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Coagulase Negative Staphylococci Isolated from Blood Cultures at Anosiala University Hospital Center, Antananarivo

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ABSTRACT

Blood cultures are bacteriological examinations to be carried out to confirm bacteremia caused by pathogenic germs. Coagulase-negative Staphylococci are so-called opportunistic bacteria that can become pathogenic for their host, especially in immunocompromised individuals. The main objective of this study was to determine the prevalence of coagulase-negative Staphylococci isolated from blood cultures and their antibiotic resistance at the Anosiala University Hospital Center. This is a retrospective descriptive study of blood culture examinations carried out in the bacteriology laboratory of the Anosiala University Hospital Center. It was carried out from January 2020 to December 2022 for a period of 2 years. Among 274 blood samples received during this period, 38 isolated cases of coagulase-negative Staphylococci were recorded, representing a prevalence of 13.86%. All blood cultures positive for coagulase-negative Staphylococci were isolated from hospitalized patients: pediatric department in 85% of cases (32/38), followed by intensive care in 10% of cases (4/38), then medicine unit in 5% of cases (2/38). In this study, 60% were identified resistant to methicillin. The most active molecules were Pristinamycin and Vancomycin. Carrying out blood culture in a developing country like Madagascar requires consensus both in the collection and in the interpretation of positive results. Clinico-biological consultation remains essential to distinguish real bacteremia from contamination.

Keywords: Blood culture, Coagulase negative Staphylococci, Prevalence, Resistance

INTRODUCTION

Blood cultures are bacteriological examinations to be carried out to confirm bacteremia caused by pathogenic germs. However, it is possible to isolate so-called commensal germs from blood samples. Coagulase-negative staphylococci (CNS) are so-called opportunistic bacteria that can become pathogenic for their host, especially in immunocompromised individuals. The pathogenicity of these germs in blood cultures is a problem of interpretation for the biologist and management for the clinician. The use of antibiotics in the event of contamination with CNS is unnecessary and promotes bacterial resistance. In addition, it is associated with additional costs for the patient, by extending the hospital stay and carrying out other series of analyses (Bates, Goldman, & Lee, 1991; Weinstein, 2003). The main objective being to describe the frequency of isolation in blood cultures and the antibiotic resistance of these CNS.

MATERIALS AND METHODS

This is a retrospective descriptive study of blood culture examinations carried out in the bacteriology laboratory of Anosiala University Hospital. It is a versatile laboratory, carrying

out routine analyzes in hematology, biochemistry, bacteriology, virology and serology. All coagulase-negative Staphylococci isolated from blood cultures constituted the study population. CNS isolated from other samples were excluded from the study. It was carried out from January 2020 to December 2022 for a period of 2 years. Dependent variables were represented by blood culture positivity for coagulase-negative Staphylococcus. The independent variables were the department, the clinical information justifying the examination, and the results of the antibiogram. The samples were inoculated into manual OXOID®-type vials then sent to the laboratory. They were incubated in an oxygen oven at 37°C for 7 days. For cases of suspected infective endocarditis, the incubation period has been extended to 21 days. The detection of positivity is carried out visually, twice the first 2 days: once in the morning and once in the evening then once a day for the last 5 days or until the 21st day. Positivity was observed in the event of a change in the turbidity of the medium by the appearance of a disorder, hemolysis with an ascent of the liquid through the indicator. In this case, a subculture was launched and the sample inoculated in blood and chocolate agar, and on the chromogenic medium such as Urinary Tract Infection UTI. A direct examination in the fresh state and after GRAM staining were also carried out and the results were communicated to the service. After 24 to 48 hours following seeding, suspicious colonies appear. Gram staining showed Gram-positive cocci grouped in clusters. The catalase test using hydrogen peroxide came back positive. The coagulase test using citrated plasma came back negative, hence coagulase negative Staphylococci. Species identification was not carried out due to lack of technical means. Antibiograms were performed and interpreted according to the EUCAST/CA-SFM 2020 recommendations.

RESULTS

Overall Results

Among 274 blood samples received during this period, 38 cases of coagulase-negative Staphylococci were recorded, representing a prevalence of 13.87% (Figure 1).

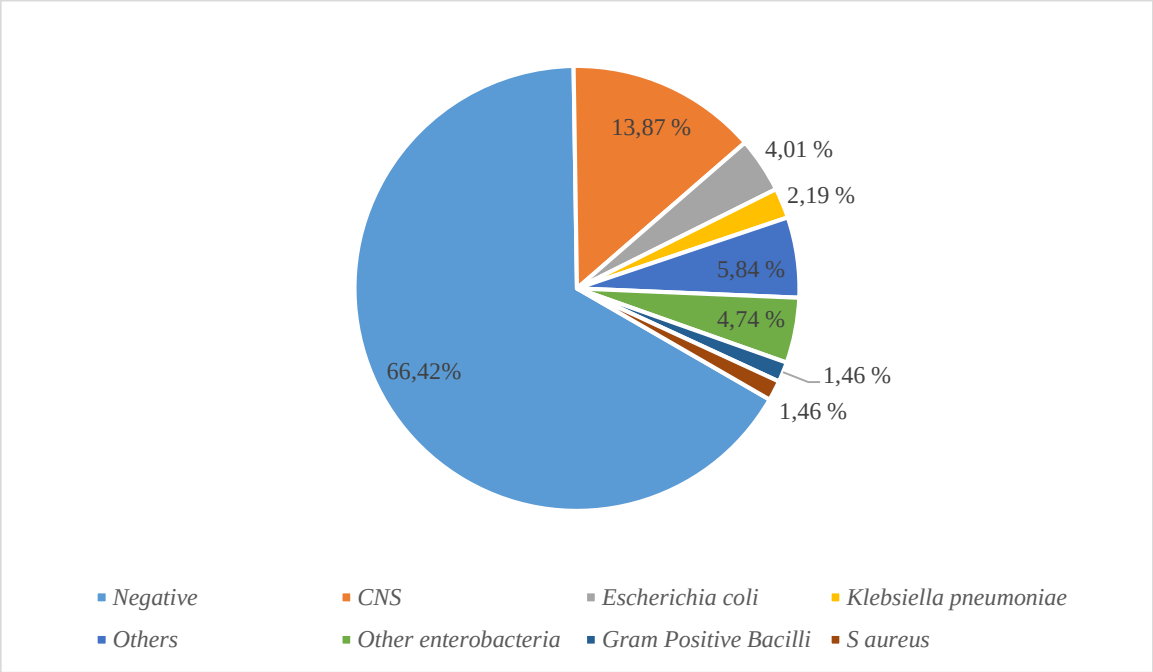

Figure 1: Distribution of Blood Cultures Result Types

The extreme ages were from 0 days to 67 years with an average age of 8 years.

The sex ratio was 1.38.

All CNS-positive blood cultures were isolated from hospitalized patients. They concerned the pediatric department in 85% of cases (32/38), followed by intensive care in 10% of cases (4/38) then medicine unit in 5% of cases (2/38) (Figure 2).

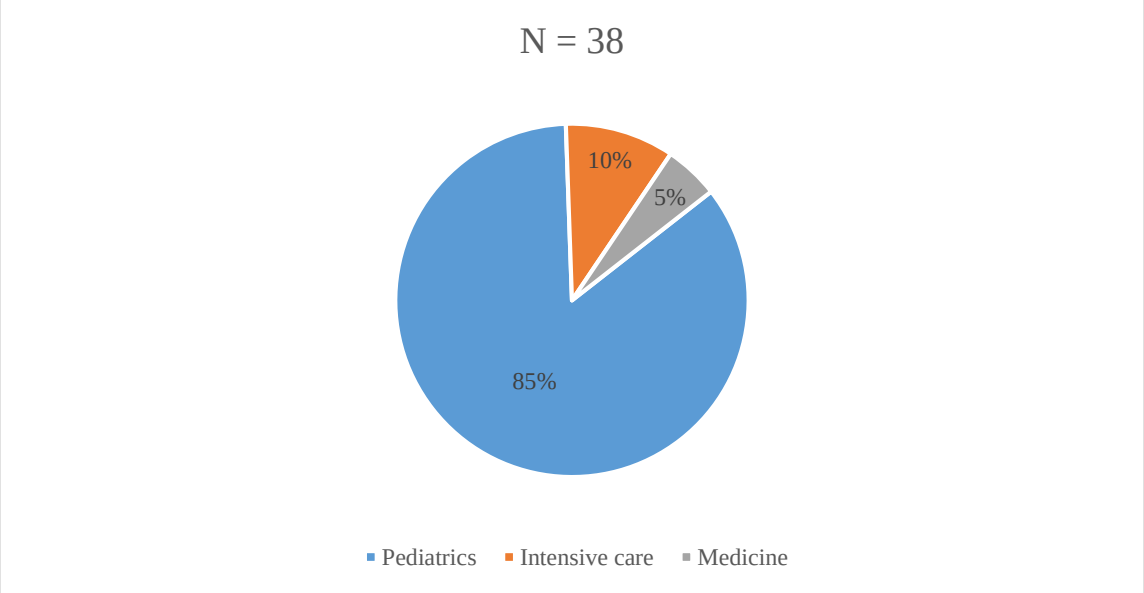

Figure 2: Distribution of cases according to clinical department

Fever was the common reason justifying the request for blood culture 95%, chills 1%, without clinical information 4% (Figure 3).

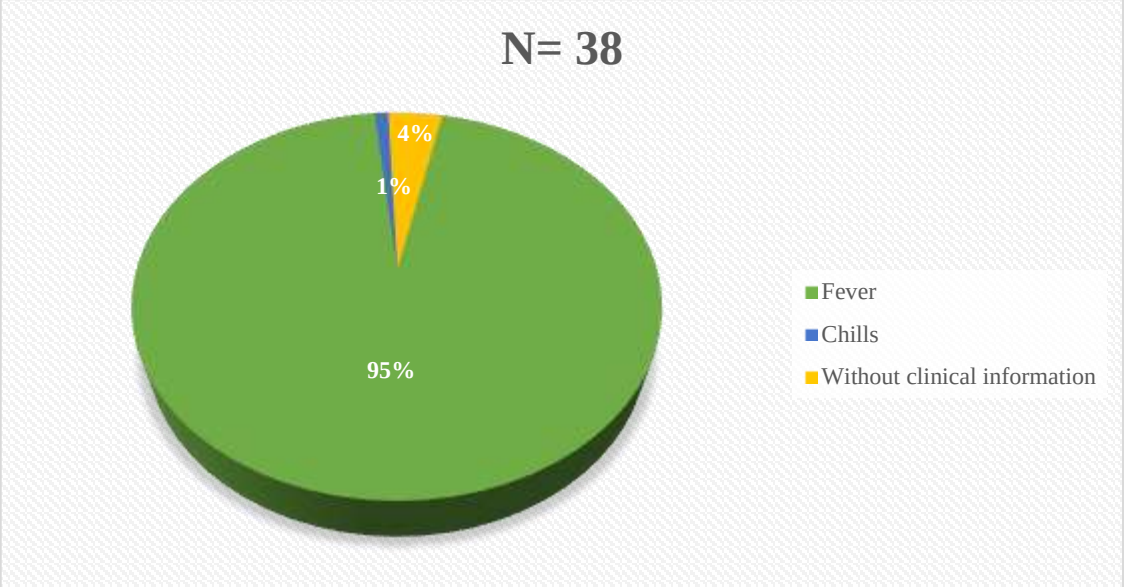

Figure 3: Distribution according to clinical information motivating the examination

Antibiotic Resistance

In this study, 60% (23/38) of the strains were resistant to Cefoxitin.

Regarding aminoglycosides, 45% (17/38) were resistant to Gentamicin and Tobramycin and 18/38 or 47% to Kanamycin.

For the macrolide-lincosamide-streptogramin (MLS) groups, there were more strains resistant to Erythromycin with 14/38 or 36.8% than to Clindamycin (11/38 or 28.9%). Resistance to Pristinamycin was found in 13.1% (5/38) of cases.

Vancomycin was sensitive in 90% of cases.

DISCUSSION

Coagulase negative Staphylococci (CNS) have always been considered by many clinicians to be of low pathogenicity. However, according to numerous studies, they are increasingly recognized among the pathogens of nosocomial infections (Elzi, 2012; Cavanagh et al., 2016; Karakulluk et al., 2017). According to studies, CNS were placed in third position among the germs responsible for bacteremia (Baudat, Chuard, & Regamey, 2005). Ours found a prevalence of 13.86% of CNS among positive blood cultures. This result is consistent with that found in Casablanca in 2019 (El Houssaini et al., 2019) which found a prevalence of 10 %. It was higher than that found in Sydney in 2008 with a prevalence of 2.6% (Van Hal et al., 2008). The difficulty is above all to distinguish true coagulase-negative Staphylococci bacteremia from contamination. Center Disease Control or CDC criteria clinically define single-germ bacteremia as at least 2 positive blood cultures within 48 hours for the same organism accompanied by signs of infection unrelated to other infections and finding the same antibiograms of isolates (National healthcare safety network, 2023). The Clinical and Laboratory Standards Institute or CLSI recommends paired blood culture sets with 4 x 10ml bottles to detect 95% of bacteremia and 6 x 10ml bottles to detect 95-99% of bacteremia (Town, Jarvis, & Hsueh, 2010). Another study by Beekmann, Diekema, and Doern (2005) was able to evaluate the significant criteria of true infections by these germs by isolating in at least two positive blood cultures, SCN within 5 days, or a positive blood culture associated with clinical signs (such as fever or hypothermia, …) and biological infection (an abnormal level of white blood cells in the blood, increased C Reactive Protein). In the present study, all samples positive for these groups of bacteria were only taken from a single vial, associated in 95% with fever, as mentioned in the clinical information. Isolation of the same CNS species from several blood cultures increases the likelihood of true bacteremia (Garcia et al., 2004). The most difficult problem in the diagnosis of CNS is the assessment of their clinical relevance. Thus, the diagnosis consists of evaluating whether a strain of CNS isolated from blood represents contamination of the sample during collection or during handling, or a physiological colonization of the skin or mucous membranes, or on the contrary a clinically serious infection. This situation remains even more difficult in the case of polymicrobial infections, in particular for the choice of antibiotics, especially if the strains present variations in the antibiotic sensitivity profile. Thus, to better appreciate the interpretation, a discussion between the clinician and the biologist would be necessary to better support the diagnosis. On the other hand, educating clinicians to perform at least 2 series of blood cultures would help to support the diagnosis of bacteremia due to this type of germ. However, most hospitalized patients cannot perform several series of blood cultures because the cost of the analysis constitutes a barrier to their performance. An algorithm is essential to guide management in the event of CNS positivity in blood cultures.

The isolation of coagulase-negative Staphylococci was found mainly in pediatric settings. A study in Casablanca showed more frequent isolation of coagulase-negative Staphylococci in pediatric departments with 47.2% followed by medical departments with 44.1%, and intensive care units with 32.9% (El Houssaini et al., 2019). The method of collection could be the cause. Indeed, the difficulty paramedical personnel have in performing venipunctures leads them to use several devices to puncture and collect blood. This would increase the risk of contamination of the sample. The hospital should have a standard protocol for collecting blood cultures using aseptic technique. A study showed that hospitals must aim

for a rate of less than or equal to 3% of contamination of samples for a blood culture examination (Dawson, 2014).

The sex ratio was 1.38. According to Aidoun and Boulazerg (2020), SCNs were isolated much more in males than in females which was similar to our study. This situation could be linked to the difficulty in sampling in the pediatric population, especially in boys who are more turbulent.

Fever was the common reason for prescribing blood culture in 95% of cases. On the other hand, it is most often secondary to a viral infection in the pediatric population (Brunet, 2019). In Madagascar, there is no consensus or precise recommendation regarding the indications for blood cultures in pediatric emergencies, apart from certain situations such as septic shock and newborn fever. It is therefore important to select patients for whom performing a blood culture presents a favorable benefit-risk ratio. In our study 60% were identified resistant to cefoxitin. However, the proportion of strains resistant to cefoxitin reflects resistance to other antibiotics belonging to the beta-lactam class (penicillin G, oxacillin) (Rakotozandrindrainy, 2018). Multi-resistance of CNS and more particularly resistance to β-lactams is very common (Bertrand et al., 2002). Pristinamycin and Vancomycin represented the most active molecule against these types of germs. The antibiotics of choice are represented by glycopeptides, rifampicin, synergistins and fusidic acid. Glycopeptides are recommended for empirical treatment of CNS infections (Bertrand et al., 2002).

SUGGESTIONS

For the diagnosis of true CNS bacteremia in patients, we suggest performing at least 2 blood cultures within 5 days. If the CNS is found combining clinical signs, patient's background and biological signs of bacterial infection, the diagnosis of bacteremia can be made. Otherwise and without signs of an infection, contamination is chosen. In the case where only one blood culture is performed, the clinical and biological signs will play an important role in opting for bacteremia. Clinico-biological consultation remains essential to distinguish real bacteremia from contamination. Moreover, educate doctors to prescribe at least 2 blood cultures for the diagnosis depending on the patient's financial means is also important. For the hospital, a standard protocol should be performed for collecting blood cultures using aseptic technique to avoid contamination.

Furthermore, multicenter studies should be carried out to be able to understand the same practices or the same difficulties in other hospital centers.

CONCLUSION

The prevalence of coagulase-negative Staphylococci was 13,87% in blood cultures. Their isolation is not negligible and leads to the adoption of an algorithm to distinguish bacteremia from contamination. Clinical-biological consultation remains important. In case of infection, the molecules that worked were Prisitnamycin and Vancomycin. To avoid contaminations, hospitals are encouraged to establish a guide for the collection of blood cultures.

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