Clinical characteristics of external bacterial ocular and periocular infections and their antimicrobial treatment patterns among a Ghanaian ophthalmic population

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Empirical antimicrobial therapy is linked to a surge in antimicrobial resistant infections. However, an insight on the bacteria etiology of ocular infections is essential in the appropriation of choice of antimicrobial among clinicians, yet there remains a dearth of data from Ghana. We investigated the bacteria etiology of external ocular and periocular infections and antimicrobial treatment patterns among a Ghanaian ophthalmic population. A multicenter study design with purposive sampling approach was employed. Patients demographics and clinical data were collated using a pretested structure questionnaire. Cornea specimens and conjunctival swabs were obtained for bacterial isolation following standard protocols. About 95% (98/103) of ocular samples were positive for bacteria culture. The proportion of Gram-negative bacteria was 58.2%, and the predominant bacteria species were Pseudomonas aeruginosa 38.8% and Staphylococcus aureus 27.6%. Conjunctivitis 40.0% and keratitis 75.0% were mostly caused by Pseudomonas aeruginosa. The routinely administered antimicrobial therapy were polymyxin B 41.2%, neomycin 35.1% and ciprofloxacin 31.6%. Participants demographic and clinical characteristics were unrelated with positive bacteria culture (p > 0.05). Our results showed a markedly high burden of ocular bacterial infections and variations in etiology. Bacterial infection-control and antimicrobial agent management programs should be urgently institutionalized to prevent the emergence of resistant infections.

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Globally, eye infections of bacterial origin remain a significant contributor to ocular morbidity and blindness, and the burden is increasing. Further, results from ocular microbial studies across different populations show no obvious pattern in prevalence estimates (ranging from 21.8 to 82.5%) across Africa, Asia, Australia, Europe, and North America. Similarly, the bacterial etiology, thus the nature of Gram bacteria and the species of bacteria commonly implicated in external ocular (surface of the eyeball) and periocular (surrounding of the eyeball) infections vary across geographical regions and settings.

Anatomically, the eye is divided into three tunics: the outer (conjunctiva, sclera, cornea), middle (lens, ciliary body, iris), and inner (retina) coats. The tear film contains innate defenses such as bacteriocin, beta-lysin, lipocalin, lysozymes, immunoglobulins (Ig A, Ig G, Ig M), lactoferrins, and with antimicrobial effect against pathogenic strain of microorganisms. The external milieu of the eyes serves as a biome for pathogenic and non-pathogenic organisms. Naturally, antimicrobial constituents within the tear film prevent opportunistic microbes from causing any infections to the eyes. Dysregulation of the homeostatic balance as a result of trauma, contact lens wear, surgery, use of topical antibiotics, and reduced systemic immunity predisposes the eyes to opportunistic pathogens such as bacteria, fungi, virus, and protozoa. However, among these microbes, bacteria are commonly implicated in external ocular and periocular infections. Based on the exterior region affected; external ocular infections can be classified as blepharitis, conjunctivitis, keratitis, dacryocystitis, preseptal and orbital cellulitis, thus eyelids, conjunctiva, cornea, lacrimal sac, pre and post-septal areas are respectively involved.

These eye infections are usually treated with broad-spectrum antimicrobial agents with varying modes of action without any proper follow up for culture and sensitivity testing to identify the implicated pathogen. In resource limited-environments such as Ghana, due to the unavailability of rapid diagnostic testing facilities, especially for identifying fastidious organisms, most clinicians: including eye care professionals engage in this prevailing empirical broad-spectrum antimicrobial treatment. Consequently, the irrational and prolonged use of broad-spectrum antibiotics in treating eye infections could alter the genetic makeup of ocular bacteria and consequently lead to antimicrobial resistance.

Ocular antimicrobial resistance is a growing public health threat in both advanced and developing countries. In the developed world nationwide surveillance programs have been institutionalized to monitor ascendant trends. Among these nationwide surveillance programs include Ocular Tracking Resistance in the U.S. Today (Ocular TRUST), Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR), European Antimicrobial Resistance Surveillance System, and Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance. However, in developing countries such as Ghana, aside from the limited accessibility to a national antimicrobial policy, there are compromise regulatory measures and poor adherence to the use of antibiotics.

Multidrug resistance (MDR) is gradually gaining attention in mainstream medicine and public healthcare generally, as it renders antimicrobial agents inefficacious against pathogenic strains of bacteria. MDR causes delays in treatment and recoveries, rise in cost of therapy as well as increase in hospitalization time. In a nationwide laboratory based surveillance studies in Ghana, Opintan et al. reported over 70% prevalence of MDR among antibiotics such chloramphenicol, gentamycin, tetracycline, and quinolones against isolated bacterial strains from various infections of the urine, blood, sputum, ears, and eyes. This finding was consistent with studies conducted in the People’s Republic of China, Italy, and Ethiopia which showed similar increasing trends. Consequently, without drastic measures, it is estimated that the world will experience over 10 million annual AMR-related deaths hence it has become imperative to devise ammunitions to curb the situation. Importantly, a decline in ocular MDR will result in increased life expectancy as ocular resistance infections and associated blindness induce mortality.

**Abbreviations**

A.E.H. Anglican Eye Hospital
A.M.R. Antimicrobial resistance
ARMOR Antibiotic resistance monitoring in ocular microorganisms
C.H.A.G. Christian Health Association of Ghana
C.H.R.P.E. Committee on human research publication and ethics
C.I.P. Ciprofloxacin
C.L.S.I. Clinical laboratory standard institute guidelines
CONS Coagulase negative Staphylococci species
C.O.R. Crude odds ratio
D.N.A. Deoxyribonucleic acid
FX Fluocoxacillin
KSH Kumasi South Hospital
G.T.M. Gentamycin
M.D.R. Multi drug resistance
R.F.R. Referral
PoB Polymyxin B
NM Neomycin
TBM Tobramycin
TX Tetracycline
O.X.T. Oxytetracycline
OFC Ofloxacin
R.N.A. Ribonucleic acid
S.M.H. St Michaels Hospital

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There is a paucity of data on the prevalence and bacteria etiology of ocular infections in Ghana. Furthermore, earlier microbiological investigations in Ghana did not exclusively focus on ocular infections and associated microbes. The absence of country-specific contemporary estimates limits the modeling of future scenarios, and assumptions with unreliable data and/or making decisions with evidence from other countries is of questionable utility given the geographic differences. An insight on bacteria etiology of ocular infections presented by Ghanaian patients is critical for desirable choice of antibiotic therapy by clinicians. Therefore, the study aims to investigate the bacteria etiology of external ocular and periocular infections, and antimicrobial treatment patterns among a Ghanaian ophthalmic population. The isolates recovered from ocular specimen will aid future antibiotic sensitivity studies and also serve as a gateway for exploration of local medicinal plants as alternative therapeutic agents.

**Results**

**Description of the sample.** Table 1 presents the sociodemographic, socioeconomic and healthcare status characteristics of the study participants. Out of the 114 patients presenting with external ocular and periocular infections, majority were females (56.1%), of median age of 17.0 (Interquartile range: 29.75) years (Table 1). The majority of the participants were aged 3–17 years (29.8%), of Akan ethnicity (93.0%), and with a protestant religion (80.7%). Most of them lived in a rural community (59.6%), with their highest education level being primary (33.6%) and major occupation as students (43.9%). An equal proportion were single (21.2%) and married (21.2%) and the remaining either cohabiting (3.5%), divorced (2.7%), widow (1.8%) or separated (0.9%). A preponderance of participants never smoked (52.6%), and with a significantly higher average alcohol intake in males compared to females (p = 0.027). Approximately 6% had hypertension and an equal proportion had diabetes (4.4%) and peptic ulcer (4.4%). The number of patients on antihypertensive, antidiabetic and antibiotic medications were 5.3%, 3.5% and 3.5%, respectively.

**Clinical characteristics of external ocular and periocular infections among study participants.** Table 2 shows the clinical characteristics of external ocular and periocular infections among study participants. Most presented with both eyes infected (66.7%) with the conjunctiva (94.7%) as the commonest affected site. The majority of the participants had previously used antimicrobials (55.8%) and have had previous eye infections (45.1%), and with duration of infection less than one-week (63.7%). There was a significant variation between males and females in terms of previous ocular trauma (p = 0.023) and previous use of mascara (p = 0.015). With respect to monocular visual acuity, majority had right eye visual acuity better than 6/18 (63.8%) and with a fewer having visual acuity worse than 6/60 (2.6%). Most had a left visual acuity within the ranges of 6/5–6/6 (67.5%) and fewer proportion (1.8%) having visual acuity better than 6/60 but worse than 6/24. The commonest presenting symptom was hyperemia/redness (69.3%), followed by discharge, (62.3%) itching (60.5%), eye pain (50.9%) and a smaller fraction having falling lashes (0.9%). Majority received a minimum of two antibiotics for treatment of infections (40.4%) and with a fewer portion (7.9%) having treatment other than antibiotics. The proportion of clinical presentations were conjunctivitis (60.5%), keratoconjunctivitis (11.4%), blepharoconjunctivitis (9.6%), keratitis (7.9%), ocular trauma (6.1%), hordeolum (2.6%), preseptal cellulitis (0.9%) and ophthalmia neonatorum (0.9%). Other associated conditions were dry eyes (10.5%), headaches (5.3%), pterygium (4.4%) and pinguecula (0.9%). The commonly used antimicrobial therapeutics were polymyxin B (41.2%), neomycin (35.1%) and ciprofloxacin (31.6%) and fewer instances gentamycin (2.6%) and ofloxacin (1.6%) as shown in Table 3.

**Bacteria etiology of external ocular and periocular infections among study participants.** One hundred and three (103/114) ocular specimens were enrolled for bacterial isolation owing to the inability to obtain swabs from uncooperative minor subjects. Ninety-eight (95.1%) of the samples were culture positive, and with the remaining either cohabiting (3.5%), divorced (2.7%), widow (1.8%) or separated (0.9%). A preponderance of participants never smoked (52.6%), and with a significantly higher average alcohol intake in males compared to females (p = 0.027). Approximately 6% had hypertension and an equal proportion had diabetes (4.4%) and peptic ulcer (4.4%). The number of patients on antihypertensive, antidiabetic and antibiotic medications were 5.3%, 3.5% and 3.5%, respectively.

**Factors associated with external ocular and periocular infections.** Table 5 shows logistic regression analyses of the association between patients’ demographics, clinical characteristics and prevalence of bacterial infection. None of the factors was significantly associated with prevalence of bacterial ocular infections (p > 0.05).

The novel study for the first time aims to investigate the bacteria etiology of external ocular and periocular infections and antimicrobial treatment patterns among a Ghanaian ophthalmic population. About 95% of the culture were positive for bacteria pathogens, and with the predominant class of bacteria being Gram negatives. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the commonly isolated bacteria species and with the former frequently isolated in cases of conjunctivitis and keratitis. The commonly used antimicrobial therapy in the clinical management of eye infections in these facilities were polymyxin B, neomycin and ciprofloxacin.

Bacteria ocular and periocular infections pose health challenges owing to associated morbidity and blindness. Globally, the burden of bacteria eye infections is higher especially in lower-and-middle income countries
### Variables

#### Total (N = 114) Males (N = 50, 43.9%) Females (N = 64, 56.1%)

| Variables                        | % (frequency) | % (frequency) | % (frequency) | p-value for linearity |
|----------------------------------|---------------|---------------|---------------|-----------------------|
| **Demographic characteristics**  |               |               |               |                       |
| **Age group (years)**            |               |               |               |                       |
| 0–2                              | 21.1 (24)     | 20.0 (10)     | 21.9 (14)     | 0.948                 |
| 3–7                              | 29.8 (34)     | 32.0 (16)     | 28.1 (18)     |                       |
| 18–39                            | 27.2 (31)     | 28.0 (14)     | 26.6 (17)     |                       |
| ≥40                              | 21.9 (25)     | 20.0 (10)     | 23.4 (15)     |                       |
| **Ethnicity‡**                   |               |               |               |                       |
| Akan                             | 93.0 (106)    | 90.0 (45)     | 95.3 (61)     | 0.271                 |
| Northerner                       | 7.0 (8)       | 10.0 (5)      | 4.7 (3)       |                       |
| **Religion**                     |               |               |               |                       |
| Catholic                         | 13.2 (15)     | 22.0 (11)     | 6.3 (4)       | 0.041                 |
| Protestant                       | 80.7 (92)     | 76.0 (38)     | 84.4 (54)     |                       |
| Muslim                           | 4.4 (5)       | 2.0 (1)       | 6.3 (4)       |                       |
| Atheist                          | 1.8 (2)       | 0.0 (0)       | 3.1 (2)       |                       |
| **Socioeconomic characteristics**|               |               |               |                       |
| **Residence**                    |               |               |               |                       |
| Rural                            | 59.6 (68)     | 60.0 (30)     | 59.4 (38)     | 0.946                 |
| Urban                            | 40.4 (46)     | 40.0 (20)     | 40.6 (26)     |                       |
| **Highest level of education**   |               |               |               |                       |
| None                             | 4.4 (5)       | 4.0 (2)       | 4.8 (3)       | 0.943                 |
| Preschool                        | 13.3 (15)     | 12.0 (6)      | 14.3 (9)      |                       |
| Primary                          | 33.6 (38)     | 30.0 (15)     | 36.5 (23)     |                       |
| Secondary                        | 29.2 (33)     | 32.0 (16)     | 27.0 (17)     |                       |
| Tertiary                         | 8.0 (9)       | 10.0 (5)      | 6.3 (4)       |                       |
| Not applicable*                  | 11.5 (13)     | 12.0 (6)      | 11.1 (7)      |                       |
| **Occupation**                   |               |               |               |                       |
| Farming                          | 4.4 (5)       | 6.0 (3)       | 3.1 (2)       | 0.092                 |
| Wage/Salary worker               | 7.0 (8)       | 6.0 (3)       | 7.8 (5)       |                       |
| Construction worker              | 2.6 (3)       | 6.0 (3)       | 0.0 (0)       |                       |
| Dressmaking                      | 1.8 (2)       | 0.0 (0)       | 3.1 (2)       |                       |
| Driver/Transport business        | 2.6 (3)       | 6.0 (3)       | 0.0 (0)       |                       |
| Businessman/woman                | 5.3 (6)       | 4.0 (2)       | 6.3 (4)       |                       |
| Welding                          | 1.8 (2)       | 4.0 (2)       | 0.0 (0)       |                       |
| Trading                          | 8.8 (10)      | 4.0 (2)       | 12.5 (8)      |                       |
| Beautician                       | 1.8 (2)       | 0.0 (0)       | 3.1 (2)       |                       |
| Hairdressing                     | 2.6 (3)       | 2.0 (1)       | 3.1 (2)       |                       |
| Student                          | 43.9 (50)     | 46.0 (23)     | 42.2 (27)     |                       |
| Unemployed                       | 5.3 (6)       | 2.0 (1)       | 7.8 (5)       |                       |
| Not applicable*                  | 12.3 (14)     | 14.0 (7)      | 10.9 (7)      |                       |
| **Marital status**               |               |               |               |                       |
| Not applicable*                  | 48.7 (55)     | 50.0 (25)     | 47.6 (30)     | 0.936                 |
| Single                           | 21.2 (24)     | 24.0 (12)     | 19.0 (12)     |                       |
| Married                          | 21.2 (24)     | 18.0 (9)      | 23.8 (15)     |                       |
| Cohabiting                       | 3.5 (4)       | 4.0 (2)       | 3.2 (2)       |                       |
| Divorced                         | 2.7 (3)       | 2.0 (1)       | 3.2 (2)       |                       |
| Separated                        | 0.9 (1)       | 0.0 (0)       | 1.6 (1)       |                       |
| Widow                            | 1.8 (2)       | 2.0 (1)       | 1.6 (1)       |                       |
| **Health status variables**      |               |               |               |                       |
| **Smoking habits**               |               |               |               |                       |
| Not applicable*                  | 44.7 (51)     | 46.0 (23)     | 43.8 (28)     | 0.237                 |
| Never smoked                     | 52.6 (60)     | 48.0 (24)     | 56.3 (36)     |                       |
| Past smoker                      | 1.8 (2)       | 4.0 (2)       | 0.0 (0)       |                       |
| Current smoker                   | 0.9 (1)       | 2.0 (1)       | 0.0 (0)       |                       |
| **Alcohol intake habits**        |               |               |               |                       |
| Not applicable*                  | 43.9 (50)     | 42.0 (21)     | 45.3 (29)     | 0.054                 |
| Continued                        |               |               |               |                       |
including Ghana. Though microscopic, the wide biodiversity of bacteria pathogens makes it burdensome for ophthalmic clinicians and physicians when selecting appropriate antibiotic therapy in routine clinical management of ocular and periocular infections. Previously, authors from several geographical jurisdictions have investigated the burden and etiology of bacteria eye infections, however, outcomes from these studies varied considerably. The prevalence estimates of medical conditions such as bacteria ocular and periocular infections are critical in informing eye care service delivery and in the development of policies to strengthen eye care practices yet there is presently limited ophthalmic data to propagate such transitions within the Ghanaian context. Importantly, gaining insight on bacteria etiology implicated in cases of external ocular and periocular infections within the Ghanaian population is essential to guide clinicians in the appropriate choice of antimicrobial therapy. Nonetheless there is paucity of data in this regard.

Overall, the prevalence of bacteria ocular and periocular infections found in this study was 95.1%. Our results are comparable with studies in Ethiopia, Saudi Arabia, Italy, and United States of America. The prevalence estimates of medical conditions such as bacteria ocular and periocular infections are critical in informing eye care service delivery and in the development of policies to strengthen eye care practices yet there is presently limited ophthalmic data to propagate such transitions within the Ghanaian context. Importantly, gaining insight on bacteria etiology implicated in cases of external ocular and periocular infections within the Ghanaian population is essential to guide clinicians in the appropriate choice of antimicrobial therapy. Nonetheless there is paucity of data in this regard.

Table 1. Description of the sample. Under age; %, percentage frequency. Northerner is a collective name for all ethnic group in the northern region of Ghana.
| Eyes affected | Total (N = 114) | Males (N = 50, 43.9%) | Females (N = 64, 56.1%) | p-value for linearity |
|---------------|---------------|----------------------|------------------------|----------------------|
|               | % (frequency) | % (frequency)        | % (frequency)          |                      |
| Right eye; oculus dexter | 16.7 (19) | 22.0 (11) | 12.5 (8) | 0.369 |
| Left eye; oculus sinister | 16.7 (19) | 14.0 (7) | 18.8 (12) | 0.247 |
| Both eyes; oculus uterque | 66.7 (76) | 64.0 (32) | 68.8 (44) | 0.065 |
| Site of eye affected |               |                      |                        |                      |
| Eyelid/eye lashes | 20.2 (23) | 22.0 (11) | 18.8 (12) | 0.668 |
| Conjunctiva | 94.7 (108) | 92.0 (46) | 96.9 (62) | 0.247 |
| Cornea | 18.4 (21) | 26.0 (13) | 12.5 (8) | 0.065 |
| Risk factors |               |                      |                        |                      |
| Previous eye infections | 45.1 (51) | 44.0 (22) | 46.0 (29) | 0.829 |
| Previous use of antimicrobials | 55.8 (63) | 52.0 (26) | 58.7 (37) | 0.474 |
| Previous usage of contact lenses | 0.9 (1) | 0.0 (0) | 1.6 (1) | 0.371 |
| Previous use of spectacles | 9.7 (11) | 10.0 (5) | 9.5 (6) | 0.932 |
| Previous ocular trauma | 20.4 (23) | 30.0 (15) | 12.7 (8) | 0.023 |
| Previous ocular surgery | 2.7 (3) | 2.0 (1) | 3.2 (2) | 0.700 |
| Duration of illness |               |                      |                        |                      |
| < 1 week | 63.7 (72) | 66.0 (33) | 61.9 (39) | 0.649 |
| 2–4 weeks | 18.6 (21) | 20.0 (10) | 17.5 (11) | 0.507 |
| > 4 weeks | 17.7 (20) | 14.0 (7) | 20.6 (13) | 0.689 |
| Previous application of mascara | 6.2 (7) | 0.0 (0) | 11.1 (7) | 0.015 |
| Previous application of breastmilk | 2.7 (3) | 2.0 (1) | 3.2 (2) | 0.700 |
| Presenting visual acuity |               |                      |                        |                      |
| Right eye; oculus dexter |               |                      |                        |                      |
| Unavailable | 2.6 (3) | 2.0 (1) | 3.1 (2) | 0.939 |
| FFL | 23.7 (27) | 24.0 (12) | 23.4 (15) | 0.507 |
| 6/5–6/18 | 65.2 (72) | 62.0 (31) | 64.1 (41) | 0.507 |
| 6/24–6/60 | 7.9 (9) | 8.0 (4) | 7.8 (5) | 0.507 |
| 3/60–1/60 | 2.6 (3) | 4.0 (2) | 1.6 (1) | 0.507 |
| Left eye; oculus dexter |               |                      |                        |                      |
| Unavailable | 2.6 (3) | 2.0 (1) | 3.1 (2) | 0.356 |
| FFL | 23.7 (27) | 24.0 (12) | 23.4 (15) | 0.507 |
| 6/5–6/18 | 67.5 (77) | 66.0 (33) | 68.8 (44) | 0.507 |
| 6/24–6/60 | 1.8 (2) | 0.0 (0) | 3.1 (2) | 0.507 |
| 3/60–1/60 | 4.4 (5) | 8.0 (4) | 1.6 (1) | 0.507 |
| Both eyes; oculus uterque |               |                      |                        |                      |
| Unavailable | 91.2 (104) | 86.0 (43) | 95.3 (61) | 0.266 |
| FFL | 0.9 (1) | 2.0 (1) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| 6/5–6/18 | 7.0 (8) | 10.0 (5) | 4.7 (3) | 0.0 (0) | 0.0 (0) |
| 3/60–1/60 | 0.9 (1) | 2.0 (1) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Presenting patient symptoms |               |                      |                        |                      |
| Eye pain | 50.9 (58) | 42.0 (21) | 57.8 (37) | 0.094 |
| Itching | 60.5 (69) | 54.0 (27) | 65.6 (42) | 0.208 |
| Falling lashes | 0.9 (1) | 0.0 (0) | 1.6 (1) | 0.375 |
| Lacrimation/watering | 61.4 (70) | 64.0 (32) | 59.4 (38) | 0.615 |
| Hyperemia/redness | 69.3 (79) | 72.0 (36) | 67.2 (43) | 0.580 |
| Swelling | 21.9 (25) | 22.0 (11) | 21.9 (14) | 0.987 |
| Discharge | 62.3 (71) | 70.0 (35) | 56.3 (33) | 0.133 |
| Burning sensation | 7.9 (9) | 6.0 (3) | 9.4 (6) | 0.507 |
| Foreign body sensation | 10.5 (12) | 14.0 (7) | 7.8 (5) | 0.285 |
| Others | 11.4 (13) | 4.0 (2) | 17.2 (11) | 0.028 |
| Test/investigations |               |                      |                        |                      |
| Visual acuity | 99.1 (113) | 98.0 (49) | 100 (64) | 0.256 |
| Slit lamp Biomicroscopy | 99.1 (113) | 98.0 (49) | 100 (64) | 0.256 |
| Ophthalmoscopy | 98.2 (112) | 98.0 (49) | 98.4 (63) | 0.860 |
| Microbial analysis | 90.4 (103) | 88.0 (44) | 92.2 (59) | 0.452 |
| Clinical signs       | Total (N=114) | Males (N=50, 43.9%) | Females (N=64, 56.1%) | p-value for linearity |
|---------------------|---------------|---------------------|-----------------------|-----------------------|
|                     | % (frequency) | % (frequency)       | % (frequency)         |                       |
| **Eyelashes**       |               |                     |                       |                       |
| Healthy             | 98.2 (112)    | 100.0 (50)          | 96.9 (62)             | 0.451                 |
| Misdirected         | 0.9 (1)       | 0.0 (0)             | 1.6 (1)               |                       |
| Crust formation     | 0.9 (1)       | 0.0 (0)             | 1.6 (1)               |                       |
| **Eyelids**         |               |                     |                       |                       |
| Healthy             | 66.7 (76)     | 66.0 (33)           | 67.2 (43)             | 0.819                 |
| Papillae            | 17.5 (20)     | 18.0 (9)            | 17.2 (11)             |                       |
| Cobblestones        | 1.8 (2)       | 2.0 (1)             | 1.6 (1)               |                       |
| Swelling            | 11.4 (13)     | 12.0 (6)            | 10.9 (7)              |                       |
| Crust               | 0.9 (1)       | 2.0 (1)             | 0.0 (0)               |                       |
| Drooping            | 0.9 (1)       | 0.0 (0)             | 1.6 (1)               |                       |
| Rashes              | 0.9 (1)       | 0.0 (0)             | 1.6 (1)               |                       |
| **Conjunctiva**     |               |                     |                       |                       |
| Healthy             | 26.3 (30)     | 28.0 (14)           | 25.0 (16)             | 0.646                 |
| Injection           | 71.9 (82)     | 72.0 (36)           | 71.9 (46)             |                       |
| Limbal papillae     | 0.9 (1)       | 0.0 (0)             | 1.6 (1)               |                       |
| Limbal pigmentation | 0.9 (1)       | 0.0 (0)             | 1.6 (1)               |                       |
| **Cornea**          |               |                     |                       |                       |
| Transparent         | 87.7 (100)    | 78.0 (39)           | 95.3 (61)             | 0.045                 |
| Opacities           | 3.5 (4)       | 4.0 (2)             | 3.1 (2)               |                       |
| Laceration          | 0.9 (1)       | 2.0 (1)             | 0.0 (0)               |                       |
| Abrasions           | 7.0 (8)       | 14.0 (7)            | 1.6 (1)               |                       |
| Ulcer               | 0.9 (1)       | 2.0 (1)             | 0.0 (0)               |                       |
| **Sclera**          |               |                     |                       |                       |
| Healthy             | 83.3 (95)     | 78.0 (39)           | 87.5 (56)             | 0.177                 |
| Pigmented           | 16.7 (19)     | 22.0 (11)           | 12.5 (8)              |                       |
| **Anterior chamber**|               |                     |                       |                       |
| Deep                | 98.2 (112)    | 96.0 (48)           | 100.0 (64)            | 0.106                 |
| Shallow             | 1.8 (2)       | 4.0 (2)             | 0.0 (0)               |                       |
| **Pupils**          |               |                     |                       |                       |
| Healthy (PERLLA)    | 99.1 (113)    | 98.0 (49)           | 100.0 (64)            | 0.256                 |
| Abnormal (RAPD)     | 0.9 (1)       | 2.0 (1)             | 0.0 (0)               |                       |
| **Iris**            |               |                     |                       |                       |
| Healthy (Dark and flat) | 99.1 (113) | 98.0 (49)           | 100.0 (64)            | 0.256                 |
| Prolapse            | 0.9 (1)       | 2.0 (1)             | 0.0 (0)               |                       |
| **Lens**            |               |                     |                       |                       |
| Transparent         | 94.7 (108)    | 92.0 (46)           | 96.9 (62)             | 0.247                 |
| Opacities           | 5.3 (6)       | 8.0 (4)             | 3.1 (2)               |                       |
| **Number of antibiotics administered** | | | | |
| None                | 7.9 (9)       | 6.0 (3)             | 9.4 (6)               | 0.351                 |
| 1                   | 33.3 (38)     | 38.0 (19)           | 29.7 (19)             |                       |
| 2                   | 40.4 (44)     | 44.0 (22)           | 37.5 (24)             |                       |
| ≥ 3                 | 18.4 (21)     | 12.0 (6)            | 23.4 (15)             |                       |
| **Clinical presentation** | | | | |
| Conjunctivitis      | 60.5 (69)     | 52.0 (26)           | 67.2 (45)             | 0.216                 |
| Blepharoconjunctivitis | 9.6 (11)  | 10.0 (5)            | 9.4 (6)               |                       |
| Keratoconjunctivitis | 11.4 (13)   | 16.0 (8)            | 7.8 (5)               |                       |
| Ophthalmia neonatorum | 0.9 (1)     | 2.0 (1)             | 0.0 (0)               |                       |
| Ocular trauma       | 6.1 (7)       | 8.0 (4)             | 4.7 (3)               |                       |
| Preseptal cellulitis | 0.9 (1)      | 0.0 (0)             | 1.6 (1)               |                       |
| Hordeolum           | 2.6 (3)       | 0.0 (0)             | 3.4 (7)               |                       |
| Keratitis           | 7.9 (9)       | 6.0 (3)             | 3.4 (7)               |                       |
| **Associated conditions** | | | | |
| Dry eye syndrome    | 10.5 (12)     | 6.0 (3)             | 14.1 (9)              | 0.164                 |
| Continued           | | | | |


United States of America\textsuperscript{26} where Gram negatives were found to be significantly lower compared to Gram positive bacteria and with proportional estimates of ranging from six to ten percent\textsuperscript{4,11,13,16,26}. Conversely, the proportionate distribution of Gram negatives to positive bacteria found in this study are parallel with results from several existing literatures\textsuperscript{2,5,8,10}. For example, among the various ocular microbiology investigations conducted across Ethiopia, by Ayebubizu et al.\textsuperscript{5}, Belyhun et al.\textsuperscript{2}, Assefa et al.\textsuperscript{10} as well as Getahun and colleagues\textsuperscript{8} the proportionate

| Types of clinical presentation | Bacteria culture results n (%) | Antimicrobial therapy employed in treating external ocular and periocular infections n (%) |
|-------------------------------|--------------------------------|--------------------------------------------------------------------------------------------------|
|                               | Positive | Negative | RFR | CIP | GM | PoB | NM | TBM | TX | OTX | OFC | FX |
| Conjunctivitis                |          |          |     |     |    |     |    |     |    |     |     |    |
| Blepharoconjunctivitis        | 11 (100.0) | 0 (0.0) |     |     |    |     |    |     |    |     |     |    |
| Keratoconjunctivitis          | 12 (92.3) | 1 (7.7)  |     |     |    |     |    |     |    |     |     |    |
| Ophthalmia neonatorum         | 1 (100.0) | 0 (0.0)  |     |     |    |     |    |     |    |     |     |    |
| Ocular trauma                 | 7 (100.0) | 0 (0.0)  |     |     |    |     |    |     |    |     |     |    |
| Preseptal cellulitis          | 1 (100.0) | 0 (0.0)  |     |     |    |     |    |     |    |     |     |    |
| Hordeolum                     | 3 (100.0) | 0 (0.0)  |     |     |    |     |    |     |    |     |     |    |
| Keratitis                     | 8 (88.9)  | 1 (11.1) |     |     |    |     |    |     |    |     |     |    |
| Total                         | 98 (95.1) | 5 (4.4)  |     |     |    |     |    |     |    |     |     |    |

Table 2. Clinical characteristics of external ocular and periocular infections among a Ghanaian ophthalmic population. FFL fixate-and-follow light, PERLLA pupils are equal, round, and reactive to light and accommodation, RAPD relative afferent pupillary defect.

| Types of clinical presentation | Bacteria isolates | Total isolates n (%) |
|-------------------------------|-------------------|----------------------|
|                               |                   |                      |
|                              |                   | Gram positive        |
|                               |                   |                      |
|                               |                   | S. aureus            |
|                               |                   | 12 (21.8)            |
|                               |                   | (72.7)               |
|                               |                   | 4 (33.3)             |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (14.3)             |
|                               |                   | 1 (100.0)            |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (12.5)             |
|                               |                   | 27 (27.6)            |
|                               |                   | CONS                 |
|                               |                   | 8 (14.5)             |
|                               |                   | (18.2)               |
|                               |                   | 1 (8.3)              |
|                               |                   | 1 (100.0)            |
|                               |                   | 1 (14.3)             |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 13 (13.3)            |
|                               |                   | Streptococcus spp    |
|                               |                   | 1 (1.8)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (1.0)              |
|                               |                   | Gram negative        |
|                               |                   |                      |
|                               |                   | Citrobacter spp      |
|                               |                   | 1 (1.8)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 2 (2.0)              |
|                               |                   | Serratia spp         |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (1.0)              |
|                               |                   | Salmonella spp       |
|                               |                   | 1 (1.8)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 3 (3.1)              |
|                               |                   | E. coli              |
|                               |                   | 1 (1.8)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (1.0)              |
|                               |                   | Klebsiella spp.      |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (1.0)              |
|                               |                   | P. aeruginosa        |
|                               |                   | 22 (40.0)            |
|                               |                   | (9.1)                |
|                               |                   | 5 (41.7)             |
|                               |                   | 0 (0.0)              |
|                               |                   | 2 (28.6)             |
|                               |                   | 0 (0.0)              |
|                               |                   | 2 (66.7)             |
|                               |                   | 6 (75.0)             |
|                               |                   | 38 (38.8)            |
|                               |                   | P. putida            |
|                               |                   | 9 (16.4)             |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (8.3)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 0 (0.0)              |
|                               |                   | 1 (12.5)             |
|                               |                   | 11(11.2)             |
|                               |                   | Total                |
|                               |                   | 55 (56.1)            |
|                               |                   | 11 (11.2)            |
|                               |                   | 12 (12.2)            |
|                               |                   | 1 (1.0)              |
|                               |                   | 7 (7.1)              |
|                               |                   | 1 (1.0)              |
|                               |                   | 3 (3.1)              |
|                               |                   | 8 (8.2)              |
|                               |                   | 98 (100.0)           |

Table 4. Distribution of bacteria isolates across different clinical presentations of external ocular and periocular infections in a Ghanaian ophthalmic population. n frequency, % percentage frequency, CCONS coagulase-negative staphylococcal species.

Table 3. Antimicrobial treatment of external ocular and periocular infections in a Ghanaian ophthalmic population. n frequency, % percentage frequency, RFR referral, CIP ciprofloxacin, GTM gentamicyn, PoB polymyxin B, NM neomycin, TBM tobramycin, TX tetracycline, OXT oxytetracycline, OFC ofloxacin, FX fluocaxicillin.
| Variable                         | Bivariate regression |   |   | p-value |
|---------------------------------|----------------------|---|---|---------|
| **Demographic characteristics** |                      |   |   |         |
| Age (years)                     | 1.04                 | 0.97–1.11 | 0.237 |
| **Age group (years)**           |                      |   |   |         |
| 0–2                             | Ref                  |   |   |         |
| 3–17                            |                      | 0.998 |   |         |
| 18–39                           |                      | 0.999 |   |         |
| ≥ 40                            | 1.00                 | 1.000 |   |         |
| **Gender**                      |                      |   |   |         |
| Man                             | Ref                  |   |   |         |
| Woman                           |                      | 0.998 |   |         |
| Not applicable*                 |                      | 0.998 |   |         |
| **Sex designated at birth**     |                      |   |   |         |
| Male                            | Ref                  |   |   |         |
| Female                          |                      | 0.32  | 0.03–2.97 | 0.316 |
| **Ethnicity**                   |                      |   |   |         |
| Akan                            | Ref                  |   |   |         |
| Northerner                      |                      | 0.999 |   |         |
| **Religion**                    |                      |   |   |         |
| Catholic                        | Ref                  |   |   |         |
| Protestant                      |                      | 0.999 |   |         |
| Muslim                          | 1.00                 | 1.000 |   |         |
| Atheist                         | 1.00                 | 1.000 |   |         |
| **Socioeconomic characteristics**|                      |   |   |         |
| Residence                       |                      |   |   |         |
| Rural                           | Ref                  |   |   |         |
| Urban                           | 0.99                 | 0.16–6.21 | 0.993 |
| **Highest level of education**  |                      |   |   |         |
| None                            | Ref                  |   |   |         |
| Preschool                       | 1.00                 | 1.000 |   |         |
| Primary                         |                      | 0.999 |   |         |
| Secondary                       |                      | 0.999 |   |         |
| Tertiary                        | 1.00                 | 1.000 |   |         |
| Not applicable*                 | 1.00                 | 1.000 |   |         |
| **Occupation**                  |                      |   |   |         |
| Not applicable*                 | Ref                  |   |   |         |
| Student                         |                      | 0.999 |   |         |
| Trading                         | 1.00                 | 1.000 |   |         |
| Welding                         | 1.00                 | 1.000 |   |         |
| Hairdressing                    | 1.00                 | 1.000 |   |         |
| Unemployed                      | 1.00                 | 1.000 |   |         |
| Construction worker             | 1.00                 | 1.000 |   |         |
| Beautician                      | 1.00                 | 1.000 |   |         |
| Wage or salary worker           | 1.00                 | 1.000 |   |         |
| Driver/Transport business       | 1.00                 | 1.000 |   |         |
| Businessman/woman               | 1.00                 | 1.000 |   |         |
| Farming                         | 1.00                 | 1.000 |   |         |
| Hairdressing                    | 1.00                 | 1.000 |   |         |
| **Marital status**              |                      |   |   |         |
| Not applicable*                 | Ref                  |   |   |         |
| Single                          | 2.24                 | 0.24–21.29 | 0.481 |
| Married                         |                      | 0.998 |   |         |
| Cohabitung                      |                      | 0.999 |   |         |
| Divorced                        |                      | 0.999 |   |         |
| Separated                       |                      | 1.000 |   |         |
| Widow                           |                      | 0.999 |   |         |
| Continued                       |                      |   |   |         |
| Variable                               | Bivariate regression | p-value |
|----------------------------------------|----------------------|---------|
| **Health status variables**            |                      |         |
| Smoking habits                         |                      |         |
| Not applicable*                        | Ref                  |         |
| Never smoker                           | 6.27                 | 0.107   |
| Past smoker                            |                      | 0.999   |
| Current smoker                         |                      | 1.000   |
| Alcohol intake habits                  |                      |         |
| Not applicable*                        | Ref                  |         |
| I never drink                          | 5.67                 | 0.128   |
| I drink only on special occasions      |                      | 0.999   |
| I drink once or twice a week           |                      | 0.999   |
| Average alcohol consumption per week   |                      |         |
| None                                   | Ref                  |         |
| 1 unit                                 |                      | 0.999   |
| 2-5 unit                               |                      | 0.999   |
| Medical history                        |                      |         |
| Diabetes                               |                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 0.999   |
| Hypertension                           |                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 0.999   |
| Tuberculosis                           |                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 1.000   |
| Sexually transmitted diseases          |                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 1.000   |
| Peptic ulcer                           |                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 0.999   |
| Are you currently taking any medication|                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 0.998   |
| Clinical characteristics               |                      |         |
| Eyes affected                          |                      |         |
| Right eye; oculus dexter               | Ref                  |         |
| Left eye; oculus sinister              | 0.47                 | 0.555   |
| Both eyes; oculus uterque              | 1.75                 | 0.655   |
| Site of the eye affected               |                      |         |
| Eyelids/lashes                         |                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 0.998   |
| Conjunctiva                            |                      |         |
| No                                     | Ref                  |         |
| Yes                                    |                      | 0.999   |
| Cornea                                 |                      |         |
| No                                     | Ref                  |         |
| Yes                                    | 0.36                 | 0.282   |
| Risk factors                           |                      |         |
| Previous eye infections                |                      |         |
| No                                     | Ref                  |         |
| Yes                                    | 0.19                 | 0.145   |
| Previous use of antimicrobials         |                      |         |
| No                                     | Ref                  |         |
| Continued                              |                      |         |
| Variable                      | Bivariate regression | p-value |
|-------------------------------|----------------------|---------|
|                               | OR       | 95% CI  |
| Previous use of contact lens  | Yes      | 0.998   |
|                               | No       | Ref     |
|                               | Yes      | 1.000   |
| Previous use of spectacles    | Yes      | 0.46    | 0.05–4.53 | 0.505 |
|                               | No       | Ref     |
| Previous ocular trauma        | Yes      | 0.998   |
|                               | No       | Ref     |
| Previous ocular surgery       | Yes      | 0.999   |
|                               | No       | Ref     |
| Duration of illness           | < 1 week  | Ref     |
|                               | 2–4 weeks | 0.998   |
|                               | > 4 weeks | 1.22    | 0.13–11.62 | 0.863 |
| Previous application of mascara | Yes    | 0.999   |
|                               | No       | Ref     |
| Previous application of breastmilk | Yes | 0.999   |
|                               | No       | Ref     |
| Patient presenting symptoms   | Yes      | 0.999   |
| Eye pain                      | No       | Ref     |
|                               | Yes      | 0.29    | 0.03–2.73  | 0.294 |
| Itching                       | No       | Ref     |
|                               | Yes      | 2.88    | 0.31–26.70 | 0.352 |
| Falling lashes                | No       | Ref     |
|                               | Yes      | 1.000   |
| Lacrimation/watering          | No       | Ref     |
|                               | Yes      | 3.10    | 0.18–6.89  | 0.920 |
| Hyperemia/redness             | No       | Ref     |
|                               | Yes      | 0.63    | 0.07–5.84  | 0.680 |
| Swelling                      | No       | Ref     |
|                               | Yes      | 0.998   |
| Photophobia                   | No       | Ref     |
|                               | Yes      | 0.32    | 0.05–2.03  | 0.315 |
| Discharge                     | No       | Ref     |
|                               | Yes      | 2.27    | 0.36–14.21 | 0.381 |
| Burning sensation             | No       | Ref     |
|                               | Yes      | 0.999   |
| Foreign body sensation        | No       | Ref     |
|                               | Yes      | 0.999   |
| Others                        | Yes      | 0.999   |
| Continued                     |          |         |
distribution of Gram-negatives were similar to Gram positives. Of note, whereas the magnitude of Gram-negative bacteria etiology found in Australia\(^{31}\), Iran\(^{30}\) and Italy\(^{24}\) were not equivalent to our findings as well as studies in parts of Ethiopia, the proportion estimates reported were relatively higher. There exist regional variations in the patterns of distribution of Gram-negative bacteria, however, the higher prevalence in our study are ascribed to hygiene as the primary mode of transmission of these enteric bacteria are through oral-fecal contamination. Specifically, we observed during data collection that most patients repeatedly clean ocular discharges with either bare hands or face handkerchief, hence predisposes eyes to contamination by fecal contaminants. Additionally, majority of our study subjects were either in preschool and/or primary hence prone to eye contamination through outdoor gaming activities in school. A considerably higher proportion of the study participants were below two years, and these age categories frequently experience oral-ocular contamination through inserting hands in mouth and touching of eyes thereafter which may have accounted for the increasingly abundance of Gram negative bacteria than positives in our study.

The predominant bacteria species found in our study were *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Although, *S. aureus* was second only to *P. aeruginosa* as the frequently isolated bacteria pathogen, however, it remains the most abundant Gram positive bacteria isolate from all obtainable ocular specimen in our study. This finding are consistent with studies in India\(^{19}\), Italy\(^{24}\), Nigeria\(^{48,49}\), and Ethiopia\(^{8,12}\). The occurrence of ocular infections with *S. aureus* etiology may be due to frequent touching of eyes with filthy hands among study subjects. The incidence of *Pseudomonas aeruginosa* in eye infections are mostly linked with the wearing of contact lens nonetheless we observed an inverse trend in our study. The blinding risk factor associated with *Pseudomonas aeruginosa* ocular infections underscores the promotion of contact lenses as an alternative to spectacle glasses in vision correction and/or cosmesis. Importantly *Pseudomonas aeruginosa* are opportunistic pathogens with devastating consequences on the ocular tissues. Specifically, they induce cornea infiltration and ulcerative keratitis when improperly managed by clinicians. Further, the conjunctiva and cornea are in close proximity landmarked by the limbus, hence pathogens of the conjunctiva can easily spread to the cornea during physiological blinking or mechanical rubbing of the eyes. Given the predominance of *Pseudomonas aeruginosa* in cases of conjunctivitis and keratitis warrants the need for clinicians to probe for other proxy predisposing factors other than relying solely on contact lenses etiology in most instances.

The commonly administered antimicrobial therapy found in this study were Polymyxin B, neomycin and ciprofloxacin. Polymyxin B is a nonribosomal peptidic antimicrobial agents used mostly in the treatment of Gram-negative infections. In particular, they exert their bactericidal effect by binding to phosphate residues within the lipopolysaccharides cell wall to induce displacement of divalent magnesium and calcium cations known to maintain membrane stabilizing properties of Gram-negative bacteria. Consequently, the intrinsic mechanism of action primarily causes an increase in cell membrane permeability resulting in a direct loss of cytoplasmic cell contents. Furthermore, they act synergistically with beta-lactam antibiotics by exposing the peptidoglycan machinery of these Gram negatives for which the latter act on\(^{51}\). On the contrary as an aminoglycoside neomycin actively inhibits protein synthesis of bacteria by insurmountably binding to the 16S ribosomal R.N.A. as well as 50S ribosomal subunits of susceptible class of Gram bacteria\(^{42,49}\). Similarly, ciprofloxacin a fluoroquinolone prevents bacteria D.N.A. replication by terminating the action of the reaction enzymes D.N.A. topoimerase IV and D.N.A. gyrase. The ensued effect is suicidal against Gram negatives as well as mixed bacteria culture\(^{46}\). Altogether, the frequent use of the aforementioned antibiotic agents in clinical management of ocular and periocular eye infections in our study are concordant with the laboratory results which identified Gram negatives as the predominant bacteria isolates.

The previous use of antimicrobials among patients is usually considered a risk factor in ocular infection due to the increased potential for contamination from improper handling or storage\(^{4,37}\). Although Getahun et al.\(^{8}\) in northwestern Ethiopia reported a significant association between the previous use of antimicrobials and the presence of positive bacterial culture, our results showed otherwise. Thus, patient characteristics, such as the prior usage of antimicrobials, were not significant determinants of positive bacterial culture. This was consistent with a similar investigation by Belyhun and coworkers\(^{37}\). Considering the varying resistance mechanism of microorganisms to single antimicrobial therapy and its negative repercussion in resistant eye infections, the administration of two/more specific antibiotic treatment underscores the patronage of a single broad-spectrum antibiotic, an essential determinant in antimicrobial resistance.

Of note, the study has several strengths worth highlighting. The study presents a preliminary and most recent data on bacterial etiology of external ocular and periocular infections among ophthalmic patients in Ghana. Although, we recommend future ocular antibiotic sensitivity studies in this setting, however, in light of the present evidence on the bacterial isolates implicated in eye infection are essential in assisting ophthalmic clinicians in their choice of antibiotic therapy. Moreover, unlike previous studies\(^{2,38}\), the present investigation

| Variable | Bivariate regression | p-value |
|----------|---------------------|---------|
|          | OR                  | 95% CI  |
| No       | Ref                 |         |
| Yes      | 0.56                | 0.06–5.42 | 0.615 |

Table 5. Factors associated with external ocular and periocular infections among a Ghanaian ophthalmic population. Bivariate regression analysis at a significance of p < 0.05. OR odds ratio, CI confidence interval, Ref reference.
utilized sample from multiple sites which underscores the selection bias usually associated with the convenience sampling approach which the study employed. On the contrary, owing to resource limitation the study could not perform direct fluorescent antibody test and/or Giemsa staining to investigate infections of *Chlamydia trachomatis* etiology. Our prevalence may have been underestimated as a considerable number of our patients where preschoolers whose uncooperative nature denied researchers from taking ocular swabs for bacteriological analyses. Although, given the nature of the studies we could not ascertain the treatment outcomes of the patients the information on the therapy was pivotal in our laboratory.

**Conclusion**

The prevalence of positive bacteria culture from external ocular and periocular infections was approximately 95%. Gram-negative organisms were commonly implicated and with *Pseudomonas aeruginosa* and *Staphylococcus aureus* as the predominant causative bacteria. Clinical presentations of conjunctivitis and keratitis infections were mostly caused by *Pseudomonas aeruginosa* and with polymyxin B, neomycin and ciprofloxacin as the frequently administered antimicrobial therapy. Given the high burden of ocular bacterial infections, measures (infections control program and antimicrobial agent management program) should be institutionalized to prevent emergence of resistant strains. We recommend future studies to focus on investigating into the potential antibiotic resistances infections within the Ghanaian ophthalmic population.

**Methods**

**Study design, setting and population.** A multi-center study was conducted among patients suspected of external ocular and periocular infections in three health facilities in Ghana, namely Anglican Eye Hospital, Jachie; St. Michaels Hospital, Pramso; and Kumasi South Hospital, Agogo from July 18, 2021 to September 18, 2021. Cornea scrapings and conjunctival specimens were obtained from infected eyes for bacterial isolation together with collation of patients sociodemographic and clinical characteristics with a pretested structured questionnaire.

**Study setting.** The Anglican Eye Hospital (A.E.H.), St. Michaels Hospital (S.M.H.) and Kumasi South Hospital (KSH) were selected for the study primarily because of their higher out-patient-department (O.P.D.) turn-out, as well as their wide catchment area and rural/urban interactions. The A.E.H. and S.M.H. are located in Bosomtwe; a rural district in Ghana whilst KSH is situated in the Asokwa municipal area, an urban settlement in the Ashanti Region of Ghana. All the facilities have either a permanent/visiting ophthalmologist, optometrists, ophthalmic nurses and opticians. All the facilities provide comprehensive eye services which range from corneal history, visual acuity assessment, refraction, dispensing of refractive glasses, management of anterior and posterior segment pathologies, prescribing of medications and performing scheduled surgeries. The S.M.H. and KSH, serve as immediate referral hospitals for the surrounding private and polyclinics. However, all clinical emergencies are referred to the Komfo Anokye Teaching Hospital, the only tertiary health facility in the region. The study facilities lack microbiology laboratory hence clinicians employ empirical approaches in their routine diagnosis and management of external ocular and periocular infections.

**Study population and sampling.** The study population involved patients who sought ophthalmic treatments/services for external ocular and periocular infections at the eye clinics of the Anglican Eye Hospital, Jachie; St Michaels Hospital, Pramso; and the Kumasi South Hospital from July 18 to September 18, 2021. Purposive sampling approach was used to recruit all patients presenting with signs and symptoms of external ocular and periocular infections following a consent (and accent for minors). Patients reporting solely for optical correction, or participants on systemic/topical antibiotics or have performed ocular surgery in the last one week were excluded. A purposive sampling approach was used to recruit all one hundred and fourteen (114) eligible subjects.

**Study variables.** The independent variables for this study were participants’ sociodemographic factors; age, sex, ethnicity, religion, facility, socioeconomic; residence, highest level of education, occupation, marital status, health status; smoking habits, alcohol intake, systemic medical conditions and clinical characteristics (eyes affected, site of the eyes affected, risk factors, patient presenting symptoms) whereas the outcome/dependent variable was prevalence of bacteria ocular and periocular infections. Participants were assessed and clinical presentations classified based on operational terms reported previously, and antimicrobial treatments documented accordingly.

**Operational definitions.** Blepharitis in the study was characterized by gritty itchy sore eyes, with crusting and/or collarattes around the base of the eyelashes coupled with clogging of the Meibomian gland, loss of eyelashes and with demodex conjunctivitis. Conjunctivitis was defined as conjunctival lesion delineated by hyperemia, chemosis, whitish tint purulent discharge and hemorrhage. Blepharocconjunctivitis presented as redness of the eye, with dry scaly eyelids and ensuing symptoms of itchiness and burning sensation. In keratoconjunctivitis, cornea and conjunctiva were implicated with complaints of dryness, itching and mucous discharge. Keratitis was defined as lesion of the cornea with characteristic cornea edema, cellular infiltration, pain, redness, photophobia and ciliary injection. Hordeolum was defined swelling and tenderness of the eyelid with acute pain, photophobia and mild epiphora. Ophthalmia neonatorum is a neonatal conjunctivitis presented within the first 28 days of life with signs of eyelid edema, erythema and purulent discharge. Preseptal and orbital cellulitis showed simi-
lar features of painful swelling and/or tenderness of the eyelid with the later distinguished from the former by decreased vision and pain on eye motility.

**Data collection. Sociodemographic and clinical data.** The patients sociodemographic, socioeconomic, and health status variables were gathered by the principal investigator and a trained research assistant using a pre-tested structured questionnaire. A comprehensive vision assessment including visual acuity, slit lamp biomicroscopy, and phthalmoscopy was performed by a registered optometrist on all study participants. Subsequently, patient medical history, primary and secondary diagnosis, and antimicrobial therapy prescribed were extracted using a data collection form.

**Specimen collection and transport.** Overall, 103 ocular specimens were obtained from the eyes of patients with external ocular and periorcular infections following aseptic procedures. With the patient eyes in an upward position of gaze, conjunctival specimens were obtained by gently rolling a moistened saline cotton bud over the lower tarsal plate of the eyelids and fornix of the conjunctiva in repeated strokes, thus from nasal to temporal and vice versa. Samples from corneal ulcer and keratitis infections were obtained utilizing a modified version of an original protocol described previously. Briefly, using slit-lamp biomicroscopy and under topical local anesthesia (1–2 drops of 0.5% fresh proparacaine), the edges of the ulcer were firmly scraped. On the contrary, none of the patients in our study presented with dacryocystitis and/or blepharitis; hence a puncture and/or aspiration of the lacrimal sac as well as swabbing on the eyelids were not undertaken. The swabs were subsequently kept in a sterile, freshly prepared nutrient broth and transported within 1–3 h in a standard triple packaging system (of an absorbent cotton wrapping primary container enclosed in a sealed bag and kept in an insulated icebox with icepacks) from the study sites to the Microbiology Laboratory of the Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology, for further microbial investigation.

**Laboratory methods. Culture and identification of bacteria pathogens.** All specimen obtained were initially inoculated on a Nutrient agar and incubated at 37 °C for 24 h and plates examined for growth afterwards. Plates with microbial growth were transferred onto various differential and selective media for preliminary isolation and identification. Specifically, bacteria were cultured on a Mannitol Agar, MacConkey Agar, Bismuth sulphite (all from Oxoid Ltd. Basingstoke, Hants United Kingdom brand), Cetrimide agar (HiMedia Laboratories Pvt. Ltd Mumbai, India), 5% sheep Blood and Chocolate agars and incubated for 24 h. Of note, with the exception of 5% blood and chocolate agars which were kept under anaerobic conditions, an aerobic atmosphere was maintained for all other differential agar media used. Conversely, plates with no growth were re-incubated for additional 48 h and consequently counted negative if no growth pattern appeared. In addition, microbial growth on differential media was again sub-cultured on a nutrient agar to obtain pure colonies and subsequently subjected to further phenotypic identification, specifically colony morphology, Gram stain, and biochemical analyses. Gram-positive bacteria isolates were characterized using coagulase, catalase, and bacitracin tests, whereas Gram-negative bacteria were differentiated using citrate utilization, lysine deacylase agar, indole, and urease tests, as well as triple sugar iron agar. Details of the methodology are summarized in Fig. 1.

**Quality assurance and control.** The questionnaires employed to gather the sociodemographic and clinical data were pretested at the Anglican Eye Hospital and revised accordingly following their feedback. Questionnaires were written in English and administered by the principal investigator and a trained research assistant. On the one hand, questionnaire was explained in local dialect for study subjects who could not comprehend instructions in English language. The data from study was double checked for accuracy and completeness. At the facility, all test tubes with ocular samples were well-labeled to avoid any mismatched. The laboratory reagents and culture media for the experiments were checked for expiry dates, and sterility control performed to ascertain the integrity of the media such as free from contamination. The media performance and/or functionality assessment was conducted using the American Type Culture Collection (A.T.C.C.) Standard Reference Strains. Specifically, *Escherichia coli* ATCC 25,922; *Pseudomonas aeruginosa* ATCC 4853; *Staphylococcus aureus* ATCC 25,923.

**Data protection and management.** The hardcopy version of the filled questionnaires was kept under lock and key and accessible only to the principal investigator and research advisor. Similarly, the softcopy of the non-aggregated dataset was protected using an alphanumeric stringed password. The research report presented to the respective facilities and for publication purposes were aggregated hence individual study participants could not be traced.

**Ethical consideration.** To undertake this study a hierarchical ethical consideration protocols were followed. A written permission was sought from the authorities of the Anglican Eye Clinic, St. Michaels Hospital, and Kumasi South Hospital. The study protocol was then approved by the Committee on Human Research, Publication and Ethics (C.H.R.E.), of the Kwame Nkrumah University of Science and Technology and the Komfo Anokye Teaching Hospital (Reference number: CHRPE/AP/282/21). Written informed consent was obtained from adult participants and for minors a written informed consent was taken from caregivers after study protocol was fully explained to the best of their comprehension. The study adhered to the tenets of the declaration of Helsinki and all laboratory procedures performed in accordance to the Clinical Laboratory Standard Institute guidelines, C.L.S.I.
Statistical analysis. Data were entered and managed in Microsoft Excel and further exported into Statistical Package and Service Solution version (I.B.M. Corporation IBM® SPSS® Statistics for Windows, version 25.0 Armonk, NY) compatible with windows. Normality assessment was performed using the Kolmogorov Smirnov statistic. The demographics, socioeconomics, health status and clinical characteristics of the sample were presented, and the difference between males and females was tested with chi-square analysis. Clinical diagnosis, cultural status and antimicrobial treatments were presented in cross tabulations using frequencies and percentages. Association between sample characteristics and prevalence of bacterial infections were investigated using bivariate logistic regression at a significance set at p < 0.05 (Supplementary Information S1).

Data availability
All relevant data and materials supporting the conclusion of this article is/are available within the manuscript and its supporting information files.

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