value 0.01) during hospital stay
- more likely to be provided with **higher dose and longer duration of vasopressors**
- than those without BSI.

Clinical Characteristics of Blood Stream Infections in IGH

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RESULTS - ANTIBIOGRAM

- For *Staphylococcus aureus* blood stream infection, no case of methicillin resistant staphylococcus aureus was identified.
- The antimicrobial resistance was not a problem in Gram positive BSI.

Clinical Characteristics of Blood Stream Infections in IGH

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RESULTS - ANTIBIOGRAM

- For *Gram negative* blood stream infection, the antimicrobial resistance was common and variable.
- **ESBL** (extended spectrum beta-lactamase producing) bacteria accounted for **47.4 percent** of Gram negative organisms.

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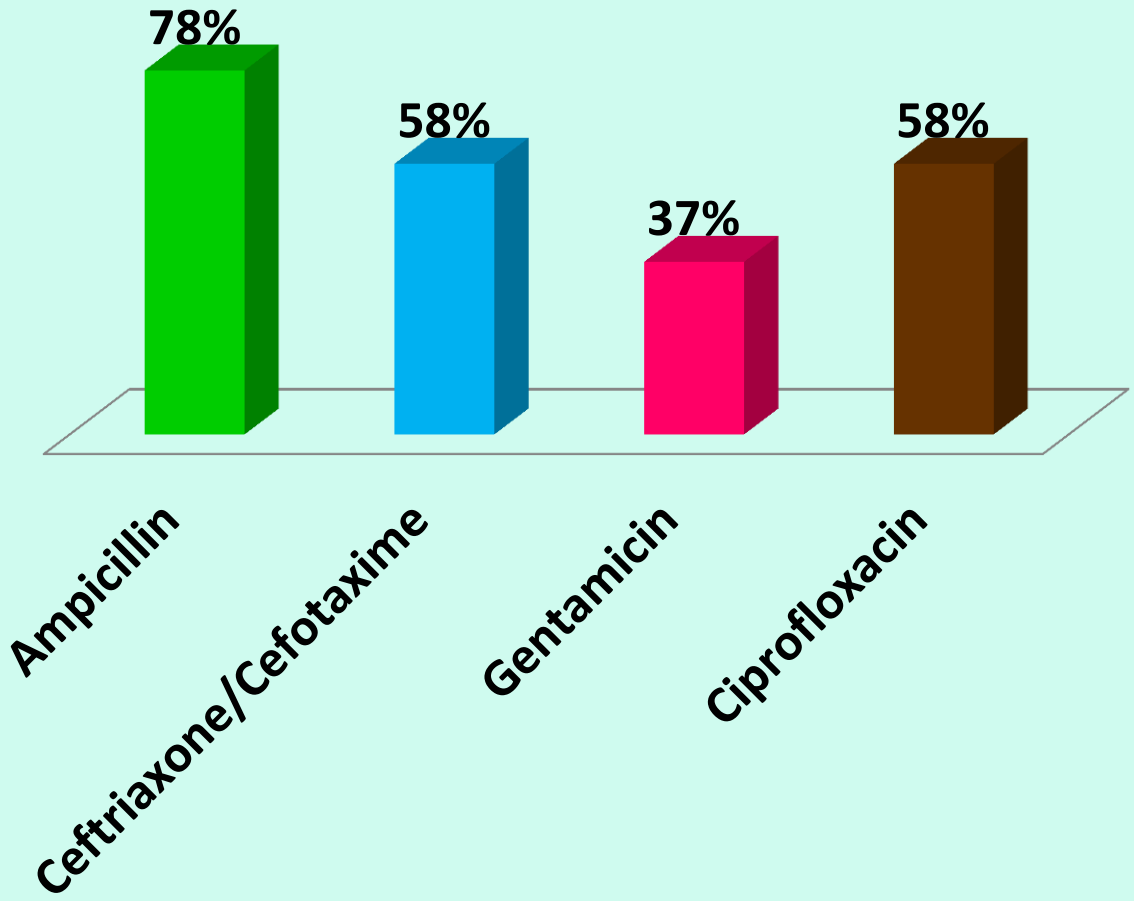
RESULTS – ANTIMICROBIAL RESISTANCE

- For *Gram negative* blood stream infection, **beta-lactam and lower generation fluoroquinolone** resistance was above 50 percent. Gentamicin resistance was 37 percent.



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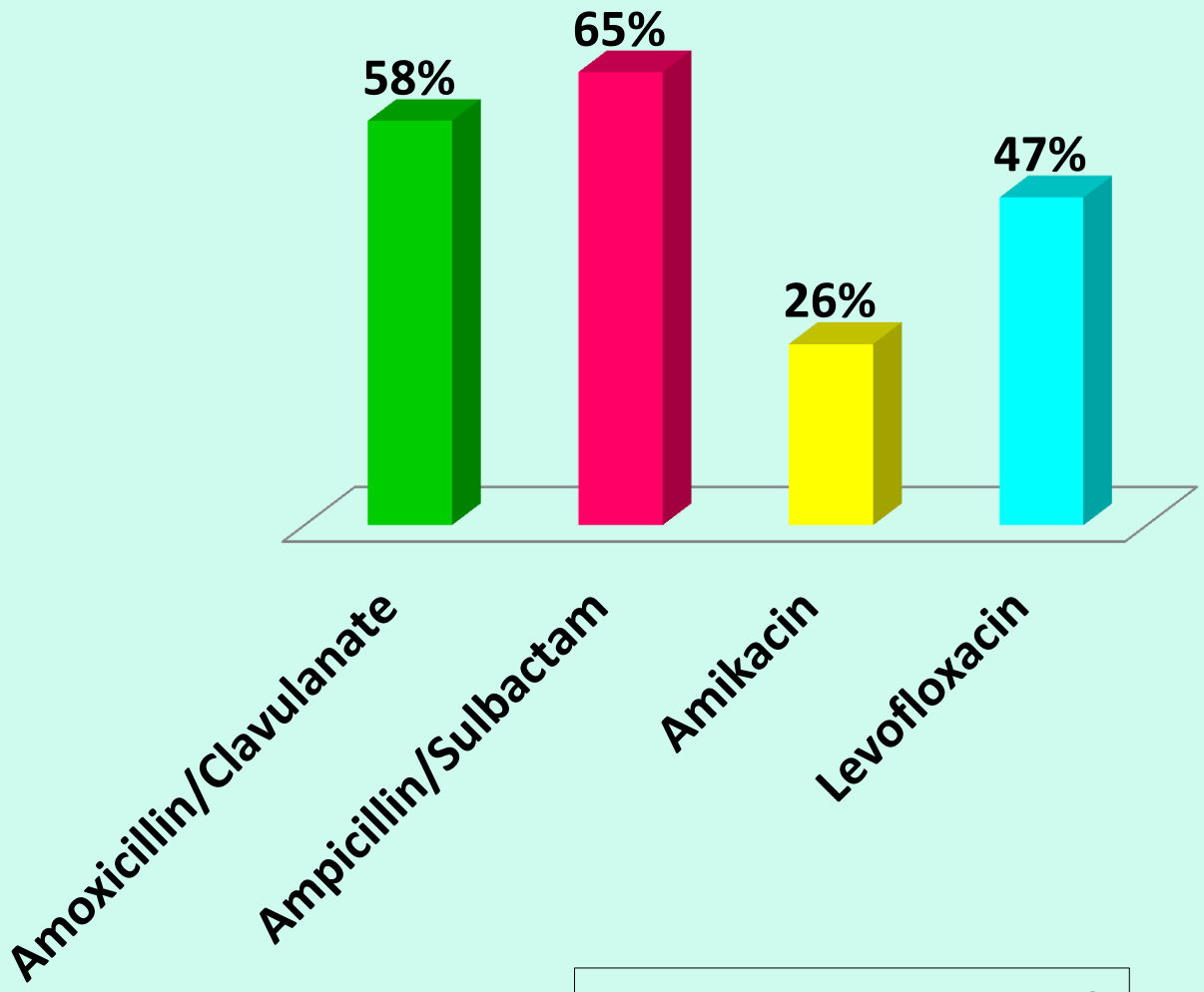

RESULTS – ANTIMICROBIAL RESISTANCE

- For *Gram negative* blood stream infection, **beta-lactamase combined penicillins** resistance was above 50 percent. Amikacin resistance was 26 percent. Levofloxacin resistance was 47 percent.

Clinical Characteristics of Blood Stream Infections in IGH

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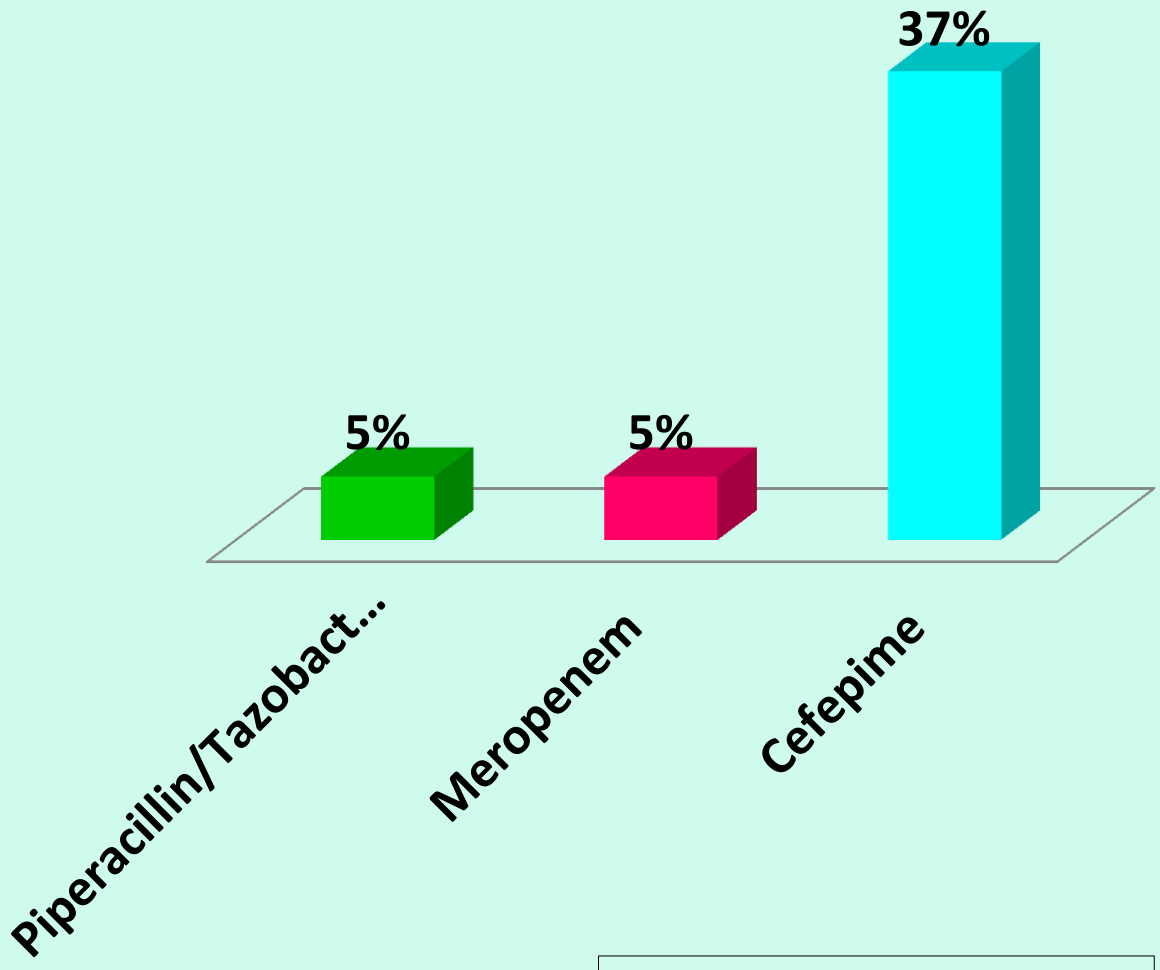

RESULTS – ANTIMICROBIAL RESISTANCE

- For *Gram negative* blood stream infection, **piperacillin/tazobactam and meropenem** resistance was low at 5 percent. Cefepime resistance was 37 percent.

Clinical Characteristics of Blood Stream Infections in IGH

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Message from our study

- Blood stream infection accounted for 18.2 percent of all forms of severe sepsis in medical ward.
- Gram negative organisms (9 in 10 cases) are the main causal organisms.
- Most of the patients with BSI (73 percent) were previously healthy and none of the cases could be identified for immunodeficiency.

DMR presentation 12.1.18

Clinical Characteristics of Blood Stream Infections in IGH

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Message from our study

- There was no clinical stigmata to differentiate between BSI and non-BSI severe sepsis.
- However reduced consciousness, reduced urine output and reduced oxygen saturation were more likely to be associated with BSI and thus the presence of these features suggest urgent intravenous antibiotic therapy.

DMR presentation 12.1.18

Clinical Characteristics of Blood Stream Infections in IGH

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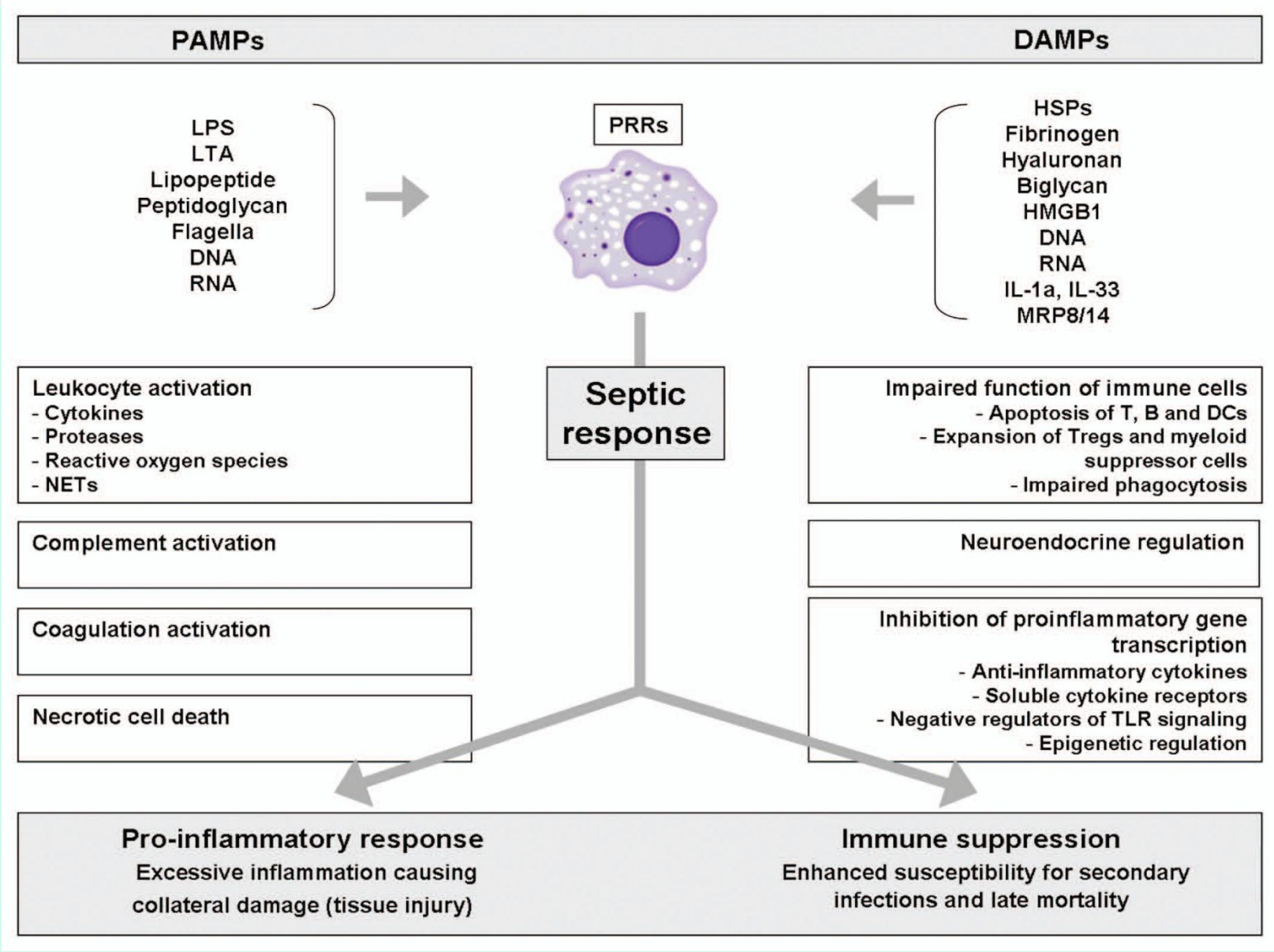
Message from our study

- The case fatality rate of BSI was high at 46 percent.
- Presence of BSI significantly increased the risk of developing shock and prolonged persistence of shock which leads to multi-organ failure.

Pathophysiology

Host innate immune responses to sepsis



INVESTIGATIONS

Investigations

DIAGNOSIS

Cultures

- Appropriate routine microbiologic cultures before starting antimicrobial therapy in patients with suspected sepsis or septic shock
- No substantial delay in the start of antimicrobials
- Always include at least two sets of blood cultures (aerobic and anaerobic).

Investigations

DIAGNOSIS

Cultures

- May include blood, cerebrospinal fluid, urine, wounds, respiratory secretions, and other body fluids.
- The decision regarding which sites to culture requires careful consideration from the treatment team.
- “Pan culture” of all sites that could potentially be cultured should be discouraged.

Investigations

DIAGNOSIS

Supportive investigations

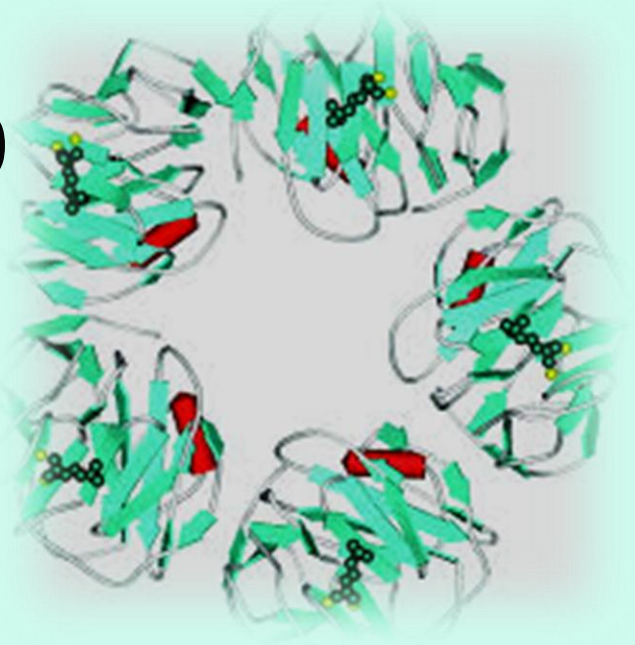
- Full blood count
- CRP
- Procalcitonin
- Urea, electrolytes, creatinine
- Coagulation profile
- Investigations to find out source of infection (urine RE, CXR, CT)
- Others (Serum (1,3)-b-1)-glucan (BDG), Combined serum mannan-antimannan testing, Molecular methods)

Investigations

DIAGNOSIS

Serum C-reactive protein (CRP)

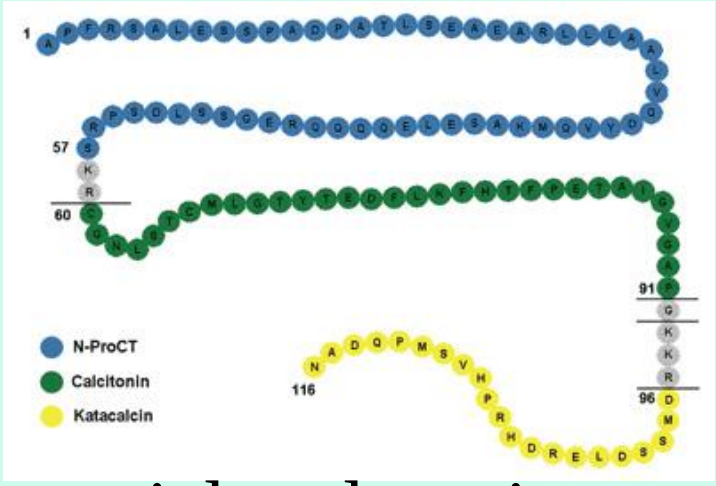
- Influenced by the use of corticosteroids and systemic inflammatory diseases



Investigations

DIAGNOSIS

Procalcitonin (PCT)



- 116 aa protein
- Exact physiological role still unclear
- Most potently stimulated by bacterial endotoxin
- Elevated levels occur in bacterial, fungal and parasitic infections
- Viral and localized infections have lower PCT levels than systemic infections.

Investigations

DIAGNOSIS

Neutrophil Lymphocyte Count Ratio (NLCR)

NLCR = Absolute neutrophil count/ Absolute lymphocyte count

- An indicator of systemic inflammation
- Used in the diagnosis of bacterial infection in patients with fever
- Can be used as prognostic marker in patient with bacteremia.
- Predict acute kidney injury in patients with severe sepsis.

- MANAGEMENT

Management

- Sepsis and septic shock are medical emergencies.
- Treatment and resuscitation must begin immediately.

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Initial Resuscitation

2012 SSC Recommendation for Initial Resuscitation (Early Goal Directed Therapy)

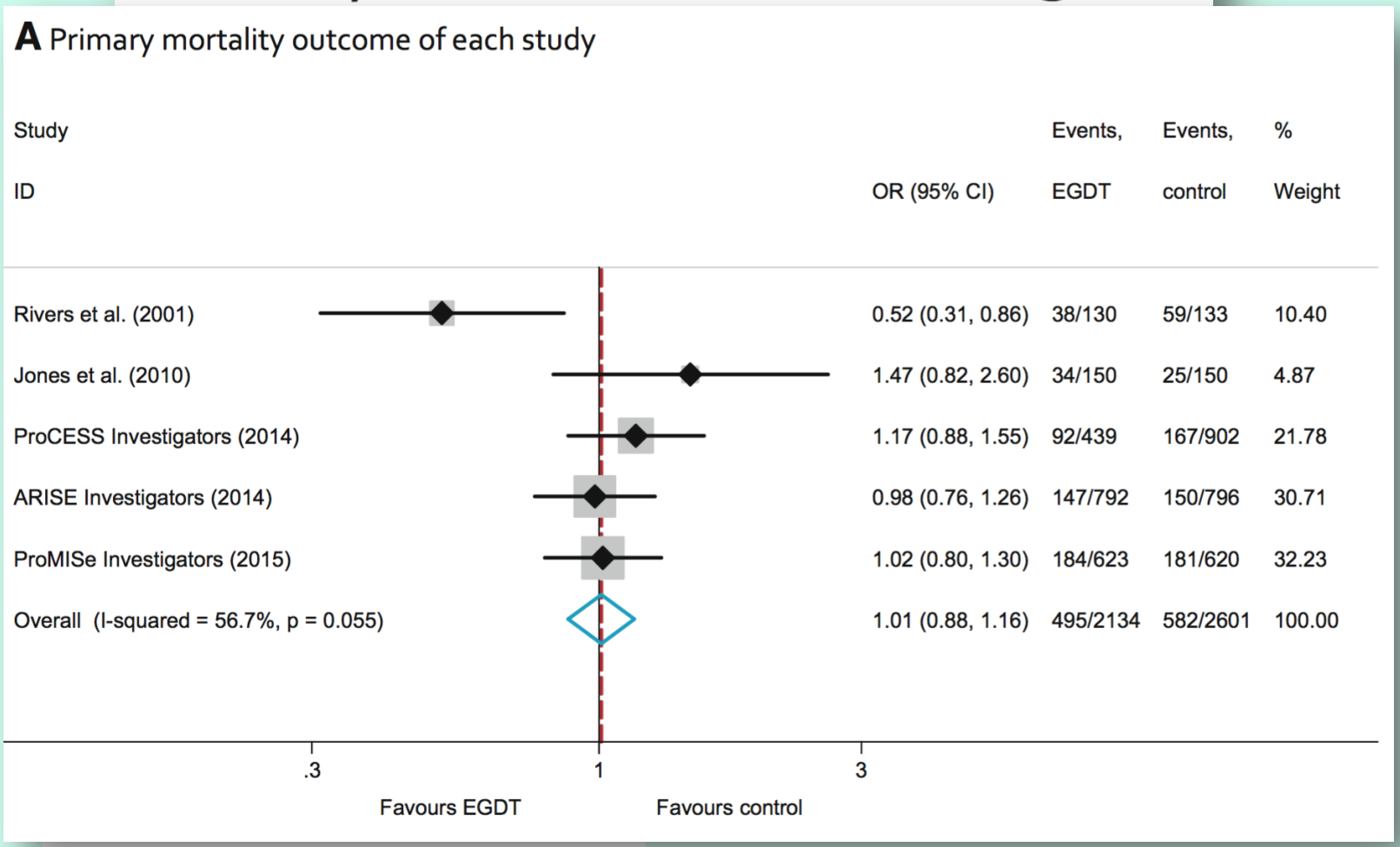
During the first 6 hours of resuscitation, the goals of initial resuscitation should include all of the following as a part of a treatment protocol:

a) CVP 8–12 mm Hg
b) MAP ≥ 65 mm Hg
c) Urine output ≥ 0.5 mL/kg/hr
d) Scvo2 ≥ 70%.

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Initial Resuscitation

A systematic review and meta-analysis of early goal-directed therapy for septic shock: the ARISE, ProCESS and ProMISe Investigators



Intensive Care Med (2015) 41:1549–1560
DOI 10.1007/s00134-015-3822-1

Management: Initial Resuscitation

- **We recommend that in the resuscitation from sepsis-induced hypoperfusion, at least 30ml/kg of intravenous crystalloid fluid be given within the first 3 hours.**

(Strong recommendation; low quality of evidence)

- **We recommend that following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status.**

(Best Practice Statement)

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Initial Resuscitation

TO BE COMPLETED **WITHIN 3 HOURS** OF TIME OF PRESENTATION

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Initial Resuscitation

"TO BE COMPLETED **WITHIN 6 HOURS** OF TIME OF PRESENTATION:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65mmHg

6. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion and document findings.

7. Re-measure lactate if initial lactate elevated.

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Initial Resuscitation

Fluid Therapy

- Crystalloids are recommended as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Initial Resuscitation

Vasoactive agents

- Norepinephrine is the first choice vasopressor
- Either vasopressin (up to 0.03 U/min) or epinephrine can be added to norepinephrine with the intent of raising MAP to target, or adding vasopressin (up to 0.03 U/min) to decrease norepinephrine dosage.

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Source Control

- A specific anatomic diagnosis of infection requiring **emergent source** control be identified or excluded as rapidly as possible.

- And any required **source control intervention** be implemented as soon as medically and logistically practical after the diagnosis is made.

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Sepsis may be devastating!

Management: Antibiotics

- Administration of IV antimicrobials should be initiated as soon as possible after recognition and **within 1 h for both sepsis and septic shock.**

- **Empiric broad-spectrum therapy** with one or more antimicrobials to cover all likely pathogens should be given.

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Antibiotics

What to choose

Causative agent	Predisposing factors	**Antimicrobial agents**
Staphylococcus aureus	Skin/soft tissue infections, prosthetic joints, prosthetic cardiac valves, cardiac electronic devices, central venous catheters	Oxacillin, cefazolin (in case of MRSA: vancomycin, daptomycin, or linezolid)
Coagulase-negative staphylococci	Central venous catheters, cardiac electronic devices, prosthetic joints, prosthetic cardiac valves	Oxacillin, cefazolin (if resistant to b-lactams: vancomycin, daptomycin, or linezolid)
Enterococci	Inflammatory bowel diseases, colorectal cancer, cirrhosis, aging, urinary tract infections	Ampicillin, ampicillin/sulbactam, vancomycin (if resistant to penicillins)

Ref: Valerio Del Bono & Daniele Roberto Giacobbe (2016) Bloodstream infections in internal medicine, Virulence, 7:3, 353-365, DOI: 10.1080/21505594.2016.1140296

Management: Antibiotics

What to choose

Causative agent	Predisposing factors	**Antimicrobial agents**
Enterobacteriaceae	Urinary tract infections, diabetes, aging, solid and hematologic cancers, inflammatory bowel diseases, Cirrhosis	Ureidopenicillins, third generation cephalosporins, gentamicin, fluoroquinolones (high rates of resistance have been reported in both community and hospitals worldwide), carbapenems (in case of ESBL-PE)
Pseudomonas aeruginosa	Bedridden patients, chronic obstructive pulmonary disease, solid and hematologic cancer, aging, prolonged hospital stay	Ureidopenicillins, anti-pseudomonal cephalosporins (ceftazidime, cefepime), amikacin, ciprofloxacin (usually not as single agent), carbapenems
Candida spp.	Elderly, solid and hematologic cancer, immunosuppressive therapies, broad spectrum antibiotics, total parenteral nutrition, diabetes, central venous catheters, prolonged hospital stay	Echinocandins, polyenes, azoles (see Table 3 for specific indications)

Relative activity of selected betalactam antibiotics against common pathogens

Bacteria	Antibiotics								
	Amoxil	Co-amoxi	Cephalaxin/cefadroxil	Cefuroxime	Cefoxitin	Ceftriaxone/Cefotaxime	Ceftaxidime	Piperacillin/Tazobactem	Meropenem
Streptococci	+++	+++	++	++	++	++	+	+++	+++
MSSA	+	+++	+	++	++	++	+	+++	+++
MRSA	-	-	-	-	-	-	-	-	-
CNS	+	+	-	+	+	+	-	+	+
Enterococcus fecalis	+++	+++	_	_	_	_	_	++	_
Enterococcus faecium	_	_	_	_	_	_	_	_	_
H influenzae	+	+++	+	++	++	+++	+++	+++	+++

Ref: Oxford Desk Reference Acute Medicine (2016)

Relative activity of selected betalactam antibiotics against common pathogens									
Bacteria	Antibiotics								
	Amoxil	Co-amoxi	Cephalaxin/cefadroxil	Cefuroxime	Cefoxitin	Ceftriaxone/Cefotaxime	Ceftaxidime	Piperacillin/Tazobactem	Meropenem
M caterrhalis	_	+++	+	++	++	+++	+++	+++	+++
N meningitisis	++	++	+	++	++	+++	+++	+++	+++
N gonorrhae	+	++	+	++	++	+++	+++	+++	+++
E coli	+	++	+	++	++	++	++	++	+++
Klebsiella	_	++	+	++	++	++	++	++	+++
Serratia/ Enterobacter	_	_	_	_	_	+	+	+	+++
Pseudomonas aeruginosa	_	_	_	_	_	_	+++	+++	+++
Anaerobes	+	+++	_	_	++	_	_	++	++

Ref: Oxford Desk Reference Acute Medicine (2016)

Relative activity of selected non betalactam antibiotics against common pathogens									
Bacteria	Antibiotics								
	Ciprofloxacin	Moxifloxacin	Clarithromycin	Gentamycin	Amikacin	Tigicycline	Daptomycin	Vanco/ Teicoplanin	Linozolid
Streptococci	+	++	++	_	_	+++	+++	+++	+++
MSSA	+	++	++	++	++	+++	+++	+++	+++
MRSA	_	_	+	+	+	+++	+++	+++	+++
CNS	+	+	+	+	+	+++	+++	+++	+++
Enterococcus fecalis	_	_	_	_	_	++	+++	++	+++
Enterococcus faecium	_	_	_	_	_	++	+++	++	+++
H influenzae	+++	+++	+++	+	+	++	_	_	_

Ref: Oxford Desk Reference Acute Medicine (2016)

Relative activity of selected non betalactam antibiotics against common pathogens									
Bacteria	Antibiotics								
	Ciprofloxacin	Moxifloxacin	Clarithromycin	Gentamycin	Amikacin	Tigicycline	Daptomycin	Vanco/ Teicoplanin	Linozolid
M caterrhalis	+++	+++	+++	+	+	++	_	_	_
N meningitisis	+++	+++	++	_	+	++	_	_	+
N gonorrhae	+	+	++	+	+	++	_	_	+
E coli	++	++	_	+++	+++	+++	_	_	_
Klebsiella	++	++	_	+++	+++	+++	_	_	-
Serratia/ Enterobacter	++	++	_	+++	+++	+++	-	_	_
Pseudomonas aeruginosa	++	_	_	+++	+++	+++	_	_	_
Anaerobes	_	_	+	_	_	+++	+	+	+

Ref: Oxford Desk Reference Acute Medicine (2016)

Management: Antibiotics

Duration of antimicrobial therapy – 7 to 10 days

Discontinuation of antimicrobial therapy

- Relosution of infection clinically

  +/_

- Strong and early decrease of serum CRP and PCT, especially PCT

Ref: Valerio Del Bono & Daniele Roberto Giacobbe (2016) Bloodstream infections in internal medicine, Virulence, 7:3, 353-365, DOI: 10.1080/21505594.2016.1140296

Management: Antibiotics

Duration of antimicrobials	
Condition	Durattion of treatment
Pylonephritis	10-14 days
CAP	7 days
DM foot with OM	42-56 days
Cholangitis	7 days
SBP	7 days
Septic arthritis	28-42 days
OM	28-42 days
Listeria meningitis	21 days
IE	14-42 days
VAP	7 days
CDI	10-14 days

Role of Corticosteroids

French multicentre trial

- Patients with septic shock unresponsive to fluids and vasopressor therapy.
- Significant shock reversal and reduced mortality in patients with relative adrenal insufficiency detected by ACTH stimulation.

Ref: Oxford Desk Reference Acute Medicine (2016)

Role of Corticosteroids

CORTICUS Study

- No mortality benefit.
- Resolution of shock was faster in those who received steroids.
- ACTH testing did not predict a faster resolution of shock.

Ref: Oxford Desk Reference Acute Medicine (2016)

Role of Corticosteroids

Consensus

- IV hydrocortisone should be given exclusively to those patients whose BP is unresponsive to fluid resuscitation and vasopressor therapy.
- Steroids have side effects. High doses of corticosteroids, equivalent to >300 mg hydrocortisone daily, should not be used in septic shock, as it is ineffective and may be harmful.
- Some septic patients may have an absolute reason for corticosteroid administration.

Ref: Oxford Desk Reference Acute Medicine (2016)

Vasopressin

Relative vasopressin deficiency

- Studies show that vasopressin levels are elevated in early septic shock, but, as the shock continues for 24-48 hours, levels fall within normal range in most patients but in the presence of hypotension.

Ref: Oxford Desk Reference Acute Medicine (2016)

Vasopressin

The VASST trial

- Noradrenaline alone Vs Noradrenaline + low dose vasopressin
- No difference in outcome

Ref: Oxford Desk Reference Acute Medicine (2016)

Vasopressin

Recommendation (SSC guideline)

- Vasopressin should not be administered as the initial, or sole, vasopressor in septic shock.
- Vasopressin at low dose (0.03 units/min) may be subsequently added to noradrenaline.

Ref: Oxford Desk Reference Acute Medicine (2016)

Glucose control

NICE-SUGAR

- Higher mortality rate in adults on intensive care units who received intensive blood sugar control.

Recommendation

- Avoid hyperglycemia
- A target bood glucose < 10mmol/L (180mg/dl)

Ref: Oxford Desk Reference Acute Medicine (2016)

Management: Performance Improvement

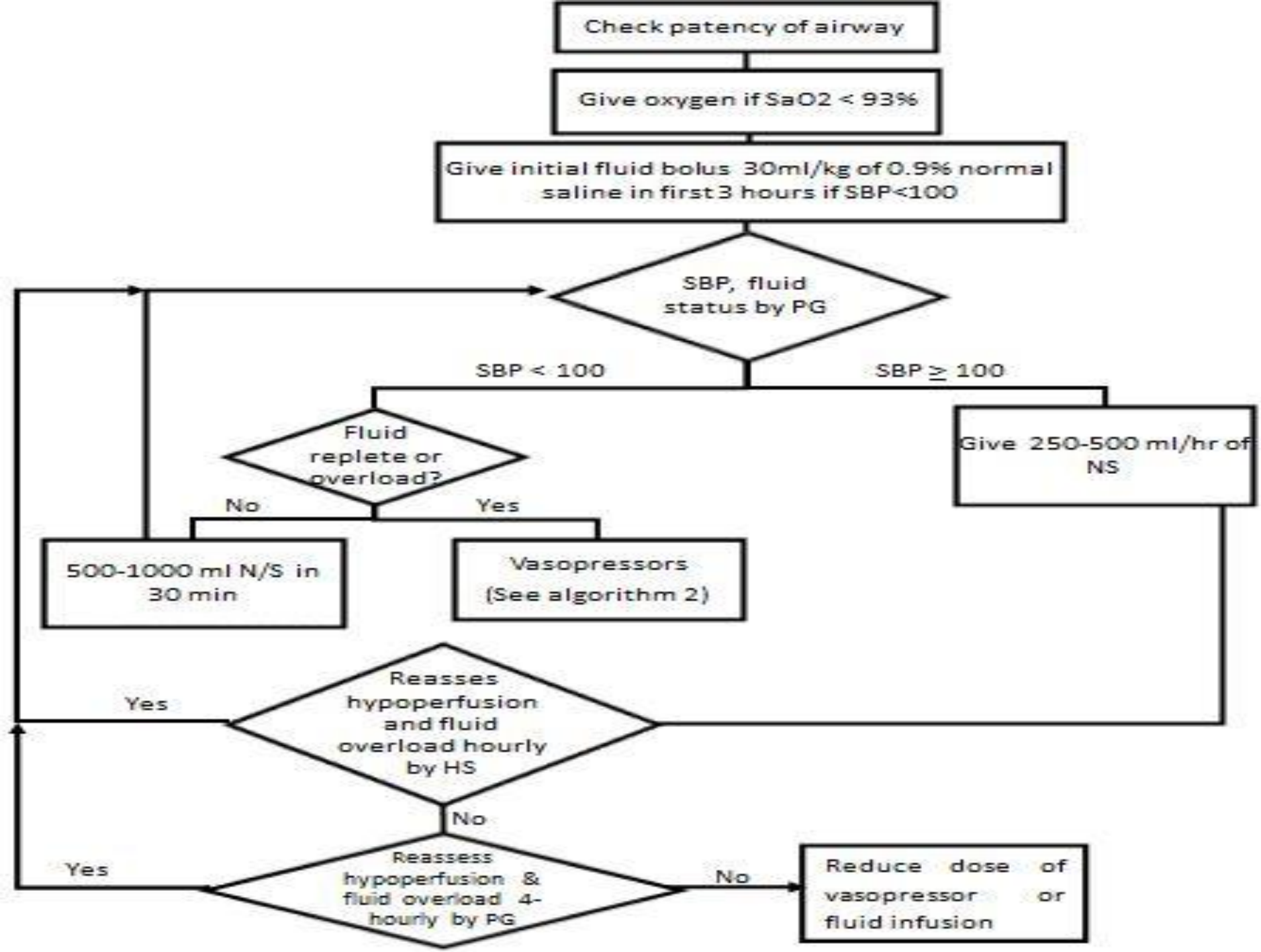
Hospitals and hospital systems should have a **performance improvement program** for sepsis including sepsis screening for acutely ill, high-risk patients.

Ref: Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Management: Performance Improvement

Standard Operating Procedure For Management of Sepsis and Septic Shock (North Okalapa General Hospital)

- Title : Management of Sepsis and Septic Shock
- Document Number: MED/SOP/001
- Lead Author : Dr. Su Yee Win
- Checked by : CS Dr. Thuzar Win
- Approved by : Professors of Medical Units
- Authorized By : Medical Superintendent
- Date : 28.3.2017
- Effective Date : 1.4.2017
- Review Date : 1.4.2018


Check patency of airway
Give oxygen if SaO2 < 93%
Give initial fluid bolus 30ml/kg of 0.9% normal saline in first 3 hours if SBP<100
SBP, fluid status by PG
SBP < 100
SBP ≥ 100
Fluid replete or overload?
No
Yes
Give 250-500 ml/hr of NS
500-1000 ml N/S in 30 min
Vasopressors (See algorithm 2)
Reasses hypoperfusion and fluid overload hourly by HS
Yes
No
Reassess hypoperfusion & fluid overload 4-hourly by PG
Yes
No
Reduce dose of vasopressor or fluid infusion

SEPSIS RECORD PROFORMA

MEDICAL WARD

NORTH OKKALAPA GENERAL HOSPITAL

Name-	Age-	Sex-	RN-	DOA- /

Recognition of sepsis	SIRS Criteria (To circle fulfilled criterion)	qSOFA (To circle fulfilled criterion)
At - : / . .17 ☐ Within 48 hrs of admission ☐ After 48 hrs of admission	T - WBC - RR - PR -	SBP - RR - GCS -

Organ dysfunction (To fill the worst & valid status)	GCS -	Cr - umol/L	Bilirubin - mg/dl	PLT - 10-3/uL
	INR -	UOP - /24 hrs	MAP - mmHg	SpO2 -
Vasopressor requirement	☐ Nil	☐ < 0.1ug/kg/min	☐ > 0.1ug/kg/min	PaO2/FiO2 -

Septic Focus	☐ CNS	☐ SSI	☐ Hepatobiliary	Remark -
	☐ GI	☐ GU	☐ Respiratory	
	☐ CVS	☐ IE	☐ Unspecify	

Comorbidities	☐ CKD	☐ Malignancy	☐ COPD	Remark -
☐ AIDS/HIV	☐ COL	☐ Diabetes mellitus	☐ Corticosteroid	
☐ Tuberculosis	☐ CCF	☐ Autoimmune d/s	☐ Immunosuppresant	

Functional status before illeness	☐ Independence	☐ Partially dependence	☐ Totally dependence
Basic ADLs – bathing, dressing, transfer, toileting, grooming, feeding			

Microbiological data (C & S) - To attach C & S result copy / To write down the result on back page

No	Sample	Send at	Send to	Organisms

Antimicrobial resistance is Challenging!

Antimicrobial resistance is Challenging!

- ANH, 20 years old gentleman from Mayangone

C/o

- High continuous fever with chills x 6 days
- Generalized rash x 2 days
- Melaena stool x 2 times

Antimicrobial resistance is Challenging!

Investigations

CBC

- Hb – 11.1 x 10^6
- WBC – 6.5 x 10^6
- Platelet – 56 x 10^3

Dengue serology

- NS1 Ag - Positive
- IgM – Positive

MP ICT – Positive

Blood for MP – Negative

Rx

IV ARTESUNATE

IV LEVOFLOXACIN 750 MG OD (Participant in ANTHEM study)

Antimicrobial resistance is Challenging!

- Blood culture result 1 week later revealed growth of *Staphylococcus aureus*.

Susceptibility Information	Analysis Time:	11.00 hours	Status:	Final
Antimicrobial	**MIC**	**Interpretation**	**Antimicrobial**	**MIC**	**Interpretation**
Cefoxitin Screen	POS	+	Inducible Clindamycin Resistance	NEG	-
Benzylpenicillin	>= 0.5	R	+Azithromycin		R
+Amoxicillin		R	Erythromycin	>= 8	R
Ampicillin			Clindamycin	8	R
+Amoxicillin/Clavulanic Acid		R	Quinupristin/Dalfopristin	>= 8	
Oxacillin	>= 4	R	Linezolid	>= 32	R
Gentamicin High Level (synergy)			Vancomycin		R
Streptomycin High Level (synergy)			+Doxycycline	>= 16	R
+Amikacin		R	Tetracycline	<= 0.12	S
Gentamicin	8	*R	Tigecycline	<= 16	S
Ciprofloxacin	>= 8	R	Nitrofurantoin	>= 32	R
Levofloxacin	>= 8	R	Rifampicin	>= 320	R
Moxifloxacin	>= 8	R	Trimethoprim/Sulfamethoxazole		
+Norfloxacin		R			

Antimicrobial Resistance

Two main mechanisms

(i) the production of ESBL

(ii) the production of carbapenemases and metallo-betalactamases

Common Organisms Causing Antimicrobial Resistance

ESCAPE

- **E**nterococcus faecium
- **S**taphylococcus aureus
- **C**lostridium difficile
- **A**cinetobacter
- **P**seudomonas aeruginosa
- **E**nterobacteriaceae (E coli, K. pneumoniae, Proteus spp, Enterobacter spp)

Take Home Message

- Awareness - Sepsis Guideline (international and local)
- Relevant specimen should be taken for culture prior to starting antibiotics.
- Choose effective antibiotics with knowledge of local antibiotic resistant pattern
- Empirical antibiotics followed by narrowest spectrum antibiotics

Take Home Message

- Right dose and route and appropriate duration of antibiotics
- Supportive therapy (Fluids, Sugar control, Nutrition, Anaemia management)
- Sensitivity pattern of local hospitals and local antibiotic guidelines should be developed including antibiotic stewardship.

References

- Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016
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Thank you!