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Original Article

Microbial Pattern and Antimicrobial Susceptibility of Ludwig's Angina : Study in a Tertiary Level Hospital in Bangladesh

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Abstract:

Background*: Ludwig's angina is a form of severe diffuse cellulitis that presents as acute onset and spreads rapidly, bilaterally affecting the submandibular, sublingual and submental spaces. Isolation of bacteria responsible for Ludwig's angina and their antibiotic susceptibility is crucial as mixed infections are common.*

Objectives: *To find out the microbes responsible for developing Ludwig's angina and their antibiotic susceptibility.*

Methods: *This cross-sectional study was conducted at Department of Otolaryngology and Head-Neck Surgery, Dhaka Medical College& Hospital, Dhaka, Bangladesh, from January 2018 to June 2019. Total 100 patients of Ludwig's angina were enrolled. Surgical drainage followed by pus culture sensitivity was done to determine microbes responsible for Ludwig's angina and analyzed the coverage rate of different antimicrobial agents.*

Results: *Mean (±SD) age of the study patients was 36.83±13.7 years and majority (45%) were in 3rd decade of life with a male predominance. Dental infection was the commonest source of infection and diabetes mellitus was the major (54.0%) predisposing factor. Isolated common organisms were* Streptococcus viridians *(30.6%),* staphylococcus aureus *(25.2%),* E.coli *(17.1%),* Pseudomonas *(11.7%),* Klebsiella *(9.9%) and* Acinetobacter (*5.4%). But no organism was found in 12 cases. Maximum patients (64%) were sensitized by Ceftriaxone, Gentamycin (55%) and Ciprofloxacin*

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(46%). However, 11 study patients developed complications. ***Conclusion:*** *Ludwig's angina is common in middle aged male. Dental infection is the commonest source of infection and diabetes mellitus is an important risk factor.* Streptococcus Viridans, Staphylococcus aureus, E.coli, Pseudomonas w*ere the common causative organism. Most effective antibiotic were Ceftriaxone, Gentamicin and Ciprofloxacin.*

Key wards: *Antibacterial susceptibility, Bacteriological study,Ludwig's angina,Microbial Pattern.*

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Introduction:

Ludwig's angina is a rapidly progressive, potentially fulminant cellulitis of the submandibular, submental and sublingual spaces[1]. It is presented with swelling of the floor of the mouth, tense edema and induration of submental soft tissues and elevation and posterior displacement of tongue[1]. The pain and trismus, along with swelling of the oral and cervical tissues and tongue displacement causes severely compromised airway[1]. More than 80 percent of patients with Ludwig's angina have a dental infection and the rest usually have an upper respiratory tract infection[2]. Other etiology includes sialadenitis, floor of the mouth trauma, mandibular fractures and peritonsillar abscess[3]. The second and third mandibular molars have roots which lie at the level of the mylohyoid muscle either adjacent to or below the submandibular space. Abscesses of these lower molar may perforate the mandible and spread into the submandibular and submental spaces, leading to Ludwig's angina[4]. It was reported that mixed infections involving both aerobes and anaerobes are common in Ludwig's angina[2,5,6]. All age groups may be affected particularly elderly and young patients are commonly affected[5]. The swelling is diffuse, and there is erythema and cellulitis of the skin[6]. The floor of the mouth appears edematous, brown in color with the tongue pushed upwards and backwards which can cause a potential airway obstruction[2]. Patients usually presented with neck swelling, pain and elevation of the tongue, trismus, excessive salivation, malaise, fever, dysphagia and stridor[5-8]. The submandibular area could be indurated, sometimes with palpable crepitus[7]. The diagnosis and treatment of deep neck space infections have been challenging for physicians and surgeons. The complexity and the deep location of this region make diagnosis and treatment of infections in this area difficult. Advancement of modern microbiology and radiology, the effectiveness of modern antibiotics and the continued development of medical intensive care protocols and surgical techniques reduce the rate of complication[7]. There are four proposed criteria to distinguish Ludwig's angina from other deep neck abscesses, which include-bilateral infection (more than one space), produce serosanguinous infiltration (with or without pus), involve connective tissue, fascia and muscles (not glandular structure) and spread by continuity (not by lymphatics)[9]. The diagnosis of Ludwig's angina is based on the history and examination that made on clinical grounds. The white cell count and the inflammatory markers are usually raised. Radiological investigations allow knowing the extent of spread. The ultrasound or computed tomography (CT) scan delineate the abscess and confirm diagnosis, although abscess

formation is rare[5]. Needle aspiration under ultrasound or CT guidance should be considered and may be helpful in some circumstances. Culture and sensitivity of collected pus/fluid might be helpful in the choice of appropriate antibiotics. However, established collections will require formal incision and drainage via an external approach.

Airway management is paramount and high-dose intravenous antibiotic therapy targeted to the causing bacteria should be commenced. Tracheostomy may be required for airway management in a significant proportion of patients with well-established Ludwig's angina[2]. Intravenous steroids could be given for 48 hours that can decrease edema and cellulitis and thus help maintain the integrity of the airway and enhance antibiotic penetration[10]. Usually Ludwig's angina is associated with other co-morbid conditions like- malnutrition, diabetes mellitus and immunosuppressive states[11]. It is very important to identify and address these co-morbidities[11]. Complication includes airway obstruction due to laryngeal edema or swelling or pushing back of tongue, extension to mediastinum causing mediastinitis, sepsis and septicemia, pleural empyema, pericarditis and pericardial tamponade and may result in the death of the patient[3]. This study was aimed to find out the microbes responsible for developing Ludwig's angina and their antibiotic susceptibility. This study provides information about the common bacteria and their antibiotic susceptibility that cause Ludwig's angina at a tertiary care hospital in Bangladesh.

Materials and Methods

Study Design

This cross-sectional study was conducted at the Department of Otolaryngology-Head and Neck Surgery, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh from January 2018 to June 2019. A total of 100 diagnosed patients of Ludwig's angina were selected purposively according to inclusion and exclusion criteria. After selection of the subjects; the nature, purpose, risk and benefit of the study were explained to each patient or to legal guardian of the patients in details. Informed written consent was taken from the participants. Ethical clearance was taken from the Institutional Review Board (IRB) and concerned authority of Dhaka Medical College.

Study Population

Patients, irrespective of age and sex, who were diagnosed as Ludwig's angina and their incision and drainage were done to obtain pus which was sent for culture and sensitivity was included in this study. All cases of Ludwig's angina that were treated conservatively or surgically elsewhere were excluded from this study.

Study Procedure

A detailed history was taken from each study patients; thereafter a thorough general and ENT examination were performed. Then clinical specimen (wound swab or pus) was sent for culture and sensitivity. All data regarding history, clinical examination, investigations and treatment were collected in a data collection sheet. Culture was done in MacConkey's agar media, blood agar mediaand/or chocolate agar media using FAN method in BACTEC machine using BACTEC blood culture bottle (Kirby Bauer method/Disc diffusion method). Incubation period was 24-48 hours, incubation temperature was 35±2ºC, incubation environment was aerobic and microaerophilic condition. Susceptibility to antibiotic reports was followed as per CLSI

(Clinical and Laboratory Standards Institute) guidelines. Following antibiotics were taken for sensitivity test. Amikacin, Amoxiclav, Ampicillin, Azithromycin, Cefixime, Ceftazidime, Ceftriaxone, Ciprofloxacin, Cloxacillin, Clotrimazole, Doxycycline, Gentamicin, Levofloxacin, Penicillin G, Vancomycin. Sensitivity pattern of isolates were categorized as Sensitive and Resistant. The culture and sensitivity tests were done in Department of Clinical Microbiology, International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B).

Statistical Analysis of Data

Data were collected, cross-checked, compiled and tabulated according to key variables and functional assessment scoring. The analysis of different variable was done according to standard statistical analysis. Quantitative data were expressed as frequency with percentage and qualitative data were expressed as mean with standard deviation. Data were processed and analyzed using software SPSS version 22.0.

Results and Observations

This cross sectional study was intended to find out the microbes responsible for developing Ludwig's angina and their antibiotic susceptibility at the Department of Otolaryngology-Head & Neck Surgery, DMCH, Dhaka, Bangladesh from January 2018 to June 2019. Most of the patients were in 3rd decade (45%) followed by 5th decade (22%) then 4th decade (11%). Minimum age, maximum age and mean (±SD) age were 17 years, 70 years and 36.83±13.7 years respectively (Table- 1). Out of 100 study cases 74% were male and 26% were female; male tofemale ratio was 2.8:1 (Figure- 1). Majority of study patients (76%) did not maintain proper oral hygiene (Figure- 2).

Table- I

Age distribution of the study patients (N= 100)

Age (years)	Frequency (n)	Percentage (%)
<20	7	7.0
21-30	45	45.0
31-40	11	11.0
41-50	22	22.0
51-60	9	9.0
>60	6	6.0
Total	100	100.0
Mean ± SD	36.83±13.7 years	
Range	17 – 70 years	

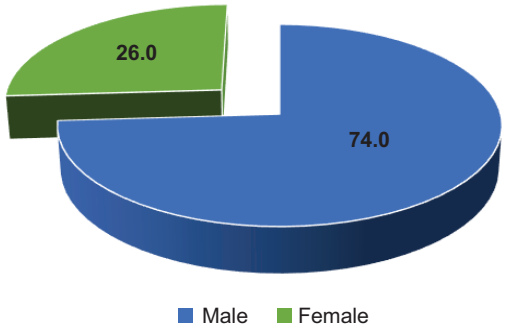

Figure-1: *Gender distribution among the study population (N= 100)*

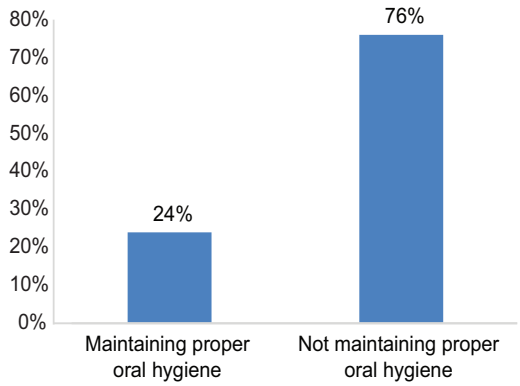

Figure- 2: *Oral hygiene maintainer among the study population (N= 100)*

Regarding clinical presentations; among all study cases (100%) presenting symptoms were swelling in the floor of the mouth and neck, pain and tenderness with fever. Of them; 90% study patients had dysphagia, 80% study patients had a history of dental disease and 10% study patients had respiratory distress 10% (Table- II).

Table-II
Clinical presentations of the study population (N= 100)

Clinical * presentations	Frequency (f)	Percentage (%)
Swelling in the floor of the mouth and neck	100	100.0
Pain and tenderness	100	100.0
Fever	100	100.0
Dysphagia	90	90.0
History of dental disease	80	80.0
Respiratory distress	10	10.0

*Multiple responses

It was observed that, the most common (78%) source of infection ofLudwig's angina was various forms of dental infection followed by submandibular sialadenitis (6%), tonsillar infection (5%), history of tooth extraction (5%) and other factors (6%) (Table- III).

Table- III
Sources of infection among the study patients (N= 100)

Sources of infection	Number of cases	Percentage (%)
Dental infection	78	78.0
Submandibular sialadenitis	6	6.0
Tonsillar infection	5	5.0
History of tooth extraction	5	5.0
Other	6	6.0

Analyzing the associated predisposing factorsthat affecting the disease (Ludwig's angina) of the study patients revealed that; maximum patients (54.0%) had diabetes mellitus followed by smoking habits (31%), betel nut chewing habits (25%), chronic kidney disease (CKD) (4%) and alcoholism (2%) (Table- IV).

Table- IV
Associated predisposing factors among the study patients (N=100)

Predisposing factors	Number of cases	Percentage (%)
Diabetes mellitus	54	54.0
Smoking habits	31	31.0
Betel nut chewing habits	25	25.0
Chronic kidney disease (CKD)	4	4.0
History of alcoholism	2	2.0

In this study, majority (89%) of the study patients had no complications, while 11 patients developed different complications like necrotizing fasciitis (5%), necrotizing fasciitis with mediastinitis (4%) and necrotizing fasciitis with septicemia (2%) (Table- V).

Table- V
Complications of Ludwig's angina among the study patients (N= 100)

Complications	Frequency (n)	Percentage (%)
No complications	89	89.0
Necrotizing fasciitis	5	5.0
Necrotizing fasciitis with Mediastinitis	4	4.0
Necrotizing fasciitis with Septicemia	2	2.0

In this study 66 study cases were infected by monomicrobes and 22 cases were infected by polymicrobes, while no organism was found in 12 study cases. Among the study cases total 111 microbes were identified. The identified common organisms were *Streptococcus viridians* (30.6%), *Staphylococcus aureus* (25.2%), *E. coli* (17.2%), *Pseudomonas* (11.7%), *Klebsiella* (9.9%) and *Acinetobacter* (5.4%) (Table- VI).

Culture and sensitivity reports revealed that most effective antibiotic was Ceftriaxone (57.7%) followed by Gentamicin (49.5%), Ciprofloxacin (41.5%), Cotrimoxazole (40.6%), Vancomycin (38.7%), Doxycycline/ Levofloxacin (28.8%), Amikacin (27%) and Amoxiclav (20.7%) (Table- VII).

Table- VI

Causative isolated bacteria in the study population (n= 111)

Isolated bacteria	Frequency (f)	Percentage (%)
Streptococcus viridians	34	30.6
Staphylococcus aureus	28	25.2
E. coli	19	17.1
Pseudomonas	13	11.7
Klebsiella	11	9.9
Acinetobacter	6	5.4

Table-VII

Causative microorganisms and their sensitivity to antibiotics among the study population (n= 111)

Antibiotics	Sensitivity pattern of isolates (of organisms)								
	Streptoc-occus viridians (34)	*Staphyloc-occus aureus* (28)	*E. coli* (19)	*Psudom-onas* (13)	*Klebsiella* (11)	*Acineto bacter* (6)	-Polymic-robes (17)	Total (111)	Percentage (%)
Amikacin	14	0	7	0	3	0	6	30	27.0
Amoxiclav	12	0	4	0	0	0	7	23	20.7
Ampicillin	8	0	4	0	0	0	5	17	15.3
Azithromycin	0	0	0	0	0	0	0	0	0
Cefixime	9	0	4	0	0	0	0	13	11.7
Ceftazidime	9	0	4	0	0	0	4	17	15.3
Ceftriaxone	24	8	11	6	4	4	7	64	57.7
Ciprofloxacin	24	0	7	0	6	4	5	46	41.5
Cloxacillin	8	6	4	0	0	0	1	19	17.1
Cotrimazole	17	15	4	0	0	0	9	45	40.6
Doxycycline	16	15	0	0	0	5	1	32	28.8
Gentamicin	15	11	13	0	3	0	13	55	49.5
Levofloxacin	20	2	4	0	0	0	6	32	28.8
Penicillin G	8	0	4	0	0	0	5	17	15.3
Vancomycin	20	15	0	0	0	0	8	43	38.7

Among the study group, majority of the patients (71%) were treated by a combination of Ceftraixone and Metronidazole followed by 19% by Ciprofloxacin with Metronidazole combination, 6% by Amoxicillin + Clavulanic acid with Metronidazole combination and 4% by Cefuroxime with Metronidazole combination before the availability of culture and sensitivity reports (Table- VIII).

Table- VIII
Antibiotics used before the culture and sensitivity results among the study patients (N=100)

Antibiotics	Frequency (f)	Percentage (%)
Ceftriaxone and Metronidazole	71	71.0
Ciprofloxacin and Metronidazole	19	19.0
Amoxicillin + Clavulanic acid and Metronidazole	6	6.0
Cefuroxime and Metronidazole	4	4.0

Discussion:

Ludwig's angina is a diffuse cellulitis of submandibular, submental and sublingual spaces due to odontogenic infection. The major predisposing factors include- poor oral hygiene, dental infection, malnutrition, diabetes mellitus and immunosuppressive states[8]. It presents as an acute onset, spreads rapidly and causing neck swelling, edema at the floor of the mouth, pain, fever, trismus, foul-smelling pus discharge, dysphagia, airway edema and tongue displacement resulting a compromised airway with stridor[10]. An early diagnosis and appropriate treatment could be a life saving[8]. In this study an attempt was made to find out the microbes responsible for developing Ludwig's angina and their antibiotic susceptibility at a tertiary care hospital in Bangladesh. The mean (±SD) age of the study patients was 36.83±13.7 years that was ranged from 17 to 70 years and majority (26.67%) of the patients were in the 3rd decade of life. Male were predominant in this study. These findings were consistent with a couple of related previous study[6,12]. In this study76% patients did not maintain proper oral hygiene that might predispose the Ludwig's angina. In accordance Fakir *et al.* reported that male are affected more than female and it mainly affects the patients having poor oral hygiene[6].

In this present study, all the study cases (100%) were presented with swelling in the floor of the mouth, pain and tenderness and fever; but dysphagia (90%), history of dental disease (80%) and respiratory distress (10%) were also observed among them. These findings were comparable with previous studies[8,12]. The source of infection for Ludwig's angina among the study cases includes dental infection (78%), sub-mandibular sialadenitis (6%), tonsillar infection (5%), history of tooth extraction (5%) and other factors (6%). These findings were supported by similar previous studies[8,13-16]. Diabetes mellitus was the most common (54%) influencing factor for Ludwig's angina among the patients in this study. Diabetes mellitus was the commonest associated co-morbidity reported by related previous studies[8,11-15]. It was reported that presence of diabetes had a significant correlation with the management of the disease[11-16]. The patients who had more severe uncontrolled diabetes at the time of admission presented with more severe symptoms of Ludwig's angina and needed an immediate attention to control of the blood sugar levels to achieve complete cure[15]. The duration of hospital stay and morbidity was more as compared to the

non-diabetic Ludwig's angina patient[11-15]. In this current study only 11 patients developed complications, of them; all patients had necrotizing fasciitis, 2 patients had necrotizing fasciitis with septicemia, 4 patients had necrotizing fasciitis with mediastinitis; these finding was an agreement of a related previous study[12].

In this study an attempt was made to know the organisms responsible for Ludwig's angina by aerobic culture. Anaerobic culture was not done because it is not available in our centre. The pus obtained after incision and drainage did not show any microbial growth in 12 study cases. In total, 111 microbes were identified. The common organisms were *Streptococcus viridians* (30.6%), *Staphylococcus aureus (*25.2%), *E.coli* (17.2%), *Pseudomonas* (11.7%), *Klebsiella* (9.9%) and *Acinetobacter* (5.4%). These findings were consistent with a couple of previous studies[8,12,16-18]. In this study, 57.7% of the microorganisms were sensitive to Ceftriaxone. But Gentamycin (49.5%), Ciprofloxacin (41.5%), Cotrimoxazole (40.6%), Vancomycin (38.7%), Doxycycline (28.8%) and Amikacin (27%) were also sensitive to different micro-organisms. Almost similar result was observed in a couple of previous study[19-20]. Among the study patients; majority of the patients (71.0%) were treated by a combination of Ceftraixone and Metronidazole. However 19% patients were treated by Ciprofloxacin and Metronidazole, 6% patients were treated by Amoxacillin+ clavulunic acid and Metronidazole, but only 4% patients were treated by Cefuroxime and Metronidazole before the availability of culture sensitivity report. Metronidazole was used for anaerobic bacteria. Antibiotics were changed according to their culture sensitivity report in resistant cases. Best response was observed by the use of Ceftraixone and Metronidazole combination. In complicated cases (11 cases), Meropenem and sometimes Piperacillin+Tazobactam combination were used.

Despite the improvement in mortality rate following antibiotic therapy and surgical intervention, Ludwig's Angina is still a dangerous disease that can have a fatal outcome mostly due to the rapid airway obstruction[21,22]. The cases presented late and had uncontrolled diabetes mellitus may be complicated by necrotizing fascitis on a background of severe sepsis and mediastinitis.

Conclusion:

This study concluded that most of the patients with Ludwig's Angina are male and majority of patients were in the 3rd decade of life. Dental infection and diabetes mellitus are the important risk factors where *Streptococci Viridans, Stahylococcus Aureus, E. Coli* and *Pseudomonas*are the common organisms. Combination of parenteral antibiotics plays an important role in the control of infection. Most effective antibiotic are Ceftriaxone, Gentamicin and Ciprofloxacin. Early diagnosis, surgical decompression and administration of effective parenteral antibiotics are the key elements for successful management of Ludwig's angina.

Limitations:

It was a single centre study with a relatively small size and the duration of the study was short. Therefore the result of this current study may not reflect the total scenario of the country. The facility to culture and sensitivity test for an anaerobic bacterium is not available in our centre, hence the possibilities of Ludwig's angina due to anaerobic micro-organisms were not considered in this study.

Recommendations:

A multi-centre study with large sample size over long period is recommended to get a more accurate result.

Conflicts of Interest:

The authors declared that they have no conflicts of interest regarding this publication.

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