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# Article tittle: Bacteriological profile, antibiotic susceptibility patterns, and Clinical Outcomes of culture-positive early-onset neonatal sepsis at Dodoma Regional Referral Hospital, Tanzania: A hospital-based cross-sectional study

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## Abstract

# Background

Neonatal sepsis remains a major cause of death among newborns, especially in low- and middle-income countries. Globally, neonatal sepsis accounts for about 27.5% of neonatal deaths. In Tanzania, it contributes to approximately 25% of neonatal deaths, making it the third leading cause of neonatal deaths. The increase in neonatal deaths, together with the growing problem of antimicrobial resistance, necessitates the need for continuous surveillance of bacterial profiles and antibiotic susceptibility patterns to achieve better outcomes

# Methods

A hospital-based cross-sectional study was conducted in the neonatal unit of DRRH from February to April 2026. Neonates aged 0–3 days with at least one WHO sign of sepsis were consecutively enrolled. Blood was cultured using an automated system; isolates were identified by standard biochemical methods and tested by CLSI disc diffusion. Outcomes were recovery or death. Factors associated with culture positivity were assessed using modified Poisson regression model, giving adjusted prevalence ratios (APR).

# Results

Of 308 neonates, 128 (41.6%) were culture-positive. Gram-negative bacteria accounted for 75.8% of isolates: Pseudomonas aeruginosa (29.7%), Klebsiella spp. (21.9%), Escherichia coli (14.0%), Enterobacter spp. (9.4%) and Citrobacter spp. (0.8%). Staphylococcus aureus made up 24.2% (methicillin-susceptible 20.3%; MRSA 3.9%). Meropenem and amikacin were the most active agents against Gram-negative isolates (susceptibility 84.6–100% and 85.7–100%), and vancomycin was active against all staphylococci. Susceptibility to ceftriaxone was 0-27.8% in Enterobactereciae, and to ampicillin-cloxacillin 38.5% in MSSA. Twenty-one of 128 culture-positive neonates (16.4%) died. Culture positivity was associated with premature rupture of membranes (APR 1.72; 95% CI 1.20–3.97), birth weight below 2.5 kg (APR 1.52; 1.27–2.31), invasive procedures (APR 1.73; 1.22–3.34), neonatal resuscitation (APR 1.57; 1.27–2.18) and maternal foul-smelling vaginal discharge (APR 1.34; 1.19–1.51); urban residence was associated with lower prevalence (APR 0.87; 0.77–0.99).

## Background

Neonatal sepsis remains a leading cause of neonatal morbidity and mortality worldwide, with the greatest burden in low- and middle-income countries (LMICs). A systematic review and meta-analysis estimated a pooled incidence of 2,824 cases per 100,000 live births and a case fatality of about 17%. Early-onset neonatal sepsis (EONS), usually defined as sepsis within the first 72 hours of life (1), is

typically acquired from the maternal genitourinary tract, either by ascending infection in utero or during passage through the birth canal (2). In high-income settings, Group B Streptococcus predominates in term infants and Escherichia coli in preterm infants(3, 4), whereas in LMICs invasive Group B Streptococcus is reported less often, possibly reflecting differences in maternal colonisation and the strains involved (5).

In LMICs, Gram-negative bacilli such as Klebsiella spp. and E. coli, together with Staphylococcus aureus, are commonly reported, and resistance to ampicillin, gentamicin and third-generation cephalosporins is increasing (6, 7). In Tanzania, most neonatal deaths occur in the first week of life (8). A recent meta-analysis described the pathogens causing neonatal sepsis in the country but did not distinguish early-onset from late-onset disease (9). Hospital-based studies from Muhimbili, Mwanza, Kilimanjaro and Dodoma have reported high blood-culture positivity and substantial resistance to commonly used antibiotics (10–13), yet few have focused specifically on neonates in the first three days of life.

At DRRH, a regional referral hospital in central Tanzania, neonatal sepsis is a leading cause of admission and of death in the neonatal unit. In 2023 the unit recorded 1,440 admissions, and about 98% of neonates started first-line antibiotics empirically (ampicillin or ampicillin–cloxacillin plus gentamicin, following WHO and national guidelines) while awaiting culture results, which often take 5 to 7 days (14). No local protocol exists, and the susceptibility profile of EONS pathogens at the hospital has not been updated. We therefore determined the bacteriological profile, antibiotic susceptibility patterns and clinical outcomes of culture-positive EONS at DRRH, and the factors associated with culture positivity among neonates with suspected EONS.

## Methods

# Study design and setting

A hospital-based analytical cross-sectional study conducted at Dodoma Regional Referral Hospital in Dodoma City, the administrative capital of Tanzania, from February to April 2026. DRRH is a referral hospital for Dodoma and neighbouring regions, and its neonatal unit admits newborns up to 28 days of life. The unit is staffed by paediatricians, medical doctors and nurses. The hospital microbiology laboratory uses the BD BACTEC FX40 automated system, follows Clinical and Laboratory Standards Institute (CLSI) procedures and uses ATCC reference strains for quality control. The study is reported in line with the STROBE statement for cross-sectional studies.

## Sample size and sampling

The sample size was calculated with the Cochran formula, $n = Z^2P(1 - P)/e^2$, using a prevalence of EONS of 23.5% from a previous study(15), a 5% margin of error and a 95% confidence level ($Z = 1.96$), giving 277 neonates. Adding 10% for non-response gave a target of 308. All eligible neonates were screened

and enrolled consecutively until the target was reached, and a screening log was maintained to limit selection bias.

## Data collection

A structured questionnaire adapted from a previous Tanzanian neonatal sepsis study (16)was programmed in KoboToolbox. Mothers or guardians were interviewed for social demographic information, and clinical information was abstracted from the neonate's record in the hospital's electronic health management system (EHMS), whose patient numbers were also used to link laboratory results. The tool was pilot-tested at DRRH for face validity, and research assistants were trained on its use. Variables collected were neonatal characteristics (sex, gestational age, birth weight,APGAR score within 5 minutes, plurality, place and mode of delivery, referral status, body temperature), maternal characteristics (age, marital status, employment, education, residence, premature rupture of membranes (PROM), offensive vaginal discharge indicating chorioamnionitis, urinary tract infection (UTI) and antibiotic use during pregnancy) and care-related factors (resuscitation at birth and invasive procedures such as intravenous cannulation, oxygen therapy, intubation or nasogastric tube insertion).

## Blood culture and identification

Blood culture was taken by trained personnel before the first antibiotic dose. After skin antisepsis with alcohol and povidone-iodine, 3 mL of blood was collected aseptically, inoculated into a paediatric blood-culture bottle and delivered to the laboratory within one hour. Bottles were incubated in the BD BACTEC FX40 at 37°C and considered negative if no growth occurred within 5–7 days. Positive bottles were Gram-stained and subcultured on 5% sheep blood agar, chocolate agar and MacConkey agar at 37°C for 24 hours. Isolates were identified by colony morphology, Gram stain and biochemical tests: catalase and coagulase for Gram-positive bacteria, and lactose fermentation on MacConkey agar, triple sugar iron, sulphide–indole–motility, urease, citrate and oxidase for Gram-negative bacteria.

## Antimicrobial susceptibility testing

Susceptibility was determined by Kirby-Bauer disc diffusion on Mueller-Hinton agar and interpreted using CLSI breakpoints. Gram-negative isolates were tested against meropenem, amikacin, ciprofloxacin, ceftriaxone, cefotaxime, gentamicin and amoxicillin-clavulanic acid (not every agent was tested for every organism; see Fig. 2). Gram-positive isolates were tested against vancomycin, ampicillin-cloxacillin, ciprofloxacin, gentamicin, amoxicillin-clavulanic acid and ceftriaxone. MRSA was identified with a 30 µg cefoxitin disc (zone ≤ 21 mm). Extended-spectrum beta-lactamase (ESBL) production was screened by double-disc synergy in Gram-negative isolates resistant to third-generation cephalosporins. *S. aureus* ATCC 25923 and *E. coli* ATCC 25922 were used for quality control.

# Outcome definitions

Culture-positive EONS was defined as growth of a bacterial pathogen from blood in a neonate aged 0–3 days with clinical features of sepsis. The clinical outcome of culture-positive neonates was recovery with discharge or in-hospital death. For the analysis of factors associated with culture positivity, the outcome was a positive blood culture among all enrolled neonates.

## Statistical analysis

Data were exported from KoboToolbox, cleaned in Microsoft Excel and analysed in SPSS version 27. Categorical variables are summarised as frequencies and percentages and continuous variables as means with standard deviations. Isolate frequencies, susceptibility results and outcomes are presented descriptively. Associations between factors and culture positivity were first examined with the chi-square test. Because culture positivity was common, modified Poisson regression was used to estimate crude and adjusted prevalence ratios (cPR, aPR) with 95% confidence intervals (CI); all variables in Table 5 were entered into the multivariable model. A p-value < 0.05 was considered statistically significant.

# Results

## Participants

During the study period, 427 newborns aged 0–3 days were screened, of whom 316 were suspected to have EONS; 308 were enrolled and their blood was cultured (Fig. 1). Of the 308 neonates, 128 (41.6%) were culture-positive and 180 (58.4%) culture-negative.

The mean age of the neonates was 1.9 ± 0.8 days, and 157 (51.0%) were female. Most were born in a health facility (284, 92.2%) and most mothers lived in urban areas (280, 90.9%). The mean maternal age was 26.9 ± 5.8 years (Table 1). Among clinical characteristics, 100 neonates (32.5%) were referred from other facilities, 137 (44.5%) were preterm, 139 (45.1%) weighed < 2.5 kg (mean birth weight 2.5 ± 0.9 kg), 80 (26.0%) had APGAR score < 7 within 5 minutes, 78 (25.3%) required resuscitation and 73 (23.7%) had undergone an invasive procedure. PROM was reported in 54 mothers (17.6%) and offensive vaginal discharge in 32 (10.4%) (Table 2).

Table 1
Sociodemographic characteristics of neonates with early-onset neonatal sepsis (N = 308)

| Characteristic | n | % |
|---|---|---|
| **Neonatal sex** | | |
| Female | 157 | 51.0 |
| Male | 151 | 49.0 |
| **Place of delivery** | | |
| Health facility | 284 | 92.2 |
| Home | 24 | 7.8 |
| **Maternal residence** | | |
| Urban | 280 | 90.9 |
| Rural | 28 | 9.1 |
| **Maternal age (years); mean 26.9 ± 5.8** | | |
| < 20 | 33 | 10.7 |
| 20–34 | 240 | 77.9 |
| ≥ 35 | 35 | 11.4 |
| **Marital status** | | |
| Married | 240 | 77.9 |
| Single | 68 | 22.1 |
| **Maternal employment** | | |
| Self-employed | 131 | 42.5 |
| Formally employed | 78 | 25.4 |
| Unemployed | 99 | 32.1 |
| **Maternal education** | | |
| None | 39 | 12.6 |
| Primary | 112 | 36.4 |
| Secondary | 129 | 41.9 |
| College or higher | 28 | 9.1 |

Table 2
Clinical Characteristics of neonates with Early-Onset Neonatal Sepsis (N = 308)

| Characteristic | n | % |
|---|---|---|
| Female sex | 157 | 51.0 |
| Urban residence | 280 | 90.9 |
| Born at a health facility | 284 | 92.2 |
| Referred from another facility | 100 | 32.5 |
| Preterm (< 37 weeks) | 137 | 44.5 |
| Birth weight < 2.5 kg (mean 2.5 ± 0.9 kg) | 139 | 45.1 |
| Multiple pregnancy | 24 | 7.8 |
| Caesarean delivery | 71 | 23.1 |
| 5-minute APGAR score < 7 | 80 | 26.0 |
| Resuscitation at birth | 78 | 25.3 |
| Invasive procedure | 73 | 23.7 |
| Maternal PROM | 54 | 17.6 |
| Maternal foul-smelling vaginal discharge | 32 | 10.4 |
| Maternal UTI in pregnancy | 80 | 26.0 |

# Bacterial isolates

Among the 128 culture-positive neonates, one organism was recovered per neonate (Fig. 2;). Gram-negative bacteria accounted for 97 isolates (75.8%) and Gram-positive bacteria for 31 (24.2%). *P. aeruginosa* was the most frequent isolate (29.7%), followed by *Klebsiella* spp. (21.9%), *S. aureus* (20.3%) and *E. coli* (14.0%). *Enterobacter* spp. accounted for 9.4%, MRSA for 3.9% and *Citrobacter* spp. for 0.8%. No Group B *Streptococcus* or coagulase-negative staphylococci were isolated.

# Antibiotic susceptibility

Meropenem and amikacin were the most active agents against Gram-negative isolates (Table 3): meropenem susceptibility was 100% in *E. coli*, 92.1% in *P. aeruginosa*, 91.7% in *Enterobacter* and 89.3% in *Klebsiella*; amikacin susceptibility was 100%, 86.8%, 100% and 85.7%, respectively. Gentamicin was moderately active (72.2% in *E. coli*, 58.3% in *Enterobacter*, 42.9% in *Klebsiella*). Ceftriaxone susceptibility was 27.8% in *E. coli* and 0% in *Klebsiella* and *Enterobacter*; cefotaxime susceptibility was 16.7–50.0%, and ciprofloxacin and amoxicillin-clavulanic acid performed poorly (16.7–52.6%). Ciprofloxacin was the only other agent tested against *P. aeruginosa* (52.6%).

All *S. aureus* isolates (MSSA and MRSA) were susceptible to vancomycin. Among MSSA, only 38.5% were susceptible to ampicillin-cloxacillin and to gentamicin, 7.7% to ceftriaxone and 30.7% to amoxicillin-clavulanic acid; all five MRSA isolates were resistant to ampicillin-cloxacillin. The single *Citrobacter* isolate was susceptible to amikacin and meropenem only.

Table 3
Antibiotics Susceptibility of bacterial isolates causing early-onset neonatal sepsis N (%) susceptible

| **Antibiotic** | ***E. coli* (18)** | ***P. aeruginosa* (38)** | ***Klebsiella* (28)** | ***Enterobacter* (12)** | **MSSA (26)** | **MRSA (5)** |
|---|---|---|---|---|---|---|
| Meropenem | 18 (100) | 35 (92.1) | 25 (89.3) | 11 (91.7) | 22 (84.6) | NT |
| Amikacin | 18 (100) | 33 (86.8) | 24 (85.7) | 12 (100) | 25 (96.2) | NT |
| Gentamicin | 13 (72.2) | NT | 12 (42.9) | 7 (58.3) | 10 (38.5) | 4 (80.0) |
| Ciprofloxacin | 5 (27.8) | 20 (52.6) | 8 (28.6) | 4 (33.3) | 10 (38.5) | 3 (60.0) |
| Cefotaxime | 9 (50.0) | NT | 13 (46.4) | 2 (16.7) | 11 (42.3) | NT |
| Ceftriaxone | 5 (27.8) | NT | 0 (0) | 0 (0) | 2 (7.7) | NT |
| Amoxicillin-clavulanate | 9 (50.0) | NT | 6 (21.4) | 2 (16.7) | 8 (30.7) | NT |
| Vancomycin | NT | NT | NT | NT | 26 (100) | 5 (100) |
| Ampicillin-cloxacillin | NT | NT | NT | NT | 10 (38.5) | 0 (0) |

NT, not tested.

# Clinical outcomes

Of the 128 culture-positive neonates, 107 (83.6%) recovered and were discharged and 21 (16.4%) died. Outcomes by characteristic are shown in Table 4; no inferential tests were done because of the small number of deaths, so these comparisons are descriptive. Mortality was higher among neonates of mothers with PROM (35.2% vs 2.7% without), offensive vaginal discharge (28.6% vs 10.5%), a 5-minute APGAR score < 7 (44.1% vs 6.4%) and invasive procedures (20.2% vs 3.4%). It was also higher among neonates with a body temperature > 37.5°C (25.0%), rural residence (25.0% vs 14.8% urban), mothers aged < 20 years (25.0% vs 14.6% at 20–34 years), single mothers (25.0% vs 13.5% married) and mothers with no formal education (30.4%). Mortality was similar by mode of delivery, referral status, place of delivery and gestational age, and was lower among neonates whose mothers had received antibiotics in

pregnancy (7.1% vs 19.0%). Mortality was not higher in low-birth-weight (12.1%) than in heavier neonates (25.0% for > 3.5 kg), nor in neonates who were resuscitated (12.9% vs 17.5%).(Table 4)

Table 4
Clinical Outcomes of of neonates with culture-positive early-onset neonatal sepsis (N = 128)

| Characteristic | Recovered, n (%) | Died, n (%) |
|---|---|---|
| **Overall** | 107 (83.6) | 21 (16.4) |
| **Sex** | | |
| Female | 57 (86.4) | 9 (13.6) |
| Male | 50 (80.7) | 12 (19.3) |
| **Place of delivery** | | |
| Health facility | 96 (83.5) | 19 (16.5) |
| Home | 11 (84.6) | 2 (15.4) |
| **Maternal residence** | | |
| Urban | 92 (85.2) | 16 (14.8) |
| Rural | 15 (75.0) | 5 (25.0) |
| **Maternal age (years)** | | |
| < 20 | 12 (75.0) | 4 (25.0) |
| 20–34 | 82 (85.4) | 14 (14.6) |
| ≥ 35 | 13 (81.3) | 3 (18.7) |
| **Marital status** | | |
| Married | 83 (86.5) | 13 (13.5) |
| Single | 24 (75.0) | 8 (25.0) |
| **Maternal education** | | |
| None | 16 (69.6) | 7 (30.4) |
| Primary | 46 (86.8) | 7 (13.2) |
| Secondary | 39 (88.6) | 5 (11.4) |
| College or higher | 6 (75.0) | 2 (25.0) |
| **Referred from another facility** | | |
| No | 73 (83.9) | 14 (16.1) |
| Yes | 34 (82.9) | 7 (17.1) |
| **Gestational age** | | |

| Characteristic | Recovered, n (%) | Died, n (%) |
|---|---|---|
| < 37 weeks | 50 (84.7) | 9 (15.3) |
| ≥ 37 weeks | 57 (82.6) | 12 (17.4) |
| **Maternal PROM** | | |
| No | 72 (97.3) | 2 (2.7) |
| Yes | 35 (64.8) | 19 (35.2) |
| **Maternal chorioamnionitis** | | |
| No | 77 (89.5) | 9 (10.5) |
| Yes | 30 (71.4) | 12 (28.6) |
| **Mode of delivery** | | |
| Spontaneous vaginal | 85 (83.3) | 17 (16.7) |
| Caesarean section | 22 (84.6) | 4 (15.4) |
| **5-minute APGAR score** | | |
| < 7 | 19 (55.9) | 15 (44.1) |
| ≥ 7 | 88 (93.6) | 6 (6.4) |
| **Birth weight (kg)** | | |
| < 2.5 | 51 (87.9) | 7 (12.1) |
| 2.5–3.5 | 44 (81.5) | 10 (18.5) |
| > 3.5 | 12 (75.0) | 4 (25.0) |
| **Invasive procedure** | | |
| No | 28 (96.6) | 1 (3.4) |
| Yes | 79 (79.8) | 20 (20.2) |
| **Resuscitation at birth** | | |
| No | 80 (82.5) | 17 (17.5) |
| Yes | 27 (87.1) | 4 (12.9) |
| **Body temperature (°C)** | | |
| < 36.5 | 20 (87.0) | 3 (13.0) |
| 36.5–37.5 | 69 (85.2) | 12 (14.8) |
| > 37.5 | 18 (75.0) | 6 (25.0) |

| Characteristic | Recovered, n (%) | Died, n (%) |
|---|---|---|
| **Maternal UTI in pregnancy** | | |
| No | 30 (88.2) | 4 (11.8) |
| Yes | 77 (82.0) | 17 (18.0) |
| **Maternal antibiotic use in pregnancy** | | |
| No | 81 (81.0) | 19 (19.0) |
| Yes | 26 (92.9) | 2 (7.1) |
| **Multiple pregnancy** | | |
| No | 96 (83.5) | 19 (16.5) |
| Yes | 11 (84.6) | 2 (15.4) |

# Factors associated with culture positivity among neonates with suspected early-onset neonatal sepsis

In unadjusted chi-square tests, PROM (p = 0.001), invasive procedures (p = 0.027), resuscitation (p = 0.012) and maternal chorioamnionitis (p < 0.001) were significantly associated with culture positivity In the multivariable modified Poisson model (Tables 5), the prevalence of culture positivity was higher among neonates whose mothers had PROM (aPR 1.72, 95% CI 1.20–3.97), neonates weighing < 2.5 kg compared with > 3.5 kg (aPR 1.52, 1.27–2.31), neonates who had invasive procedures (aPR 1.73, 1.22–3.34), neonates who were resuscitated at birth (aPR 1.57, 1.27–2.18) and neonates of mothers with offensive vaginal discharge (aPR 1.34, 1.19–1.51). Body temperature > 37.5°C was also significant in the adjusted model (aPR 1.35, 1.24–1.62; p = 0.046). Neonates of mothers living in urban areas had a lower prevalence than those from rural areas (aPR 0.87, 0.77–0.99; p = 0.040). Sex, place of delivery, maternal age, marital status, employment, education, referral, gestational age, mode of delivery, maternal UTI and multiple pregnancy were not significantly associated with culture positivity.(Table 5)

Table 5
Factors associated with culture positivity among neonates with suspected EONS: modified Poisson regression (N = 308)

| Factor | Culture-positive, n/N (%) | cPR (95% CI) | aPR (95% CI) | p (adjusted) |
|---|---|---|---|---|
| **Sex** | | | | |
| Female | 67/157 (42.7) | 1 | 1 | |
| Male | 61/151 (40.4) | 0.98 (0.91–1.06) | 0.98 (0.91–1.06) | 0.654 |
| **Place of delivery** | | | | |
| Health facility | 115/284 (40.5) | 1 | 1 | |
| Home | 13/24 (54.2) | 1.10 (0.95–1.25) | 1.08 (0.94–1.23) | 0.259 |
| **Maternal age (years)** | | | | |
| < 20 | 17/33 (51.5) | 1 | 1 | |
| 20–34 | 95/240 (39.6) | 0.92 (0.81–1.03) | 0.93 (0.82–1.07) | 0.345 |
| ≥ 35 | 16/35 (45.7) | 0.96 (0.82–1.12) | 0.98 (0.83–1.17) | 0.870 |
| **Maternal residence** | | | | |
| Rural | 16/28 (57.1) | 1 | 1 | |
| Urban | 112/280 (40.0) | 0.89 (0.78–1.01) | 0.87 (0.77–0.99) | 0.040 |
| **Marital status** | | | | |
| Single | 33/68 (48.5) | 1 | 1 | |
| Married | 95/240 (39.6) | 1.06 (0.97–1.16)† | 1.04 (0.90–1.11)† | 0.937 |
| **Maternal employment** | | | | |
| Employed | 35/78 (44.9) | 1 | 1 | |
| Self-employed | 58/131 (44.3) | 0.99 (0.90–1.10) | 0.98 (0.89–1.10) | 0.829 |
| Unemployed | 35/99 (35.4) | 0.93 (0.84–1.03) | 0.93 (0.84–1.03) | 0.172 |
| **Maternal education** | | | | |
| None | 18/39 (46.2) | 1 | 1 | |

| Factor | Culture-positive, n/N (%) | cPR (95% CI) | aPR (95% CI) | p (adjusted) |
|---|---|---|---|---|
| **Sex** | | | | |
| Primary | 51/112 (45.5) | 0.99 (0.87–1.13) | 1.01 (0.89–1.14) | 0.837 |
| Secondary | 50/129 (38.8) | 0.94 (0.76–1.07) | 0.96 (0.85–1.08) | 0.514 |
| College or higher | 9/28 (32.1) | 0.90 (0.76–1.07) | 0.89 (0.75–1.06) | 0.190 |
| **Referral** | | | | |
| No | 87/208 (41.8) | 1 | 1 | |
| Yes | 41/100 (41.0) | 0.99 (0.91–1.08) | 0.96 (0.87–1.04) | 0.325 |
| **Gestational age** | | | | |
| ≥ 37 weeks | 69/171 (40.4) | 1 | 1 | |
| < 37 weeks | 59/137 (43.1) | 1.43 (1.34–1.51)† | 1.72 (0.98–1.21)† | 0.116 |
| **Maternal PROM** | | | | |
| No | 107/254 (42.1) | 1 | 1 | |
| Yes | 21/54 (38.9) | 1.98 (1.26–3.45)† | 1.72 (1.20–3.97)† | 0.032 |
| **Mode of delivery** | | | | |
| Caesarean section | 25/71 (35.2) | 1 | 1 | |
| Spontaneous vaginal | 103/237 (43.5) | 1.86 (1.12–4.16) | 1.73 (1.10–3.92) | 0.064 |
| **Birth weight (kg)** | | | | |
| > 3.5 | 16/36 (44.4) | 1 | 1 | |
| 2.5–3.5 | 54/147 (36.7) | 0.93 (0.85–1.01) | 0.91 (0.81–1.02) | 0.094 |
| < 2.5 | 58/125 (46.4) | 1.46 (1.37–1.55)† | 1.52 (1.27–2.31)† | 0.018 |
| **Invasive procedure** | | | | |
| No | 98/235 (41.7) | 1 | 1 | |

| Factor | Culture-positive, n/N (%) | cPR (95% CI) | aPR (95% CI) | p (adjusted) |
|---|---|---|---|---|
| **Sex** | | | | |
| Yes | 30/73 (41.1) | 1.99 (1.12–3.49)† | 1.73 (1.22–3.34)† | 0.038 |
| **Resuscitation at birth** | | | | |
| No | 96/230 (41.7) | 1 | 1 | |
| Yes | 32/78 (41.0) | 1.41 (1.35–1.48)† | 1.57 (1.27–2.18)† | 0.026 |
| **Body temperature (°C)** | | | | |
| < 37.4 | 104/248 (41.9) | 1 | 1 | |
| > 37.5 | 24/60 (40.0) | 1.42 (1.36–1.48)† | 1.35 (1.24–1.62)† | 0.046 |
| **Maternal UTI in pregnancy** | | | | |
| No | 95/228 (41.7) | 1 | 1 | |
| Yes | 33/80 (41.3) | 0.99 (0.91–1.08) | 0.99 (0.91–1.08) | 0.947 |
| **Multiple pregnancy** | | | | |
| No | 115/284 (40.5) | 1 | 1 | |
| Yes | 13/24 (54.2) | 1.10 (0.95–1.25) | 1.11 (0.96–1.27) | 0.132 |
| **Maternal chorioamnionitis** | | | | |
| No | 114/289 (39.4) | 1 | 1 | |
| Yes | 14/19 (73.7) | 1.32 (1.20–1.46)† | 1.34 (1.19–1.51)† | < 0.001 |

# Discussion

In this study of neonates aged 0–3 days with suspected EONS at Dododma regional referral hospital in central Tanzania, 41.6% had a positive blood culture. Three-quarters of isolates were Gram-negative, led by *P. aeruginosa* and *Klebsiella* spp., with *S. aureus* the main Gram-positive pathogen and no Group B *Streptococcus*. Meropenem, amikacin and, for *S. aureus*, vancomycin retained high in-vitro activity, whereas third-generation cephalosporins, amoxicillin–clavulanate and ampicillin–cloxacillin performed poorly and gentamicin only moderately. Case fatality among culture-positive neonates was 16.4%.

# Bacteriological profile

The predominance of Gram-negative organisms agrees with Tanzanian and regional reports (6, 9, 15) and with a pooled analysis of developing-country studies (17), and contrasts with high-income settings where Group B *Streptococcus* and *E. coli* dominate (3, 4). Culture positivity of 41.6% is within the range reported in Tanzanian neonatal units (about 31–50%) (8, 9), although most of those studies did not restrict enrolment to the first 72 hours.

The absence of Group B *Streptococcus* is in line with other African reports (5, 9). Three explanations are plausible: a genuine local shift towards Gram-negative organisms; maternal antibiotic exposure, since 20.3% of mothers of culture-positive neonates took antibiotics in pregnancy; and laboratory limitations, notably the lack of selective enrichment broth.

1. *aeruginosa* was the commonest isolate (29.7%). This organism is typically associated with moist hospital environments, contaminated equipment and breaches of hand hygiene rather than maternal colonisation, and about a third of our neonates were referred from other facilities. Its prominence among babies who were at most three days old may therefore point to health care-associated acquisition, either at birth, during referral, or in the first hours on the unit, and to gaps in cleaning, equipment reprocessing and hand hygiene; this should prompt an infection prevention and control audit, though we collected no environmental or molecular data to confirm transmission. *Klebsiella* spp. are likewise linked to multidrug resistance and neonatal unit outbreaks (7, 9). *S. aureus*, the leading Gram-positive isolate (24.2% including MRSA), has been reported as dominant in Muhimbili and in Nigeria (7, 18).

# Antibiotic susceptibility

Meropenem and amikacin retained activity against most Gram-negative isolates, and vancomycin against all staphylococci, consistent with data from KCMC, Muhimbili and Egypt (7, 9, 13, 18)Ceftriaxone and cefotaxime were unreliable against *Klebsiella*, *Enterobacter* and *E. coli* (ceftriaxone 0-27.8%), amoxicillin-clavulanic acid and ampicillin-cloxacillin were weak, and gentamicin was only moderately active (42.9–72.2% in Gram-negative bacilli; 38.5% in MSSA). These findings are consistent with the earlier DRRH report of resistance to commonly used agents (10) and with national and international evidence of progressive resistance to ampicillin-based and cephalosporin regimens (6, 9, 13, 14, 19).Together they indicate that the current first- and second-line empirical regimens would leave a substantial proportion of culture-positive neonates on ineffective therapy while awaiting a result that takes five to seven days. Note that ampicillin alone and gentamicin against *P. aeruginosa* were not tested, so conclusions about the full ampicillin-gentamicin combination are inferential.

Carbapenems and amikacin cannot simply replace first-line therapy. Meropenem should be reserved to protect its activity, and amikacin requires monitoring for ototoxicity and nephrotoxicity. The practical implications are to base any change in the DRRH protocol on a formal review of local susceptibility data

with antimicrobial stewardship input, to ensure blood cultures are taken before antibiotics, and to de-escalate promptly once susceptibilities are known.

# Clinical outcomes

Case fatality of 16.4% is close to the pooled Tanzanian estimate of 16% (6), although higher figures (29–33%) have been published from other settings (12). Low APGAR score and fever were the clearest markers of death in our descriptive data, in keeping with studies identifying birth asphyxia and temperature instability as predictors of death in EONS (6, 20, 21). Mortality did not decrease with increasing birth weight, and mortality by gestational age was similar, unlike what is usually reported; with only 21 deaths, these subgroup figures are imprecise and we did not test for differences or adjust for confounding, so they should not be over-interpreted. We also did not link outcomes to organism or to whether the empirical regimen was active against the isolate, which is an important next step.

# Factors associated with culture positivity

PROM and maternal foul-smelling discharge, a clinical marker of intra-amniotic infection, are recognised routes for ascending infection and have been associated with EONS in Dodoma and elsewhere (6, 21, 22). Low birth weight was independently associated with culture positivity, as in other studies (23), and reflects immature skin barriers and immune function. Invasive procedures and resuscitation were also associated, as reported earlier in Dodoma (6); this may reflect contamination of equipment or hands, but also reverse causation, since sicker infants require more procedures. The lower prevalence in urban residents agrees with an Ethiopian study (24), although residence is likely a proxy for access to antenatal care and for unmeasured environmental factors. Because the data are cross-sectional, these results indicate association, not causation.

# Strengths and limitations

*Strengths* include consecutive enrolment, a 100% response rate, blood cultures taken before antibiotics, automated culture and CLSI-standard susceptibility testing, and a focus on neonates in the first 72 hours, in whom data are scarce.

**Limitations**

the study was conducted in a single referral hospital over three months, so organism distribution and resistance may not be generalizable and may vary seasonally. We enrolled only clinically suspected cases, and culture-negative neonates (58.4%) may include infections missed because of small blood volume, prior maternal antibiotics or fastidious organisms. Not all antibiotics were tested against all organisms; ESBL and multidrug-resistance prevalence are not reported here; and there was no molecular typing or environmental sampling, so clusters of *P. aeruginosa* or *Klebsiella* could not be excluded. Group B *Streptococcus* may have been under-detected. Analysis of outcomes was descriptive and unadjusted, and the sample was not powered for mortality.

# Conclusions

Gram-negative bacteria, particularly *P. aeruginosa* and *Klebsiella* spp., were the most frequent causes of culture-positive EONS at DRRH, and susceptibility to ceftriaxone, cefotaxime, amoxicillin–clavulanate, ampicillin–cloxacillin and gentamicin was limited, while meropenem, amikacin and vancomycin were highly active. Case fatality was 16.4%. PROM, chorioamnionitis, low birth weight, invasive procedures and resuscitation were associated with culture positivity. We recommend regular review of empirical guidelines against local susceptibility data, antimicrobial stewardship, to strengthen infection prevention and control measures during labour, resuscitation and neonatal care, continued culture-based surveillance, and studies of the sources and routes of transmission.

# Abbreviations

- **APGAR**: Appearance, Pulse, Grimace, Activity, Respiration (score)
- **aPR**: adjusted prevalence ratio
- **ATCC**: American Type Culture Collection
- **CI**: confidence interval
- **CLSI**: Clinical and Laboratory Standards Institute
- **cPR**: crude prevalence ratio
- **DRRH**: Dodoma Regional Referral Hospital
- **EHMS**: electronic health management system
- **EONS**: early-onset neonatal sepsis
- **ESBL**: extended-spectrum β-lactamase
- **LMIC**: low- and middle-income country
- **MIC**: minimum inhibitory concentration
- **MRSA**: methicillin-resistant *Staphylococcus aureus*
- **MSSA**: methicillin-susceptible *Staphylococcus aureus*
- **NT**: not tested
- **PROM**: premature rupture of membranes
- **SPSS**: Statistical Package for the Social Sciences
- **STROBE**: Strengthening the Reporting of Observational Studies in Epidemiology
- **TZS**: Tanzanian shilling
- **UTI**: urinary tract infection
- **WHO**: World Health Organization

# Declarations

*Ethics approval and consent to participate*: The study was approved by the Institutional Research Review Ethics Committee of The University of Dodoma (reference MA.84/261/99/3), 21 January 2026; reviewed

at its 99th meeting on 19 January 2026). Permission was obtained from the Regional Administrative Secretary and the DRRH administration. Written informed consent was obtained from the mothers or guardians of all participating neonates. Participation was voluntary, data were de-identified using unique study numbers, and all neonates received standard care irrespective of participation. The study followed the Declaration of Helsinki

**Clinical trial number** :Not applicable

**Consent for publication**: Not applicable.

**Availability of data and materials**: The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests**: The authors declare that they have no competing interests.

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**Authors' contributions**: IMB conceived and designed the study, collected and analysed the data and drafted the manuscript. EN and MLM supervised the study, contributed to design and interpretation, and critically revised the manuscript. All authors read and approved the final manuscript.

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# Figures

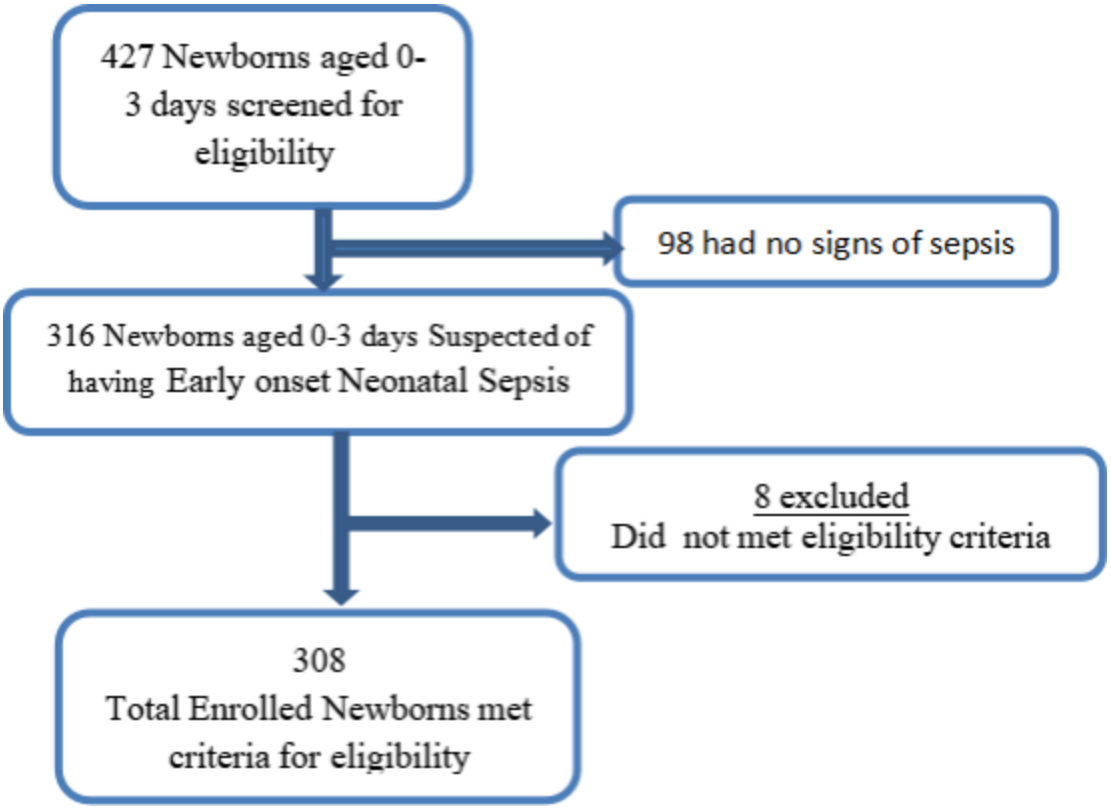


**Figure 1**

Flow of participants

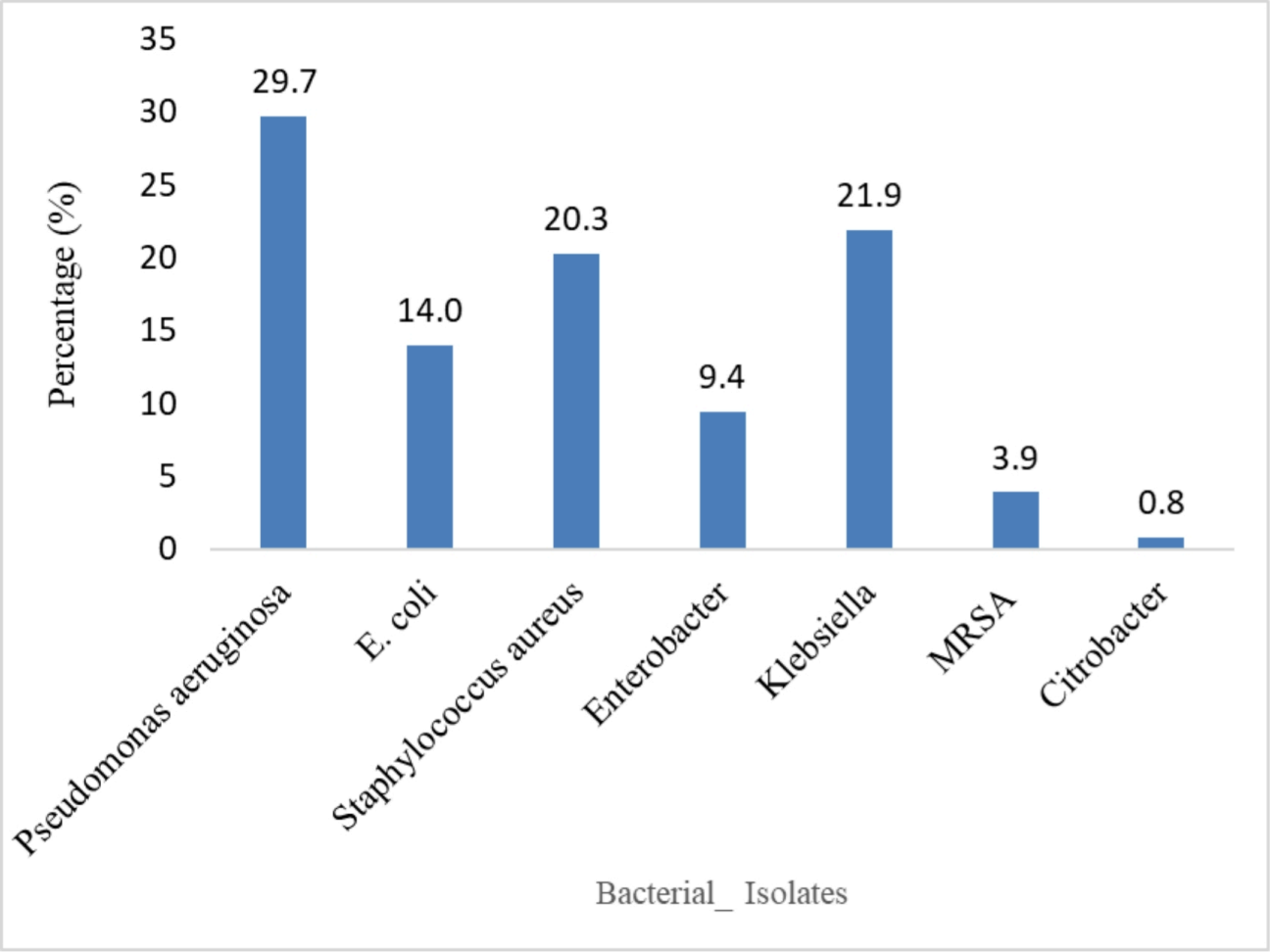


**Figure 2**

Bacterial isolates from neonates with culture-positive EONS (N = 128)