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ORIGINAL RESEARCH

COVID-19, Diabetes Mellitus, and Ludwig's Angina: A Case Series Exploring Immune Compromise and Complications

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ABSTRACT

Background: This case series discussion explores the relationship between COVID-19 and diabetes-induced immune compromise and its association with the development of Ludwig's angina, a potentially life-threatening deep neck space infection. **Aim:** A retrospective study which was aimed to assess the risk factors, microbiological profile, management strategies of Ludwig's angina patients and its association with odontogenic infections and diabetes mellitus in COVID-19 pandemic. **Methods:** The study population consisted of 38 patients of Ludwig's angina those presented to and were managed in the department of ENT, Government Medical College, Amritsar, Punjab, India, from January 2021 to March 2024. All the patients exhibiting clinical symptoms and signs of Ludwig's angina were examined and a detailed history of the duration of each symptom, present and past illness, dental infection, throat infection, diabetes mellitus was taken. **Results:** Results: It was observed that in 60.52% cases of Ludwig's angina history of dental infection, followed by tonsillar infection (15.78%), oral musosal injury (13.15%) and tooth extraction (10.5%). Streptococcus viridans was found in 23.68% patients, Staphylococcus aureus (13.15%), no growth in 50% cases. Major co-morbidity was diabetes mellitus (63.15%), followed by viral infections (HIV and HCV) in 15.78% and COVID-19 infections in 11.89% patients. Surgical drainage was performed in 81.57% cases including tracheostomy in 12.5% cases whereas rest treated medically. **Conclusions:** Ludwig's angina should be actively treated as a surgical and medical emergency in which incision and drainage is required as early as possible. Uncontrolled diabetes mellitus delayed treatment of odontogenic infection in COVID-19 pandemic that developed Ludwig's angina and highlight the importance of early recognition and intervention to mitigate potential life-threatening complications.

Keywords: Ludwig angina, Odontogenic infection, COVID-19 pandemic, Immunocompromise.

INTRODUCTION

Ludwig's angina is a rapidly progressive, potentially life-threatening cellulitis that affects the submandibular, sublingual, and submental spaces of the neck. It is typically caused by polymicrobial infections, most commonly originating from dental or oropharyngeal sources. The condition is characterized by rapid neck swelling, airway compromise, and the potential for septicemia if not promptly treated. Individuals with underlying medical conditions such as diabetes mellitus are at an increased risk of developing serious complications, including Ludwig's angina. In the context of the COVID-19 pandemic, individuals with diabetes face an elevated risk of severe infection due to their compromised immune response.

COVID-19 and Immune Compromise

COVID-19, caused by the novel coronavirus SARS-CoV-2, is notorious for its ability to undermine the immune system. The virus primarily infects the respiratory system, where it can cause pneumonia and severe respiratory distress. In individuals with diabetes, the risk of developing severe COVID-19 is significantly higher due to the immunocompromised state commonly associated with this metabolic disorder (1).

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Diabetes mellitus is characterized by elevated blood glucose levels and impaired insulin production or utilization. This chronic condition weakens the immune response, making individuals more susceptible to infections. In the case of COVID-19, diabetic patients may experience a delayed and less effective immune response, which increases the likelihood of viral replication and spread throughout the body (2).

Understanding Diabetes and Immune Compromise

Diabetes, particularly Type 2 diabetes, is recognized for its multifaceted impact on the immune system. The condition disrupts the normal functioning of immune cells, impairing their ability to combat infections effectively. Chronically high blood sugar levels associated with diabetes can lead to reduced functionality of various immune cells, such as neutrophils and macrophages, which are crucial for fighting off bacterial infections.

Moreover, diabetes affects the body's ability to heal wounds and injuries, thereby increasing the susceptibility to infections. When coupled with poor blood circulation, a common issue in diabetic individuals, this creates an environment conducive to the development of infections, particularly in the oral cavity.

Ludwig's Angina: A Rare but Serious Complication

Ludwig's Angina is an uncommon, rapidly progressing, and potentially life-threatening condition that affects the soft tissues of the mouth and throat, particularly the floor of the mouth. It results from a polymicrobial infection, commonly involving Streptococcus and Staphylococcus bacteria, and can lead to severe swelling and compromise of the airway (3).

In diabetic individuals with COVID-19, the combination of immune compromise and the viral infection can create a perfect storm for the development of Ludwig's Angina. The weakened immune response in diabetics allows oral bacteria to flourish, and COVID-19 may further impair the body's ability to control and eliminate these pathogens. This synergistic effect can lead to a rapid and severe soft tissue infection in the mouth and throat, potentially leading to Ludwig's Angina (4). The most feared complication of Ludwig’s angina is airway obstruction. Other complications include mediastinitis, internal jugular vein thrombophlebitis, empyema, necrotizing fascitis, osteomyelitis, and aspiration pneumonia. (5). If left untreated, the condition often leads to asphyxia resulting in mortality rate of 50%. However, with aggressive surgical intervention, the administrationy of the antibiotics, and improvement of dental care, the mortality rate can be reduced to less than 10% (6).

MATERIALS AND METHODS

The study population consisted of cases of Ludwig angina that were presented to and managed by the Department of ENT, Government Medical College, Amritsar, Punjab, India, from January 2021 to March 2024. All the patients exhibiting clinical symptoms and signs of Ludwig angina were included in this study with informed consent and after ethical approval. A detailed history of duration of each symptom, present and past illness, dental infection, throat infection, diabetes mellitus and past COVID 19 infection was taken. Local and systemic examination was conducted and routine blood investigations including random blood sugar/fasting blood sugar, renal function test, HIV, and hepatitis B surface antigen were performed for all cases. Where odontogenic infection was thought to be the predisposing factor, dental consultation and orthopantogram were done.

Computed tomography and magnetic resonance imaging were performed to rule out impending complications. Incision and drainage were performed in most of the cases presenting with significantly large swelling causing dysphagia and respiratory distress. Pus samples were sent for culture and sensitivity testing. After incision and drainage, the patients were treated with IV fluid, parental antibiotics, injectable analgesic, and hydrogen peroxide mouth wash gargles for maintaining oral hygiene. Antibiotic treatment was adjusted based on the culture report. Tooth extraction was done in cases where the source of infection was found to be of dental origin. Adequate wound care and daily dressing were done under aseptic precautions. Most of the patients improved gradually within a few days and were discharged in satisfactory condition with instructions regarding dental care and control of diabetes.

Statistical analysis was performed using SPSS software. Descriptive data presented as percentages and means ± standard deviation (SD). Kendall’s tau-B was used for ordinal values. Chi-squared analysis was used for relationships of nominal variables. Student t test (2-tailed) used for comparisons of parametric data. Results were deemed significant with a p value of < 0.05.

RESULTS

Thirty-eight patients who presenting with features suggestive of Ludwig angina were included in the study. The most common age group involved was 15-45 years. Females (57.89%) were more commonly affected than males (42.1%). Figure No.1 and Tables No. 1-5.

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Table No. 1: Association with risk factors

Etiology	No. of patients	Percentage
Dental infection	23	60.52
Tonsillar infection	6	15.78
Tooth extraction	4	10.52
Oral mucosal injury	5	13.15

Figure No 1 : Patients presented with Ludwig angina.

Table No. 2: Clinical presentation of patients

Presentation	No. of patients	Percentage
Neck swelling	30	78.94
Pain	32	84.21
Fever	10	26.31
Dysphagia	26	68.42
Respiratory distress	9	23.68
Trismus	22	57.89
Sore throat	6	15.78

Table No. 3: Associated Comorbities with ludwig angina

Co-morbidities	No. of patients	Percentage
Diabetes	24	63.15
HIV and HCV	6	15.78
Blood disorders	3	7.89
Chronic heart failure	2	5.26
Post chemotherapy	2	5.26
COVID-19 infection	4	11.89

Table No. 4: Organisms isolated from the pus

Organism	No. of patients	Percentage
S. Viridans	9	23.68
S. Aureus	5	13.15
E.coli	3	7.89
Klebsiella	2	5.26
No growth	19	50

Table No.5: Complications

Complications	No. of patients	Percentage
Necrotizing fasciitis	1	2.63
Peritonsillar abscess	2	5.26
Tracheostomy	5	13.15
Death	1	2.63
No complications	29	76.31

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DISCUSSION

The COVID-19 pandemic has brought to light the complex interplay between viral infections and underlying medical conditions. There is a complex interplay between COVID-19 and diabetes mellitus, leading to immune compromise and predisposing individuals to severe infections such as Ludwig's angina. The inflammatory response triggered by SARS-CoV-2 in patients with diabetes can impair their ability to combat polymicrobial infections, as seen in the rapid progression of deep neck space infections.(7) Several factors may contribute to the increased risk of Ludwig's angina in patients with COVID-19 and diabetes mellitus, including hyperglycemia, compromised neutrophil function, and microvascular complications. Hyperglycemia can impair immune cell function and promote bacterial growth, facilitating the development of severe infections. In addition, diabetes-related microvascular complications may reduce blood flow to infected tissues, making them more susceptible to infection. (8)

In the present study, most of the patients (31.5%) were between 31-45 years of age, followed by 15-30 years (28.9%). Females (57.89%) were more commonly affected than males (42.1%). The main etiological factors in our study were caries tooth (60.52%), followed by tonsillar infection (15.78%), oral mucosal injury (13.15%) and tooth extraction (10.5%). (Table No. 1). In a study done to evaluate the medical treatment of Ludwig's angina in 47 patients, the odontogenic cause was found in 85.1% of cases. (9) Thus, poor oral hygiene accounted for the majority of cases. In a study by Ojoke et al odontogenic focus was present in almost all the 13 patients of Ludwig's angina. (10) A study by Neal et al concluded that odontogenic infection is the main cause of Ludwig's angina. (11)

The most common symptoms reported by patients in our study were neck swelling (78.94%), neck pain (84.21%), dysphagia (68.42%), trismus (57.89%) and fever (26.31%). Some patients reported complain of difficulty in breathing (23.68%) and amongst these five patients had stridor at presentation so tracheostomy was performed (Table No. 2). A study conducted by Fakir et al in 50 cases of Ludwig angina showed neck swelling, neck pain and fever in 100% of cases, whereas dysphagia was present in 80% of cases. (8)

In our study most common co-morbidity was diabetes mellitus in 63.15% cases, followed by HIV and HCV infections in 15.78% and 11.89% with COVID-19 infection. There was 1 (2.5%) case each of CKD, anemia, post chemotherapy and 2 (5.26%) cases of chronic heart disease (Table No. 3). In a study involving 185 cases of deep neck infections, 34.1% had underlying systemic disease, among them 88.8% had diabetes mellitus, 9.5% had chronic renal failure, 4.8% had liver cirrhosis, 2.4% had myelodysplastic syndrome and 1.2% had gastric malignancy. (12)

In another study conducted by John et al in 30 patients diabetes mellitus was present in 63.3% patients. (13)

Surgical drainage was performed in 31 cases whereas only 7 patients received only medical treatment.

Figure No. 2. Emergency tracheostomy was performed in 5 (12.5%) patients who were having respiratory distress with stridor at the time of presentation. All patients were given systemic antibiotics based on culture sensitivity report. In a study conducted in Dhaka, out of 50 cases, 40 (80%) had to be drained surgically, whereas only 10 cases could be treated medically, the reason for surgical drainage again being abscess formation and airway compromise. (8) Study by Ojoke et al also showed that surgical intervention was done in almost all the 13 patients of Ludwig's angina. (10) Ambikavathy et al in the study of 40 patients concluded that only 25% of patients were managed conservatively and surgical intervention was done in rest the 75% patients. (14)

The most common organisms found in our study was *S. viridans* which was found in 9 cases (23.68%), followed by S. Aureus in 5 cases (13.15%).Some patients had Escherichia coli (7.89%) and Klebsiella infections (5.26%). No growth was observed in 50.5% cases. Thus, the majority of cases were associated with aerobic bacterial growth (Table No. 4). In a study done by Fakir et al out of 32 samples, *Streptococcus* was the most common organism (13) followed by *Staphylococcus* (6), *E. coli* (4) and *Pseudomonas* (3). (8) In another study conducted by Sharma et al 12 samples were cultured, anaerobic growth was not seen in any sample, whereas five samples showed no growth. (9) In another study of 30 patients on culture examination *S. viridans* was found in 36.6% patients, *S. aureus* in 16.6%, *S. pyogenes* in 13.3% patients and no growth was seen in 23% patients. (13)

In the present study, 9 patients experienced complications 1 patients developed necrotizing fasciitis requiring ICU management. 2 patients presented along with peritonsillar abscess, which was later drained. 5 patients presented with stridor and respiratory distress requiring emergency tracheostomy. 1 patient died due to septicemia (Table No. 5). In another study by Okoje et al out of 13 patients 2 patients died during treatment. (10) In a study conducted in Nigeria, septicemia, mediastinitis, empyema thoracis, necrotizing fasciitis, laryngeal spasm and renal failure were the complications recorded in five cases (31.3%).(15) In a study by Prasad et al out of 15 patients 1 patient died during the course of treatment. (16)

COVID-19 infection further complicates the management of Ludwig angina as it can worsen pneumonia, leading to pulmonary embolism or septic shock (17, 18). Thus, despite the availability of antibiotics in the present era, systemic illnesses pose a major threat in development of life threatening complications. The disease can be fatal if neglected. We advocate that surgical management should be

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done at earliest in presence of respiratory difficulty as medical treatment alone cannot be sufficed. (19)

Case Presentations

Case 1: A 58-year-old male with a long-standing history of poorly controlled type 2 diabetes mellitus presented to the emergency department with symptoms suggestive of COVID-19. After testing positive for SARS-CoV-2, the patient was managed as an outpatient. However, he returned to the hospital five days later with rapidly progressing neck swelling and difficulty swallowing. Imaging confirmed the diagnosis of Ludwig's angina. The patient was promptly intubated and underwent surgical drainage of the infected spaces. Despite aggressive treatment, the patient succumbed to septic shock.

Case 2: A 52-year-old female with type 1 diabetes mellitus of 25 years duration was admitted with confirmed COVID-19. She exhibited mild respiratory symptoms but developed progressively worsening neck pain and swelling over three days. Imaging showed Ludwig's angina, and she was promptly taken to surgery for drainage. The patient's course was complicated by sepsis and respiratory failure but ultimately survived with intensive medical management. Figure No.2.

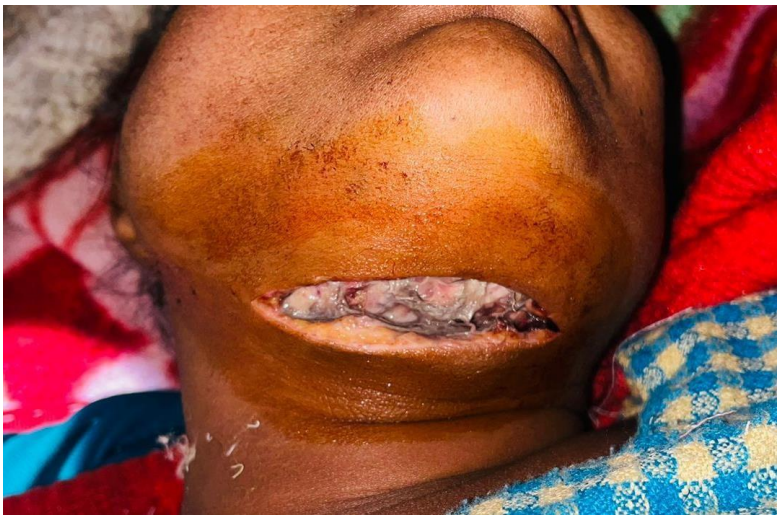

Figure No. 2: Patient presented with Ludwig angina and incision and drainage done.

3: A 49-year-old male with a recent diagnosis of type 2 diabetes mellitus was admitted with severe COVID-19 pneumonia. He initially responded well to antiviral and oxygen therapy. However, on day 10 of hospitalization, he developed rapidly progressing neck swelling. Imaging confirmed Ludwig's angina, and surgical intervention was performed. The patient recovered following a prolonged hospital stay and antibiotic treatment. Figure No. 3

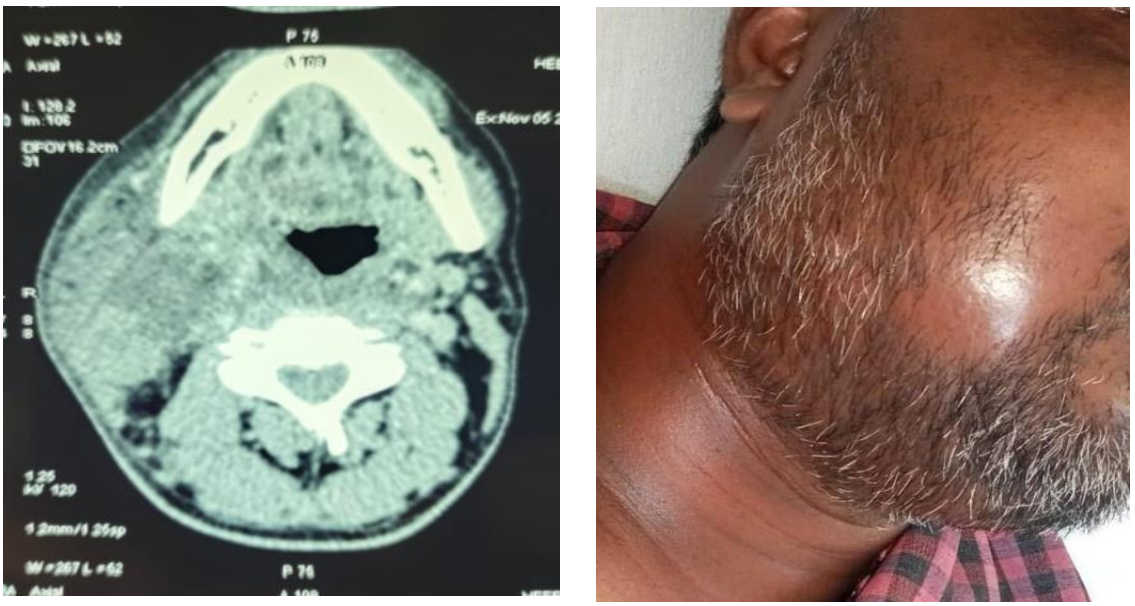

Figure No.3: The CECT axial view showing involvement of right submandibular space.

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Case 4: Necrotising fasciitis

One patient developed necrotizing fasciitis requiring ICU management (Figure 2). A male patient in his 40s presented to the ED with the complaint of shortness of breath. He had not gone to the dentist due to fear of being infected with COVID-19. The oxygen saturation of the patient was 80%, and his other vital signs were stable. There was widespread pitting oedema, tenderness and crepitation on his neck. His right molar tooth was broken and bruised, and his tongue was pushed to the right side on oropharyngeal examination. Free air was observed under the skin of the cervical region, around the thyroid gland and the clavicle, between the muscular structures of the neck, and around the soft tissues on the CT of the neck. The neck tissues were necrotic and black in colour. Figure No. 4

Figure No. 4: Patient with necrotizing fascitis

Preventive Measures and Recommendations: To mitigate the risk of Ludwig's angina in diabetic individuals during the COVID-19 pandemic, several strategies can be implemented: Early recognition and aggressive management are crucial in preventing fatal outcomes in such cases. Close monitoring of patients with diabetes and COVID-19 for signs of neck space infections, including neck pain, swelling, and difficulty swallowing, is imperative. Once diagnosed, immediate surgical intervention, appropriate antibiotics, and intensive care support are essential. (20)

Control Blood Sugar Levels: Diabetic individuals should focus on maintaining optimal blood sugar control to minimize the negative impact of hyperglycemia on their immune function.

Oral Health and Regular Dental Check-ups: Diabetic individuals should prioritize good oral hygiene practices and seek regular dental check-ups to address any oral infections promptly.

COVID-19 Vaccination: Getting vaccinated against COVID-19 is crucial for individuals with diabetes, as it can reduce the risk of severe infection and its associated complications.

Adherence to Health Guidelines: Following public health guidelines, such as wearing masks, practicing good hand hygiene, and social distancing, can help reduce the risk of COVID-19 infection.

SUMMARY

This case series underscores the importance of recognizing the potential life-threatening consequences of COVID-19 and diabetes mellitus-induced immune compromise, leading to conditions such as Ludwig's angina. Healthcare providers should maintain a high index of suspicion in these at-risk patients and act swiftly to mitigate the progression of deep neck space infections through early diagnosis and intervention. Patients with diabetes and COVID-19 should receive diligent medical management, including glycemic control, to reduce the risk of severe complications like Ludwig's angina.

CONCLUSION

We advocate that surgical management should be done at earliest in presence of respiratory difficulty as medical treatment alone cannot be sufficed. Diabetic patients and patients with history of COVID infection are susceptible to frequent infections which increase the risk of complications, hospital stay and can also lead to mortality.

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