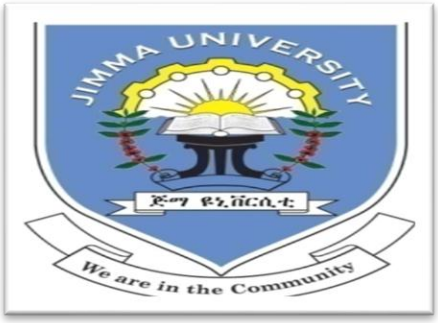
BACTERIAL PROFILE, ANTIMICROBIAL SUSCEPTIBILITY, AND TREATMENT OUTCOMES OF BACTERIAL CONJUNCTIVITIS AMONG PATIENTS TREATED AT THE OPHTHALMOLOGIC CLINIC OF JIMMA MEDICAL CENTER, ETHIOPIA



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ABSTRACTS

Background: Bacterial conjunctivitis is a common ocular infection in Ethiopia with high ocular morbidity and complications. Antimicrobial resistance to agents commonly used for infectious conjunctivitis makes it crucial to consider changing resistance trends when prescribing; however, data in this area are limited in Ethiopia.

Objective: To assess bacterial profile, antimicrobial susceptibility, and treatment outcomes of bacterial conjunctivitis among patients treated at the Ophthalmologic Clinic of Jimma Medical Center, Ethiopia, 2022.

Methods: Hospital-based longitudinal study was conducted at the Ophthalmologic Clinic of Jimma Medical Center, from January-June 2022. Conjunctival swabs were collected from 190 patients clinically diagnosed with bacterial conjunctivitis. All Ocular specimens were collected using an aseptic technique for gram stain and culture. Bacteria were identified by a series of biochemical tests using the standard microbiological method. Antimicrobial susceptibility testing was done using the disk diffusion method. Sociodemographic, Clinical characteristics, treatment, clinical response, and complications were recorded prospectively from the first visit (diagnosis) to 30-day. Data were entered into EPI data 3.1 and exported to SPSS version 21 for data analysis. Bivariate and multivariable logistic regressions were done to identify factors associated with poor treatment outcomes. P-value <0.05 was taken as statistically significant.

Results: Among 190 patients included in this study, 97 (51.1%) were males, and more than half 107(56.3) were under 18 years. The bacterial growth rate from bacterial conjunctivitis was 160 (84.2%) (95%CI: 78.4, 89.5). The most frequently isolated bacteria were gram-positive 124 (77.5%); predominantly *Coagulase-negative staphylococcus* 57 (35.6%) and *Staphylococcus aureus* 35 (21.9%) with a higher resistance rate against penicillin, ampicillin, and tetracycline. Common gram-negative isolates were *Pseudomonas aeroginosa* 13 (8.1%) and *Klebsiella pneumonia* 7 (4.4%) with a higher resistance rate to penicillin and ampicillin. Multidrug-resistant bacteria were detected among 124 (77.5%) of the 160 bacterial isolates. A total of 84 (44.2%) patients had poor treatment outcomes (persistent or worsened symptoms from baseline). Factors associated with poor treatment outcomes were comorbid chronic diseases [AOR=11, 95%CI (2.8-43)], traditional eye medicine use [AOR=3.7, 95%CI (1.3-10)], infection with *Coagulase-negative staphylococcus* [AOR = 4.2, 95%CI (1.4-12)], treatment with Zoxan D [AOR =10, 95%CI (3-13)], Topical steroids use [AOR =14, 95%CI [4-48)], fortified antibiotics[AOR=10, 95%CI (3-35)], and non-adherence to a treatment regimen [AOR= 3.3, 95%CI (1.1-9.5)]. Blepharoconjuntivitis 17 (8.9%) was the most common type of complication experienced by the study participants.

Conclusions: *Coagulase-negative staphylococcus* and *Staphylococcus aureus* were the most predominant bacterial isolates with high resistance to frequently used antibiotics for ocular infections such as ciprofloxacin, gentamycin, and tetracycline. Almost half of the patients had poor treatment outcomes. Therefore, empirical treatment of bacterial conjunctivitis in the study area should be supported by antimicrobial susceptibility tests.

Keywords: Conjunctivitis, Antibiotic resistance, Ocular Infections, Antimicrobial susceptibility, Treatment outcome

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TABLE OF CONTENTS

Contents

ABSTRACTS..... iii

ACKNOWLEDGMENTS..... iv

TABLE OF CONTENTS..... v

LIST OF TABLES..... viii

LIST OF FIGURES..... ix

ABBREVIATIONS /ACRONYMS/INITIALISMS..... x

1.INTRODUCTION..... 1

1.1. Backgrounds..... 1

1.2. Statement of the problem..... 3

1.3. Significance of the study..... 5

2.LITERATURE REVIEW..... 6

2.1 Bacterial profile and their antimicrobial susceptibility patterns..... 6

2.2. Treatment outcomes of bacterial conjunctivitis..... 10

2.3 Conceptual framework..... 11

3. OBJECTIVES..... 12

3.1. General Objective..... 12

3.2. Specific Objectives..... 12

4. MATERIALS AND METHODS..... 13

4.1. Study Area..... 13

4.2. Study period..... 13

4.3. Study Design..... 13

4.4. Population..... 13

4.4.1 Source population..... *13*

4.4.2. Study Population ... *13*

4.5. Eligibility ... 13

4.5.1. Inclusion criteria ... *13*

4.5.2. Exclusion criteria ... *14*

4.6. Sample size determination and Sampling technique ... 14

4.7. Study variables ... 15

4.7.1. Dependent variables ... *15*

4.7.2. Independent variables ... *15*

4.8. Data collection procedures (tool, personnel, technique) ... 15

4.8.1. Clinical procedures ... *15*

4.8.2 Sample collection, handling, and transport of specimen ... *16*

4.8.3. Isolation and Identification of bacterial pathogens ... *16*

4.8.4. Antimicrobial susceptibility testing ... *17*

4.8.5 Data collection tool and Process ... *19*

4.9. Data quality assurance ... 19

4.10. Data processing and analysis ... 19

4.11. Outcome measures and validating method ... 20

4.11. A. Treatment outcome ... *20*

4.11. B. Complications of bacterial conjunctivitis ... *20*

4.12. Ethical considerations ... 21

4.13. Dissemination Plan ... 21

4.14. Operational Definition and definition of terms ... 21

5. RESULTS ... 22

5.1 Study Participant's Enrolment ... 22

5.2. Socio demographic characteristics ... 22

5.3. Baseline clinical characteristics 23

5.4. Medical and Medication history 24

5.5 Prevalence of bacterial isolates 25

5.6. Antimicrobial susceptibility patterns among gram positive bacterial isolates 26

5.7. Antimicrobial susceptibility pattern among gram negative bacterial isolates 28

5.8. Multidrug resistance patterns of bacterial isolate 32

5.9. Treatments of bacterial conjunctivitis 32

5. 10. Outcomes 34

5.10. A Treatment outcome 34

5.10. B Complications of bacterial conjunctivitis 34

5.10. C Factors associated with treatment outcomes 35

6. DISCUSSION 37

7. CONCLUSION 41

8. IMPLICATION FOR QUALITY IMPROVEMENT 42

9. REFERENCES 42

10. Annexes 46

Annex I English version Questionnaire 46

Annex IIAmharicversion Questionnaire 52

Annex III Afan Oromo version Questionnaire 55

LIST OF TABLES

Table 1: Lists of independent variables 15
Table 2: Socio-demographic characteristics of patients with bacterial conjunctivitis presented at Ophthalmic Clinic of JMC, January-June 2022..... 22
Table 3: Medical and medication history of patients diagnosed with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January - June 2022..... 24
Table 4: The prevalence of bacterial aetiologies isolated from patients diagnosed with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January - June 2022. 25
Table 5: Antimicrobial susceptibility patterns of gram positive isolates from patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January - June 2022. 27
Table 6: Antimicrobial susceptibility patterns of gram negative isolates identified from patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January - June 2022. 28
Table 7: Multidrug-resistance patterns of bacterial isolates collected from patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January - June 2022. 32
Table 8: Pharmacologic and non-pharmacologic management of patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January- June 2022. 33
Table 9: Factors associated with poor treatment outcomes of patients diagnosed with bacterial conjunctivitis on binary and multiple logistic regression analysis presented at Ophthalmologic Clinic of JMC, January - June 2022..... 36

LIST OF FIGURES

Fig. 1: Conceptual framework 11

Fig. 2: laboratory procedures 18

Fig. 3: Participant enrollment at Ophthalmologic Clinic of JMC, January-June 2022..... 22

Fig.4: Baseline clinical characteristics of patients with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January-June 2022..... 24

Fig.5: Treatment outcomes of bacterial conjunctivitis at Ophthalmologic Clinic of JMC January-June, 2022 34

Fig.6: Types of complications developed during follow-up among patients with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January-June 2022 35

ABBREVIATIONS /ACRONYMS/INITIALISMS

AMR= Antimicrobial Resistance

AST=Antimicrobial susceptibility test

ATM=Amiens transport media

CKD= Chronic kidney disease

CLSI= Clinical and laboratory standard institute.

CoNS=*Coagulase negative staphylococcus*

DM= Diabetic mellitus

E. coli= Escherichia coli

HIV= Human immunodeficiency virus

H. influenza= Haemophilus influenza

JMC=Jimma Medical Center

K. pneumoniae= Klebsiella pneumoniae

MDR=Multidrug resistance

MHA=Muller Hinton Agar

MRSA=Methicillin resistant staphylococcus

P. aeruginosa= Pseudomonas aeruginosa

SLE= Systemic lupus erythematosus

S. aureus= Staphylococcus aureus

S.pneumonia=Streptococcus pneumoniae

TEM=Traditional eye medicine

WHO=World-Health-Organization.

1. INTRODUCTION

1.1. Backgrounds

Conjunctivitis is a general term for a variety of diseases that are characterized by inflammation of the conjunctival membrane as a result of either infectious (mainly bacterial and viral) or non-infectious (immunological/allergic reactions, mechanical irritation, neoplasm or toxic substances irritation) etiologies ([1, 2]. It is one of the leading reasons people seek eye care due to the associated symptoms ([3]. Immunological or allergic reactions are the most common cause of non-infectious conjunctivitis and can significantly impact the quality of life ([4, 5]. Viral infection is the commonest(80%) form of infectious conjunctivitis, followed by bacterial conjunctivitis ([3]. Bacterial conjunctivitis is the most common(50%-75%) type of conjunctivitis in children ([6].

The etiology of bacterial conjunctivitis may differ based on age and geographical location. According to earlier literature, gram-positive bacteria such as *Coagulase-negative staphylococcus (CoNS), Staphylococcus aureus (S. aureus)* and *Streptococcus pneumoniae (S. pneumoniae)* are the most common cause of ocular infections including conjunctivitis ([7-10]. Among gram-negative, frequent isolates of conjunctivitis include *Pseudomonas aeruginosa (P. aeruginosa), Escherichia coli (E. coli),* and *Klebsiella pneumoniae* (*K. pneumoniae)* ([11, 12]. Early diagnosis and initiation of appropriate treatment are essential for early recovery and to prevent severe complications that can lead to visual impairment and blindness ([13]. Diagnosis of conjunctivitis and identification of specific etiology (eg, bacterial, viral, or allergic) needs comprehensive slit-lamp bio-microscopic ocular examinations, microbiological tests, and other laboratory investigations ([13, 14]. Patient history and clinical presentations play a significant role in the diagnosis of bacterial conjunctivitis. For instance, a purulent or mucopurulent discharge, glued eyelids, unilateral infection, rapid onset of conjunctival redness, diminished visual acuity, eye tenderness, and swollen lymph nodes are often due to bacterial conjunctivitis ([15, 16].

A 7- day course of broad-spectrum topical antibiotics are usually effective for mild bacterial conjunctivitis ([17] and this has been shown to decrease symptoms, improve resolution times, decreased transmission, and reduced further complications ([2]. Since there is no clinical evidence to support the superiority of one antibiotic over another, the least expensive option can be

selected ([17]). The isolation rate of methicillin-resistant *Staphylococcus aureus(MRSA)* from patients with bacterial conjunctivitis is increasing ([18, 19]), colonization of *MRSA* among nursing home residents is increasing ([20]) and the incidence of community-acquired *MRSA* infections also has risen ([21]) and *MRSA* organisms are resistant to many commercially available topical antibiotics ([18, 19, 22]). Therefore, the results from microbiological tests should serve as a guide when selecting antimicrobials for the treatment of moderate to severe bacterial conjunctivitis, which is characterized by purulent discharge, ocular pain, and marked inflammation, due to increased resistance to the commonly used antibiotics ([23]).

1.2. Statement of the problem

Worldwide approximately 43.3 million individuals suffer from blindness and about 295 million persons have a significant visual impairment in 2020 ([24]). Globally, the disability-adjusted life years (DALYs) due to blindness and vision loss increased from 12.4 million in 1990 to 22.6 million in 2019 ([25]). Blindness and visual impairment are associated with a huge financial impact globally with an estimated potential productivity loss of 410.7$ billion annually ([26]). Sub-Saharan Africa (SSA) disproportionately carries a high number of blindness and vision impairments ([27]). Ethiopia is one of the countries with the world's highest prevalence of blindness (1.6%) and visual impairment (3.7%) with more than 80% being avoidable cases (either preventable or treatable) ([28, 29]). According to World Health Organization (WHO) report, effective prevention or treatment has not been given for more than one-third of people with visual impairments ([30]).

Conjunctivitis is one of the most frequent causes of ocular diseases globally([1]). In the United States only, bacterial conjunctivitis affects more than 6 million people annually with an estimated direct cost of $800 million([31]). Although bacterial conjunctivitis is believed to be more common in developing countries where the hygienic-sanitary condition is poor, we found no quality data on bacterial conjunctivitis incidence, economic burden, and clinical outcomes in the area. Likewise, there is no nationwide data on bacterial conjunctivitis in Ethiopia. Nevertheless, prior observational studies in Ethiopia reported that conjunctivitis accounts for 20.2% to 60.4% of all external ocular infections ([8, 32, 33]) and it is reported as the main cause of ocular morbidity (35%) among rural children in Ethiopia ([34]).

Although most (about 60%) viral and bacterial conjunctivitis are self-limiting ([35]), bacterial conjunctivitis can be associated with persistent symptoms and long-term sequelae. These complications include keratoconjunctivitis, corneal ulcer, erosion, and other systemic complications ([36]). In addition infection with drug-resistant bacteria such as *Methicillin Resistant Staphylococcus aureus (MRSA)* and *pseudomonas aurigeunosa* can cause sight threatening-complication([37]).

Globally, antimicrobial-resistant pathogens from ocular infection are becoming more frequent and these microbes are challenging to treat and led to poor outcomes([37]). In Ethiopia, most bacterial isolates from different clinical samples are resistant to the most frequently used antibiotics ([38]). Particularly, *(MRSA)* is extremely resistant to common antibiotics used in

Ethiopian healthcare including ophthalmology ([38, 39]). From the ophthalmology perspective, *Staphylococcus aureus* is the leading cause of ocular infections in Ethiopia and other settings ([33, 39, 40]). Furthermore, the steady increasing prevalence of antibiotic-resistant *P. aeruginosa and extended beta-lactames producing Enterobacteriaceae (E.coli and K. pneumonia)* poses a substantial challenge to the ophthalmologists who are responsible to prescribe empiric antibiotics in resource-limited settings such as Ethiopia ([41, 42]). Moreover, these resistant bacteria compromise patient care and negatively affect visual outcomes ([43]). Hence, studies that characterize antibiotic susceptibility patterns in ocular infections with a particular focus on MDR organisms are urgently needed to tailor empiric antibiotic treatment for ocular infections and where possible, to amend local treatment guidelines accordingly ([44, 45]).

Although there were studies on antimicrobial susceptibility patterns in ocular infections in different parts of Ethiopia including Jimma ([33, 39, 40, 46]), the trends of antibiotic resistance vary from setting to setting and from time to time. Understanding this rapid emergence and dynamic nature of antimicrobial resistance, WHO and Ethiopian Food and Drug Authorities (EFDA) recommends continuous surveillance of antimicrobial resistance ([44, 45]). Furthermore, as far as our knowledge is concerned, none of these studies describe the common antibiotics regimens used for the treatment of bacterial conjunctivitis and they did not evaluate treatment outcomes comprehensively. Hence, this study is aimed to assess the bacterial profile, antimicrobial susceptibility, and treatment outcome of patients with bacterial conjunctivitis presented to the Ophthalmology Clinic of Jimma Medical Center Ethiopia.

1.3. Significance of the study

This study provides up-to-date data on bacterial profiles involved in bacterial conjunctivitis and their antimicrobial resistance patterns which will guide ophthalmologists in selecting appropriate and effective empirical antibiotics that will cover the most common pathogens. In addition, this study will be used as input to strengthen the national survey of antimicrobial resistance. Furthermore, the knowledge of bacterial etiologies and their antimicrobial susceptibility is crucial to developing institution-specific antibiogram.

This study will alert ophthalmologists by depicting treatment outcomes and associated factors. Moreover, the present study also identified areas that need patient education such as unsupervised use of traditional eye medicine and medication non-adherence since they contribute to poor treatment outcomes.

2. LITERATURE REVIEW

2.1 Bacterial profile and their antimicrobial susceptibility patterns

One of the most common causes of ocular infections worldwide is bacteria ([47]. The prevalence and isolation rate of bacteria in samples collected from the eye and their antimicrobial susceptibility patterns have been studied in different parts of the world ([48-50]. Different classes of antibiotics are commonly used for the treatment of ocular infections. These are Penicillin, cephalosporins, aminoglycosides (gentamycin, tobramycin, amikacin, and netilmicin), fluoroquinolones, and macrolides. Gentamycin and tobramycin are active against most Staphylococci, Proteus, and Enterobacteriaceae, but resistant strains are now being reported ([51].

Previous literature from different parts of the world reported different prevalence of bacterial conjunctivitis. For instance, the observational study conducted in New York, the USA among Children under 17 years reported that bacteria were the most common (64.7%) cause of conjunctivitis ([52]. However, studies conducted in Pakistan and Iraq reported that bacteria contributed to only about one-fourth of conjunctivitis ([53, 54]. Surprisingly, one study conducted in India reported that bacteria accounted for just 13.3% of conjunctivitis ([55].

Regarding bacterial profile, generally, *S. aureus*, *CoNS*, *S. pneumonia*, and *P.auroginosa* were the leading bacterial isolates that play a key role in bacterial conjunctivitis ([56]. Most studies showed that gram positive bacteria such as *S. aureus*, *CoNS*, and *S. pneumoniae* were the most common cause of bacterial conjunctivitis ([6, 18, 22, 53, 57-59]. However, there are also plenty of studies that reported gram-negative bacteria such as *H. influenza* and *P.auroginosa* as the predominant cause of bacterial conjunctivitis ([52, 54, 60, 61]).

Two hundred seventy-three samples were collected from patients with ocular infections over 2 years in one observational study conducted in Italy. Out of 273 samples processed, 86.4% yielded growth: of them, 77.5% were bacterial, 11% were fungal, and 9.7% specimens showed the presence of Acanthamoeba. Among bacterial infections, 54.5% of bacterial isolates were gram-positives, and (44.8%) were gram-negatives. Among gram-positives, Tigecycline showed the greatest susceptibility 93.8%, followed by Linezolid 97% and Daptomycin 95.18%. Gram-negative bacteria strains were susceptible to Imipenem 95%, Meropenem 98.5%, and Amikacin

91%. Multidrug resistance (resistance ≥3 classes of antibiotics) was found in 63% of gram-positive bacteria, and 44% of gram-negative([62]).

A hospital-based prospective cross-sectional study was conducted in Assam Medical College and Hospital in India with 110 culture-proven bacterial conjunctivitis cases for a period of 1 year. In this study, the microbiological test result showed that *S. aureus* 32.1% was the predominant organism isolated throughout the year [*MRSA* (2.7%)] followed by *CoNS* 29.1%, *S. pneumoniae*, *diphtheroid* 12.8% and *streptococcus beta hemolyticus* 8.4%. *Moraxella catarrhalis* 4.5%, *H. influenza* 4.5%, *Klebsiella* 3.6%, *P.auroginosa* 3.6%, *Escherichia coli* 1.8%, *Neisseria gonorrhea*, 1.8%, *Enterobacter* 0.9% and *Corynebacterium diphtheria* 0.9% were isolated less frequently in our study population. Regarding AMR, more than 70% of isolates of *MSSA* were sensitive to aminoglycosides (amikacin, gentamycin, tobramycin), doxycycline, chloramphenicol, cephalosporins, vancomycin, and linezolid, whereas >70% of isolates were resistant to ciprofloxacin and moxifloxacin. More than 80% of *staphylococcus epidermidis* isolates were sensitive to aminoglycosides (amikacin and tobramycin), doxycycline, chloramphenicol and cephalosporins. More than 20% of isolates were resistant to fluoroquinolones (ciprofloxacin and moxifloxacin)([63]).

A cross-sectional study was conducted in Nigeria between February-September 2010 among 83 patients with conjunctival infection. All collected specimens were culture-positive, with a total growth of 155 bacterial isolates. Among identified bacterial isolates, gram-positive cocci comprising *S. aureus* 27.7% and *CoNS* spp. 22.6% accounted for 50.3% (of bacterial conjunctivitis cases, followed by gram-positive bacilli 22.6%, gram-negative bacilli 21.3%, and gram-negative cocci 4.5%. *Corynebacterium* species were the most commonly isolated 16.1% gram-positive bacilli. *P. aeruginosa* topped with 9.7% as the most commonly isolated gram-negative bacilli. Antimicrobial resistance test results revealed that chloramphenicol and ofloxacin were the least and most effective antibiotics tested, as 63.9% and 96.1% of the 155 recovered isolates were sensitive to them. On the whole, the least susceptible pathogen was *P. aeruginosa* with sensitivities ranging from 20% - 80%, while Moraxella sp. represented the most sensitive pathogen with sensitivities ranging from 71.4% - 100% ([9]).

Another study conducted in Ibadan, Nigeria among 365 patients who were clinically diagnosed with bacterial conjunctivitis revealed that the bacterial growth rate from conjunctival samples was 93.7%. From the identified pathogens, 86.5% were gram-positive whereas the rest 13.5% were gram-negative. *S. aureus* 74.9%, CoNS 10.2%, and *P. aeruginosa* 6.4% were the most commonly isolated pathogens. In this study, *S. aureus* showed a higher rate of susceptibility to ceftriaxone 69.1% and showed a higher rate of resistance to ofloxacin 27%. *P. aeruginosa* displayed a higher resistance rate to amoxicillin, amoxicillin-clavulanate, cloxacillin and chloramphenicol, and erythromycin each 100% and some of them were susceptible to gentamycin 54.6%, ofloxacin 63.6% and ceftriaxone 54.6% ([64].

In a cross-sectional study conducted at Hawassa University Hospital from December 2012 to April 2013, 48.8% of the 281 collected ocular specimens had positive cultures. The majorities of bacterial isolates were gram positive 61.5%. *S. aureus* 21%, *CoNS* 18.2%, and *S. pneumoniae* 14.0% were the predominant pathogens in descending order. Ciprofloxacin was effective against 86% of the isolated pathogens. Multi-drug resistance was observed in 69.9% of the bacterial isolates. Gram-positive isolates were more susceptible to amoxicillin-clavulanic acid and Vancomycin, whereas gram-negative isolates were more susceptible to ciprofloxacin and gentamycin. Relatively, ciprofloxacin was effective against most isolated pathogens ([56].

A retrospective study was conducted in Gondar University Hospital on a total of 102 ocular specimens collected from patients with ocular infections. Of the collected specimens, 60.8% of them had bacterial growth. The most frequent isolates were gram-positive bacteria 74.2%. Among them, *CoNS* 27.4% and *S.aureus* 21% were the two predominant bacterial isolates identified from these patients. Most of the bacterial isolates were resistant to ampicillin 71%, amoxicillin 62.9%, erythromycin 43.5%, gentamycin 45.2%, penicillin 71%, Trimethoprim-sulphamethoxazole 58.1%, and tetracycline 64.6%; while Ceftriaxone and Ciprofloxacin showed 75.8% and 80% susceptibility respectively. Out of the total bacterial isolates, 87.1% showed multi-drug resistance to two or more drugs ([65].

A cross sectional study conducted in Borumeda on 160 patients with ocular infections showed that from the total ocular samples collected, 59.4% were culture positive. The majority of the isolates 93.7% were gram positive. CoNS 31.9% were the leading isolate among gram positive

bacteria followed by *S. aureus* 13.1% and *S. pneumoniae* 6.2%. All gram-isolates were susceptible to Vancomycin but most were resistant to ampicillin and amoxicillin. Most gram-negative were sensitive to gentamycin but resistant to tetracycline, norfloxacin, ceftriaxone, and ciprofloxacin ([66].

A hospital-based cross-sectional study was conducted at Quiha Ophthalmic Hospital, Tigray region, northern Ethiopia among 270 patients diagnosed with ocular infections. The bacterial growth rate from ocular specimens was 66.7%. The predominant bacterial isolates were *S. aureus* 22.2%, *CoNS* 17.2%, and *P. aeruginosa* 11.7%. Regarding antimicrobial susceptibility results, most isolates were susceptible to amikacin 93.2%, gentamicin 89.1%, and ciprofloxacin 89.2%. The rate of multidrug resistance was found to be 34.8% ([46].

A facility-based cross-sectional study conducted among 323 patients diagnosed with ocular infections from January-April 2019 at Menelik II Referral Hospital, Addis Ababa, Ethiopia, showed that the bacterial growth rate was 54.5%. *CoNS* 41.3% and *S. aureus* 36.4% were the most common bacteria identified from the collected ocular specimen. The antimicrobial resistance test results explained that gram-positive isolates were sensitive to tobramycin, gentamicin, chloramphenicol, vancomycin, and ceftriaxone. In contrast, 94.0% of these gram-positive isolates were resistant to penicillin. The overall rate of MDR was 73.4% ([67].

A facility-based cross-sectional study was conducted at Jimma Medical Center (JMC) Ophthalmologic clinic including 319 patients with ocular infections from March-June 2017. From a total of 319 ocular specimens collected, the bacterial growth rate was 46.1%. The predominant bacterial isolates were *CoNS* 27.7% followed by *S. aureus* 19.7%. Among Gram-negative groups, *P. aeruginosa* 6.8% was the leading isolate. Increased antimicrobial resistance rate was observed to tetracycline 64%, erythromycin 66.7%, and penicillin 77.1%. Amoxicillin-clavulanic acid, ciprofloxacin, and gentamicin were the most effective drugs for external eye infections due to susceptibility ranging from 70-100% among both gram-negative and gram-positive groups. Methicillin-resistant *S. aureus* (MRSA) accounted for 13.8%. The rate of multidrug resistance (MDR) was 68.7% ([40].

2.2 . Treatment outcomes of bacterial conjunctivitis

Study done in the U.S among 246 patients with signs of bacterial conjunctivitis were randomized to receive either norfloxacin or chloramphenicol for one week in double-masked parallel group study. Ninety-two percent of the norfloxacin-treated patients and 93% of the chloramphenicol-treated patients were rated as either clinically improved or cured at the end of the treatment period. Whereas, two norfloxacin-treated patients and three chloramphenicol-treated patients had adverse experiences, predominantly ocular discomfort, which required cessation of drug therapy ([68].

Another study conducted in the Netherlands that compares the treatment of infectious conjunctivitis with fusidic acid versus placebo found out that among patients who were randomized to fusidic acid group 62% of them were recovered after 7 days of treatment; whereas 38% of them were not recovered and (14%) of them developed adverse effects ([69].

In a placebo-controlled trial of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis conducted in USA including a total of 249 patients; 126 were randomly assigned to the 0.5% levofloxacin treatment group, and 123 were randomly assigned to receive placebo. Of these, 227 patients completed the study and the reasons for discontinuation included adverse events 7, lost to follow up 6, non-compliance 4, clinical worsening 3, and others. Clinical cure rates were significantly greater 88% in the 0.5% levofloxacin treatment group than in the placebo group 53%. Resolution rates for ocular signs and symptoms were consistently higher in the 0.5% levofloxacin treatment group than in the placebo group at all study visits. Statistically significant differences favouring 0.5% levofloxacin were observed for resolution of the ocular signs and symptoms ([70].

2.3 Conceptual framework

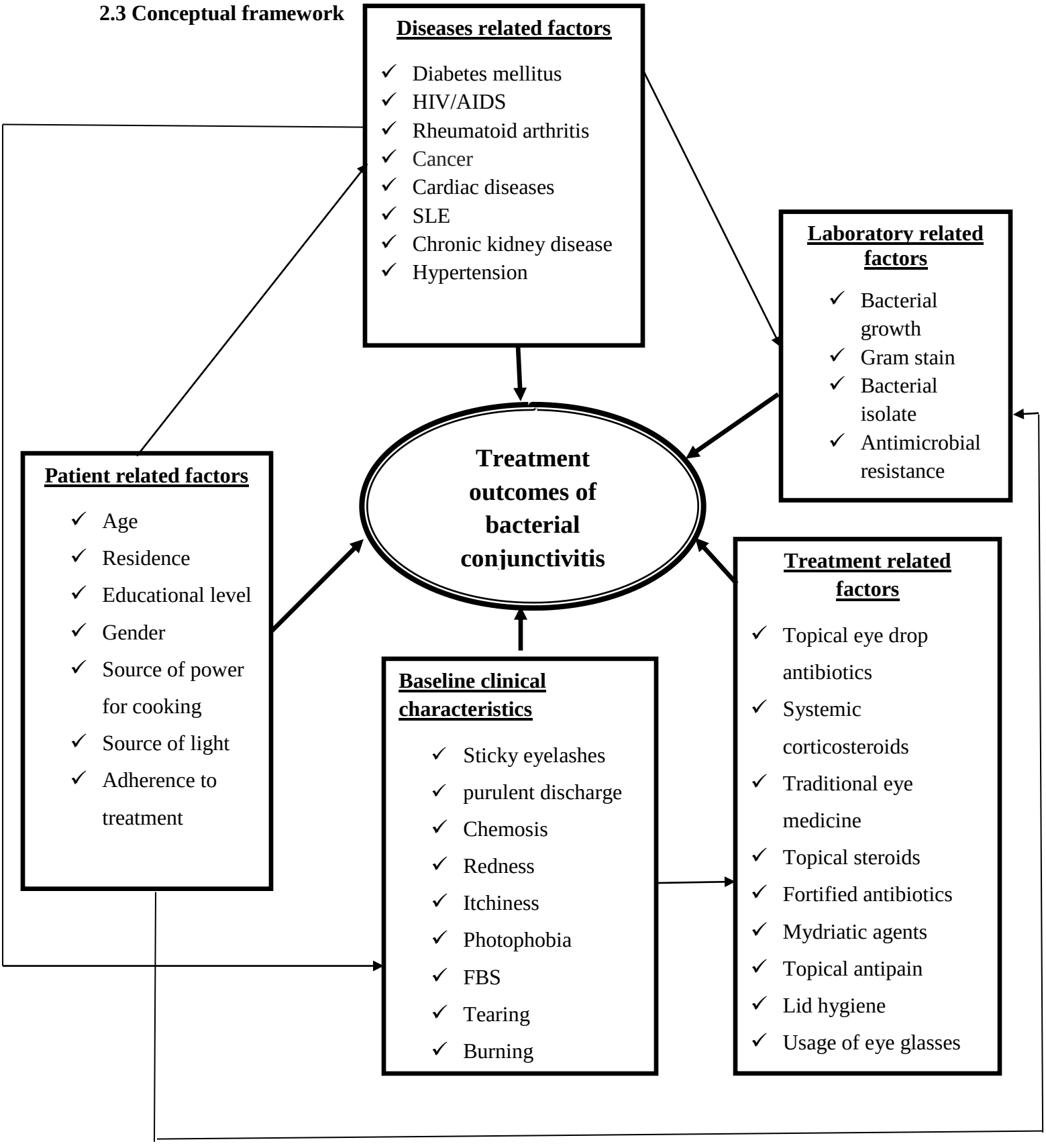


Fig. 1: Conceptual framework

3. OBJECTIVES

3.1. General Objective

To assess bacterial profile, antimicrobial susceptibility, and treatment outcome of patients diagnosed with bacterial conjunctivitis treated at the Ophthalmologic Clinic of Jimma Medical center (JMC), Ethiopia, 2022.

3.2. Specific Objectives

1. To identify bacterial etiologies among patients diagnosed with bacterial conjunctivitis
2. To assess the antimicrobial susceptibility patterns of bacterial isolates from patients diagnosed with bacterial conjunctivitis
3. To assess the treatment outcomes of patients diagnosed with bacterial conjunctivitis
4. To identify the complications that occurred among patients diagnosed with bacterial conjunctivitis.
5. To identify predictors of poor treatment outcomes among patients treated for bacterial conjunctivitis.

4. MATERIALS AND METHODS

4.1. Study Area

This study was conducted at Ophthalmologic Clinic of JMC which is located about 354 kilometers away from Addis Ababa ([71]. JMC is the only tertiary referral center in southwest Ethiopia, with a catchment population of more than 20 million, 800 inpatient beds, and about 3000 hospital workers. It has 32 service units including Ophthalmologic Clinic. The ophthalmologic clinic serves as a referral eye center for a population residing in the southwestern part of Ethiopia. It is the only tertiary eye center in the area. This clinic has also different components, such as the wards for inpatients, an operation room, and Outpatient department.

Jimma University microbiology laboratory was established 8 years back in 2014. Currently, it has eight microbiologists and it is one of the six reporting centers for GLASS (Global Antimicrobial Resistance and Use Surveillance System) which is governed by WHO. It serves around 5000 patients with duties including gram stain, cultures, and antimicrobial sensitivity tests annually.

4.2. Study period

This study was conducted from January 3 to June 3, 2022

4.3. Study Design

Facility based longitudinal study was conducted at the Ophthalmologic Clinic of JMC.

4.4. Population

4.4.1 Source population

All patients who were diagnosed with bacterial conjunctivitis visit the Ophthalmologic Clinic of JMC.

4.4.2. Study Population

All patients diagnosed with bacterial conjunctivitis that visited Ophthalmologic Clinic of JMC during the study periods and fulfill the inclusion criteria.

4.5. Eligibility

4.5.1. Inclusion criteria

- ✓ Patients who were newly diagnosed with bacterial conjunctivitis

- ✓ Patients who were willing to participate in the study
- ✓ Children whose guardian agreed to participate and give assent

4.5.2. Exclusion criteria

- ✓ Patients who were on antibiotics within the last 7 days.
- ✓ Lost to follow up

4.6. Sample size determination and Sampling technique

The sample size was calculated using a single population proportion formula using the prevalence of poor treatment outcome of bacterial conjunctivitis to be 0.5(p=0.5) as there was no study conducted in Ethiopia that is related to this topic. Using 95% CI and a margin of error of 5% and a 10% non-response rate, the sample size was calculated as,

The sample size $\boldsymbol{n = z\,(\alpha/2)2p\,(1-p)/d2}$

Where

n = Sample size

α = level of significance

z = at 95% confidence interval Z value (α = 0.05) =>Z α/2 = 1.96

p = 0.5

d = Margin of error at (5%) (0.05)

n = ((1.96)2 x .5(1-.5))/ (0.05)2

n = **384**

Since the source population is **360,** we used the correction formula to get the final sample size as the following.

A consecutive sampling Technique was used.

Finite population correction to sample size (nc) =N*n/N+ (n-1)

nc=360*384/384+359=**186**

nc: corrected sample size

N: source population

n: calculated sample size.

10% non-response rate=18, so the final sample size (n) will be

n = 186+ 18 =**204**

4.7. Study variables

4.7.1. Dependent variables

- ✓ Treatment outcome(good or poor)
- ✓ Bacterial profile
- ✓ Antimicrobial resistance

Table 1: Lists of independent variables

4.7.2. Independent variables

Patient-related factors	Clinical characteristics	Disease-related factors	Treatment-related factors
✓ Age ✓ Gender ✓ Educational level ✓ Source of light ✓ Source of power ✓ Residence ✓ Adherence to treatment	✓ Redness ✓ Burning sensation ✓ Tearing ✓ Itching ✓ Foreign body sensation ✓ Photophobia ✓ Sticky eyelashes in the morning ✓ purulent conjunctival discharge ✓ Chemosis ✓ Ocular pain ✓ Reduced vision	✓ Diabetes mellitus ✓ HIV/AIDS ✓ Hypertension ✓ Cardiac diseases ✓ Chronic kidney diseases ✓ Rheumatoid arthritis ✓ Cancer ✓ Lupus	✓ Topical eye drops antibiotics ✓ Systemic corticosteroids ✓ Topical steroids ✓ Usage of traditional eye medicine ✓ Systemic antibiotics ✓ Topical antipain ✓ Mydriatic agents ✓ Fortified antibiotics ✓ Non pharmacologic interventions ✓ Duration of treatment
Investigation related factors ✓ Culture ✓ Gram stain			

4.8. Data collection procedures (tool, personnel, technique)

4.8.1. Clinical procedures

Every patient was examined on the slit-lamp bio microscope by either residents or ophthalmologists. Visual acuity (VA) was measured under conditions of high contrast, using

printed or projected charts with optotypes; typically they are letters or “tumbling E’s. The result was expressed in numbers like 6/6. The first number represented the distance between the chart and the patient. The second number means that a "normal” eye can see this size letter at the indicated distance. The result of visual acuity measured using projected or printed charts ranged from 6/6-3/60. VA worse than 3/60 was determined by counting fingers (CF). The patient cannot count fingers at less than 6m, he/she was tested for hand movement (HM). Patients having VA worsen than HM were tested for light perception (LP) then reported as LP and no light perception (NLP).

Comorbid medical conditions such as diabetic mellitus, hypertension, HIV/AIDS, chronic kidney disease, rheumatoid arthritis, lupus, cancer, cardiac diseases, and the history of corticosteroids, and traditional eye disease use, and all baseline clinical presentations were recorded through direct interview and assessment of patient records. After a detailed ocular examination, the diagnosis was made depending on the examination obtained through slit microscopy and clinical manifestation of patients. After that standard empirical treatment was established for each patient.

4.8.2 Sample collection, handling, and transport of specimen

After detailed ocular examinations using standard techniques, conjunctival specimens for culture and gram stain were collected using sterile cotton swabs by gently swabbing the eye, the lower conjunctival sac according to Clinical and Laboratory Standard Institute (CLSI) 2020 guideline ([72]. Swabs of conjunctival samples from patients were obtained aseptically from infection sites before the eye was cleaned with an antiseptic solution and antibiotic used. Two swabs were collected from each patient; one for gram stain and the other for culture. The swabs were immersed in 3 ml of Amiens transport media with charcoal, placed in a cold box, and transported to the JMC Microbiology laboratory for bacterial isolation and identification.

4.8.3. Isolation and Identification of bacterial pathogens

Ocular specimens were inoculated onto MacConkey agar, Mannitol Salt Agar, Blood agar, and Chocolate agar plates. The plates were incubated at 37 °C for 24 to 48 hours aerobically. For fastidious organisms, Chocolate agar (heated 5% Sheep’s blood agar) was incubated at 37 °C for 24 to 48 hours in a 5-10% CO2 atmosphere. All plates were examined for growth after 24 hours and cultures with no growth were further incubated for another 24 hours. After obtaining pure

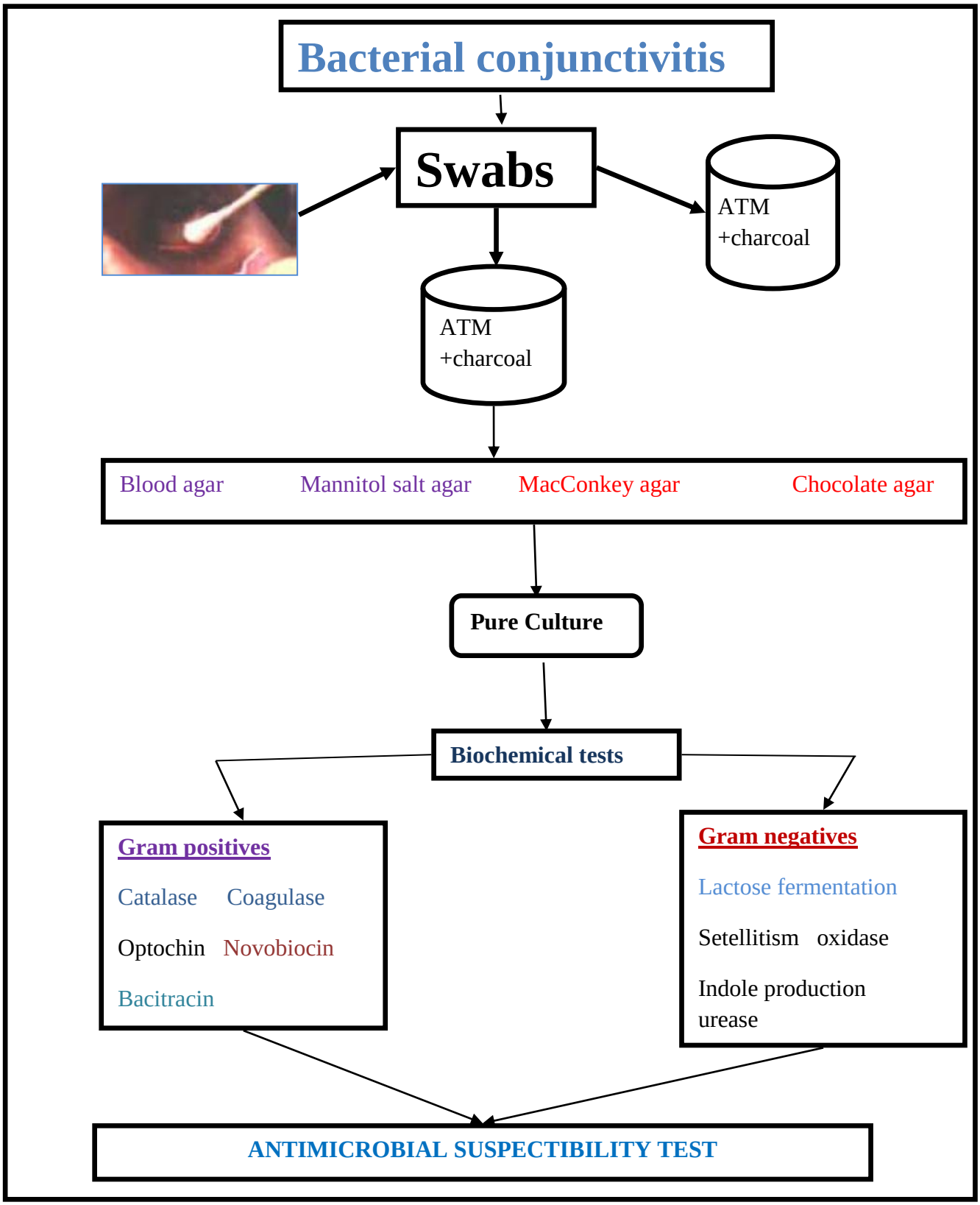
colonies, further identification was conducted using standard microbiological techniques including gram reaction and biochemical tests

Gram-positive bacteria were identified using hemolytic activity on sheep blood agar, catalase and coagulase test, optochin disk sensitivity, novobiocin, and bacitracin tests. Gram-negative bacteria were identified by performing a series of biochemical tests namely, lactose fermentation, indole production test, urease test, oxidase test, and satellitism test. For *Hemophilus* species, a satellitism test was done in which *Hemophilus* species grown on blood agar were streaked with *S.aureus* that provide a growth factor required for Haemophilus species (small colonies surrounding *S. aureus* colonies).

4.8.4. Antimicrobial susceptibility testing

For every identified bacteria, antimicrobial susceptibility test was carried out on Muller Hinton agar (MHA) using the disk diffusion method described by CLSI 2020 guideline. From a pure culture, three to five colonies of the test organisms were emulsified in 3 ml of sterile nutrient broth and mixed gently. The suspension was diluted and incubated at 37 °C till the turbidity of the suspension becomes adjusted to 0.5 McFarland standards. The suspension was swabbed uniformly onto MHA agar entirely by rotating the plate 60 degrees between streak for non-fastidious organisms and MHA with defibrinated sterile sheep blood (5%) for fastidious organisms. The antimicrobial impregnated disks were placed using sterile forceps on the MHA plate's surface and the plates were incubated at 37°C for 18-24 hours and the zone of inhibition around the disk was measured to the nearest millimeter using a graduated caliper in millimeters, and the isolates were classified as sensitive, intermediate and resistant according to CLSI, 2020.

The following 12 antibiotics with the respective concentrations were used to determine the antibiogram of the strains and impregnated antibiotic disks were used in the following concentrations: Ampicillin (AMP) 10µg, Ceftriaxone (CRO) 30µg, Chloramphenicol (C) 30µg, Ciprofloxacin (CIP) 5µg, Clindamycin (DA) 2µg, Erythromycin (E) 15µg, Gentamicin (CN) 10µg, Penicillin-G (P) 10IU, Tetracycline (TE) 30µg, Trimethoprim-sulphamethoxazole (SXT) 1.25/23.75µg, piperacillin/tazobactam(100/10µg) and meropenem(10 µg).



ATM=Amiens transport media

Fig. 2: laboratory procedures

4.8.5 Data collection tool and Process

The questionnaire was prepared by reviewing different relevant literature related to the topic ([40, 73-75]). The data collection tool has six parts which include socio-demography, clinical characteristics, medical history, laboratory data collection format, management, and treatment outcome. After completion of the patient/caregiver consent form, data were collected by four ophthalmology residents through medical record reviews and patient interviews using a pretested structured questionnaire. All patients included in the study were followed from the time of their first hospital visit to the Ophthalmology clinic to one month using a follow-up chart included in the questionnaire.

4.9. Data quality assurance

The questionnaire was prepared in English and translated to Afan Oromo and Amharic and again it was translated back to English. The data collectors were trained for three days on the aim of study, eligibility criteria and sampling technique before data collection. The questionnaire was pretested on 10% (20) of the sample population to test for validity. All ophthalmic specimens were collected following CLSI guidelines 2020 by professional ophthalmology residents. The sterility of culture media was ensured by incubating 5 % of each batch of the prepared media at 37 °C for 24 hours. The performance of the Catalase reagent was checked *against S. aureus* (positive control) and *S. pyogene* (negative control). The test for coagulase was also checked by known *S. aureus* (positive control) and *S. epidermidis* (negative control). To preserve the quality of results, physical changes including cracks, excess moisture, change in color, dehydration, contamination, and expiration dates of culture media were checked routinely. Incubators' and refrigerator's temperature was monitored on daily basis. All collected data were checked for completeness by the principal investigator on daily basis. To ensure the accuracy of data, double data entry method was used.

4.10. Data processing and analysis

The collected data were checked for completeness and coded. And then entered into EPI data 3.1 and exported to SPSS version 21 software to analyze, manage, and produce graphical visualizations of data. The continuous variable was reported by median and the categorical variables were summarized using percentages and frequency tables. Bivariate and multivariable logistic regression models were used to identify factors associated with poor treatment outcomes.

Variables having a p-value of ≤0.25 in the bivariate analysis were subjected to multivariable analysis to identify independent predictors of poor treatment outcomes. A p-value <0.05 was considered statistically significant.

4.11. Outcome measures and validating method

Patients diagnosed with bacterial conjunctivitis were enrolled in the study for a period of 30 days. All patients on follow-up with appointments were followed up every week.

4.11. A. Treatment outcome

The main treatment Outcome Measure was a response to treatment as a cure, improved, stable, and worsened as per the following criteria during a one-month follow-up period.

- ✓ Cure- if there is no sign or symptom of bacterial conjunctivitis
- ✓ Improved-if there is a sign or symptom of bacterial conjunctivitis but with less severity than the baseline
- ✓ Stable- if there is no change in sign or symptom of bacterial conjunctivitis from baseline severity
- ✓ Worsened- if there is sign or symptom of bacterial conjunctivitis with increased severity from baseline([76]).

Treatment outcome was defined as **"good"** if

- ✓ The patient's status of the response is either cured or improved during the follow up period

The treatment outcome is defined as "**poor"** if

- ✓ The patient's status of response is either stable or worsened during the follow up period

4.11. B. Complications of bacterial conjunctivitis

- ✓ Development of complications: any complication from bacterial conjunctivitis was confirmed by an ophthalmologist through microscopic examination and clinical assessment([6]).

4.12. Ethical considerations

Ethical clearance was obtained from Jimma University Institutional Review Board. Supportive letter was written to Jimma medical center medical directors/managers. Data collection was started after obtaining permission from hospital managers/medical directors and informed consent from the study participants/caregivers. The study subjects/guardians were informed that their responses would remain confidential.

4.13. Dissemination Plan

The study result will be presented during the thesis defense and will be submitted to Jimma university department of Clinical pharmacy's post-graduate coordinating office. Results of the study will be compiled in the form of thesis, and will be communicated to all concerned bodies and attempts will be made to present findings in scientific journals.

4.14. Operational Definition and definition of terms

Multidrug resistance: Microorganisms resistant to at least three antibiotics of different classes([77]).

Good adherence: - is defined as a score of ≥ 3 out of 4 Morisky medication adherence scale test([78]).

Treatment Outcomes: The clinical consequence of treatment was explained in terms of good or poor treatment outcomes.

Complication: a secondary disease or condition aggravating an already existing bacterial conjunctivitis.

5. RESULTS

5.1 Study Participant's Enrolment

Out of a total of 209 patients newly diagnosed with bacterial conjunctivitis that had a follow up at Ophthalmologic Clinic of JMC during the study period, 190 patients fulfilled the inclusion criteria and enrolled in this study (Figure 3).

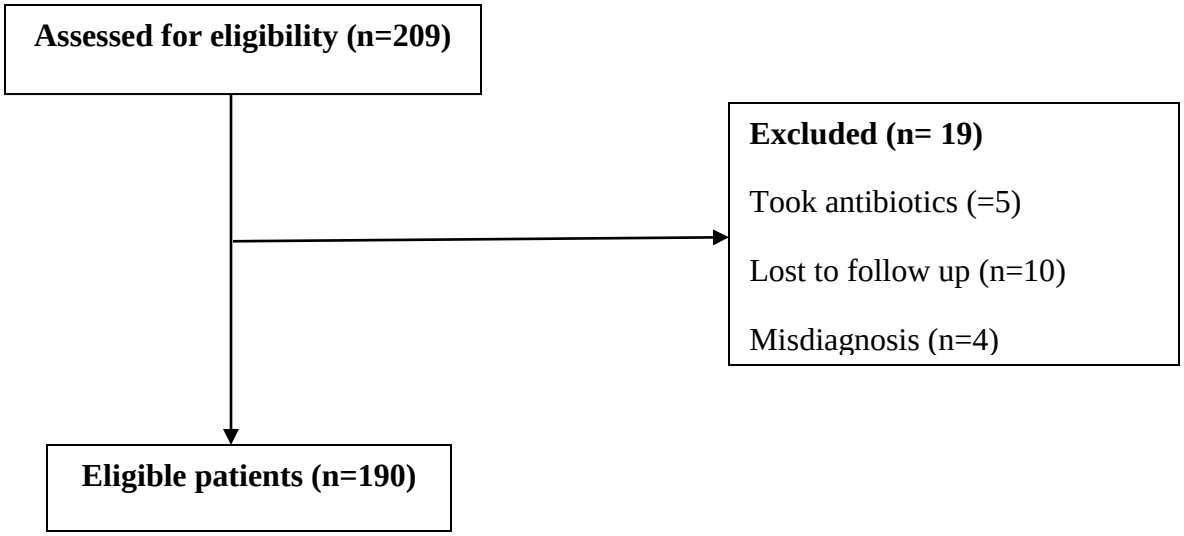


Fig. 3: Participant enrollment at Ophthalmologic Clinic of JMC, January-June 2022.

5.2. Socio demographic characteristics

Among 190 study participants included in this study proportion of males 97 (51.1%) and females 93 (48.9%) was almost similar. More than half 107 (56.3%) of the patients were younger than 18 years. One hundred thirteen (59.5%) of the total participants were from the urban areas and use electricity as a source of light. All most all 185 (97.4%) of the study participants/their families use wood as a source of power for cooking (Table2).

Table 2: Sociodemographic characteristics of patients with bacterial conjunctivitis presented at Ophthalmic Clinic of JMC, January-June 2022

Variables	Category	Frequency	Percentage
Age[Median,12 (IQR;29)]	0-4	39	20.5
	5-17	68	35.8
	18-64	68	35.8
	>=65	15	7.9
Gender	Male	97	51.1
	Female	93	48.9
Residence	Urban	113	59.5
	Rural	77	40.5
Educational status	Preschoolers	46	24.2
	No formal education	40	21
	Primary	71	37.4
	High school	16	8.4
	College and above	17	9
Source of light	Electric	115	60.5
	Kerosene	43	22.6
	Artificial solar	27	14.2
	Wood	5	2.7
Source of power for cooking			
Wood		185	97.4
Electric		82	43.2
Kerosene		40	21.1

5.3. Baseline clinical characteristics

Almost all of the patients presented with redness of eye/eyes 183(96.3%) that is why conjunctivitis is called the red eye. A significant number of study participants 163(85.8%) were presented with purulent discharge which is a common characteristic of bacterial conjunctivitis. The least common clinical feature was Chemosis 10(5.3%) of the involved eye/eyes (figure 4). Bilateral eye involvement was seen in 128(67.3%).

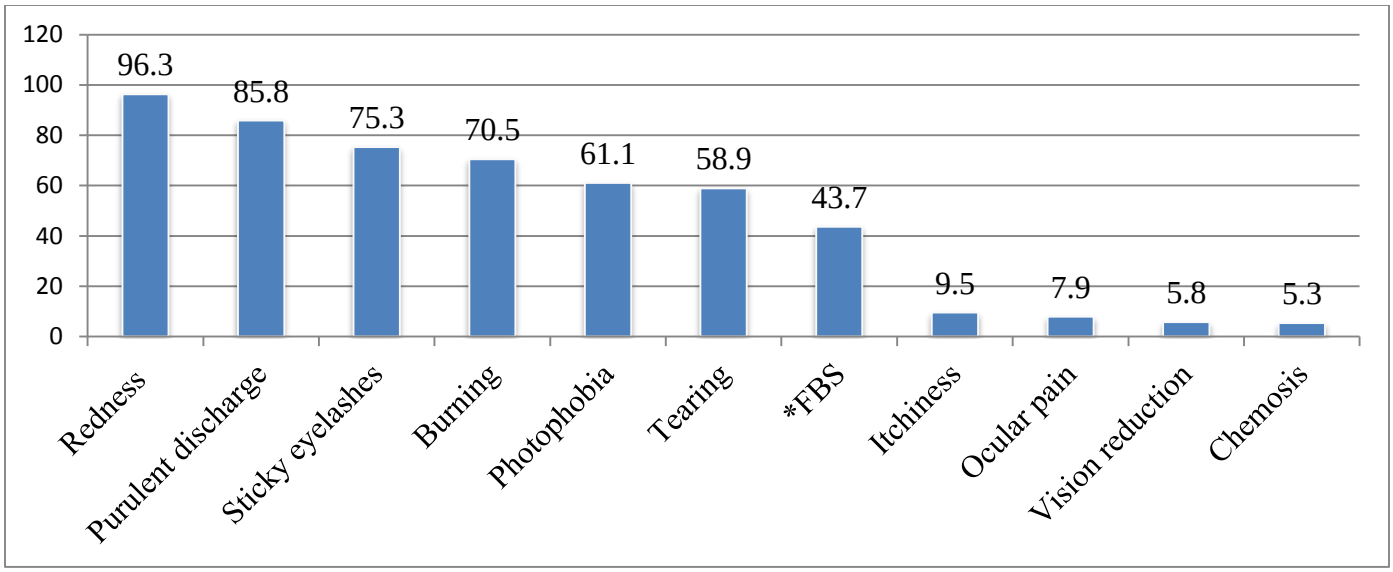


Fig. 4: Baseline clinical characteristics of patients with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January-June 2022.

**: Foreign body sensation*

5.4. Medical and Medication history

Out of 190 study participants, 65 (34.2%) of them had a history of chronic medical conditions with diabetes mellitus being the most common 28 (14.7%) followed by HIV/AIDS 19 (10%). History of systemic steroid use was recorded in 54 (28.4%) of study participants and 88 (46.3%) of study participants reported the use of traditional eye medicine (Table 3).

Table 3: Medical and medication history of patients diagnosed with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January - June 2022

Medical and Medication History	Category	Frequency	Percentage
Chronic diseases	Yes	65	34.2
	No	125	65.8
	Diabetes	28	14.7
	HIV/AIDS	19	10
	Hypertension	13	6.8
	Cardiac disease	8	4.2
	Kidney disease	9	4.7

	SLE	5	2.6
	Cancer	4	2.1
	RA	3	1.6
Systemic Steroids	Yes	54	28.4
	No	136	71.6
	Prednisolone	30	15.8
	Dexamethasone	17	8.9
	Hydrocortisone	7	3.7
TEM	Yes	88	46.3
	No	102	53.7

SLE: systemic lupus erythematosus; TEM: traditional eye medicine; RA: rheumatoid arthritis;

5.5 Prevalence of bacterial isolates

Among 190 conjunctival swabs cultured, 160 (84.2%) had bacterial growth. About three-quarters of bacterial isolates were gram-positive 124 (77.5%). *Coagulase-negative staphylococcus* was the most predominant 57 (35.6%) bacterial isolate followed by *S. aureus* 35(21.9%). The two common gram-negative bacterial isolates were *P. aeroginosa* 13 (8.1%) *and K. pneumoniae* 7 (4.4%) (Table 4).

Table 4: The prevalence of bacterial etiologies isolated from patients diagnosed with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January - June 2022.

Variable		Frequency (N=190)	Percentage
Bacterial growth		160	84.2
Gram-positive		124	77.5
	CoNS	57	35.6
	S. *aureus*	35	21.9
	S. *pneumonia*	26	16.3
	S. *pyogenes (group B)*	5	3.1
	S. *viridians (mutans)*	1	0.6
Gram-negative		36	22.5
	P. *aeruginosa*	13	8.1
	K. *pneumonia*	7	4.4
	E.coli	5	3.1
	K. *ozaenae*	2	1.3
	E. *aerogenes*	2	1.3
	P. *mirabilis*	2	1.3
	Acinobactersp	2	1.3
	H. *influenza*	2	1.3
	S. *maltophilia*	1	0.6

CoNS=Coagulase-negative staphylococcus

5.6. Antimicrobial susceptibility patterns among gram positive bacterial isolates

Antimicrobial susceptibility pattern were done on twelve antibiotics belonging to ten drug classes. Among gram-positive isolates, *Coagulase-negative staphylococcus* acquired a higher resistance rate to penicillin 55 (96.5%), ampicillin 54 (94.7%), and tetracycline 47 (82.5%). Likewise, *S. aureus* showed a high resistance rate to penicillin 34 (97.1%), ampicillin 33 (94.3%), and tetracycline 32 (91.4%). Both *Coagulase negative staphylococcus and S. aureus* maintained susceptibility to meropenem (71.9% and 74.3%) and piperacillin/tazobactam (68.4% and 71.4%) respectively (Table 5).

Table 5: Antimicrobial susceptibility patterns of gram positive isolates from patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January - June 2022.

		Antibiotics tested												
Bacterial isolate	**Pattern**	AMP N (%)	CIP N (%)	GEN N (%)	PCN N (%)	TTC N (%)	CAF N (%)	ERY N (%)	CLI N (%)	CEF N (%)	TMX N (%)	MER N (%)	PIP N (%)	Total
CoNS	R	54(94.7)	32(56.1)	37(64.7)	55(96.5)	47(82.5)	38(66.7)	41(71.9)	37(64.9)	36(63.2)	33(57.9)	16(28.1)	18(31.6)	57
	S	3(5.3)	25(43.9)	20(35.1)	2(3.5)	10(17.5)	19(33.3)	16(28.1)	20(35.1)	21(36.8)	24(42.1)	41(71.9)	39(68.4)	
S. *aureus*	R	33(94.3)	14(40)	21(60)	34(97.1)	32(91.4)	22(62.8)	20(57.1)	18(51.4)	19(54.3)	16(45.7)	9(25.7)	10(28.6)	35
	S	2(5.7)	21(60)	14(40)	1(2.9)	3(8.6)	13(37.2)	15(42.9)	17(48.6)	16(45.7)	19(54.3)	26(74.3)	25(71.4)	
S. *pneumonia*	R	24(92.3)	8(30.8)	17(65.4)	24(92.3)	22(84.6)	15 (57.7)	14(53.8)	12(46.2)	6(23.1)	9(34.6)	3(11.5)	4(15.4)	26
	S	2(7.7)	18(69.2)	9(34.6)	2(7.7)	4(15.4)	11(42.3)	12(46.2)	14(53.8)	20(76.9)	17(65.4)	23(88.5)	22(84.6)	
S. *pyogene*	R	4(80)	1(20)	2(40)	4(80)	2(40)	2(40)	2(40)	2(40)	1(20)	1(20)	1(20)	1(20)	5
	S	1(20)	4(80)	3(60)	1(20)	3(60)	3(60)	3(60)	3(60)	4(80)	4(80)	4(80)	4(80)	
S. *viridians*	R	_	_	_	1(100)	1(100)	1(100	1(100)	_	_	_	_	_	1
	S	1(100)	1(100	1(100)	_	_	_	_	1(100	1(100	1(100	1(100	1(100	

CoNS=Coagulase negative staphylococcus, S=Sensitive, R= Resistant, AMP = Ampcillin, CIP = Ciprofloxacin, GEN=gentamycin, PCN=penicillin, TTC=tetracycline, CAF=chloramphenicol, ERY=erythromycin, CLI=clindamycin, CEF=ceftriaxone, TMX= Trimethoprim-sulphamethoxazole, MER=meropenem, PIP= piperacillin/tazobactam.

5.7. Antimicrobial susceptibility pattern among gram negative bacterial isolates

Among gram negative bacteria, all identified isolates of *P. aeruginosa* 13(100%) were resistant to ampicillin, penicillin, and tetracycline; whereas, about half of them were susceptible to meropenem and piperacillin/tazobactam. All 7(100%) identified isolates of *K. pneumonia* were resistant to both penicillin and ampicillin (Table 6).

Table 6: Antimicrobial susceptibility patterns of gram negative isolates identified from patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January - June 2022.

		Antibiotics tested												
Bacterial isolate	Pattern	AMP N (%)	CIP N (%)	GEN N (%)	PCN N (%)	TTC N (%)	CAF N (%)	ERY N (%)	CLI N (%)	CEF N (%)	TMX N (%)	MER N (%)	PIP N (%)	Total
P.*aurogi nosa*	R	13(100)	12(92.3)	12(92.3)	13(100)	13(100)	10(76.9)	11(84.6)	12(92.3)	12(92.3)	11(84.6)	7(53.8)	6(46.2)	13
	S	_	1(7.7)	1(7.7)	_	_	3(23.1)	2(15.4)	1(7.7)	1(7.7)	2(15.4)	6(46.2)	7(53.8)	
K. *pneumo nia*	R	7(100)	5(71.4)	5(71.4)	7(100)	5(71.4)	5(71.4)	5(71.4)	5(71.4)	6(85.7)	6(85.7)	5(71.4)	5(71.4)	7
	S	_	2(28.6)	2(28.6)	_	2(28.6)	2(28.6)	2(28.6)	2(28.6)	1(14.3)	1(14.3)	2(28.6)	2(28.6)	
E. *coli*	R	5(100)	1(20)	2(40)	5(100)	5(100)	3(60)	3(60)	2(40)	2(40)	_	_	_	5
	S	_	4(80)	3(60)	_	_	2(40)	2(40)	3(60)	3(60)	5(100)	5(100)	5(100)	
K.ozaen	R	2(100)	_	1(50)	2(100)	2(100)	1(50)	1(50)	2(100)	_	2(100)	1(50)	1(50)	2

ae	S	_	2(100)	1(50)	_	_	1(50)	1(50)	_	2(100)	_	1(50)	1(50)	
E.*aerogenes*	R	2(100)	1(50)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	1(50)	2(100)	2
	S	_	1(50)	_	_	_	_	_	_	_	_	1(50)	_	
P.*mirabilis*	R	1(50)	1(50)	2(100)	2(100)	2(100)	2(100)	1(50)	1(50)	1(50)	1(50)	_	_	2
	S	1(50)	1(50)	_	_	_	_	1(50)	1(50)	1(50)	1(50)	2(100)	2(100)	
Acinobactersp	R	2(100)	1(50)	1(50)	2(100)	1(50)	1(50)	1(50)	1(50)	1(50)	1(50)	1(50)	1(50)	2
	S	_	1(50)	1(50)	_	1(50)	1(50)	1(50)	1(50)	1(50)	1(50)	1(50)	1(50)	
H. *influenza*	R	2(100)	_	_	2(100)	2(100)	_	_	_	_	_	_	_	2
	S	_	2(100)	2(100)	_	_	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	
S.*maltophilia*	R	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	_	1
	S	_	_	_	_	_	_	_	_	_	_	_	1(100)	

CoNS=Coagulase negative staphylococcus, S=Sensitive, R= Resistant, AMP = Ampcillin, CIP = Ciprofloxacin, GEN=gentamycin, PCN, PCN=penicillin, TTC=tetracycline, CAF=chloramphenicol, ERY=erythromycin, CLI=clindamycin, CEF=ceftriaxone, TMX= Trimethoprim-sulphamethoxazole, MER=meropenem, PIP= piperacillin/tazobactam, S.*maltophilia* =Stenotrophomonas *maltophilia*

5.8. Multidrug resistance patterns of bacterial isolate

From total of 160 bacterial isolates, 124 (77.5%) of them were found to be multidrug resistant. *Coagulase-negative staphylococcus* 48 (30%) and *S. aureus* 26 (16.3%) exhibited a higher rate of multi-drug resistance among gram-positive pathogens. Regarding gram-negative isolates, almost all identified *P. aeruginosa* 12 (7.5%) and K. *pneumoniae* 6 (3.8%) showed multi-drug resistance (Table 7).

Table 7: Multidrug resistance patterns of bacterial isolates collected from patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January - June 2022.

Bacterial isolate	**Resistance patterns**			
	R3	**R4**	**>=R5**	**Total**
CoNS	5(3.1)	4(2.5)	39(24.4)	48(30)
S. aureus	4(2.5)	-	22(13.8)	26(16.3)
S.*pneumonia*	2(1.3)	1(0.6)	15(9.4)	18(11.3)
S. *pyogene*	-	-	2(1.3)	2(1.3)
S.*viridians*	1(0.6)	-	-	1(0.6)
P. *aeroginosa*	-	-	12(7.5)	12(7.5)
K. *pneumonia*	1(0.6)	-	5(3.1)	6(3.8)
E. *coli*	-	-	3(1.9)	3(1.9)
K.*ozaenae*	-	1(.6)	1(0.6)	2(1.3)
E.*aerogenes*	-	-	2(1.3)	2(1.3)
P.*mirabilis*	-	1(0.6)	1(0.6)	2(1.3)
Acinobacter*sp*	-	-	1(0.6)	1(0.6)
S.*maltophilia*			1(0.6)	1(0.6)
Total	13(8.1)	7(4.4)	104(65)	124(77.5)

CoNS=Coagulase negative staphylococcus R3= bacterial isolate resistance to 3 antibiotics of different classes, R4= bacterial isolate resistance to 4 antibiotics of different classes, and >R5= bacterial isolate resistance to 5 and above antibiotics of different classes

5.9. Treatments of bacterial conjunctivitis

Topical ophthalmic eye drops and/or ointment were prescribed for all study participants.

Tetracycline 1% eye ointment 136 (71.6%) was the most frequently prescribed topical antibiotic.

Topical steroids were prescribed for 80 (42.1%) patients. Fortified antibiotics were prescribed for the majority 113 (59.5%). Prolonged duration of treatment (>21 days) was recorded among 21 (19.5%) and systemic antibiotics were prescribed for a few 17 (8.9%) of the study participants. (Table 8).

Table 8: Pharmacologic and non-pharmacologic management of patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January- June 2022

Treatments		Frequency (N=190)	Percent
Systemic antibiotics		17	8.9
	Amoxicillin/clavulanate	9	4.7
	Azithromycin	2	1.1
	Doxycycline	6	3.1
Topical antibiotics		190	100
	CIP0.3%+dexamethasone1%	70	36.8
	CIP 0.3% eye drop	79	41.6
	TTC 1% eye ointment	136	71.6
	GEN 0.3 % eye drop	27	14.2
Duration of treatment with topical antibiotics			
	1 week	56	29.5
	2 weeks	66	34.7
	3 weeks	31	16.3
	4 weeks	37	19.5
Topical steroids		80	42.1
	Dexamethasone	60	31.6
	Fluorometholone	20	10.5
Topical antipain	Flurbiprofen	15	7.9
Mydriatic agents		62	32.6
	Tropicamide	54	28.4
	Atropine	8	4.2
Fortified antibiotics		113	59.5
	Vancomycin eye drop 50mg/ml (5%)	81	42.6
	Gentamycin eye drop 14mg/ml	103	54.2

	(1.4%)		
Non pharmacologic treatment		39	20.5
	Lid hygiene	25	13.2
	Eyeglass	18	9.5

5. 10. Outcomes

5.10. A Treatment outcome

A total of 106 (55.8%) patients were improved or cured within 30-day of the follow-up period. However, the rest of them had persistent/worsened signs and symptoms of bacterial conjunctivitis.

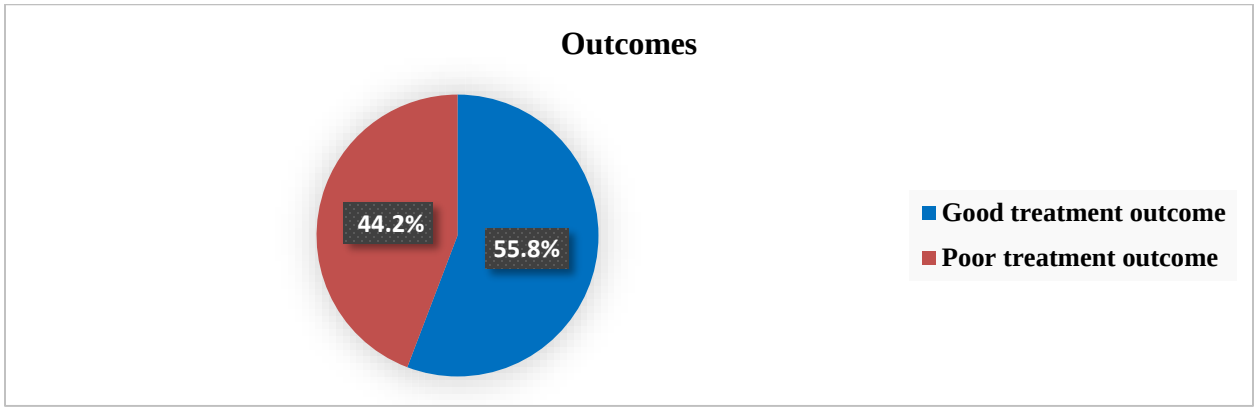


Fig. 5: Treatment outcomes of bacterial conjunctivitis at Ophthalmologic Clinic of JMC January-June, 2022

5.10. B Complications of bacterial conjunctivitis

Among a total of 190 patients who enrolled in this study, 34 (17.9%) of them developed complications from bacterial conjunctivitis. Out of these, blepharo-conjunctivitis 17 (8.9%) was the most commonly observed complication *(*Figure 5).

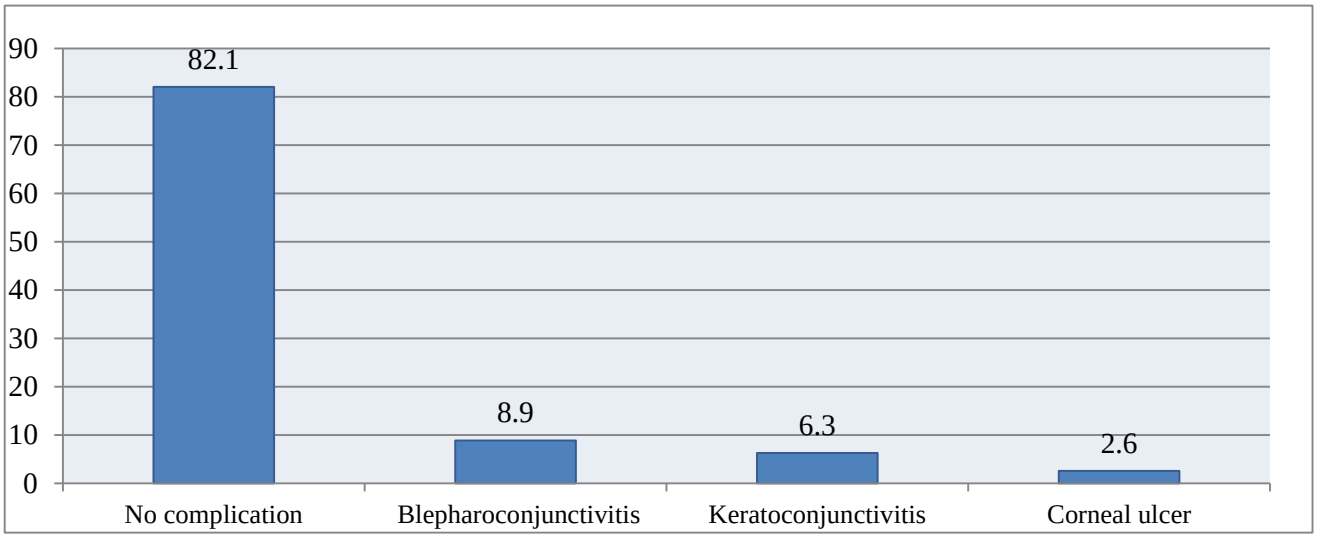


Fig. 6: Types of complications developed during follow-up among patients with bacterial conjunctivitis at Ophthalmologic Clinic of JMC, January-June 2022

5.10. C Factors associated with treatment outcomes

Nine Variables having a p-value of < 0.25 in the bivariate analysis were subjected to multivariable analysis to identify independent predictors of poor treatment outcomes. Among these, seven variables showed significant association with poor treatment outcome. These variables were, chronic diseases [AOR=11, 95%CI (2.8-43) p= 0.001], TEM use [AOR=3.7, 95%CI (1.3-10) p= 0.017], infection with CoNS [AOR = 4.2, 95%CI (1.4-12) p= 0.009], treatment with Zoxan D [AOR =10, 95%CI (3-30) p< 0.001], topical steroids[AOR =14, 95%CI 4-48) p<0.001] and fortified antibiotics[AOR=10, 95%CI (3-35) p<0.001] and non-adherence to a treatment regimen [AOR= 3.3, 95%CI (1.1-9.5) p= 0.027] (Table 9).

Table 9: predictors of poor treatment outcomes among patients diagnosed with bacterial conjunctivitis presented at Ophthalmologic Clinic of JMC, January - June 2022.

Variables	**Category**	**Treatment outcome**		**Bivariate Analysis**		**Multivariate analysis**	
		Good	**poor**	**COR (95%CI**	**P- value**	**AOR (95%CI)**	**P- value**
Kerosene	Yes	16	24	2.3[1.1,4.6]	0.026	1.3[.4,5]	0.654
	No	90	60	1			
*Chronic diseases	Yes	14	51	10.2[5,20.7]	<0.001	11[2.8,43]	0.001
	No	92	33	1			
Systemic steroids	Yes	19	35	3.3[1.7,6.3]	<0.001	1.1[.2,4.8]	.935
	No	87	49	1			
*TEM	Yes	36	52	3.2[1.7,5.7]	<0.001	3.7[1.3,10]	.017
	No	70	32	1			
*CoNS	Yes	17	40	4.8[2.4,9.3]	<0.001	4.2[1.4,12]	.009
	No	89	44	1			
*Zoxan D	Yes	20	50	6.3[3.3,12.2]	<0.001	10[3,30]	<0.001
	No	86	34	1			
*Topical steroids	Yes	23	57	7.6[4,14.6]	<0.001	14[4,48]	<0.001
	No	83	27	1			
*Fortified antibiotics	Yes	49	64	3.7[2,7]	<0.001	10[3,35]	<0.001
	No	57	20	1			
*Adherence	Adherent	86	29	1			
	Non adherent	20	55	3.7[2,6.8]	<0.001	3.3[1.1,9.5]	0.027

* *=value statistically significant AOR= Adjusted Odds ratio COR= Crude odds ratio TEM= traditional eye medicine 1= reference Zoxan D= ciprofloxacin 0.3% + Dexamethasone 0.1% Hosmer and Lemeshow test= 0.4*

6. DISCUSSION

The overall prevalence of bacterial growth in the present study was 84.2%. This finding was comparable to previous studies from JMC and Saudi Arabia which reported 74.7% ([8]) and 78.7% ([79]) respectively. However, relatively lower bacterial growth rates (46.1% to 66.7%) were reported from different studies conducted in different parts of Ethiopia ([32, 46, 66, 67, 80]). This discrepancy might be due to differences in the study population, geographic location and climate, specimen collection procedure, eligibility criteria and transportation methods.

The leading bacterial isolates from bacterial conjunctivitis were gram-positive cocci. This is supported by numerous prior studies from Ethiopia including, Jimma ([8]), Borumeda ([66]), Gondar ([39]), southern Ethiopia ([81]), and other countries like Nigeria ([82]), Japan ([83]) and Rwanda ([84]). Among gram-positive, *CoNS* was the most predominant pathogen in this study with an overall prevalence of (35.6%). This finding was in line with studies conducted in Gondar (27.4%) ([65]), Rwanda (51.4%) ([84]), and Uganda (65.9%) ([85]) which reported a higher rate of CoNS among identified bacteria. In the past, CoNS has been overlooked as a cause of severe infections since it was considered normal flora. Recently, *CoNS* has emerged as a significant source of nosocomial bloodstream infections in recent years, owing to an increased usage of intravascular devices and an increase in the number of hospitalized immunocompromised patients ([86]).

In regards to AMR, *CoNS* (96.5%), (94.7%), (82.5%) and *S.aureus* (97.1), (94.3%), (91.4%) had a higher resistance rate to penicillin, ampcillin, and tetracycline respectively. However, significant number of *CoNS* (71.9%), (68.4%) and *S.aureus* (74.3%), (71.4%) were susceptible to meropenem and piperacillin/tazobactam respectively. This finding is comparable to a study conducted at Felege Hiwot Hospital which showed similar pattern of resistance of *CoNS* (94.8%), (93.7%) and S.aureus (96.1%), (96.1%) to penicillin and ampicillin respectively ([33]).

Among gram-negative pathogens, all identified isolates of *P. aeruginosa* were resistant to ampcillin, penicillin and tetracycline; whereas, about half of them were susceptible to meropenem and piperacillin/tazobactam. Furthermore, all identified isolates of *K. pneumonia* were resistant to both penicillin and ampcillin. This finding was similar to studies conducted at Felege Hiwot and Menelik II Hospital which reported a 100% resistance rate of *K. pneumonia to* ampicillin ([33, 67]. Self-medication, misuse of antibiotics, and improper preparation of fortified antibiotics with low adherence to treatment regimens might have played a significant role in the emergence of resistant pathogens.

The prevalence of multidrug resistance (resistance to three or more than three antimicrobials) in the present study was 77.5%. This is higher than the previous study done in the same setting where the rate of MDR was reported to be 68.7% ([8]. However, the rate of MDR observed in this study is lower compared to studies conducted at Gondar ([65]) and Alert Hospital ([80]) which reported MDR rates of 87.1% and 93.0% respectively. This difference might be due to the difference in the operationalization of the term multidrug resistance because those studies defined it as a resistance to two or more antibiotics. In general emergence of MDR bacteria is increasing steadily which indicates the urgent need for antimicrobial stewardship and infection prevention and control practice in the hospital.

Regarding treatment outcomes, almost half (44.2%) of patients with bacterial conjunctivitis had poor outcomes (worsened or persistent symptoms). This finding was unlike other studies which reported that conjunctivitis had a good prognosis with almost half of the cases being self-limiting ([2, 35, 36]). The difference is probably because this study was conducted at a tertiary eye care hospital that treats patients with severe ocular diseases. On top of that, a significant number of patients were presented after trying traditional eye medicines and they have one or more

comorbid conditions such as diabetes, hypertension, and HIV/AIDS which contributed to poor patient outcomes. In the presenting setting, the treatment of bacterial conjunctivitis was empirical and common pathogens such as *CoNS* and *S aureus* had already developed resistance to commonly prescribed antibiotics. Therefore, we recommend that empiric treatment should be guided by microbiological test results.

In the present study, factors associated with poor treatment outcomes were presence of comorbid conditions, history of TEM, CoNS infection, treatment with Zoxan D, topical steroids and fortified antibiotics and non-adherence to a treatment regimen. Prior studies have also identified diabetes as a major risk factor for bacterial conjunctivitis ([87] and reported that diabetes results in fragile epithelial and poor wound healing that increase the risk of corneal erosions and persistent eye infections such as conjunctivitis ([88]. HIV/AIDS especially those who have low CD4 count had a higher risk of developing conjunctivitis with poor treatment outcomes ([89].

About 46% of the study participant used TEM and they had four times more likely to have a poor prognosis compared to none users. This finding is concordant with the studies conducted in South Africa and rural India which reported that 50.0% and 61.4% of patients visiting eye clinics use traditional medication respectively ([90, 91]. Ample evidence are available regarding the deleterious effect of unsupervised TEM use ([92-94]. Proposed mechanisms are reduction in the number of bulbar conjunctival goblet cells, introducing high microbial load (lack of aseptic technique during preparation), and the direct toxic effect they may cause corneal epithelial breakdown and thus aid in bacterial penetration to deeper corneal layers, which overall scales up disease severity and impair the healing process ([93, 94]).

A combination of topical steroids and antibiotics in the treatment of bacterial conjunctivitis was associated with poor outcomes in the present study. Available evidence in this area are limited and controversial. Also, management guidelines recommend against the use of corticosteroids in bacterial conjunctivitis ([2, 36], review of available evidence suggests that a combination of steroids with anti-infective, could be a promising treatment option for acute conjunctivitis ([13]. This issue is also controversial in bacterial keratitis that review of four clinical trials to date showed that a combination of steroids with anti-infective has no benefit or adverse effect compared to a placebo ([95]. This study is not powered enough to recommend against the use of combination of steroids with anti-infective. So, we recommend further studies to clarify the benefit and negative impact of topical corticosteroids in bacterial conjunctivitis.

Study participants who were taking fortified antibiotics experienced poor treatment outcomes as compared to those who didn't and this distinction could be explained by breaks in the aseptic technique during preparation and improper storage condition experienced by our staff. Fortified eye drops should be prepared by a pharmacist in a sterile pharmaceutical dispensary. Since there is a risk of contamination, because it is preservative free, it should be refrigerated at 4°C and can be used for a maximum of seven (7) days once prepared ([96]. In contrast to this guideline, in our clinic, fortified antibiotics were prepared by non-pharmacy professionals (nurse professionals), there was a breakage in a sterile procedure as antibiotics were prepared at OPD and in a ward which paves the way for bacterial contamination and these products were not kept in the refrigerator which threatens these products effectiveness. Additionally, these products were used for longer periods usually for more than 2 weeks. The fortified stock solution of vancomycin is prepared by adding 33 ml of 0.9% sodium chloride for injection and artificial tears to 500 mg

vials of vancomycin to produce a solution of 15 mg/ml ([96]). But in our setting artificial tear is not part of the procedure.

Strengths and limitations

The present study prospectively enrolled patients with bacterial conjunctivitis and laboratory specimens were collected following standard procedure. This study also followed patients for 30-day and recorded treatment outcomes and important variables that had impact on patient outcomes. Moreover, this research provided the recent trend of antimicrobial resistance in bacterial conjunctivitis that can be used by ophthalmologists and healthcare providers to tailor patient treatment and clinical guidelines accordingly. However, this study has also limitations. First of all, the sample size was small which will affect the generalizability of our studies to a large population. Second, important antibiotics such as vancomycin, tobramycin, amikacin, amoxicillin clavulanate, cefepime, methicillin, and others were not included in AMR tests in the present study. Finally, bacteria that are not easily cultured by routine laboratory diagnoses such as Chlamydia trachomatis, Corynebacterium species, and anaerobic bacteria were not investigated due to financial issues.

7. CONCLUSION

The prevalence of bacterial isolates from conjunctival specimens among patients with bacterial conjunctivitis was high in the present study area and the isolates were predominantly gram-positive cocci (*CoNS* and *S. aureus).* The two common gram-negative bacteria identified were *P. aeroginosa and K. pneumoniae.* Over three quarters of bacterial isolates were multidrug-resistant and a high resistance rate was observed to frequently used antibiotics for ocular infections such as ciprofloxacin, gentamycin, and tetracycline. Meropenem and piperacillin/tazobactam were the two effective antimicrobials against most gram positive and gram negative bacteria in the present study area.

Nearly half of the patients had poor treatment outcomes. Factors associated with poor outcomes in this study were the presence of comorbid conditions, TEM use, CoNS infection, topical steroid use, fortified antibiotics use, and non-adherence to the treatment regimen. A significant number of study participants developed complications such as blepharoconjunctivitis, keratoconjunctivitis, and corneal ulcers.

8. IMPLICATION FOR QUALITY IMPROVEMENT

- We recommend Ophthalmologists to give attention to gram-positive cocci (CoNS and *S.aureus*) and guide empiric treatment of bacterial conjunctivitis with microbiological test results as a significant number of patients had poor outcomes.
- It is better if JMC Ophthalmologic clinic and pharmacists collaborate to provide training on the safe preparation, storage and, use of fortified antibiotics.
- We recommend Ophthalmologists and other healthcare professionals create awareness for the community regarding the negative impact of traditional eye medicine.
- In general emergence of MDR bacteria is steadily increasing. Therefore we recommend JMC strengthen antimicrobial stewardship and infection prevention and control practice in the hospital.
- We recommend further studies to clarify the benefit and negative impact of topical corticosteroids in the management of bacterial conjunctivitis.
- It is better if MoH and EFDA conduct a nationwide surveillance on AMR
- We recommend JMC to develop local guidelines on treatment of common eye infections including bacterial conjunctivitis.

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10. Annexes

Annex I English version Questionnaire
Information sheet English version

JIMMA UNIVERSITY

Institute of Health

School of pharmacy

Clinical pharmacy course team

TITLE: BACTERIAL PROFILE, ANTIMICROBIAL SUSCEPTIBILITY, AND TREATMENT OUTCOMES OF BACTERIAL CONJUNCTIVITIS AMONG PATIENTS TREATED AT THE OPHTHALMOLOGIC CLINIC OF JIMMA MEDICAL CENTER, ETHIOPIA

Name of advisors:

Mr. Korinan Fanta

Dr. Jafer Kedir

Sponsor: Mettu University

Benefits for participants

Study participants doesn't have any financial incentives or other inducements from participating in this study and the result of the study will be beneficial for planning, screening or prevention strategies of disease.

Risks and complication

There are no anticipated risks to your participation

Confidentiality

On the request paper your name or your identities will not be mentioned and any information given to me will remain confidential and your privacy will be respected.

Right to refuse or withdraw

I have read and I understand the provided information and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without cost. I understand that I will be given a copy of this consent form. I voluntarily agree to take part in this study.

Person to contact

If you have any questions about this study you should feel free to ask now or anytime throughout the study by contacting:

PI Address::school of pharmacy, Jimma University, Jimma, Ethiopia

Cell phone: +251912275694

Email: eyosiasteklemariam77@gmail.com

Date of interview……. Signature ----------

 Interviewer name…… Code ----------

Consent form

I am informed fully in a language I understand about the aim of the above mentioned research. I understood the purpose of the study entitled **BACTERIAL PROFILE, ANTIMICROBIAL SUSCEPTIBILITY, AND TREATMENT OUTCOMES OF BACTERIAL CONJUNCTIVITIS AMONG PATIENTS TREATED AT THE OPHTHALMOLOGIC CLINIC OF JIMMA MEDICAL CENTER, ETHIOPIA**

I have been informed this study which involves collecting conjunctival swab sample. I have also read the information sheet or it has been read to me. In addition I have been told all the

information collected throughout the research process will be kept confidential. I understood my current and future medical services will not be affected if I refuse to participate or withdraw from the study. I----------, after being fully informed about the detail of this study, hereby gave my consent to participate in the study and approve my agreement with signature.

Patient name---------- Signature ---------- Date ----------

Investigator name----------Signature----------Date----------

1. SOCIO DEMOGRAPHIC CHARACTERISTICS AND PATIENT IDENTIFICATION.		
Sr. No	Background information	
	Questions	Response
1	Patient Card No.	
2	Age in years	
3	Gender	1. Male 2. Female
4	Residence	1. Rural 2. Urban
5	Educational status	1. Preschool 2. No formal education 3. Elementary 4. Secondary 5.College and above
6	What is the source of light in your home at night?	1. Wood 3. Kerosene 2. Electric 4. Artificial solar
7	What is the source of power for cooking in your home?	1. Wood 3. Kerosene 2. Electric

2. BASELINE CLINICAL MANIFESTATIONS		
1.	What are the clinical characteristics at baseline?	1. Redness 2. Burning 3. Tearing 4. Itching 5. Foreign body sensation 6. Photophobia 7. gluey or sticky eyelids/eyelashes in the morning 8. Purulent conjunctival discharge 9. Others
2.	Which eye is involved?	1. Right 2. Left 3. Both
3. CLINICAL HISTORY		
1.	Do you have chronic medical condition?	1. Yes 2. No
2.	If yes to the above question, Which of the following medical conditions do you have?	1. Rheumatoid Arthritis 2. HIV/AIDS 3. Diabetes 4. Systemic cancer 5. Cardiac diseases 6. SLE 7. Hypertension 8. CKD
3.	Are you currently taking systemic steroids?	1. Yes 2. No
4.	If yes is the response to the above question, which of the followings are you taking?	1. Dexamethasone 2. Prednisolone 3. Hydrocortisone 4. Others
5.	Do you use traditional eye medicine?	1. Yes 2. No

4. LABORATORY DATA COLLECTION FORMAT		
s. no	Question	Response
1	Patient ID	
3	Date of sample collection	
5	Type of diagnosis	Bacterial conjunctivitis
7	Culture growth	1. Yes 2. No
6	If yes to culture growth, what is the gram stain result?	1. Gram positive 2. Gram negative
8	If the bacterium is isolated, what is the name of the isolate?	

1. Antimicrobial susceptibility testing	**S (mm)**	**I(mm)**	**R (mm)**
Ampcillin (AMP) (10µg)	----------	----------	----------
Ceftriaxone (CRO) (30µg)	----------	---------	----------
Chloramphenicol (C) (30µg)	----------	----------	----------
Ciprofloxacin (CIP) (5µg)	----------	----------	----------
Clindamycin (CLN) (2µg)	----------	----------	----------
Erythromycin (ERY) (15µg)	----------	---------	----------
Gentamicin (CN) (10 µg)	----------	----------	----------
Penicillin (PE) (10 IU)	----------	----------	----------
Tetracycline (TE) (30µg)	----------	----------	----------
Trimethoprim-Sulfamethoxazole (SXT) (1.25µg)	----------	----------	---------
Piperacillin/tazobactam	----------	---------	---------
Meropenem	----------	------	----------

5. TREATMENT PART		
S.	**Questions**	**Response**

no		
1	Was there any systemic antibiotics prescribed for the patient?	1. Yes 2. No
	If yes to the above question, which one was prescribed for the patient (write the name dose, frequency and duration of treatment)?	1. Amoxicillin-Clavulinic 2. Doxycycline 3. Azithromycin
	Which of the following topical antimicrobial agent/agents is/are being taken?	1. Ciprofloxacin/Dexamethasone eye drop 2. Ciprofloxacin eye drop 3. Tetracycline eye ointment 4. Gentamycin eye drop
	What is the duration of treatment?	1. One week 2. Two weeks 3. Three weeks 4. Four weeks
	Was any topical steroid prescribed for the patient?	1. Yes 2. No
	If yes to the above question, which one of the following was it?	1. Dexamethasone eye drop 2. Fluorometholone
	Was any mydriatic agent prescribed for the patient?	1. Yes 2. No
	If yes to the above question, which mydriatic agent was it?	1. Tropicamide 2. Atropine
	Was there any topical antipain prescribed?	1. Yes 2. No
	If yes to the above question, which topical antipain was it?	1. Flurbiprofen 2. Others
	Was there any Fortified Antibiotics prescribed?	1. Yes 2. No
	What are the used for treatment?	1. Vancomycin eye drop 50mg/ml (5%) 2. Gentamycin eye drop 14mg/ml (1.4%) 3. Both
	Is there any non-pharmacologic intervention?	1. Yes 2. No
	If yes to the above question, Which non-pharmacological intervention is given for the patient?	1. Lid hygiene 2. Eye glasses

FOLLOW UP CHART AND LOST TO FOLLOW-UP

6A. OUTCOME MEASURE		Date	Date	Date	Date
Primary outcome measures	Response status	visit 1	Visit 2	Visit 3	Visit 4
1.	Cured				
2.	Improved				

3.	Stable				
4.	Worsened				

6B. COMPLICATIONS OF BACTERIAL CONJUNCTIVITIS		
1.	Does the patient develop complication	1. Yes 2. No
2	If yes, which of the following complications did the patient experienced?	1. Blepharo-conjunctivitis. 2. Keratoconjunctivitis 3. Corneal ulcer
6C. MEASURE OF ADHERENCE TO MEDICATIONS AND LOSS TO FOLLOW-UP		
1.	Are you taking the medication prescribed for you appropriately?	1. Yes 2. No
2.	If No to the above question how much dose did you miss?	
3.	Why you missed to take your medication?	1. Un availability of medication 2. Forgetfulness 3. Side effects (toxicities) 4. Expensiveness of medication 5. Others(specify)----------
4.	If you feel better do you stop taking your medications	1. Yes 2. No

Annex IIAmharicversion Questionnaire

አባሪII፡ተሳታፊመረጃወረቀት
ጂማ ዩኒቨርሲቲ

የጤና እንስቲትዩት የፋርማሲ/ቤት

ክሊንካልፋርማሲኮርሥቲም

ርዕሥ: BACTERIAL PROFILE, ANTIMICROBIAL SUSCEPTIBILITY, AND TREATMENT OUTCOMES OF BACTERIAL CONJUNCTIVITIS AMONG PATIENTS TREATED AT THE OPHTHALMOLOGIC CLINIC OF JIMMA MEDICAL CENTER, ETHIOPIA

የ አማካሪዎችስምዝርዝር:

አቶኮሪናንፋንታ

ዶርጃፈርከድር

ስፖንሰር: መቱ ዩኒቨርሲቲ

የጥናቱ ሂደት
ለያንዳንዱተሳታፊየተቀነባበረቃለመጠይቅይደረግላቸዋል፤፤

የታካሚዉንጥቅምበተመለከተ

ማንኛዉምታካሚምንምአይነትየገንዘብድጎማአያገኝም፤፤.
ነገርግንበሚደረገዉየምርመራዉጤትላይተመሥርቶትክክለኛዉንህክምናያገኛል፤፤

የተሳታፊዉንስጋትበተመለከተ

ይህጥናትበተሳታፊዎችላይምንምአይነትጉዳትአያደርሥም ።

ምስጢራዊነት

የያንዳንዱታካሚምሥጢርእናግላዊነትበጥብቅየተጠበቀነዉ፤፤

የታካሚዉ መብት

ማንኛዉምታካሚበጥናቱእላይያለመሳተፍመብቱየተጠበቀነዉ፤፤
በዬትኛዉምጊዜጥናቱንለቆየመውጣሙሉመብትአለዉ፤በዚህምምንምአይነትችግርአይደርሥበትም፤፤

የተመራማሪዉ አድራሻ::ጂማ

ስልክ: +251912275694

የኢሜይል አድራሻ: eyosiasteklemariam77@gmail.com

የቃለመጠይቅ ቀን…… ፊርማዉ---------- የጠያቂዉ ስም…… ኮድ----------

<u>የስምምነት ቅጽ</u>

የጥናቱዓላማበደንብመረዳትበሚችለዉቋንቋተነግሮኛል፤፤ **“BACTERIAL PROFILE, ANTIMICROBIAL SUSCEPTIBILITY, AND TREATMENT OUTCOMES OF BACTERIAL CONJUNCTIVITIS AMONG PATIENTS TREATED AT THE OPHTHALMOLOGIC CLINIC OF JIMMA MEDICAL CENTER, ETHIOPIA**

“ዓላማተረድቸዋለሁኝ፤፤በዚህጥናትከዓይንናሙናእንደሚወሰድተነግሮኛል፤፤ህንንቅጽአንብበዋለሁኝ/ተነቦልኛል፤፤በተጨማሪምበጥናቱ ላይስለኔየሚሰበሰበውመረጃበሚሥጥርእንደሚያዝአስረድተዉኛል፤፤በጥናቱላይባልሳተፍወይምጥናቱንአቋርጩብወጣበሚሠጠኝየህክምና ገልግሎትላይምንምአይነትተፅዕኖእንደሌለዉተረድቸዋለሁኝ፤፤. እኔ----------,
ስለጥናቱበዝርዝርበመረዳትበጥናቱላይለመሳተፍፈቃደኛመሆኔንበፊርማዬአረጋግጣለሁኝ፤፤

የታካሚዉስም_____ፊርማዉ_____ቀን_____

የተመራማሪዉ ስም_____ ፊርማዉ _____ ቀን _____

QUESTIONNAIRE PART 1, 3, and 6CAMHARIC VERSIONS.

ትእዛዝ፡ ከተዘጋጁምረጫዎችአንዱንምረጥወይምበተዘጋጀቦታላይጻፍ

ተ.ቁ	**1. ማህበራዊ መረጃዎች**	
	ጥያቄ	**መልስ**
1	የህመምተኛዉየካርድቁጥር	
2	ዕድሜ	
3	ፆታ	1.ወንድ 2. ሴት
4	የመኖርያ አድራሻ	1. ገጠር 2. ከተማ
5	የትምርት ሁኔታ	1. ያልተማረ/ች 2. ዕድሜዉ/ዋ ያልደረሰ 3. አንደኛ ደረጃ 4. ሁለተኛ ደረጃ 5. ሶስተኛ ደረጃ
6	በቤታችዉየብረሃንምንጭምንድንነዉ?	1. እንጨት 2. ኩራዝ 3. ኤላክትሪክ 4. ሰው ሠራሽ ብርሀን
7	በቤታቸዉምግብለማብሰልየሚጠቀሙትምንድንነዉ?	1. እንጨት 2. ቡታጋዝ 3.ኤላክትሪክ
3.**የህክምና መረጃ**		
1	ከነዚህበሽታዎችዬትኛዉንአለቦት?	1. ሬሁማቶይድ አርትራይተስ 2. ኤድስ 3. የስኮር በሽታ 4. ካንሠር 5. የልብ በሽታ 6. ሉፐስ 7. የደም ግፊት 8. የኩላሊት በሽታ 9. የለብኝም
2	ሲስተሚክስቴሮድሥእየተጠቀሙነዉ?	ነ. አዎ 2.አይ

5	ለዓይንህ/ሽየባህልመድሐኒትወስደህ/ታዉቃለህ/ሽ?	ነ. አዎ 2.አይ
QUESTIONNAIRE PART 6C: ABOUT ADHERENCE TO MEDICATIONS		
1	መድኃኒቱንበአግባቡአየወሰዱነዉ?	ነ. አዎ 2.አይ
2	መልሥዎ2ከሆነምንያክልጊዜዘለዋል?	----------
3	መድሃኒትዎንለምንአልወሰዱም?	ሀ)የመድኃኒት እጥረት ለ)መርሳት ሐ)የጎንዮሽ ጉዳቶች መ)የመድኃኒት መወደድ ሠ)ሌሎች(ይጥቀሱ) ---------
4	ጥሩስሜትከተሰማዎትመድኃኒቶዎንመውሰድያቆማሉ	ነ. አዎ 2.አይ

አመሰግናለሁኝ፤

Annex III Afan Oromo version Questionnaire
Information sheet Afan Oromo

YUNIVARSIITII JIMMAA

Instiitiyuutiifayyaa, ManabaruumsaaFaarmaasii, KilinikaalFaarmaasii

Title: Bacterial profile, antimicrobial susceptibility, and treatment outcomes of bacterial conjunctivitis among patients treated at Jimma medical center ophthalmology clinic, Ethiopia

Maqaagorsitootaa: ObboKoorinaanFaantaa **fi** Dr. JaafarKadir

Ispoonsara: Mattuuyunivarsiitii

Adeemsaqorannichaa- Hirmaattotaafgaaffiifdeebiinnitassifamaaf.

Faayidaahirmaattotaailaalchisee-Hirmaataankamiyyuuqarshiihinargatu.Haatahumalee, qorannoorrattihundaayeeyaaliigaariinnitaasifamaaf.

Miidhaaqorannichaa-QorannoonKunMiidhaahingeessisu.

IccitiieeguuIccittiinhirmaattotaahaalanKaneegamuudha.

MirgadiduuyknqorannooaddaankutuuAdeemsaqorannoorrattiyerookamiyyuuaddaankutuunyk ntasumahirmaachuudhiisuunnidandahama.**Teessooqorataa**:Jimma

Lakk.Bilbilaa: +251912275694

Email: eyosiasteklemariam77@gmail.com

GuyyaaGaaffiifdeebii……. Mallattoo----------

Maqaagaaffataa…… koodii----------

GucawaliigalteeAfaanOromootin

Kayyoonqorannookanaaloqodanhubachuudanahuunnaafibsameera. **BACTERIAL PROFILE, ANTIMICROBIAL SUSCEPTIBILITY, AND TREATMENT OUTCOMES OF BACTERIAL CONJUNCTIVITIS AMONG PATIENTS TREATED AT THE OPHTHALMOLOGIC CLINIC OF JIMMA MEDICAL CENTER, ETHIOPIA** isaas haalan hubadheera.Qorannoonkunnaamudaaijarraafudhatamuakkabarbaachisuhaalaannaafibsameera.Waraqaa kanahaalaandubbiseeraykknaafbubbifameera.Dabalataanoddeeffannowwanyerooqorannookanaattiguuram aniccittiinakkaeegamunaafhimameera.Yeroonbarbaadeyoonqorannookanakeessaabahehaallitajaajilummaa fayyaakootasumaakkahinmiidhamne hubadheera.ani_____,haalajiruhundaerganhubadheebooda,hayyamummaakootiinqoran nookanarrattifedhiikoonhirmaachuukootiifmallattookoonmirkaneesa.
Maqaadukkubsataa_____Mallattoo_____Guyyaa_____

Maqaaqorataa_____Mallattoo_____Guyyaa_____
QUESTIONNAIRE PART 1, 3, AND 6C: AFAN OROMO VERSION

B. **GaragalchaGaaffii Afaan Oromoo**

Sr. No	**ODEEFFANNOO HAWWASUMMAA**	
	Gaaffii	**Deebii**
1	Lakk. Kaardiidhukkubsata	
2	Umrii(waggaan)	
3	Saala	1. Dhiira 2. Dubara
4	Iddoojireenyaa	1. Baadiyyaa 2. Magaala
5	Haalabaruumsaa	1. Kanhinbaranne 2. barressuufdubbisuukandandahu 3.umriin hingeenye 4. sadarkaa 1ffaa 5.sadarkaa 2ffaa 6. sadarkaa 3ffaa

6	Maddiifamanakeettifayyadamtumaali?	1. Qoraan 2. Kurraazii 3. Elektirikii 4. Soolarii
7	Nyaatabilcheessuufmaalfayyadamtu?	1. Qoraan 2. Buttaagaazii 3. Elektirikii
3.RAGA FAYYAA		
2	Dhukkubaqaamamiidhankamqabdan?	1. Qurxumaata 2. Eedsii 3. Dhibeesukkaara 4. kaanserii 5. Dhibeeonnee 6. Luupasii 7. Dhiibbaadhiigaa 8. Dhibeekalee 9. hinqabu
5	Siistemiikisteeroyidiifayyadamaajirtaa?	1. Eeyyee2. Lakki
	Ijakeefqorichaaaadaafudhatteejirtaa?	1. Eeyyee 2. Lakki
6C.GAAFIWWAN HAALA QORICHA ITTI FUDHATAN MADAALUF QOPHAAYE		
2	Qorichasiifajajameakkaataasittihimameensirriittifudhachaajirtaa?	1. Eeyyee 2. Lakki
3	Yoohinfudhanneta'ehangamotoohinfudhatinhafte?	----------
4	Maaliifhinfudhatin	1. Sababaqorichidhabameef 2. Waaninirraanffadhuuf 3. Miidhaaqaamakiyyairraanwaangayuuf D. Gatiinisaawaanqaala'uuf E.Kanbirooyoojiraate (ibsi)……
	Yoodhukkubnikeesittifooyya'uqorichakeeaddaankuttaa?	1. Eeyyee 2. Lakki

Maqaaqorataa _____ Mallattoo _____ Guyyaa _____

GALATOOMAA