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Bacteriological pattern and their correlation with complications in culture positive cases of acute bacterial conjunctivitis in a tertiary care hospital of upper Assam

A cross sectional study

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Abstract

Acute conjunctivitis is inflammation of conjunctiva of less than 3 to 4 weeks duration, characterized by cellular infiltration and exudation. It may also result into corneal, lid or orbital involvement which may lead to various complications.

A hospital based prospective study was conducted in Assam Medical College and Hospital with 110 culture proven acute bacterial conjunctivitis cases. Primary objective was to evaluate the bacteriological pattern and secondary objectives were to evaluate seasonal variation, association of different organisms with various complications and antibiotic sensitivity pattern of the isolates.

Maximum frequency of bacterial conjunctivitis observed from May to September. SA was the predominant organism isolated throughout the year (32.1%). Commonest single organism isolates were SE (26.1%) and SA (21.6%). True membrane formation was significantly associated with CD ($P < .05$), whereas pseudo-membrane formation was associated with SA and STBH isolation ($P < .05$). Isolation of SE, SA, and PA was associated with corneal involvement ($P < .05$). Lid involvement was seen with SA and Diphtheroid, whereas SP isolation was associated with concomitant dacryocystitis ($P < .05$). All the major organisms were (SE, SA, D, STBH, SP) highly sensitive to amino-glycosides, cephalosporins, chloromphenicol, vancomycin and linezolid, whereas high level of resistance was seen towards fluroquinolones (ciprofloxacin and moxifloxacin).

All acute bacterial conjunctivitis cases don't require antibiotic therapy. In case if required, periodical culture and sensitivity may guide initial pre-emptive antibiotic therapy. Further choice of antibiotic should be govern by culture and sensitivity status.

Abbreviations: CD = corynebacterium diphtheriae, D = diphtheroid, E = enterobacter, EC = Escherichia coli, HI = hemophilus influenza, K = klebsiella, MC = Moraxella catarrhalis, MRSA = methicillin resistant staph aureus, NG = neisseria gonorrhoea, PA = pseudomonas aeruginosa, SA = staph aureus, SE = *staphylococcus epidermidis*, SP = *streptococcus pneumonia*, STBH = streptococcus beta hemolyticus.

Keywords: acute bacterial conjunctivitis, antimicrobial sensitivity, bacterial profile, complications, seasonal variation

1. Introduction

Acute conjunctivitis is defined as the inflammation of conjunctiva of less than 3 to 4 weeks duration, characterized by cellular infiltration and exudation.[1,2] Commonest presentation is foreign body sensation, redness and blurring of vision with associated purulent or mucopurulent discharge.[1,3] The route of spread is mainly reported to be contagious or from own conjunctival flora.[4] In severe cases, corneal, lid or orbital involvement may be seen resulting into various complications.[5]

Prevalence and etiology of acute bacterial conjunctivitis varies from place to place, even within the same country owing to geographical, cultural and socioeconomic variation.[6,7] Till now no data is available regarding pattern of bacteriological flora of acute bacterial conjunctivitis in north-east Indian population. Studies evaluating association of different organisms and complications of acute bacterial conjunctivitis is not reported till date. The north-east Indian region needs a separate investigation as this area is very humid, rains heavily, its typical geographic location, wide temperature variation, predominance of low and middle socioeconomic class of people, ethnic and socio-cultural variation as compared to mainstream India. Again antibiotic sensitivity pattern of the organisms (conjunctival swab culture) in this region is also unknown. Here comes the need of

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AB and PS have contributed equally to this work. So both are designated as first author.

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the study. The primary objective of our study was to evaluate the bacteriological pattern in culture positive cases of acute bacterial conjunctivitis. The secondary objectives were evaluation of seasonal variation of organism profile, evaluation of the association between different organisms involved and complications of acute bacterial conjunctivitis and antibiotic sensitivity profile of different organisms.

2. Material and method

A hospital based cross sectional study was conducted in the department of ophthalmology, Assam Medical College and Hospital, Assam (duration of study: 1 year).

All culture positive cases of acute bacterial conjunctivitis were included (both gender, any age group). Patients who had pre-existing ocular surface disorders, foreign body or trauma, patients already on antibiotic therapy, patient on steroid therapy at the time of first contact were excluded.

Conjunctival swab culture was done in all patients with clinical symptoms of acute bacterial conjunctivitis willing to get enrolled into the study. Culture positive patients were recruited and were further evaluated for any complications. Culture positive cases were further subjected to antibacterial sensitivity screen.

2.1. Clinical evaluation and complication assessment

After taking detailed patient history, a through local and systematic evaluation was done. Snellen chart was used for visual aquity evaluation. Patients were examined under first by torch light examination followed by detailed evaluation under slit lamp to detect associated complications. Patients were evaluated in details for occurrence of different complications of acute bacterial conjunctivitis e.g. occurrence of true and pseudo-membrane, different form of keratitis (marginal keratitis, punctate epithelial keratitis, peripheral ulcerative keratitis etc.), corneal erosion, corneal thinning, corneal ulcer, corneal opacity and lid and adnexa involvement.

For the study, acute bacterial conjunctivitis was defined as, presence of conjunctival congestion, chemosis, purulent or mucopurulent discharge, matted eyelash with less than 4 week duration.[3]

2.2. Collection and processing of conjunctival swab

Purulent material from conjunctival sac and inner canthus (with special precaution not to touch the eyelid) were collected with 2 sterile cotton swabs. Both the swabs were sent immediately to the Department of Microbiology. Gram staining and direct microscopy was done in one part and the other part was used for bacterial culture. Culture media used were blood agar enriched with 5% sheep blood, Mac Conkey agar, and chocolate agar (incubated at 37°C for 24–48 hours). In case no organism was grown, it was reported as 'No Growth.' Positive culture was considered if growth was observed at least any of the two media.[8,9] Various biochemical tests and identification methods were utilized to identify the growth identified.[10]

2.3. Antibiotic susceptibility test

Kirby-Bauer disc diffusion method was used for antibiotic susceptibility testing on Mueller Hinton agar according to CLSI recommendation.[11] Zone of inhibition were measured and the antibiotic sensitivity was reported as sensitive, intermediate or resistant to the specific antibiotic tested according to manufacturer guideline (HiMedia, Mumbai, India).[12]

2.4. Sample size calculation

From our clinical practice, assuming a prevalence of 7% of acute bacterial conjunctivitis amongst all the patients attending ophthalmological OPD, with 5% precision, 95% confidence interval, with infinite population, a sample size of 101 was calculated. Taking a 10% drop out rate a total of 111 sample size was calculated.

2.5. Ethical considerations

Ethical approval for the study was obtained from the institutional Ethics committee of Assam Medical College and Hospital (ethics permission number AMC/EC/PG: 7269 dated 31.5.2014). Informed consent was taken from all participants and from legally acceptable representatives in case of children before enrolling into the study.

2.6. Statistical analysis

Continuous data was presented as mean ± SD or Median (Range), whereas categorical data was represented as frequency (%). Logistic regression model was used for evaluation of predictors of complications. SPSS version 22 was used in analysis of data. P value $< .05$ was taken as criteria for statistical significance.

3. Result

The study is reported as per STROBE guidelines.[13] Participant flow chart is showed in Figure 1. We have screened 172 patients showing clinical signs and symptoms of acute bacterial conjunctivitis. Out of which, 110 patients came out to be culture positive and were included in the study.

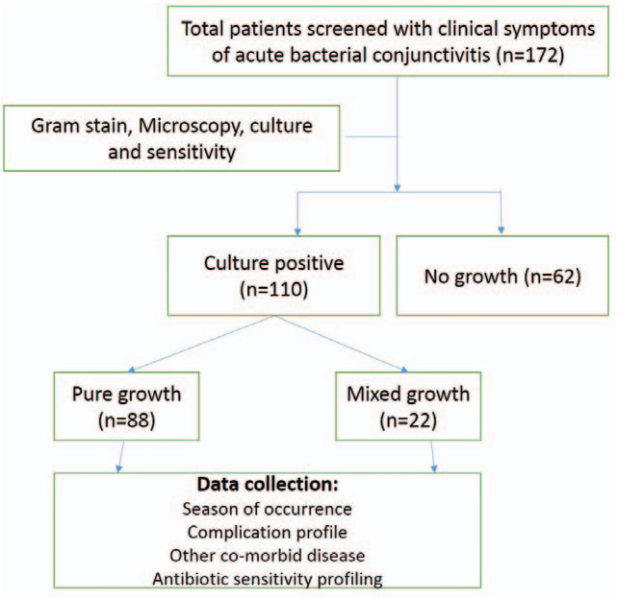

Figure 1. Participant flow chart.

3.1. Demographic characteristics

Data is showed in Table 1. Total no of culture positive cases in our study were 110 with median age of 31.5 year (Range 1 year to 85 year). Single eye involvement were seen in 45.45% patients (N=50) and bilateral involvement was seen in 54.54% (N=60). Middle class socio economic group has the maximum no of cases 40.90% (N=45) followed by lower socioeconomic group 36.36% (N=40). Higher socioeconomic group was less frequently involved which consisted of 22.72% (N=25).

3.2. Seasonal variation

Maximum no of cases was seen in the month of June which consisted of 20.9% of total cases. Increased frequency were seen in the months of May (10%), June (20.9%), July (19.09%), August (12.72%) and September (12.72%). Overall, highest number of cases were found in the season of May to September (n=83, 75%). In the month of October to April, the no of bacterial conjunctivitis cases were less (25%). Month wise frequency of bacterial pathogen and seasonal variation is shown in Table 1.

3.3. Clinical presentation of acute bacterial conjunctivitis

All the patients complained of blurring of vision, photophobia and foreign body sensation, while only 80% cases complained pain. On examination, conjunctival congestion was seen in all the cases (100%). Mucopurulent and purulent discharge was seen in 58.18% and 41.8% cases. Lid involvement was seen in 20% patients and corneal involvement was seen in 42.72% patients. Lymphadenopathy was seen in 10% of total cases. Data showed in Table 2.

Table 1

Demographic characteristics of acute bacterial conjunctivitis.

Parameter		Value
Total number of cases enrolled (n)		110
Age (Years)		31.5 (1–85)
Sex		
	Male	80 (72.7%)
	Female	30 (27.3%)
Unilateral/Bilateral involvement		
	UL	50 (45.45%)
	BL	60 (54.54%)
Socioeconomic status		
	Higher	25 (22.72%)
	Middle	45 (40.90%)
	Lower	40 (36.36%)
Month of occurrence	JAN	3 (2.72%)
	FEB	5 (4.54%)
	MAR	2 (1.81%)
	APR	5 (4.54%)
	MAY	11 (10%)
	JUNE	23 (20.9%)
	JULY	21 (19.09%)
	AUG	14 (12.72%)
	SEPT	14 (12.72%)
	OCT	7 (6.36%)
	NOV	3 (2.72%)
	DEC	2 (1.81%)

Table 2

Clinical presentation of acute bacterial conjunctivitis.

Signs and symptoms	N (%)
Redness	110 (100%)
Purulent discharge	46 (41.8%)
Mucopurulent discharge	64 (58.18%)
Blurring of vision	110 (100%)
Photophobia	110 (100%)
Foreign body sensation	110 (100%)
Pain	88 (80%)
Diminish vision (DOV)	0 (0%)
Congestion	110 (100%)
Chemosis	55 (50%)
Discharge	110 (100%)
Lid involvement	22 (20%)
Cornea involvement	47 (42.72%)
Lymphadenopathy	11 (10%)

3.4. Microbiological profile

SA (32.1%) was the predominant organism isolated throughout the year [MRSA (2.7%)] followed by SE (29.1%), SP (14.5%), D (12.8%) and STBH (8.4%). MC (4.5%), HI (4.5%), Klebsiella (3.6%), PA (3.6%),EC (1.8%), NG (1.8%), Enterobacter (0.9%) and CD (0.9%) were isolated less frequently in our study population. [Data showed in Table 3].

Maximum number of SE cases isolated was from May to September (62.5% cases). Similarly occurrence of maximum no of cases of STBH and SP were in the month of May to August (66.7%) and May to September (75%). SA and Diphtheroid were isolated all throughout the year. Minor constituents of bacterial profile namely MC, HI, K, PA, MRSA, EC, NG, E and catarrhalis were seen randomly in the year with no predominance in any season. Frequency of occurrence of organism and maximum occurrence in the year showed in Table 3.

3.5. Complications of conjunctivitis and associated organisms

3.5.1. True membrane. True membrane was seen in 0.9% of all cases of culture positive acute bacterial conjunctivitis. Isolation of *C Diphtheria* was significantly associated with true membrane formation (n=1, $P=.009$).

3.5.2. Pseudo membrane. Pseudo membrane was seen in 20% cases. The organisms isolated STBH (31.8%), SA (54.5%), SP (9%) and SE (18.1%). However, only STBH and SA isolation were significantly associated with occurrence of pseudo membrane ($P < .001$and $P=.006$ respectively).

3.5.3. Punctate epithelial keratitis (PEK). PEK was seen in 20% of all cases. Maximum no of isolation associated with occurrence of PEK were seen in SA (36.2%) and SP (27.2%) isolation in culture. But no statistical significance association was seen with any of the isolates.

3.5.4. Marginal keratitis. Marginal keratitis was seen in a single case (0.9%), where mixed growth was seen (components were SE, MC, and D). However none of the isolation in culture was significantly associated with occurrence of marginal keratitis.

3.5.5. Peripheral ulcerative keratitis (PUK). PUK was seen in 2.7% cases. Organisms isolated were SA (100%) and SE

Table 3

Organism, frequency month wise and total occurrence.

Organism		Overall frequency (%)	Frequency		Month of maximum occurrence [n, (%)]
			Pure growth [n = 88, (80%)]	Mixed growth [n = 22, (20%)]	
Staph aureus	MSSA	35 (32.1%)	19 (21.6)	16 (72.7%)	All throughout the year
	MRSA	3 (2.7%)	3 (3.5%)	0	Random (n = 3)
Staph epidermidis		32 (29.1%)	23 (26.1%)	9 (40.9%)	May to sept [20 (62.5%)]
Streptococcus pneumoniae		16 (14.5%)	13 (14.8%)	3 (13.6%)	May to sept [12 (75%)]
Diphtheroid		14 (12.8%)	6 (6.8%)	8 (36.4%)	All throughout the year
S. beta haemolyticus		9 (8.4%)	5 (5.7%)	4 (18.2%)	May to august [6 (66.7%)]
M. catarrhalis		5 (4.5%)	3 (3.4%)	2 (9.1%)	Random (n = 5)
H influenza		5 (4.5%)	3 (3.5%)	2 (9.1%)	Random (n = 5)
Klebsiella		4 (3.6%)	4 (4.5%)	0	Random (n = 4)
Pseudomonas-A		4 (3.6%)	2 (2.3%)	2 (9.1%)	Random (n = 4)
E coli		2 (1.8%)	2 (2.3%)	0	Random (n = 2)
N gonorrhoea		2 (1.8%)	2 (2.3%)	0	Random (n = 2)
Enterobacter		1 (0.9%)	1 (1.1%)	0	Random (n = 1)
C. Diphtheria		1 (0.9%)	1 (1.1%)	0	Random (n = 1)

(33.3%). Significant association was found between SA isolation and occurrence of PUK ($P = .03$).

3.5.6. Corneal erosion. Corneal erosion was seen in 5.4% cases. Organisms isolated were SA and SP, however, only isolation of SA were significantly associated with occurrence of corneal erosion ($P = .001$).

3.5.7. Corneal thinning. Corneal thinning was seen in 3.6% cases. Organisms isolated were PA (75%), SA (25%), SP (25%) and HI (25%). However, only PA isolation was found to be significantly associated with corneal thinning ($P < .001$).

3.5.8. Corneal ulcer. Corneal ulcer was seen in 3.6% cases. Organisms isolated were SA (75%), SP (25%), HI (25%) and PA (25%). None of the isolates were significantly associated with occurrence of corneal ulcer.

3.5.9. Corneal opacity. Corneal opacity was seen in 7.2% cases. Organisms isolated were SE (75%) and SP (25%). Only STBH isolation (75%) in culture was significantly associated with occurrence of corneal opacity. ($P = .007$).

3.5.10. Lid edema. Lid edema was seen in 13.6% cases. Organisms isolated were SA (53.3%), SE (13.3%), SP (26.6%) and STBH (13.3%).

3.5.11. Blepharitis. Blepharitis was seen in 5.4% cases. Organisms isolated were SA (66.6%), D (50%), SE (16.6%), SP (16.6%) and MC (16.6%). Isolation of Diphtheroid in culture were significantly associated with occurrence of blepharitis ($P = .0027$) and near significance was seen in case of SA ($P = .083$).

3.5.12. Dacryocystitis. Dacryocystitis was seen in 1.8% cases and organisms isolated were SP as single isolate. Significant association was seen between of SP isolation and occurrence of concomitant dacryocystitis ($P = .02$).

3.5.13. Pre-septal cellulites. Pre-septal cellulitis was seen in 0.9% cases. SA was the single organism isolated. [Organism associated with specific complication showed in Table 4]

3.6. Conjunctivitis as a part of other systemic disease

3.6.1. Otitis media. Concomitant otitis media was seen in 4.5% of cases and SP was isolated from all the cases. Significant association was seen between SP isolation in culture and occurrence of concomitant otitis media ($P \leq .001$).

3.6.2. Rrihonorrhoea. Rhinorrhea was seen in 2.7% cases. No significant association was seen in any of the isolates (SP, HI, and STBH) with concurrent rhinorrhea.

3.6.3. Meningitis. Conjunctivitis associated with meningitis was seen in 1 case in which MRSA was isolated in culture.

3.6.4. Septicemia. In 2 cases, concomitant septicemia was there and organisms isolated were MRSA (50%) and STBH (50%).

3.6.5. Orbital abscess. In one case concurrent orbital abscess was seen and MRSA growth was found in culture. [Conjunctivitis as a part of other systemic disease has been showed in Table 5]

3.7. Antibiotic sensitivity pattern of individual organism

More than 70% isolates of MSSA were sensitive to aminoglycosides (amikacin, gentamycin, tobramycin), doxycycline, chloramphenicol, cephalosporins, vancomycin, and linezolid, whereas highest number of isolates were resistant to ciprofloxacin and moxifloxacin (>70% isolates).

More than 70% Diphtheroid isolates were sensitive to aminoglycosides (amikacin, gentamycin and tobramycin), doxycycline, chloramphenicol and cephalosporins, whereas more than 50% isolates were resistant to fluroquinolones (ciprofloxacin, moxifloxacin) and amoxicillin-clavulinic acid.

More than 70% STBH isolates were sensitive to aminoglycosides (amikacin and gentamycin), chloramphenicol, cephalosporins and macrolides (Azithromycin) whereas more than 50% isolates showed intermediate or high level resistance to doxycycline and fluroquinolones (ciprofloxacin and moxifloxacin).

More than 70% of SP isolates were sensitive to aminoglycosides (amikacin, gentamycin and tobramycin), chloramphenicol,

Table 4

Complications of conjunctivitis and associated organisms.

Complication	Frequency (%)	Organism	N (%)	OR (95% CI)	*P* value
True membrane	1 (0.9%)	CD	1 (100%)	–	.009
Pseudo membrane	22 (20%)	STBH	7 (31.8%)	21 (3.9–111.58)	<.001
		SA	12 (54.5%)	3.768 (1.4–10.1)	.006
		SP	2 (9%)	0.529 (0.111–2.52)	.52
		SE	4 (18.1%)	0.476 (0.147–1.538)	.159
Punctate epithelial keratitis	22 (20%))	SP	6 (27.2%)	2.888 (0.918–9.087)	.0888
		SE	4 (18.1%)	0.468 (0.145–1.513)	.198
		SA	8 (36.2%)	1.249 (0.468–3.33)	.657
		STBH	2 (9%)	1.173 (0.225–6.105)	1.000
		D	1 (4.5%)	–	.204
		MC	1 (4.5%)	–	1.000
Peripheral ulcerative keratitis	3 (2.7%)	SA	3 (100%)	–	.031
		SE	1 (33.3%)	1.266 (0.107–14.01)	1.000
Marginal keratitis	1 (0.9%)	SE	1 (100%)	–	.291
		MC	1 (100%)	–	.045
		D	1 (100%)	–	.128
Corneal erosion	6 (5.4%)	SA	6 (100%)	1.207 (1.038–1.403)	.001
		SP	1 (16.6%)	1.187 (0.129–10.878)	1.000
Corneal thinning	4 (3.6%)	PA	3 (75%)	309 (15.38–6207)	<.001
		SA	1 (25%)	0.717 (0.072–7.157)	1.000
		SP	1 (25%)	2 (0.195–20.52)	.475
		HI	1 (25%)	8.417 (0.709–99.898)	.173
Corneal Ulcer	4 (3.6%)	SA	3 (75%))	6.844 (0.685–68.329)	.096
		SP	1 (25%)	2.022 (0.197–20.746)	.472
		HI	1 (25%)	8.5 (0.716–100)	.172
		PA	1 (25%)	11.333 (0.896–143)	.141
Corneal opacity	8 (7.2%)	SE	6 (75%)	8.769 (1.66–46.171)	.007
		SP	2 (25%)	2.095 (0.384–11.432)	.329
Lid oedema	15 (13.6%)	SA	8 (53.3%)	2.836 (0.936–8.592)	.076
		SE	2 (13.3%)	0.333 (0.071–1.5)	.223
		SP	4 (26.6%)	2.515 (0.689–9.179)	.228
		STBH	2 (13.3%)	2.048 (0.38–11.026)	.334
Blepharitis	6 (5.4%)	SA	4 (66.6%)	4.645 (0.808–26.699)	.083
		D	3 (50%)	8.364 (1.5–46.6)	.0027
		SE	1 (16.6%)	0.471 (0.053–4.199)	.67
		SP	1 (16.6%)	1.187 (0.129–10.878)	1.000
		MC	1 (16.6%)	5 (0.468–53)	.249
Dacryocystitis	2 (1.8%)	SP	2 (100%)	1.143 (0.950–1.375)	.02
Pre-septal Cellulites	1 (0.9%)	SA	1 (100%)	1.029 (0.973–1.09)	.321

cephalosporins, co-trimoxazole and macrolides (erythromycin and azithromycin). The 5% to 20% isolates were resistant to doxycycline, fluroquinolones, amoxicillin-clavulinic acid and erythromycin.

More than 80% of SE isolates were sensitive to aminoglycosides (amikacin and tobramycin), doxycycline, chloramphenicol and cephalosporins. More than 20% isolates were resistant to fluroquinolones (ciprofloxacin and moxifloxacin).

All the major organisms (SA, SE, D, STBH, and SP) were sensitive to vancomycin and linezolid. [Antibiotic sensitivity pattern of major organisms (>5 isolates) has been shown in Table 6].

Table 5

Conjunctivitis as a part of other systemic disease.

Systemic disease	N (%)	Organism	N (%)	OR (95% CI)	*P* value
Otitis media	5 (4.5%)	SP	5 (100%)	1.455 (1.045–2.024)	<.001
Rhinorrhoea	3 (2.7%)	SP	1 (33.3%)	3.067 (0.262–35.956)	.379
		HI	1 (33.3%)	12.875 (0.956–173.3)	.131
		STBH	1 (33.3%)	6 (0.489–73.56)	.234
Meningitis	1 (0.9%)	MRSA	1 (100%)	–	.0027
Septicaemia	2 (1.8%)	MRSA	1 (50%)	53 (2.376–1182)	.054
		STBH	1 (50%)	12.125 (0.692–212.65)	.162
Orbital abscess	1 (0.9%)	MRSA	1 (100%)	1.5 (0.0674–3.33)	.0027

Table 6

Antibiotic sensitivity pattern of various organisms.

Organism (N, %)	AK	Gen	TB	DO	Chlor	Cip	Moxi	Amoxyclav	Cefoxitin	Cotrimoxa	VA	LZ	ER	Azithro
MSSA														
N	35	35	35	35	28	33	35	35	35	30	35	30	34	34
S	26 (74.3)	25 (71.4)	30 (85.71)	31 (88.6)	26 (92.9)	1 (3)	2 (5.7)	24 (68.57)	35 (100)	12 (40)	35 (100)	30 (100)	17 (50)	22 (64.7)
I	8 (22.9)	9 (25.7)	4 (11.4)	4 (11.4)	2 (7.1)	8 (24.2)	9 (25.7)	2 (5.7)	0	6 (20)	0	0	12 (35.3)	10 (29.4)
R	1 (2.9)	1 (2.85)	1 (2.85)	0	0	24 (72.7)	24 (72.7)	9 (25.71)	0	12 (40)	0	0	5 (14.7)	2 (5.9)
D														
N	14	14	10	14	14	13	13	11	13	10	13	13	13	-
S	10 (71.4)	10 (71.4)	9 (90)	13 (92.9)	12 (85)	2 (15.4)	2 (15.4)	4 (36.4)	13 (100%)	5 (50)	13 (100)	13 (100)	7 (53.8)	-
I	3 (21.4)	3 (21.4)	0	1 (7.1)	2 (14.28)	2 (15.4)	3 (23.1)	1 (9.1)	0	1 (10)	0	0	3 (23)	-
R	1 (7.1)	1 (7.1)	1 (10)	0	0	9 (69.2)	8 (61.5)	6 (54.5)	0	4 (40)	0	0	3 (23)	-
STBH														
N	9	9	-	8	9	9	9	9	8	9	9	9	9	9
S	7 (77.8)	8 (88.8)	-	3 (37.5)	8 (88.8)	3 (33.3)	3 (33.3)	6 (66.7)	7 (87.5)	4 (44.4)	9 (100)	9 (100)	6 (66.7)	7 (77.8)
I	2 (22.2)	1 (11.1)	-	2 (25)	1 (11.1)	5 (55.5)	4 (44.4)	2 (22.2)	1 (12.5)	3 (33.3)	0	0	3 (33.3)	2 (22.2)
R	0	0	-	3 (37.5)	0	1 (11.1)	2 (22.2)	1 (11.1)	0	2 (22.2)	0	0	0	0
SP														
N	15	15	15	14	12	15	15	13	15	15	12	14	15	15
S	12 (80)	13 (86.7)	11 (73.3)	7 (46.7)	12 (100)	7 (46.7)	10 (66.7)	8 (61.5)	11 (73.3)	13 (86.7)	12 (100)	14 (100)	11 (73.3)	11 (73.3)
I	3 (20)	2 (13.3)	4 (26.7)	5 (33.3)	0	5 (33.3)	3 (20)	4 (30.8)	4 (26.7)	2 (13.3)	0	0	3 (20)	4 (26.7)
R	0	0	0	2 (13.3)	0	3 (20)	2 (13.3)	1 (7.7)	0	0	0	0	1 (6.7)	0
SE														
N	32	-	32	25	30	32	32	21	30	20	32	30	23	30
S	27 (84.37)	-	26 (81.25)	24 (96)	24 (80)	17 (53.12)	18 (56.25)	7 (33.3)	26 (86.7)	9 (45)	32 (100)	30 (100)	10 (43.5)	19 (63.3)
I	2 (6.25)	-	3 (9.37)	1 (4)	5 (16.7)	6 (18.75)	5 (15.62)	1 (4.8)	3 (10)	0	0	0	11 (47.8)	8 (26.7)
R	3 (9.37)	-	3 (9.37)	0	1 (3.33)	9 (28.12)	9 (28.12)	13 (61.9)	1 (3.33)	11 (55)	0	0	2 (8.7)	3 (10)

AK = Amikacin; Gen = Gentamycin; TB = Tobramycin; DO = Doxycycline, Chlor: Chloramphenicol; Cip = Ciprofloxacin; Moxi = Moxifloxacin, Amoxyclav: Amoxicillin clavulinate, Cotrimoxa: cotrimoxazole; VA = Vancomycin; LZ = Linezolid; ER = Erythromycin; Azithro: Azithromycin; N = total no of organism; S = highly sensitive; I = Intermediate; R = Resistant.

4. Discussion

4.1. Demographic profile

In our study, out of 172 patients screened with signs and symptoms of acute bacterial conjunctivitis, 110 (63.95%) showed culture positivity. Median age of presentation was 31.5 year (Range 1–85 year). Bilateral eye involvement was seen in 54.54% cases.

4.2. Seasonal variation

World-wide, both the frequency and the etiology of bacterial conjunctivitis vary according to climate, socioeconomic status and hygienic conditions.[2,14,15] In our study population, prevalence of acute bacterial conjunctivitis was more in middle and lower socioeconomic group. Maximum number of cases was seen in the month of May to September (75%). In the month of November to January, there was a declining trend of culture positive bacterial conjunctivitis cases were seen. Similar finding was reported by Aggarwal et al, where it was found that the frequency of bacterial conjunctivitis follows a step ladder pattern.[6] During the month of March to September (summer) its frequency was increased, sudden decreases in frequency was seen in autumn and remained low during winter season (November).[6] SA and Diphtheroid were isolated throughout the year, whereas SE and SP were mainly isolated during the season "May to September", and STBH cases were isolated from "May to August" (data showed in Table 3). Results of our study is supported by findings by Aggarwal et al.[6]

4.3. Clinical presentation

Redness and conjunctival congestion were the most common clinical presentation (seen in 100% cases) in the first contact. All the patients complained of blurring of vision, photophobia and foreign body sensation, while only 80% cases complained of pain. None of the patients complained diminished vision. Mucopurulent and purulent discharge was seen in 58.18% and 41.8% cases. Lid involvement was seen in 20% and corneal involvement was seen in 42.72% patients. Lymphadenopathy was seen in 10% among all our study participants. Our findings are in accordance with previous literatures.[14,15]

4.4. Culture profile: Mixed growth versus single organism growth

In our study mixed growth was seen in 20% cases whereas 80% cases showed single organism growth. Mixed growth is commonly reported in conjunctival swab culture. Aggarwal et al reported 39.4% single organism growth, 30.5% mixed infection and no growth in 30% cases.[6] On the other hand, Perkins et al, reported 84.7% mixed growth in their study.[6,16] In a study by Hashish et al mixed growth of 2 organisms were 38% whereas mixed growth of three or more organisms were reported to be 9.8% among all samples.[17]

4.5. Microbial profile

Overall, SA (32.1%) was the predominant organism [MRSA (2.7%)] followed by SE (29.1%), SP (14.5%), D (12.8%) and STBH (8.4%) in our study. MC (4.5%), HI (4.5%), K (3.6%), PA

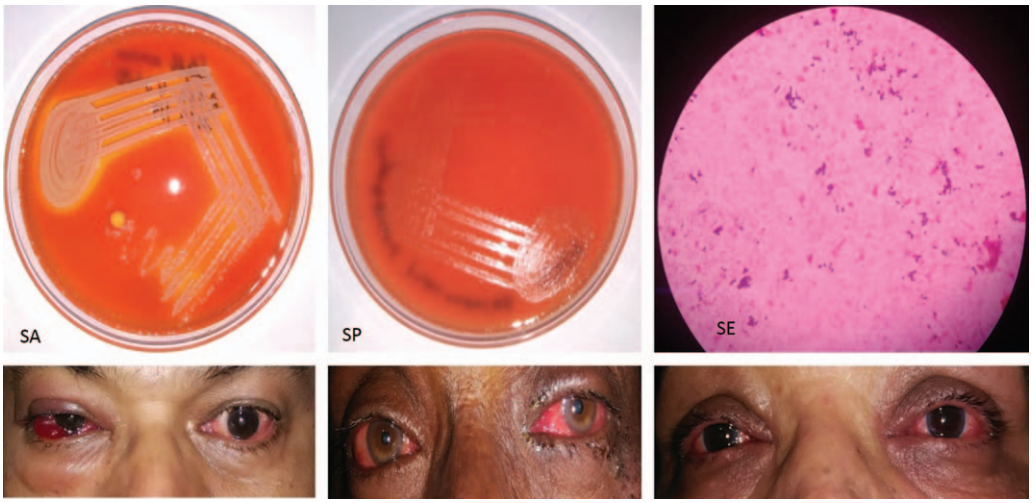

Figure 2. Culture plate and microscopic picture of organism.

(3.6%), EC (1.8%), NG (1.8%), E (0.9%) and CD (0.9%) were isolated less frequently in our study population.

SA was the most common isolate (Overall) and second most common single isolate in our study population. Our finding is in accordance with Seal et al and Mahajan et al, where SA is reported to be the most frequent single isolate in bacterial conjunctivitis cases.[2,18–20] Ramesh et al, Boralkar et al, and Stenson et al also reported SA to be the predominant single isolate from in eyelids and conjunctival infections.[21–23] mong the Staph aureus infection, 3% is estimated to be methicillin-resistant S aureus (MRSA) conjunctivitis. [4] In our study population, MRSA was seen in 2.7% of all the positive culture cases and the cases were seen randomly in the study period.

SE was the second most common isolate (29.1%) and commonest single organism isolates (26.1%).Our finding is in accordance with Aggarwal et al[6] and Perkin et al.[16]

SP was the third most common single organism isolate in our study population (14.5%). Rao and Rao observed SP as the second most prevalent organism (Mysore, India)[6] while Perkin et al reported SP to be most common isolate in acute bacterial conjunctivitis cases.[16] Martin et al reported uncapsulated strain of SP to be the most predominant organism in Florida and non typable SP as single or as component of mixed growth in New York State as the predominant organism in epidemic bacterial conjunctivitis.[2,24]

STBH was isolated in 8.4% of cases and it was component of both mixed and single growth. In a study by Aggarwal et al STBH was isolated in 1.1% cases (0.4% was single growth and 0.7% was mixed growth).[6] Similarly, Rajbanshi et al reported hemolytic streptococci to be 6.8% of total cases of bacterial conjunctivitis.[25]

In our study, Diphtheroid was present in 12.8% of total cases. Although Diphtheroid is commonly considered as commensel and contaminant in clinical samples, Rajbanshi et al reported Diphtheroid to be associated with bacterial conjunctivitis.[25–28] Similarly Watkins et al, Rubinfield et al, Joussen et al, Chace and Locatcher also considers Diphtheroid as causative agent of bacterial conjunctivitis.[29–32]

MC was isolated in 4.5% culture positive cases which was the most frequent gram negative isolate which was seen both as single growth (3.4%) and as a part of mixed growth (9.1%) in our study population. Although many authors consider MC as a commensel of conjunctiva and upper respiratory tract, however, Verduine et al reported it to be an emerging pathogen, both in healthy and immune compromised patients. [33]

Other micro-organisms that were isolated from the bacterial conjunctivitis cases were MC, HI, K, PA, MRSA, EC, NG, Enterobacter and CD. [Culture plate and microscopic picture of organisms isolated has been shown in Fig. 2]

5. Complication

5.1. Membrane formation

Both true and pseudo membrane formation is reported as complication of bacterial conjunctivitis is reported in literature.[34] In our study, true membrane were seen in 0.9% of all cases and association with *C Diphtheria* was statistically significant. Pseudo membrane was seen in 20% cases and organisms isolated were STBH, SA, SP and SE, however, STBH and SA isolation were significantly associated with occurrence of pseudo membrane.

C diphtheria is known for its association with occurrence true membrane but due to mass vaccination its prevalence is decreased except in population of lower socioeconomic status due to crowded environment.[34] Pseudo membranous conjunctivitis has been reported by various authors.[35,36] Bernaeuer et al reported S. beta hemolyticus and *C. diphtheria* as bacterial etiology for true and pseudo membrane formation.[34] Beta hemolytic Streptococcus is an invasive microorganism producing exotoxin causing severe purulent conjunctivitis with both type of membrane formation with cornea involvement.[34] Pseudo membranous conjunctivitis by Staph aureus, pneumococci, meningococci and Klebsiella has been reported in previous literature.[35–37]

5.2. Cornea involvement

In our study, corneal involvement in different forms of corneal involvement was seen [punctate epithelial keratitis (in 20% cases), marginal keratitis (0.9% cases), peripheral ulcerative keratitis (2.7%), corneal erosion (5.4%), corneal ulcer (3.6%) and corneal opacity (7.2%)] and organisms significantly isolated

with different forms of conjunctival involvement were SP, SA, MC, PA, and SE.

Overall, risk of cornea involvement is around 60% amongst all acute bacterial conjunctivitis cases.[2] Dry eye, abnormal blinking pattern and meibomian gland dysfunction are risk factors in development of keratitis in conjunctivitis patients.[2,38,39] Punctate epithelial keratitis and marginal keratitis are often associated with bacterial conjunctivitis by Staph. aureus specially in patients with dry eye[2] and staphylococcal exotoxin is hypothesized to be the culprit.[2,38] Regarding other organisms, there are reports of Moraxella and Corynebacterium species causing keratitis.[21] In a study in New Zealand, coagulase negative staphylococci was the commonest gram positive organism whereas Moraxella was the predominant gram negative organism responsible for bacterial keratitis cases.[20] Punctate epithelial keratitis is also associated with Streptococcus group.[38] Maske et al[40] reported Staph epidermidis as a causative agent of corneal ulcer and Mahajan et al[18]as a pathogen for kerato-conjunctivitis supports the tendency of this organism to opacity formation. This supports our finding of corneal opacity formation in keratitis by *S epidermidis*.[18,40] In our study, 60% cases all the corneal opacity developed were not visually significant and only complaints were glare and blurring of vision. It takes an average of 5 months for the symptoms to disappear.

5.3. Lid and adnexa involvement

Lid edema was seen in 13.6% cases and SA was isolated in maximum (53.3%). Blepharitis was seen in 5.4% cases [SA (66.6%) and Diphtheroid (50%)]. Isolation of Diphtheroid was significantly associated with occurrence of blepharitis. Our finding is in accordance with that of previous literature.[16,38,41,42] Associated dacryocystitis was seen in 1.8% cases and SP was isolated in all the cases. Association between dacryocystitis and *S Pneumonia* isolation in culture is previously reported[21,43].The blockage of the lacrimal duct system results in accumulation of tears and creates a fertile environment for secondary bacterial infection.[2] Also infection can spread from nasopharynx via the nasolacrimal duct.[2]Pre-septal cellulitis was seen in 0.9% cases. Staph aureus was the single organism isolated. SA and SP are reported to be associated with preseptal cellulitis.[44,45]

5.4. Rare complications

In our study, 4 cases of corneal thinning were seen and the commonest organism isolated was PA (in 75% cases). Corneal involvement is reported with PA and emergency treatment is recommended.[46]

5.5. Conjunctivitis as part of other systemic disease

In our study, conjunctivitis was seen to be occurring as part of other systemic diseases e.g. URTI presenting as rhinorrhea (2.7%), otitis media (5.4%), meningitis (0.9%), septicemia (1.8%) and orbital abscess (0.9%) and organisms isolated were SP, HI, STBH and MRSA. Concurrent occurrence of otitis media and upper respiratory tract infection (URTI) with acute bacterial conjunctivitis by *H. Influenza and S. pneumonia* is reported in literatures and examining ears and lymph node is recommended with special emphasis on pediatric population.[1,2,47,48]*Streptococcus species are also reported to be rare associates.*[14,48,49] In a case series by McKinley et al, *Staphylococcus* was the commonest organism isolated in cases of orbital abscess; among them 36% were methicillin resistant *Staph. aureus* followed by *Streptococcus*.[44,45]

5.6. Antibiotic sensitivity pattern

Although, in around 60% cases of acute bacterial conjunctivitis resolves within 1 to 2 weeks of presentation, topical antibiotics reduce the duration of disease.[1,4] In case of culture positive conjunctivitis cases, topical antibiotics seem to be more effective in achieving clinical and microbiological cure. [1,4]

In our study, most of the major isolates were sensitive to aminoglycosides, chloramphenicol, cephalosporins, macrolides (Azithromycin) and were also sensitive to important reserved antibiotic like vancomycin and linezolid.

One important finding of our study is high level of fluroquinolones resistance amongst Staph aureus (>70% isolates), Diphtheroid (>60% isolates), S. beta hemolyticus (50% cases are intermediate level and 10–20% cases resistant), *S. pneumonia* (13–20% isolates resistant) and staph. epidermidis (>28% isolates). Although, moxifloxacin is a fourth generation fluroquinolones with high activity towards both gram negative and positive organisms, and is taken as an agent of choice for empirical therapy,[50] the emerging pattern of resistance is a matter of concern and highlights its irrational use, wide marketing practices. Higher antibiotic prescription practices (upto 44% of all prescriptions) and fluroquinolones being most common of them, both at community level and at tertiary case level, definitely carries risk of high level of resistance.[51]

One of the factors that underlie the irrational use of antibiotics is that, many a time differentiating bacterial conjunctivitis from viral conjunctivitis is tough. Non-specificity of signs and symptoms is a reason of the same[4] and is a cause of irrational antibiotic use. We need a good scale study to distinguish acute bacterial conjunctivitis from acute viral conjunctivitis highlighting differentiating different bacterial and viral subtypes or some good biomarker and also need personalized antibiotic therapy in those who needs it.[52]

6. Summary and conclusion

In our study, most of the cases occurred in May to September and SA was the predominant organism isolated throughout the year (overall data) followed by SE, SP, D and STBH. Amongst single organism cultures also, most common organism were SE, followed by SA, SP, D and STBH.

One important finding of our study is isolation of SE, D and MC as single organism culture from acute bacterial conjunctivitis cases.

Membrane formation was seen in association with C. diphtheria (true membrane), STBH and SA (pseudo membrane). Cornea involvement was seen in association with SP, SA, MC, PA and SE. Lid and adnexa involvement was seen in association with SA and D. Although Diphtheroid is commonly considered as contaminant, its frequent isolation as single organism growth and existing literature reports highlights its growing importance.

Most of the isolates were sensitive to aminoglycosides, chloramphenicol, cephalosporins, macrolides (Azithromycin) and were also sensitive to important reserved antibiotic like vancomycin and linezolid, however high level of resistance was seen towards fluroquinolones.

6.1. Recommendations and conclusion

1. Detailed ophthalmic evaluation with special reference to occurrence of any complications to be carried out.
2. Systemic evaluation to see whether conjunctivitis is a local disease or part of a systemic disease.
3. Presumptive identification of organism involved from complications caused and other systemic clinical features and organism specific features.[53]
4. Initial choice of therapy should be based on presumptive organism involved and its regional sensitivity pattern.
5. Season of occurrence and contact exposure can guide to antibacterial therapy
6. Once culture and sensitivity report is available choice of antibiotic should be govern by culture and sensitivity.
7. In case of presumptive antibiotic therapy, the local organism profile periodic culture and sensitivity reports can guide to antibiotic therapy.
8. In case of limited resource settings, simple gram staining and microscopy can guide initial empirical antibiotic therapy.

6.2. Strengths and limitations of the study

This is the first study addressing all these issues from North-east India. Another issue is most of the existing literature evaluated the association between different organisms and complications using simple frequency approach. In our study, we have used measures of association to measure the strengths of the relations and their significance (odds ratio and regression analysis) highlighting a strong methodology of our study.

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