Sepsis among Neonates in a Ghanaian Tertiary Military Hospital: Culture Results and Turnaround Times

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Abstract: In this study, we described the bacterial profile, antibiotic resistance pattern, and laboratory result turnaround time (TAT) in neonates with suspected sepsis from a tertiary-level, military hospital in Accra, Ghana (2017–2020). This was a cross-sectional study using secondary data from electronic medical records. Of 471 neonates clinically diagnosed with suspected sepsis in whom blood samples were collected, the median TAT from culture request to report was three days for neonates who were culture-positive and five days for neonates who were culture-negative. There were 241 (51%) neonates discharged before the receipt of culture reports, and of them, 37 (15%) were culture-positive. Of 471 neonates, twenty-nine percent (n = 139) were bacteriologically confirmed, of whom 61% (n = 85) had late-onset sepsis. Gram-positive bacterial infection (89%, n = 124) was the most common cause of culture-positive neonatal sepsis. The most frequent Gram-positive pathogen was coagulase-negative Staphylococcus (55%, n = 68) followed by Staphylococcus aureus (36%, n = 45), of which one in two were multidrug resistant. The reasons for large numbers being discharged before the receipt of culture reports need to be further explored. There is a need for improved infection prevention and control, along with ongoing local antimicrobial resistance surveillance and antibiotic stewardship to guide future empirical treatment.

Keywords: neonatal sepsis; bacteria; neonatal intensive care unit; turnaround time; antibiotic resistance; sort it; operational research

1. Introduction

Neonatal sepsis remains the most common cause of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries [1]. Neonatal sepsis is defined as an infection with systemic signs which is diagnosed initially clinically, then confirmed through blood culture, within the first four weeks of life [2]. Neonatal sepsis is sub-classified by the time of presentation into early onset sepsis (EOS) if within 72 h of birth, and late-onset sepsis (LOS) if it occurs from three to 28 days of age [3]. EOS is typically acquired by exposure to microorganisms that colonize the maternal genital tract (vertical transmission) during the perinatal period [4]. Group B Streptococcus is the most common isolated bacteria in developed countries, though other bacteria have been implicated [4,5]. LOS is usually caused by pathogens from the home or hospital environment [4,5]. Staphylococcus species and Gram-negative bacteria, mostly from the Enterobacteriaceae family, are the most frequently identified pathogens with LOS [5,6].
Even though neonates are particularly susceptible to sepsis and subsequent high mortality, few countries provide incidence data for this age group [7]. The 2016–2017 global burden of disease study estimated an incidence of 1.3 million cases of neonatal sepsis [7,8]. During 1979–2019, neonatal sepsis incidence was estimated at 2824 per 100,000 live births, of which an estimated 17.6% died [6]. The estimated incidence and mortality were higher in EOS than in LOS. From 2009 to 2018, the incidence of both EOS and LOS in low- and middle-income countries (3930 per 100,000 live births) was higher than the global incidence [6]. Within Africa, the neonatal mortality ratio is estimated at approximately 27 per 1000 live births [9]. Sub-Saharan Africa accounts for 36% of neonatal deaths worldwide [10]. The projected economic cost associated with neonatal sepsis and mortality in this region is up to USD 469 billion (2014 data) [11].

The high rates of neonatal sepsis-related mortality and the types of pathogens commonly implicated in developing countries suggest that the lack of appropriate hygiene during labor and delivery, postnatal care, and feeding are the key contributors [4]. To reduce this burden, improved infection-control practices (i.e., hand hygiene, isolation, aseptic techniques, disinfection, or sterilization of equipment) have been recommended [4]. Neonatal sepsis is initially treated empirically with broad-spectrum antibiotics while waiting for culture confirmation [1]. This approach likely increases the risk of antimicrobial-resistant (AMR) bacteria, leading to an increased risk of mortality for neonatal sepsis [1,12]. Though empirical antibiotic treatment is used, it should be ideally guided by local susceptibility patterns and the Access, Watch and Reserve (AWaRe) grouping of antibiotics developed by the World Health Organization (WHO), to minimize the possibility of AMR [13]. Knowledge of the local antibiotic resistance profiles has been demonstrated to improve the probability of selecting effective empirical therapy in low-resource settings, which should lead to lower AMR risk [14].

In Ghana, where a neonate dies approximately every 15 min, neonatal mortality is an enormous problem [15]. The Greater Accra region, where the capital city of Ghana is located, has an estimated neonatal mortality ratio of 25 deaths per 1000 live births [16]. There is a paucity of reports on neonatal sepsis from the West African sub-region and Ghana specifically. Findings of significant antibiotic resistance, including multidrug resistance (MDR), have been previously reported in two studies from Ghana, one conducted in 2010–2013 at a teaching hospital [5], and the other in 2016 at two public hospitals [17]. The culture positivity rate for suspected neonatal sepsis was approximately 20% in both studies. However, neither study measured the turnaround time (TAT) from collection of the blood sample to culture and antibiotic susceptibility testing (AST) reporting, which is important in choosing the most effective antibiotics to reduce morbidity, mortality, and AMR risk. Additionally, further study is needed to evaluate if local pathogens and antibiotic susceptibility patterns are changing over time.

Therefore, in a large tertiary-level military hospital in Accra, Ghana (2017–2020), we aimed to determine the culture positivity, the TAT, and the availability of the culture report before discharge among neonates with suspected sepsis. We then described the bacterial profile and antibiotic susceptibility pattern (including MDR) among neonates with confirmed (culture-positive) sepsis.

2. Materials and Methods
2.1. Study Design

This was a hospital-based cross-sectional study using secondary data.

2.2. Setting
2.2.1. General Setting

Ghana is a country located in West Africa along the Gulf of Guinea and the Atlantic Ocean [18] and has a population of approximately 32 million [19]. Healthcare in Ghana is largely administered by the Ministry of Health and the Ghana Health Service [20]. Ghana has instituted a national universal medical insurance system, the National Health Insurance
Scheme (NHIS), which covers most basic inpatient and primary care outpatient services for patients that purchase the insurance [20]. However, those who do not enroll in the NHIS are left to pay for all services and medications out of pocket.

2.2. Specific Setting

The “37 Military Hospital” is a 600-bed level 4 hospital located in the Ayawaso East Municipality of Accra. It serves mainly the military and their dependents as well as civilians mostly from Accra. The hospital records about 95 admissions per day. The outpatient department records approximately 30,000 patients per month. The hospital covers all medical specialties and provides referral healthcare services to an estimated population of 30 million. For the serving and ex-military personnel, civilian employees, and their < 18-year dependents (called “entitled”), all the services are provided within the hospital free of cost. For civilians not employed by the military and non-dependents (called “non-entitled”), the services are either covered by the NHIS or paid out of pocket. The hospital record-keeping system utilizes both paper-based and electronic medical records (EMR). EMR includes clinical, laboratory, imaging, and pharmacy data.

The neonatal intensive care unit (NICU) has a bed capacity of 29 beds and admits about 60 neonates a month. The nursing staff-to-patient ratio is approximately 1:4. All blood samples from neonates with suspected sepsis are sent to the microbiology laboratory (on-site) for culture and AST after the laboratory request is made electronically. Aside from the NICU, other wards that record neonatal visits but less often include the pediatric emergency unit, pediatric outpatient department, and Nkrumah ward. The empirical antibiotics used for suspected neonatal sepsis are amikacin and ciprofloxacin, according to local and NICU guidelines.

2.2.3. Bacteriological Procedures for Suspected Neonatal Sepsis

For patients with suspected neonatal sepsis, 1–3 mL of blood is inoculated directly into Paediatric Bactec® blood culture vials and incubated for five days in the Bactec Fx blood culture system (Becton Dickinson, NJ, USA) as per the manufacturer’s instructions. Where bacterial growth is detected (on any day) within the five days, initial Gram stains are performed and preliminary results are shared with the attending clinicians to guide their choice of empirical treatment. Subcultures are made onto blood, MacConkey, and Saboraud agars and incubated aerobically at 37 °C for 18 to 24 h. Similarly, the sample is subcultured onto chocolate agar plates and incubated anaerobically at 37 °C for 18 to 24 h. Bacterial isolates are identified using Gram stain and routine biochemical methods. Bacteria speciation and AST are performed using the Pheonix100 identification system (Becton Dickinson, NJ, USA) in accordance with the clinical and laboratory standards institute guidelines [21]. Resistance to oxacillin in S. aureus isolates is interpreted as methicillin-resistant S. aureus [21]. When no bacterial growth is detected after five days of incubation, a final negative culture report is entered electronically onto the EMR and is accessed by the attending clinicians.

2.3. Study Population

All admitted neonates with suspected sepsis, whose blood samples were received for culture at the microbiology laboratory from January 2017 through December 2020, formed the study population.

2.4. Variables, Sources of Data, and Data Collection

The following variables were extracted from the EMR into Excel 2010 (Microsoft, Redmond, WA, USA): laboratory number (unique identifier), hospital folder number, date of admission, sex, age in days at admission, birth weight in kilograms, ward (NICU, pediatric emergency), type of beneficiary (entitled/non-entitled), neonatal sepsis categorization (EOS/LOS), date of culture request, outcome (discharged after receiving culture report, discharged before receiving culture report death), date of outcome, date of culture report along with AST, culture result (non-contaminant growth, contaminant, no growth), isolate (species and Gram +/−), sensitivity to antibiotics (sensitive or resistant).
For positive cultures, organisms including *Micrococcus* spp., *Bacillus* spp., and *Diptheroids* were classified as contaminants. An isolate was considered to be multidrug resistant when resistance was observed for at least one agent in three or more antimicrobial categories [22]. TAT (in days) was calculated using the date of culture request and the date of culture report (available in the EMR). The proportion of culture reports released after discharge or death was inferred based on the date of outcome and the date of culture report.

The source of data was from the EMR and the variables extracted were cross-checked record by record, using the paper-based database in the laboratory and the wards (NICU/pediatric emergency/others). Duplicates were removed using the hospital folder number. If a child had more than one culture, the first one was considered for the purpose of this study. During the data extraction process, we de-identified blood culture reports to ensure complete anonymity from laboratory archives.

### 2.5. Data Analysis

Patient-level data were cleaned and imported to EpiData analysis software (version 2.2.2.186, EpiData Association, Odense, Denmark). Numbers and proportions were used to summarize categorical variables. TAT and admission duration (in days) were presented as median and interquartile ranges (IQR). Antibiotic resistance, stratified across the AWaRe group of antibiotics and derived as MDR, was also described. Differences in proportions were assessed for statistical significance using chi-square and chi-square for trend test, as appropriate.

### 3. Results

#### 3.1. Characteristics of Neonates with Suspected Sepsis

There were 471 blood samples collected from neonates with suspected sepsis (Figure 1 and Table 1). Over the four-year period, the largest number of suspected cases with blood samples collected were reported in 2019 (220, 47%). The majority of neonates were <7 days of age (72%), of normal birth weight (69%), and from the non-entitled group (83%) (72%).

| Characteristics                             | N   | (%)  |
|---------------------------------------------|-----|------|
| **Year of admission**                       |     |      |
| 2017                                        | 79  | (16.8)|
| 2018                                        | 58  | (12.3)|
| 2019                                        | 220 | (46.7)|
| 2020                                        | 114 | (24.2)|
| **Age in days**                             |     |      |
| <7                                          | 337 | (71.5)|
| 7–13                                        | 81  | (17.2)|
| 14–20                                       | 17  | (3.6 )|
| 21–28                                       | 36  | (7.6 )|
| **Mean (SD)**                               | 5.4 | (7.0 )|
| **Sex**                                     |     |      |
| Male                                        | 248 | (52.7)|
| Female                                      | 223 | (47.3)|
| **Birth weight in kilograms**               |     |      |
| Very low (1.00–1.49)                        | 63  | (13.4)|
| Low birth weight (1.50–2.49)                | 85  | (18.0)|
| Normal (≥2.50)                              | 323 | (68.6)|
| **Mean (SD)**                               | 2.92|(1.0)|
| **Name of ward**                            |     |      |
| NICU                                        | 198 | (42.0)|
| PEU                                         | 268 | (57.0)|
| POPD/ Yeboah ward/ outside                  | 3   | (0.6) |

Table 1. Baseline characteristics and exit outcomes of neonates with suspected sepsis who underwent culture and antibiotic sensitivity testing at the 37 Military Hospital, Accra, Ghana (2017–2020).
Table 1. Cont.

| Characteristics                        | N   | (%)  |
|----------------------------------------|-----|------|
| Total                                   | 471 | (100.0) |
| Not recorded                            | 2   | (0.4) |

Type of beneficiary
- Entitled * 81 (17.2)
- Non entitled 389 (82.6)
- Not recorded 1 (0.2)

Category of sepsis
- Early onset (<3 days) 228 (48.4)
- Late-onset (within 3–28 days) 243 (51.6)

Hospital exit outcomes
- Clinically improved and discharged 439 (93.2)
- Died 32 (6.8)

NICU = neonatal intensive care unit, PEU = paediatric emergency unit, POPD = paediatric outpatient department, SD = standard deviation; * Entitled = dependents of serving and ex-military personnel as well as civilian employees.

Figure 1. Culture positivity and multidrug resistance among neonates with suspected sepsis who underwent culture sensitivity testing at the 37 Military Hospital, Accra, Ghana (2017–2020). GP = Gram-positive isolate, GN = Gram-negative isolate, MDR = multidrug resistant (resistance to at least one antibiotic from three or more antimicrobial categories).
3.2. Turnaround Time and Admission Outcomes of Neonates with Suspected Sepsis

The median TAT from sample submission to culture and AST reports was five days (IQR 3–5): it was three days for culture-positive samples and five days for culture-negative samples. Of the 471 neonates, 439 (93%) clinically improved and were discharged, while 32 (7%) died. Of 471 neonates, 241 (51%) received the culture report after the admission outcome and of them, 37 (15%) were culture positive. Of the 32 neonates who died, 19 received the culture report after death and 11% of those had positive cultures. The median admission duration was four days (IQR 4–6), six days for those that were discharged after receiving culture results, and three days for those who either died or were discharged before receiving culture results.

3.3. Characteristics of Neonates with Culture Confirmed Sepsis

Of the 471 neonates with suspected sepsis, 139 (29%) were confirmed by culture. Of 139 culture-confirmed neonates, 54 (39%) were EOS and 85 (61%) were LOS (Table 2). There was a decreasing trend in the proportion of LOS over the four years, with the highest being 68% in 2017 and the lowest being 54% in 2020, although these differences were not statistically significant ($p = 0.246$). Very low birth weight neonates were more likely to have EOS when compared to low and/or normal birth weight (77% vs. 32%, $p < 0.001$). A similar proportion of entitled/non-entitled neonates had EOS (37% vs. 39%) and LOS (63% vs. 61%). Neonates with EOS and LOS were both more likely to have a Gram-positive etiology for sepsis.

Table 2. Baseline characteristics of neonates with culture-confirmed sepsis, stratified by early and late-onset sepsis, at the 37 Military Hospital, Accra, Ghana (2017–2020).

| Characteristics          | Total | Early Onset | Late-Onset |
|--------------------------|-------|-------------|------------|
|                          | N     | N (%)       | N (%)      |
| Total                    | 139   | 54 (38.8)   | 85 (61.2)  |
| Year of admission        |       |             |            |
| 2017                     | 28    | 9 (32.1)    | 19 (67.9)  |
| 2018                     | 12    | 4 (33.3)    | 8 (66.7)   |
| 2019                     | 62    | 24 (38.7)   | 38 (61.3)  |
| 2020                     | 37    | 17 (45.9)   | 20 (54.1)  |
| Sex                      |       |             |            |
| Male                     | 77    | 30 (39.0)   | 47 (61.0)  |
| Female                   | 62    | 24 (38.7)   | 38 (61.3)  |
| Birth weight in kilograms|       |             |            |
| Very low (1.00–1.49)     | 22    | 17 (77.3)   | 5 (22.7)   |
| Low birth weight (1.50–2.49) | 17    | 5 (29.4)    | 12 (70.6)  |
| Normal (≥2.50)           | 100   | 32 (32.0)   | 68 (68.0)  |
| Name of ward             |       |             |            |
| NICU                     | 42    | 34 (81.0)   | 8 (19.0)   |
| PEU                      | 95    | 20 (21.1)   | 75 (78.9)  |
| POPD/Yeboah ward/outside | 1     | 0 (0.0)     | 1 (100.0)  |
| Not recorded             | 1     | 0 (0.0)     | 1 (100.0)  |
| Type of beneficiary      |       |             |            |
| Entitled *               | 27    | 10 (37.0)   | 17 (63.0)  |
| Non entitled             | 112   | 44 (39.3)   | 68 (60.7)  |
| Gram reactivity          |       |             |            |
| Positive                 | 124   | 44 (35.5)   | 80 (64.5)  |
| Negative                 | 15    | 10 (66.7)   | 5 (33.3)   |

Row percentages (denominators are the values in column N); NICU = neonatal intensive care unit, PEU = paediatric emergency unit, POPD = paediatric outpatient department, SD = standard deviation; * Entitled = dependents of serving and ex-military personnel as well as civilian employees.
3.4. Pathogens Isolated

Among Gram-positive pathogens, coagulase-negative *Staphylococcus* (CoNS) was the most common isolate (55%, 68/124), followed by *Staphylococcus aureus* (36%, 45/124). For Gram-negative infections, *Klebsiella pneumoniae* was the most common isolate (40%, 6/15). CoNS and *S. aureus* were the most frequent pathogens for both EOS (48% and 30%, respectively), and LOS (49% and 34%, respectively).

3.5. Antimicrobial Susceptibility including MDR

All culture-confirmed infections were resistant to at least one antibiotic (Tables 3 and 4). Of the 139 positive cultures, MDR was seen in 71 (51%) isolates. The year wise trend in MDR was: 2017—54%, 2018—58%, 2019—60% and 2020—32% (*p* = 0.141). Gram-positive bacteria were more frequently MDR (67/124, 54%) compared to Gram-negative bacteria (4/15, 27%); however, the difference was statistically non-significant (*p* = 0.121) (Table 5).

MDR among EOS was 50% (27/54) and among LOS was 52% (44/85).

Table 3. Antibiotic susceptibility testing patterns of Gram-positive isolates (n = 124) among neonates with culture-confirmed sepsis at the 37 Military Hospital, Accra, Ghana (2017–2020).

| Isolates   | CoNS (n = 68) | *S. aureus* (n = 45) | Enterococcus spp. (n = 7) | *S. agalactiae* (n = 2) | *S. mitis* (n = 1) | *S. faecalis* (n = 1) |
|------------|---------------|----------------------|--------------------------|------------------------|-------------------|---------------------|
| Antibiotics | Test RES (%)  | Test RES (%)         | Test RES (%)             | Test RES (%)           | Test RES (%)      | Test RES (%)        |
| Amoxicillin clavulanic acid | 60 23 (38) | 39 13 (33) | 6 2 (33) | 1 1 (100) | 1 0 (0) | 1 1 (100) |
| Ampicillin | 68 54 (79) | 40 40 (89) | 7 6 (86) | 2 2 (100) | 1 1 (100) | 1 1 (100) |
| Cefotaxime | 61 35 (57) | 27 27 (61) | 6 4 (67) | 1 1 (100) | 1 0 (0) | 1 1 (100) |
| Cefoxitin | - - | 45 13 (29) | - - | - - | - - | - - |
| Chloramphenicol | 68 27 (40) | 28 28 (62) | 7 5 (71) | 2 0 (0) | 1 1 (100) | 1 1 (100) |
| Ciprofloxacin | 63 9 (14) | 10 10 (23) | 7 2 (29) | 2 1 (50) | 1 0 (0) | 1 0 (0) |
| Cotrimoxazole | 63 47 (73) | 29 29 (66) | 7 5 (71) | 2 2 (100) | 1 1 (100) | 1 1 (100) |
| Erythromycin | 62 32 (52) | 41 41 (78) | 6 5 (83) | 1 1 (100) | 1 0 (0) | 1 1 (100) |
| Gentamicin | 63 22 (35) | 17 17 (39) | 7 3 (43) | 2 1 (50) | 1 1 (100) | 1 0 (0) |
| Levofloxacin | 63 8 (13) | 8 8 (18) | 7 0 (0) | 2 0 (0) | 1 0 (0) | 1 0 (0) |
| Oxacillin | 60 28 (47) | 41 41 (78) | 6 3 (50) | 1 1 (100) | 1 1 (100) | 1 1 (100) |
| Penicillin | 60 42 (70) | 39 39 (78) | 6 6 (100) | 1 1 (100) | 1 1 (100) | 1 1 (100) |
| Tetracycline | 68 44 (65) | 45 45 (75) | 7 5 (51) | 2 2 (100) | 1 1 (100) | 1 1 (100) |
| Vancomycin | 61 27 (44) | 41 41 (76) | 6 4 (67) | 1 1 (100) | 1 1 (100) | 1 1 (100) |

| Isolates   | *K. pneumoniae* (n = 6) | *A. baumannii* (n = 3) | *E. coli* (n = 2) | Aeromonas veronii bv sobria (n = 1) | Pseudomonas spp. (n = 1) | *M. catarrhalis* (n = 1) | Salmonella spp. (n = 1) |
|------------|-------------------------|------------------------|------------------|-------------------------------------|--------------------------|--------------------------|------------------------|
| Antibiotics | Test RES (%)             | Test RES (%)           | Test RES (%)     | Test RES (%)                        | Test RES (%)             | Test RES (%)             | Test RES (%)           |
| Amikacin | 6 0 (0) | 3 0 (0) | 2 0 (0) | 1 0 (0) | 1 0 (0) | 1 0 (0) |
| Amoxicillin clavulanic acid | 6 1 (17) | 3 0 (0) | 2 0 (0) | 1 1 (100) | 1 1 (100) | 1 1 (100) | 1 1 (100) |
| Ampicillin | 6 6 (100) | 3 3 (100) | 2 1 (50) | 1 1 (100) | 1 1 (100) | 1 1 (100) | 1 1 (100) |
| Cefotaxime | 5 3 (60) | 3 0 (0) | 2 1 (50) | 1 1 (100) | 1 1 (100) | 1 1 (100) | 1 1 (100) |
| Cefuroxime | 6 2 (33) | 3 1 (33) | 2 1 (50) | 1 0 (0) | 1 0 (0) | 1 0 (0) |
| Chloramphenicol | 6 3 (50) | 3 2 (67) | 2 1 (50) | 1 1 (100) | 1 1 (100) | 1 0 (0) | 1 0 (0) |
| Ciprofloxacin | 6 2 (33) | 3 0 (0) | 2 0 (0) | 1 0 (0) | 1 0 (0) | 1 0 (0) |
| Cotrimoxazole | 5 4 (80) | 3 2 (67) | 2 0 (0) | 1 1 (100) | 1 0 (0) | 1 0 (0) | 1 1 (100) |
| Gentamicin | 6 2 (33) | 3 0 (0) | 2 0 (0) | 1 0 (0) | 1 0 (0) | 1 1 (100) | 1 0 (0) |

Row percentages; CoNS = coagulase-negative *Staphylococcus*, RES =resistant, n = number of isolates.
Table 4. Cont.

| Isolates     | K. pneumoniae (n = 6) | A. baumannii (n = 3) | E. coli (n = 2) | Aeromonas veronii bv sobria (n = 1) | Pseudomonas spp. (n = 1) | M. catarrhalis (n = 1) | Salmonella spp. (n = 1) |
|--------------|-----------------------|----------------------|-----------------|-------------------------------------|--------------------------|------------------------|------------------------|
| Levofloxacin | 6 (0)                 | 3 (0)                | 2 (0)           | 1 (100)                             | 1 (0)                    | 1 (0)                  | 1 (0)                  |
| Meropenem    | 6 (0)                 | 3 (0)                | 2 (0)           | 1 (0)                               | 1 (0)                    | 1 (0)                  | 1 (0)                  |
| Tetracycline | 5 (40)                | 3 (1)                | 2 (0)           | 1 (100)                             | 1 (0)                    | 1 (0)                  | 1 (0)                  |

Row percentages; RES = resistant, n = number of isolates.

Table 5. Multidrug resistance among neonates with suspected sepsis who underwent culture and antibiotic sensitivity testing at the 37 Military Hospital, Accra, Ghana (2017–2020).

| Bacteria Isolates | Number of Isolates | MDR Isolates |
|-------------------|--------------------|--------------|
|                   | n                  | (%)          |
| Overall           | 139                | 71 (51.1)    |
| Gram-positive isolates | 124             | 67 (54.0)    |
| Coagulase Negative | 68                | 35 (51.5)    |
| Staphylococcus     | 45                 | 23 (51.1)    |
| Staphylococcus aureus | 7               | 5 (71.4)     |
| Enterococcus spp.  | 2                  | 2 (100.0)    |
| Streptococcus aqualectiae | 1         | 1 (100.0)    |
| Streptococcus mitis | 1                 | 1 (100.0)    |
| Streptococcus faecalis | 1            | 1 (100.0)    |
| Gram-negative isolates | 15              | 4 (26.7)     |
| Klebsiella pneumoniae | 6               | 2 (33.3)     |
| Acinetobacter baumannii | 3              | 1 (33.3)     |
| Escherichia coli   | 2                  | 0 (0.0)      |
| Aeromonas veronii bv sobria | 1           | 1 (100.0)    |
| Pseudomonas spp.   | 1                  | 0 (0.0)      |
| Moraxella catarrhalis | 1              | 0 (0.0)      |
| Salmonella spp.    | 1                  | 0 (0.0)      |

MDR = multidrug resistant, n = number of isolates.

The proportion of CoNS and S. aureus isolates that were MDR were 52% and 51%, respectively. Gram-positive bacteria showed high resistance to multiple antibiotics including ampicillin (79% CoNS, 89% S. aureus), 2nd–3rd generation cephalosporins (57%, CoNS and 29–61% S. aureus), methicillin (59% S. aureus) and vancomycin (44% CoNS, 76% S. aureus). We found a varying range of resistance by Access (0–85%) and Watch (0–63%) categorization (Table 6).

Table 6. Resistance of isolates to antibiotics, stratified by AWaRe category, among neonates with confirmed sepsis at the 37 Military Hospital, Accra, Ghana (2017–2020).

| Classes of Antibiotics | Antibiotics | AWaRe Category | Tests | Resistant |
|-----------------------|-------------|----------------|-------|-----------|
| Aminoglycosides       | Amikacin    | Access         | 15    | 0 (0)     |
| Amphenicols           | Gentamicin  | Access         | 133   | 47 (35.3) |
| Beta-lactams—Beta lactamase inhibitor | Amoxacillin-clavulanic acid | Access | 148   | 20 (13.5) |
| Carbapenems           | Meropenem   | Watch          | 15    | 0 (0)     |
Table 6. Cont.

| Classes of Antibiotics                        | Antibiotics       | AWaRe Category | Tests | Resistant | n (%) |
|-----------------------------------------------|-------------------|----------------|-------|-----------|-------|
| Cephalosporins-2nd Generation                 | Cefoxitin         | Watch Access   | 45    | 13        | (28.9) |
|                                               | Cefuroxime        | Watch          | 15    | 4         | (26.7) |
| Cephalosporins-3rd Generation                 | Cefotaxime        | Watch          | 128   | 75        | (58.6) |
| Fluoroquinolones                              | Ciprofloxacin     | Watch          | 133   | 24        | (18.0) |
|                                               | Levofloxacin      | Access         | 133   | 17        | (12.8) |
| Glycopeptides                                 | Vancomycin        | Watch          | 111   | 65        | (58.6) |
| Penicillin                                    | Penicillin        | Access         | 110   | 84        | (76.4) |
|                                               | Ampicillin        | Access         | 137   | 118       | (84.9) |
|                                               | Oxacillin         | Access         | 110   | 58        | (52.7) |
| Macrolides                                    | Erythromycin      | Watch          | 112   | 71        | (63.4) |
| Tetracyclines                                 | Tetracycline      | Access         | 138   | 81        | (58.7) |
| Sulfonamides                                  | Cotrimoxazole     | Access         | 132   | 93        | (70.5) |

AWaRe = Access, Watch, Reserve, CoNS = coagulase negative Staphylococcus, n = number of isolates.

4. Discussion

4.1. Key Findings

In this study of neonatal sepsis at a large tertiary-level military hospital in Accra, Ghana, during 2017–2020, we had the following key findings: (1) the turnaround times from culture request to report were satisfactory but due to a large number of neonates being discharged within three days, the culture report was not received before discharge for every second neonate; (2) one in three neonates with suspected sepsis were culture-confirmed and three in five neonates with confirmed sepsis were late-onset; (3) the most common pathogen was CoNS, followed by *S. aureus*, of which one in two of the isolates were MDR.

4.2. Strengths and Limitations

The strengths of this study include having access to all submitted blood samples for all neonates with suspected sepsis at a single hospital over a four-year period, which limits the chance of bias. This study also included all patients, regardless of the payer source. The major limitation was the use of retrospective data, which limits the collection of more patient and provider-specific level data for analysis. As we used laboratory data from EMR and not the clinical data, we were not able to assess the proportion of neonates with suspected sepsis who did not undergo culture and AST. In addition, this study was from a single capital city hospital setting. The results may be more representative of neonatal care within Ghana as a whole, if multiple facilities were included, particularly from outside of Accra. Finally, study isolates were not checked for resistance to WHO Reserve category antibiotics.

4.3. Implications and Recommendations

The median TAT from request for culture to culture results, overall (five days) and stratified by culture confirmation (three days for culture-positive and five days for culture-negative), was expected and not surprising considering the bacteriological procedures used. These results indicate that around half of the culture-confirmed neonates with sepsis may have to wait for three days before a more specific and narrow-spectrum antibiotic choice can be made. Others have reported that the average TAT for blood culture and AST reporting in sepsis should be closer to 3 days and with more advanced technological techniques, could be reduced to 50 h [23]. This “need for speed” could be directly translated into improved patient outcomes and reduced risk of AMR in the future not only for neonates, but for all patients under investigation for sepsis [24]. This is an area where further improvements could be leveraged with a possible high return on investment, especially in low- and middle-income countries where rapid diagnostics remain cost-prohibitive.
Our finding is similar to a study performed in Nepal where the median TAT was approximately six days [25], and where, in around two-thirds of the neonates, the antibiotic was changed based on the culture report. In our study due to a large number of neonates being discharged within three days (we speculate that this was due to an improvement in the clinical condition of the neonate), the culture report was not received before discharge for every second neonate. This needs further in-depth qualitative exploration.

In the present study, clinical sepsis was confirmed (29%) more frequently than in previous reports from Ghana (17% and 22%) [5,16], Saudi Arabia (16%) [26], but was similar to Nepal (29%) [25] and lower than in Myanmar (42%) [27]. Additionally, our proportion of reported culture-confirmed neonates was higher than reported from high-income countries [28]. Low culture confirmation rates of clinical neonatal sepsis have been attributed to multiple etiologies including maternal antibiotics before delivery, antibiotic initiation before culture, difficulty in neonatal sampling, and the challenge of making the clinical diagnosis of sepsis [28]. Our findings suggest that at this hospital, there is improving diagnostic acumen and antibiotic stewardship compared to previous studies from Ghana [5,16].

However, we found that three in five neonates with confirmed sepsis were LOS, which implies that there continue to be challenges in preventing nosocomial infections. This finding supports the need for improved infection control as a primary means of decreasing the risk of LOS.

In the present study, CoNS predominated in culture-confirmed cases (55%) and this has been found to be the major etiology of LOS in neonates [29]. This finding is similar to the most recent study from Saudi Arabia (58%) [26] and previous studies from Ghana (59%, 53%) [5,16]. Additionally, we found a high rate of MDR among those with CoNS infections (52%), although this was lower than a recent report from Myanmar (70%) [27]. This calls for improving the focus on infection prevention and control (aseptic techniques, hand hygiene, disinfection, and sterilization) among health care providers and mothers [4,27].

A previous study from Ghana showed a similar proportion of MDR of 53% [5]. This high proportion of MDR, including methicillin and vancomycin resistance to S. aureus, makes it difficult to choose the most appropriate empiric antibiotic regimen and argues for the need for ongoing local AMR surveillance and antibiotic stewardship. These findings could guide improved antibiotic selection in the future. Fortunately, there was a much lower proportion of Gram-negative infections (11%, 15/139) in this study, which has been associated with worse neonatal outcomes [30].

5. Conclusions

In this study of neonatal sepsis at a large tertiary-level military hospital in Accra, Ghana, during 2017–2020, we assessed the TAT from culture request to report, culture positivity, common bacteria, and their AST along with MDR. We found the TAT to be satisfactory. Despite this, due to large numbers of neonates being discharged within three days, the culture report was not received before discharge for every second neonate. The reasons for the high rate of discharge before receiving the culture report need to be explored. One in three neonates with suspected sepsis were culture-confirmed and three in five neonates with confirmed sepsis were late-onset. The most common pathogen was CoNS, followed by S. aureus, of which one in two of the isolates were MDR. This indicates the need for better infection prevention and control along with the need for ongoing local AMR surveillance and antibiotic stewardship.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ijerph191811659/s1, Annex 1.

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Institutional Review Board Statement: Ethics approval was obtained from the Institutional Review Board of the 37 Military Hospital, Accra (37MH-IRB IPN/NFP/409/2020 dated 30 November 2020) and the Ethics Advisory Group (EAG), the International Union against Tuberculosis and Lung Disease, Paris, France (EAG 43/21, dated 13 December 2021). Administrative approvals were obtained before data collection.

Informed Consent Statement: As the study involved secondary data, a waiver for written informed consent was sought and approved by the ethics committee(s).

Data Availability Statement: The data and codebook used in this study have been shared as Supplementary Material (Annex 1).

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