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Research Article

Bacteriological Patterns of Sepsis in Lagos State University Teaching Hospital Medical Emergency during an Outbreak of Lassa Fever in 2016

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ABSTRACT

Objective: This study was conducted to identify the bacteriological patterns of sepsis syndrome seen during a Lassa Fever outbreak with a view to distinguishing clinical features seen in bacterial, protozoal, fungal and viral haemorrhagic fevers. Sepsis is a clinical syndrome characterized by systemic inflammatory responses due to invasion of tissues by pathogens.

Method: Eighty patients with the sepsis syndrome were evaluated during a Lassa fever outbreak in Nigeria in 2016. The evaluation involved Triaging using an epidemiological tool, blood culture and identification of suspected pathogens with antibiotic susceptibility profile. Screening of suspected cases for haemorrhagic fever using Reverse Transcriptase Polymerase Chain Reaction(RT-PCR) was also carried out.

Result: Eighty patients of the male preponderance of 58.8% were reviewed. Fever (52.6%) was the main symptom. Other symptoms were bleeding from the skin and other orifices (14.6%), hypotension (7.5%), diarrhoea (7.5%) and skin rash (7.5%). Blood culture was positive in 25% of cases with *Staphylococcus aureus* (25%), *Klebsiella pneumoniae* (20%), *Enterococcus faecalis* (15%), *Acinetobacter baumanii* (15%), *Escherichia coli*(10%), *Pseudomonas aeruginosa* (10%) and *Enterobacteragglomerans* (5%). The antibiotic susceptibility pattern showed high antibiotic resistance among the isolates. Only 15 (18.8%) of the patients fulfilled the criteria for suspected case of viral haemorrhagic fever with only one case (6.7%) positive for Dengue virus.

Conclusion: Sepsis remains a phenomenon even during outbreaks of viral haemorrhagic fevers. Blood culture was positive in a quarter of the patients studied underscoring the need for patients to be investigated appropriately during such outbreaks.

INTRODUCTION

Sepsis is among the most common causes of death in hospitalized patients.[1,2] Infections are responsible for an estimated 300 million annual deaths worldwide, the majority from developing countries.[3] Sepsis can be triggered by almost any infection and is responsible for an estimated 8 million annual deaths worldwide.[1,2] Sepsis involves a dysregulation of the normal inflammatory process that leads to uncontrolled release of pro-inflammatory mediators which act synergistically with the bacterial toxins, to induce widespread tissue injury especially within the vascular endothelium. The endothelium is metabolically active in coagulation and fibrinolysis hence derangement of these activities is highly lethal, causing circulatory failure and death.[1,2]

Sepsis is a hidden public health disaster and patient's outcomes are determined by the virulence of the invading pathogen, which can be directly toxic and destructive; and the host response, which maybe out of proportion to the dose of the infecting organism. This results in collateral organ and tissue damage because the highly potent effectors molecules and acute phase reactants proteins do not discriminate between microbial and host targets.[1-4]

The causative agents of sepsis syndrome include bacterial, protozoan, fungal and viral agents.[2,3] Clinical manifestations are nonspecific and usually superimposed on the symptoms and signs of the patient's underlying illness and primary infection. There are striking individual variations in presentation and the rate at which symptoms develop may differ from patient to patient. Patients usually present with fever or hypothermia. A normal temperature on presentation is uncommon but may occur in neonates, the elderly, alcoholics and the severely immunosuppressed. Early symptoms and signs may include hyperventilation and sometimes confusion or disorientation. Occasionally, skin lesions that suggest a specific pathogenic aetiology may be present at the sites of haematogenous seeding of organisms and/or toxins to the skin. Nausea, vomiting and diarrhoea are usually nonspecific manifestations of the septic response, but may signify acute gastroenteritis as primary infection. [2,3]

Sepsis-related coagulopathy ranges from mild laboratory alterations to severe disseminated intravascular coagulation (DIC). There is evidence that DIC is involved in the pathogenesis of microvascular dysfunction contributing to organ failure. Additionally, the systemic activation of coagulation, by consuming platelets and coagulation factors, may cause bleeding. Thrombin generation via the tissue factor/factor VIIa route, contemporary depression of antithrombin and protein C anticoagulant systems, as well as impaired fibrin degradation, due to high circulating levels of PAI-1, contribute to enhanced intravascular fibrin deposition. This deranged coagulopathy is an independent predictor of clinical outcome in patients with severe sepsis.[6-10]

Lassa fever is a severe and often fatal haemorrhagic illness caused by Lassa virus; a member of the Arenaviridae virus family. Humans contract the virus primarily through contact with the contaminated excreta of *Mastomysnatalensis* rodents (commonly known as the Multimammate rat), which is the natural reservoir for the virus. The rodents live in houses with humans and deposit excreta on floors, tables, beds and food. Since its original discovery in 1969 in the village of Lassa in Borno State, Nigeria, there have been numerous outbreaks of various magnitude and severity across West Africa.

Between August 2015 and 17 May 2016, the World Health Organization (WHO) has been notified of 273 cases of Lassa fever, including 149 deaths in Nigeria. Of these, one hundred and sixty-five (165) cases and eighty-nine (89) deaths were confirmed through laboratory testing (CFR: 53.9%). The cases were reported from twenty-three (23) states in Nigeria.

The clinical presentations of septicaemia due to other pathogens and that due to Lassa fever are similar. The close similarity in presentation of both Sepsis Syndrome and Lassa fever disease poses a diagnostic dilemma especially in settings with poor laboratory backups for Reverse Transcriptase Polymerase Chain Reaction testing (RT-PCR).[5,9,10] The inflammatory response and the course for both is also similar with an incompletely understood pathogenesis: hallmarks are microvascular thrombosis, vasodilation, free radical damage and Capillary Leak.[15]

METHOD

Eighty (80) patients who presented at the Lagos State University Teaching Hospital Medical Emergency Department were reviewed during the period of the Lassa fever outbreak in Nigeria. The unit is part of the viral haemorrhagic fever (VHF) Response Team and is tasked with the responsibility of reviewing all those that presented with features pathognomonic of VHF.

The Epidemiological Triage Screening Tool (Figure 1) was used in screening and isolation of probable cases pending the collection of blood for virologic screening.

Sample collection

Trained personnel collected 5mls of blood into EDTA bottles that were then triple packed for onward transportation to the Virologic Laboratory at Lagos University Teaching Hospital on ice box for RT-PCR to identify Haemorrhagic fever viruses.

Another 20 ml of blood was collected and divided into 10 ml each for inoculation into Oxoid Signals Blood Culture system for aerobic and anaerobic culture.[19] The samples were processed microbiologically and identification of pathogens was done by using semi-automated Microbact Identification System.[20,21]

Antibiotics susceptibility testing was carried out by using the Modified Kirby Bauer Method and CLSI guideline for Antibiotic susceptibility Testing.[22]

RESULT

Thirty-three (41%) of the participants were female while 47(59%) were male. The predominant clinical feature was fever(52.6%), bleeding from different parts of the body (14.6%) and dyspnoea (13.8%), while skin rashes, hypotension and diarrhoea were seen in 5.7%, 7.3% and 7.3 % of patients, respectively (Figure 2). Blood culture was positive for bacteria in 25% of patients with *Klebsiella pneumoniae* 4(20%), *Escherichia coli* 2(10%), *Pseudomonas aeruginosa* 2(10%), *Acinetobacter baumanii* 3(15%), *Enterobacter agglomerans*1 (5%), *Staphylococcus aureus*5 (25%) and *Enterococcus faecalis*3 (15%). The antibiotic susceptibility pattern was as depicted in Table 2.

The virologic screening was carried out for only fifteen (18.8%) patients who fulfilled the criteria for suspected cases of viral haemorrhagic fever and only one (6.7%) was positive for Dengue fever.

Table 1: Definition of terms [1,2]

	DEFINITION OF TERMS
Infection Bacteraemia	Presence of a micro-organism in a normally sterile site – differentiate from colonisation Bacteria cultured from blood – poor correlation with severe sepsis, may be transient without any clinical consequences
Systemic inflammatory response syndrome (SIRS)	Two or more of the following: ✓ Temperature >38°C or ✓ Tachycardia 90 beats/min ✓ Respiratory rate >20 breaths/min or PaO2 < 4Kpa ✓ 12, 000cell/mm^3 or 10% immature (band) forms
Sepsis Hypotension Tissue hypoperfusion	If SIRS is associated with infection (proven or suspected) Systolic blood pressure of < 90 mmHg; MAP 40 mmHg from baseline (exclusive of other causes of hypotension) Manifests as one or more of the following:
Severe sepsis	● Septic shock ● Serum lactate >2.0 mmol/l ● Oliguria (1 hour, not responding to vasopressor therapy
Septic shock	Sepsis associated with dysfunction of organ(s) distant from the site of infection – hypotension or hypoperfusion, if present, must be reversible with adequate fluid resuscitation
Refractory sepsis	Sepsis-induced hypotension not responding to adequate fluid resuscitation and requiring vasopressor therapy Septic shock for >1 hour, not responding to vasopressor therapy

Table 2: Pathogens isolated from the patients with Sepsis Syndrome and their Antibiotic susceptibility patterns

Antibiotics	*Escherichia coli* n=2	*Enterobacter agglomerans* n = 1	*Klebsiella pneumoniae* n=4	*Acinetobacter iwoffii* n=3	*Pseudomonas aeruginosa* n=2	*Staphylococcus aureus* n=5	*Enterococcus faecalis* n=3
Amikacin	50	100	75	67	100	40	1 (100.0)
Ceftazidime	100	100	75	67	50	40	33
Amoxycillin-clavulanic acid	0	0	25	0	0	20	0
Levofloxacin	50	100	50	33	100	75	33
Meropenem	100	0	75	33	50	80	67
Erythromycin	0	0	0	0	0	0	0
Cefotaxime	50	100	75	67	0	60	33
Ceftriaxon	50	0	50	33	0	40	33
Ciprofloxacin	50	100	50	67	50	60	67

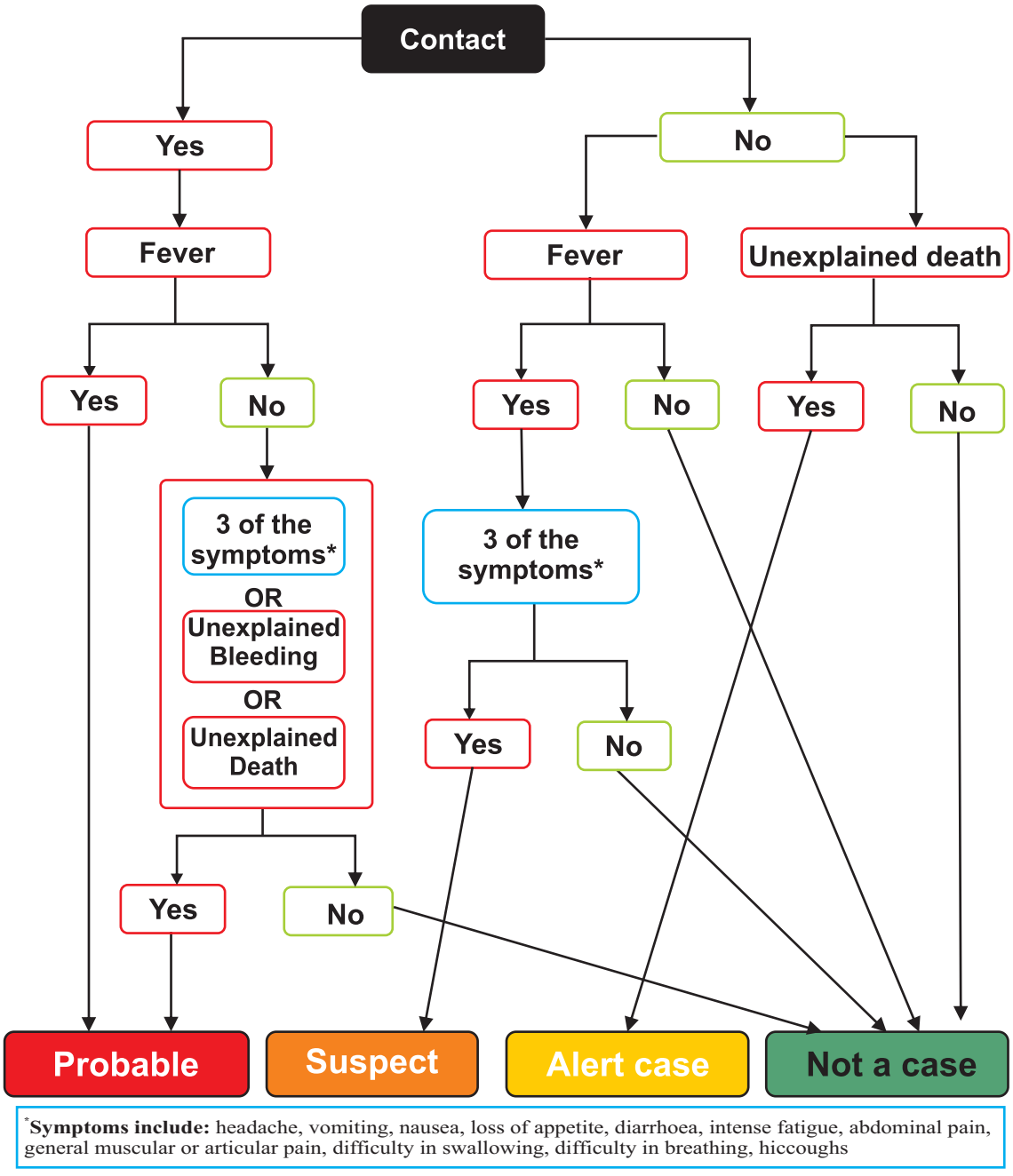

Figure 1: The Triage Epidemiological tool used for Isolating Suspected cases

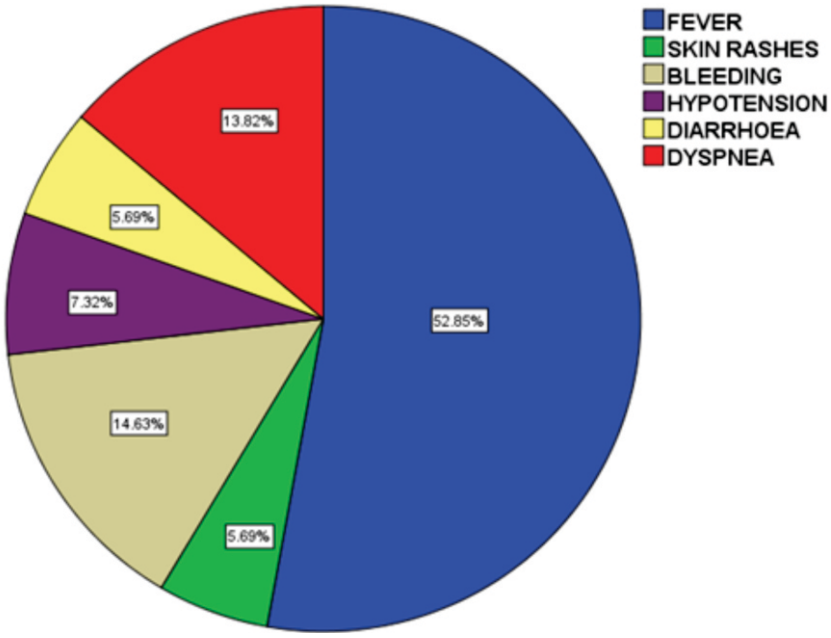

Figure 2: Clinical presentation of patients presenting at Lagos State University Teaching Hospital with Sepsis Syndrome

DISCUSSION

Septicaemia is a major cause of death. Bacterial agents of septicaemia and their susceptibility to antibiotics are influenced by geographical location and time,[23] thus necessitating periodic reviews of bacterial septicaemia to aid in empiric therapy of this life threatening condition. This study focused on determining the causative agents of septicaemia among adults presenting at the LASUTH Medical Emergency during an outbreak of Lassa fever as well determining their susceptibility profiles. An overall bacterial isolation rate of 25% was observed in this study. This result is higher than that of the value previously reported elsewhere[24] which may be due to the cohort of study population and the peculiar prevailing condition.

The finding of this study that there is a male preponderance which at variance with the findings of Komolafe *et al*.[24] However, in other studies among neonates, it has been reported that male sex is a risk factor for septicaemia.[25] This observation is in agreement with the findings in this study even though the age of the study population is different. The finding that *Staphylococcus aureus* and *Klebsiella pneumoniae* were the most prevalence Gram positive and Gram negative isolates respectively agrees with previous report.[23,24] The clinical presentation still shows that fever is one of the cardinal signs to look for in cases presenting with sepsis syndrome. This is similar to other studies in Nigeria and West Africa.[23,24,25]

The susceptibility pattern is really a cause for concern bearing in mind that the antibiotics tested for were mainly used in bloodstream infections. The resistance noted may be due to long term uncontrolled usage without appropriate monitoring of response through appropriate culture and sensitivity testing.[26-29]

Even though the positivity rate for viral haemorrhagic fever among the screened population is low, 6.7%, it is imperative that patients presenting with features of fever and bleeding should always be screened for haemorrhagic fever viruses.

LIMITATION

The findings in this report are subject to limitations. First, the assessment examined a small sample of patients at the Medical Emergency Department within the hospitals; characteristics of patients with sepsis could be different elsewhere, Second, the patients had prompt access to the VHF Response Team hence were not under financial constraint to pay for blood culture. Thirdly, there was a targeted approach in the management of these patients, rather than waiting for the usual hospital machinery hence the results cannot be generalized.

CONCLUSION

This study indicates that concerted effort should always be made to identify the aetiological agent of sepsis in patients who present with clinical features that are indistinguishable from those seen in viral haemorrhagic fever.

Conflict of interest

The authors declare no competing interest.

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