Co-infection of Methicillin Resistant *Staphylococcus aureus* Bacteremia and Malaria in Children Attending Cottage Hospital Ogidi Ilorin Kwara State, Nigeria

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DOI: 10.36348/sjpm.2021.v06i09.006 | Received: 02.08.2021 | Accepted: 04.09.2021 | Published: 20.09.2021

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Abstract

*Staphylococcus aureus* is a major agent of bacteremia in children in African where malaria is endemic and always presented with the same symptoms. The main objective of this study is to determine the co-infection of malaria and *Staphylococcus aureus* bacteremia in children less than 5 years using standard procedures from a major secondary health center in Ilorin, Kwara State and determine antibiotics susceptibility of *S. aureus*. A total number of 235 samples blood from febrile children suspected of having bacteremia were screened, 138 of the children were females and 97 were males. A total of 39 (16.6%) with positive blood culture was recorded in this study and *Staphylococcus aureus* bacteremia (SAB) detected is 20.5%. Age distribution of bacteremia were 14.3, 17.4, 27.3, 13.5 and 14.3 % for children in the age group ≤1, 1-2, 2-3, 3-4 and 4-5 years respectively while SAB distribution were 24.4, 12.5, 22.2, and 66.6 for children in the age group 1 month-1, 1-2, and 4-5 years above respectively. Also, a total number of 148 (63%) have a positive malaria parasite test, co-infection of malaria and bacteremia detected in 18 children with 6 (33.3%) having SAB and malaria co-infection. Age distribution of co-infection of malaria and SAB were 33.3, 50, and 25% with no co-infection recorded in age group 3-5 years. A total of 2 (25%) methicillin resistant *Staphylococcus aureus* were isolated. Antibiotic sensitivity profile shows that 62.5% of *S. aureus* were resistance to cefuroxime, 80% to cefepime and 100% sensitivity to augmentin, linezolid, teicoplanin, ofloxacin, gentamicin and vancomycin. Age is an important risk for development of SAB and prompt treatment with a suitable antibiotics is required to reduce mortality associated with bacteremia.

Key words: Co-infection, *Staphylococcus aureus*, bacteremia, malaria, MRSA.

INTRODUCTION

Bacteremia is one of the major and serious infections caused by *Staphylococcus aureus* and *Staphylococcus aureus* bacteremia (SAB) infections are one of the most difficult infection with significantly higher morbidity and mortality compared with bacteremia caused by other microorganisms (Naber, 2009).

Entrance of *S. aureus* into the blood stream can result in its dissemination, resulting in metastatic and serious infection of almost all the internal organs of the body leading to many complications such as infective endocarditis (Tong et al., 2015). The increase incidence of SAB complications are mainly due to higher number of immune-compromised patients, increase frequency of invasive surgeries and use of intravascular devices (Rasmussen et al., 2011). Invasive bacterial diseases was responsible for about 1.4 million worldwide and Nigeria as the largest country in Sub Saharan African contributes large percentage to the global mortality rate of 100-250 per 1000 in under 5 years children (WHO, 2019). Also research has shown that mortality as a result of non typhoidal *Salmonella*-bloodstream infection in children below 5 years exceeds that of malaria globally (Takem et al., 2014). Studies have also shown that more than 50% of SAB patients lack clinical symptoms consistent with staphylococcal infection making drug prescription difficult thus resulting in high mortality (Ahman and Zupan, 2007).

Despite the well documentation of severity and frequency of *S aureus* bacteraemia, the choice of antibiotics is not well documented most especially in the developing world. This study thus aimed at
determining the determining co-infection of *Staphylococcus aureus* bacteremia and malaria in a secondary health centre in Ilorin, Nigeria.

**Ethical Considerations**

Ethical approval was approved by Kwara State Ministry of Health, Kwara State University Center for Community development while all the parents/guardians of the participants gave a written consent.

**Study Area**

The study was conducted between October, 2017 and December, 2020 at Cottage Hospital Ogidi a Secondary Health Center in Ilorin, the Capital City of Kwara State, Nigeria.

**Blood Sample collection**

The physician that is well informed on the study protocol collects the venous blood aseptically by venipuncture from children into a sterile syringe using a butterfly attachment.

This is done after cleaning thoroughly the patient’s skin with alcohol and allowing the skin to dry before the blood samples were collected. About 2 mL to 3 mL of blood was cultured in Brain heart infusion broth unless these volumes could not be collected, in such case the maximum volume that was collected was cultured. Samples were transported to the laboratory immediately for appropriate analysis. Two drops of blood were each place on separate spots of a slide. A spot was spread to make thick blood film while the second was spread to make thin blood film.

**Patients**

All the febrile children suspected of bacteremia were screened for *S. aureus* bacteremia as well as malaria parasite.

**Malaria Screening**

Malaria parasite screening was done by microscopy of thick and thin blood films. The thin film formed was fixed thoroughly with methanol, after which the slide was stained with a 1:10 dilution of freshly prepared Giemsa stain for 10 minutes. The stain is later washed off with buffer water and allow to air-dried. The stain was subsequently examined under the light microscopy at ×1000 magnification.

**Bacterial isolation and identification**

The blood cultures were incubated at 37°C for seven consecutive days. After 24 hours incubation, a sterile loopfuls of broth were sub-cultured on to nutrient agar and blood agar and incubated aerobically for 18-24 hours at 37°C.

On a daily basis haemolysis, broth coagulation and gas production (air bubbles presence) were observed for the presence of positive growth of microorganisms. Subcultures were done on the 3rd, 5th and 7th day on selective and enriched media such as Blood agar and mannitol salt agar.

The agar plates were subsequently incubated and colonies on solid agar plates were later identified based on characteristic morphology and biochemical tests.

Isolation and identification of *Staphylococcus aureus* was done through the exploitation of its biochemical activities and culture characteristics using appropriate standard microbiological techniques. These include usage of selective culture media, catalase production, Gram reaction, slide and tube coagulase test.

**Antibiotic susceptibility testing**

Resistance and susceptibility to antimicrobial agents used in the treatment of blood stream infections was done by the disc diffusion technique according to the guidelines used by the Clinical and Laboratory Standards Institute (CLSI, 2018). The antibiotic discs to be used include Linezolid (30 µg), Teicoplanin (30 µg), augmentin (30 µg), gentamicin (10 µg), ofloxacin (5 µg), cefuroxime (30 µg), vancomycin (30 µg) and cefepime (30 µg) All from Oxoid UK. The discs was placed on to the surface of inoculated Mueller- Hinton agar plates. After overnight/ 24-hours incubation, the inhibition zone diameters was measured to the nearest millimeter. Antimicrobial susceptibility testing was performed by the disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) guidelines (2018). *S. aureus* ATCC 25923 was used as controls. Phenotypic identification of MRSA was done by determination of resistance to cefoxitin (30 µg).

**RESULTS**

Table-1: Age distribution of children with *Staphylococcus aureus* bacteremia and *Plasmodium falciparium* co-infection

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Sample</th>
<th>Positive bacteria growth</th>
<th>SAB</th>
<th><em>P. falciparum</em></th>
<th><em>P. falciparum</em> and bacteremia</th>
<th><em>P. falciparum</em> and SAB</th>
</tr>
</thead>
<tbody>
<tr>
<td>0≥1</td>
<td>98</td>
<td>14</td>
<td>3</td>
<td>53</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>1≥2</td>
<td>46</td>
<td>8</td>
<td>1</td>
<td>27</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>2≥3</td>
<td>33</td>
<td>9</td>
<td>2</td>
<td>21</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>3≥4</td>
<td>37</td>
<td>5</td>
<td>-</td>
<td>29</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>4≥5</td>
<td>21</td>
<td>3</td>
<td>2</td>
<td>18</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

percentage

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DISCUSSION

This study examined a total number of 235 blood from children with febrile condition suspected of having bacteremia or malaria infection who are under 5 years old at a major Secondary Health Center in Ilorin (Cottage Hospital Ogidi). 138 of the children are females while the remaining 97 were males. A total of 39 (16.6%) positive blood culture was recorded in this study. This is higher than 10.8% recorded by Obaro et al. (2011) at Abuja but lower than 22.4% reported by Arowosegbea et al. (2017). Also in this study the prevalence of Staphylococcus aureus bacteremia (SAB) detected is 20.5%. Obaro et al. (2011) reported that Staphylococcus aureus is the number causative agent of bacteremia in Nigeria. The total children with Plasmodium falciparum parasitemia were 148 (63%) and Co-infection of malaria and bacteremia is seen in 7.7% with co-infection of malaria and SAB been 33.3%. In most Africa countries including Nigeria where malaria is endemic, majority of febrile presentation are always presumed as malaria, however this study shows that bacteremia is alaway a major factors that could responsible as reported in many other studies (Chowdhary et al., 2006; Fortuin-de et al., 2015; Carpenter et al., 2016; McMullan et al., 2016; Arrieta et al., 2018). Age distribution shows that 0-1 the highest bacteremia (27.3%) compare to other age groups while the highest SAB (66.6%) were detected in the children between 4years to 5 years old. Children between the age group 3 years to 4 years have the highest Plasmodium falciparum parasitemia with 78.4% while the lowest were seen in children less than 1 year old. Also the the highest co infection of malaria and bacteremia were seen in age group 1 year to 2 years old with 13% with the lowest seen in age group 3-5 years old. The lowest co-infection of SAB and plasmodium falciparum were seen in children between the age group 3 years to 5 years while the highest was recorded in children between the age group 1year to 2 years. One of the major risk factors for SAB is young age, infants of 1 year of age have been reported in some studies to have higher incidence of SAB in comparison to children with older age (CDC, 2016).

In a study by Vanderkooi et al. (2011), 7/ 100,000 popualtion bacteremia prevalence were recorded in infants and 124.8/100,000 recorded in the neonates. Also Shane et al. (2012) reported that younger age and lower birth weight is proportional to the frequency of SAB while Kempley et al. (2021) repored that theses factors is associated with poorer outcome in Neonatal intensive care unit.

Also, incidence of SAB in children have been shown to correlate with household crowding, geographic factors and or socioeconomic status (Tong et al., 2012). In the United State of America, African-American ethnicity has been shown to be associated with a higher incidence of invasive methicillin-resistant S aureus (MRSA) infection compare to white (Kempker et al., 2010), however in another study by Shane et al. (2012) in NICU, no significant difference was reported regarding ethnicity. One of the major factors responsible for development of SAB in this study as reported else where could be malnutrition, previous hospitalization, presence of central venous catheter, HIV/AIDS infection, and residence in a long-term care facility (Liu et al., 2011). Also S aureus frequently cause bacteremia in healthy children but Hamdy et al. (2017) reported 48% of children having MRSA bacteremia lacked any serious underlying medical conditions.

However, medical co-infection is a major factor in development of bacteremia. SAB can vary in severity from mild infection to severe form of infection, and apparently asymptomatic isolation from the blood stream as a result of contamination is rare (Roediger et al., 2021).
al., 2017) therefore, any positive culture with *S. aureus* is always considered to clinically significant and treated promptly. Antibiotic sensitivity against the isolated *Staphylococcus aureus* shows that 62.5% and 80% resistance was recorded against cefuroxime and cefepime respectively with 100% sensitivity recorded against augmentin, linezolid, teicoplanin, ofloxacin, vancomycin and gentamicin. Age distribution shows that the highest resistance (50%) were recorded against cefuroxime in children in the age group 2 years to 3 years. A total of 2 (25%) methicillin resistance *Staphylococcus aureus* (MRSA) was detected in this study with 100% resistance against cefuroxime which is one of the major antibiotics used in empirical treatment of SAB in children. This percentage is higher compare to the study by Oren et al. (2019) involving 427 episodes of SAB, where 284 SAB were hospital acquired and 15% MRSA detected with 2% Community acquired – MRSA.

Empirical pretreatment is a common in the study hospital and drug abuse by the patients before getting to hospital is a major factor that could contribute to antimicrobial resistance. Higher antimicrobial usage in the community could also be responsible for some patients with bacteremia to postpone seeking additional healthcare thus reducing pathogen recovery rate in those who do seek medical support. As noticed in this study beta lactam antibiotics has been reported as first line drug in the treatment of MSSA-B with a superior outcome compare to glycopeptides. Furthermore, McMullan et al. (2016) reported increase in mortality in children treated with glycopeptides in a study involving 1000 cases of SAB. Vancomycin is the first-line and major antibiotics for the MRSA bacteremia and beta lactam allergic patients at starting doses of 45 to 60mg/kg per day while linezolid an oxazolidinone antibiotic with a very high tissue penetration and bioavailability is also a drug of choice that could be used in the treatment of MRSA infections, however toxicity from linezolid usage may include peripheral neuropathy, optic and bone marrow suppression and this could occur after third week of treatment (Gould, 2011).

Gentamicin sensitivity in this study is 100% sensitivity however due to increased risk of nephro-toxicity gentamicin therapy is no longer indicated in the treatment of SAB (Selby et al., 2009).

**CONCLUSIONS**

*Staphylococcus aureus* bacteremia is a major factors to be considered in febrile children reported to hospital as malaria may not be responsible and it is recommended that care must be taken in the choice of antibiotics in pretreatment of bacteremia. Also, setting up of microbiology laboratory in all the hospitals should be a priority and early screening of bacteremia using high technology equipment is also recommended for early diagnosis and prompt treatment to reduce mortality rate associated with bacteremia.

**REFERENCES**


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