

## A STUDY OF CLINICAL AND AETIOLOGICAL PROFILE OF LOWER RESPIRATORY TRACT INFECTIONS IN PATIENTS WITH DIABETES MELLITUS

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### ABSTRACT

#### BACKGROUND

Diabetes Mellitus (DM) is one of the most common metabolic disorders causing damage in multiple organs. The normal role of polymorphonuclear leukocytes, leukocyte adherence, chemotaxis, and the processes of phagocytosis may all be compromised and associated with an increased incidence or severity of common upper or lower respiratory tract infections. The impact that these disturbances have on the development and outcomes of infectious diseases has been poorly studied.

The objectives of this study were to evaluate the aetiological, demographic profile, clinical presentation and risk factors of lower respiratory tract infections and the severity of illness and outcome in patients with Diabetes Mellitus.

#### MATERIALS AND METHODS

This study includes 50 patients with Diabetes Mellitus admitted in ICU and Medical wards of Sri Venkateswara Ramnarain Ruia Government General Hospital, Tirupati, with lower respiratory tract infection.

#### RESULTS

In the current study, 45 patients got discharged without any complications and 5 patients expired. The cause of death is Tuberculosis in three patients and staphylococcal pneumonia and streptococcal pneumonia one each.

#### CONCLUSION

Increased incidence of respiratory infections is seen in males with poor glycaemic control. Streptococcus pneumoniae is the most common pathogen with unilobar involvement. Mortality is due to advanced age, increased duration of diabetes, prolonged duration of illness, poor drug compliance and increased severity of illness.

#### KEYWORDS

Diabetes, Pneumonia, Tuberculosis.

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#### BACKGROUND

Diabetes Mellitus is a major and increasing public health and clinical problem.<sup>1,2</sup> According to an estimate the world prevalence of Diabetes among adults will increase to 7.7% or 439 million adults by 2030, with a 69% increase in numbers of adults with Diabetes in developing countries and a 20% increase in developed countries.<sup>3</sup> Diabetes Mellitus (DM) is one of the most common chronic diseases worldwide and is associated with high morbidity and mortality<sup>4</sup> Several aspects of immunity are altered in patients with Diabetes. The normal role of polymorphonuclear leukocytes, leukocyte adherence, chemotaxis, and the processes of phagocytosis

may all be compromised.<sup>5</sup> Antioxidant systems involved in bactericidal activity can also be impaired.<sup>6</sup>

Lower respiratory tract infections in Diabetes Mellitus are characterized by alterations in host defense, function of respiratory epithelium and ciliary motility. Hyperglycaemia can cause an alteration in host defense and increased susceptibility to infections. Infections caused by certain microorganisms (Staphylococcus aureus, gram-negative organisms, and Mycobacterium tuberculosis) occur with increased frequency. Infections due to other microorganisms (Streptococcus pneumonia and influenza virus) are associated with increased mortality and morbidity.

Diabetes is a risk factor for bacteraemia in patients with pneumococcal pneumonia and is associated with increased mortality.<sup>7,8</sup> There is increased mortality and an increased incidence of bacterial pneumonia and ketoacidosis among diabetic patients during epidemics of influenza pneumonia.<sup>5</sup> Guidelines recommend influenza and pneumococcal vaccines for all patients with Diabetes.<sup>9</sup>

The incidence of tuberculosis in diabetic individuals is 4–5 times greater than among the non-diabetic population. It is thought that malfunction of monocytes in patients with

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Diabetes may contribute to the increased susceptibility to tuberculosis and / or a worse prognosis.<sup>10</sup> Diabetes, especially the uncontrolled one, predisposes to fungal infections; the most common are candidiasis and mucormycosis.<sup>10</sup>

Respiratory tract infections are the cause of increased hospitalizations in diabetic individuals compared to those without Diabetes.<sup>11,12,13</sup>

**MATERIALS AND METHODS**

*Study Design*

Prospective study

*Study Subjects and Settings*

Patients with Diabetes Mellitus admitted in ICU & Medical wards of Sri Venkateswara Ramnarayan Ruia Government General Hospital, Tirupati with Lower respiratory tract infection.

*Study Sample*

50 In-patients studied prospectively.

*Study Period*

October 2014 –October 2015

*Study Methods*

In-patients with Diabetes Mellitus admitted with lower respiratory tract infection are studied, analysed for various symptoms & signs, investigated accordingly to know the aetiology.

*Inclusion Criteria*

Diabetics >14 years of age on oral hypoglycaemic drugs or insulin and denovo diagnosed Diabetics with symptoms & signs of lower respiratory tract infection.

*Exclusion Criteria*

Diabetics <14 years age, Patients with other immunocompromised states (HIV, Autoimmune disorders, Lymphoproliferative disorders), Patients using immunocompromising drugs, (corticosteroids, anti-cancer agents)

*Statistical Analysis*

The study results are analysed using EPI INFO software Version 7.1.4.0 by: 1) Calculation of frequencies, percentages and mean, 2) Calculation of standard deviation, 3) p value calculation done using one-way ANOVA test. (p value less than 0.05 is considered statistically significant).

*Ethical Clearance*

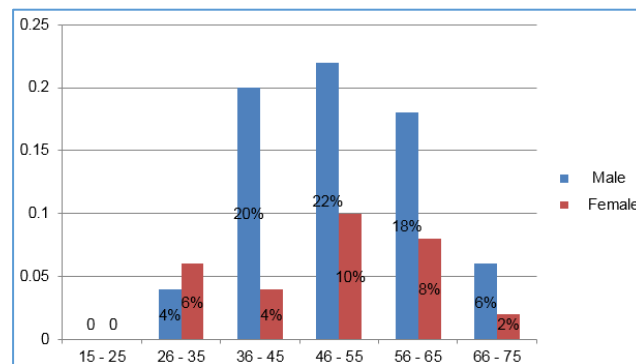
Patients are informed prior to the study and written informed consent taken from the patients or their attendants.

**RESULTS**

Results of the study are-

Age Group	Serial No.	Male	Female	Total
15 - 25	1	0	0	0
26 - 35	2	2 (4%)	3 (6%)	5 (10%)
36 - 45	3	10 (20%)	2 (4%)	12 (24%)
46 - 55	4	11 (22%)	5 (10%)	16 (32%)
56 - 65	5	9 (18%)	4 (8%)	13 (26%)
66 - 75	6	3 (6%)	1 (2%)	4 (8%)
		<b>35 (70%)</b>	<b>15 (30%)</b>	<b>50 (100%)</b>

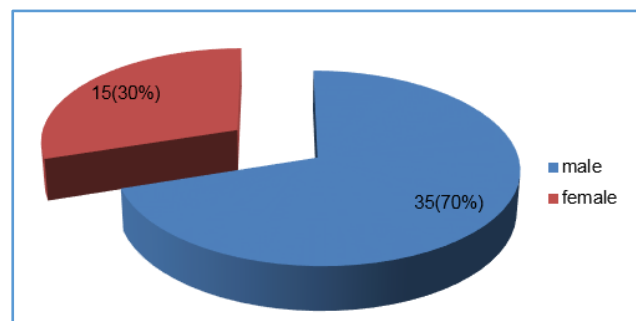
**Table 1. Age and Sex Distribution of the Patients (n = 50)**



**Figure 1. Age and distribution of the patient's sex**

Sex	Age - Mean	± Standard Deviation
Female	50	± 11.89
Male	52	± 9.89
<b>Total</b>	<b>52</b>	<b>± 10.46</b>

**Table 2. Mean age distribution of patients according to sex**

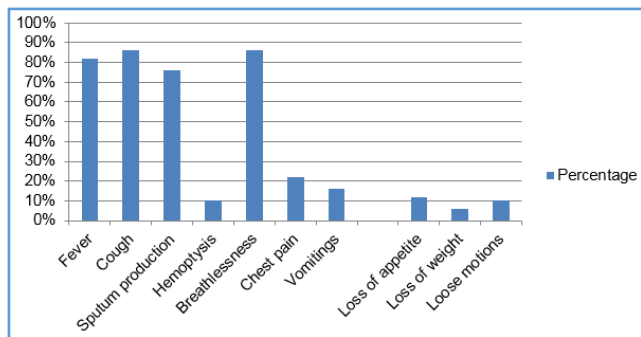


**Figure 2. Sex Distribution**

The study group consisted of 50 patients, among whom 70% were males and 30% females. The peak incidence of illness was in the age group of 46-55 yrs. for both sexes.

	Symptoms	No. of Patients	Percentage
1	Fever	41	82%
2	Cough	43	86%
3	Sputum production	38	76%
4	Haemoptysis	5	10%
5	Breathlessness	43	86%
6	Chest pain	11	22%
7	Vomiting	8	16%
8	Loss of appetite	6	12%
9	Loss of weight	3	6%
10	Loose motions	5	10%

**Table 3. Incidence of Presenting Symptoms of the Patients (n = 50)**

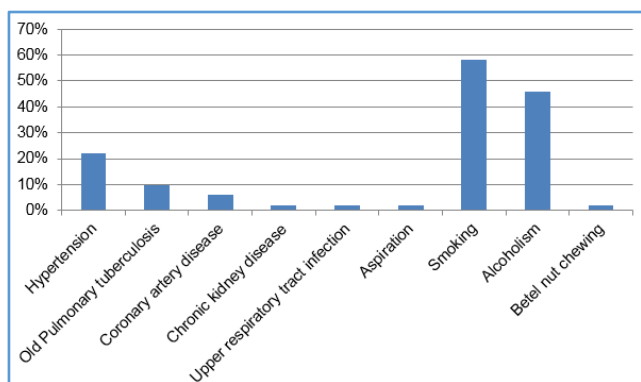


**Figure 3. Incidence of Presenting Symptoms of the Patients**

Most common presenting symptoms in our study were cough and breathlessness in 86% of patients each followed by fever in 82% of patients. Least common presenting symptoms were haemoptysis (10%), loose motions (10%) and loss of weight (6%).

Serial No.	Risk factors & Comorbidities	No. of Patients	Percentage
1	Hypertension	11	22%
2	Old Pulmonary tuberculosis	5	10%
3	Coronary artery disease	3	6%
4	Chronic kidney disease	1	2%
5	Upper respiratory tract infection	1	2%
6	Aspiration	1	2%
7	Smoking	29	58%
8	Alcoholism	23	46%
9	Betel nut chewing	1	2%

**Table 4. Risk Factor Profile of the Patients**

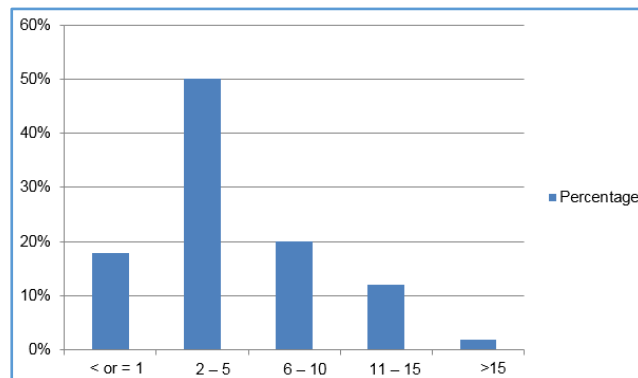


**Figure 4. Risk Factor Profile of the Patients**

Smoking (58%) was the most important risk factor in our study followed by alcoholism (46%) and hypertension (22%). Least common risk factors associated were coronary artery disease (6%) followed by chronic kidney disease (2%).

Serial No.	Duration of Diabetes (in Years)	No. of patients	Percentage
1	< or = 1	9	18 %
2	2 – 5	24	48 %
3	6 – 10	10	20 %
4	11 – 15	6	12 %
5	>15	1	2 %

**Table 5. Duration of Diabetes of the Patients**



**Figure 5. Duration of Diabetes of the Patients**

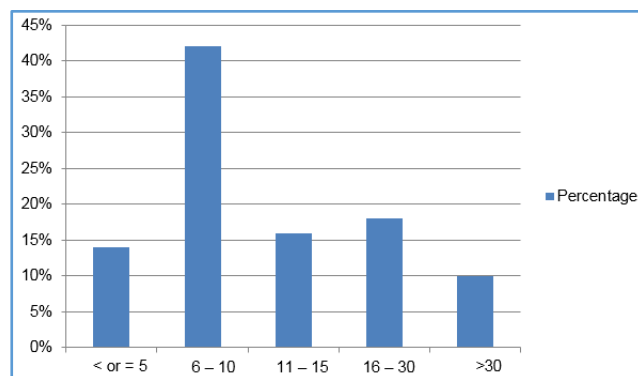
Sex	Diabetes duration mean (years)	± Standard deviation
Female	5.27	± 4.12
Male	5.74	± 4.79
Total	5.60	± 4.56

**Table 6. Mean Duration of Diabetes According to Sex**

In this study, 48 % of patients had their duration of Diabetes between 2-5 years followed by 20% had their duration between 6-10 years.

Serial No.	Duration of illness (in days)	No. of Patients	Percentage
1	< or = 5	7	14 %
2	6 – 10	21	42 %
3	11 – 15	8	16 %
4	16 – 30	9	18 %
5	>30	5	10 %

**Table 7. Duration of Illness of Patients**



**Figure 6. Duration of Illness of Patients**

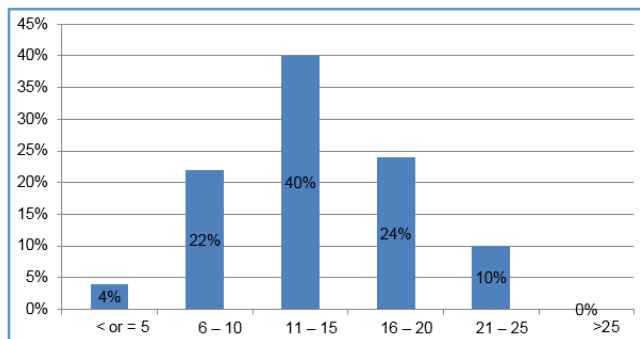
Illness duration mean (days)	Median (days)	± Standard deviation
18.46	10.00	± 20.20

**Table 8. Duration of Illness**

In our study, 42 % of patients had their duration of illness between 6 – 10 days followed by 18 % had their duration between 16 – 30 days.

Serial No.	Duration of Hospital stay (in days)	No. of Patients	Percentage
1	< or = 5	2	4 %
2	6 – 10	11	22 %
3	11 – 15	20	40 %
4	16 – 20	12	24 %
5	21 – 25	5	10 %
6	>25	0	0 %

**Table 9. Duration of Hospital Stay of Patients**



**Figure 7. Duration of Hospital Stay of Patients**

Median duration of hospital stay = 12 days (Male - 13, Female – 11).

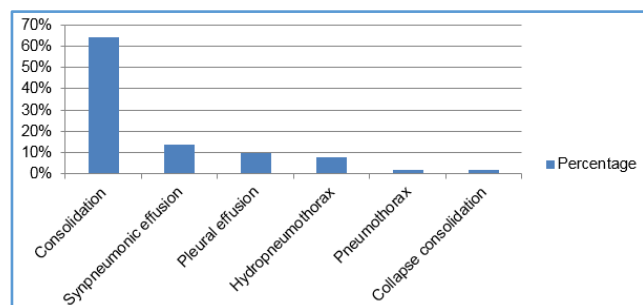
Sex	Hospital stay duration Mean (days)	± Standard Deviation
Female	12.27	± 3.43
Male	14.09	± 4.99
Total	13.54	± 4.62

**Table 10. Mean duration of Hospital Stay according to Sex**

40% of patients had their duration of stay in hospital as 11 – 15 days followed by 24% had stayed for 16-20 days.

Serial No.	Clinical Diagnosis	No. of Patients	Percentage
1	Consolidation	32	64 %
2	Synpneumonic effusion	7	14 %
3	Pleural effusion	5	10 %
4	Hydropneumothorax	4	8 %
5	Pneumothorax	1	2 %
6	Collapse consolidation	1	2 %

**Table 11. Clinical Diagnosis**

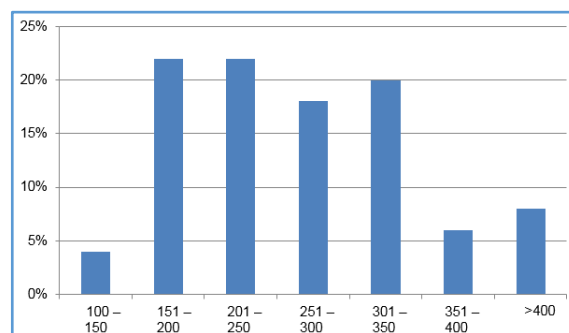


**Figure 8. Clinical Diagnosis**

Most common clinical diagnosis was consolidation present in 64% of patients followed by synpneumonic effusion (14%) and pleural effusion (10%).

Serial No.	Presenting Blood Sugars (mmol/L)	No. of Patients	Percentage
1	5.5 – 8.3	2	4 %
2	8.4 – 11.1	11	22 %
3	11.2– 13.8	11	22 %
4	13.9 – 16.6	9	18 %
5	16.7 – 19.4	10	20 %
6	19.5 – 22.2	3	6 %
7	>22.2	4	8 %

**Table 12. Presenting Blood Sugars of Patients**



**Figure 9. Presenting Blood Sugars of Patients**

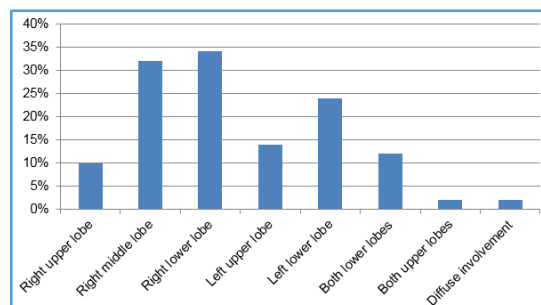
44% of patients had their presenting blood sugars in the range of 151 – 250 mg/dl followed by 20% had their presenting blood sugars in the range of 301 – 350 mg/dl.

Mean blood glucose	271.12 (15.05 mmol/L)
Median	257 (14.27 mmol/L)
Standard deviation	± 89.58 (± 4.97)

**Table 13. Presenting Blood Sugars**

Serial No.	Site Involved	No. of Patients	Percentage
1	Right upper lobe	5	10 %
2	Right middle lobe	16	32 %
3	Right lower lobe	17	34 %
4	Left upper lobe	7	14 %
5	Left lower lobe	12	24 %
6	Both lower lobes	6	12 %
7	Both upper lobes	1	2 %
8	Diffuse involvement	1	2 %

**Table 14. Site of Involvement of Lung**



**Figure 10. Site of Involvement of Lung**

Most common site of involvement in lung was right lower lobe present in 34% of patients followed by right middle lobe in 32%.

Serial No.	Total Patients	Cases with positive Gram stain and/or culture (%)	Cases with positive AFB stain (%)
1.	50 (100 %)	28 (56%)	8 (16%)

**Table 15. Cases where Pathogen Could be Isolated (n=50)**

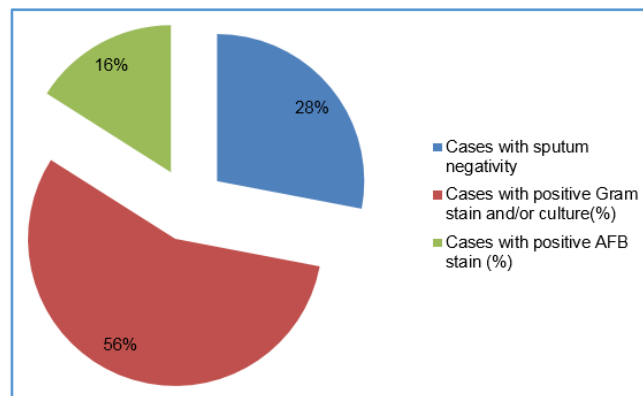


Figure 11. Cases where Pathogen Could be Isolated

In a total of 50 patients studied, pathogen could be isolated in 36 (72%) patients.

Serial No.	Organisms	Number of Patients	Percentage (%)
1	Streptococcus pneumoniae	17	34 %
2	Mycobacterium tuberculosis	8	16 %
3	Staphylococcus aureus	3	6 %
4	Klebsiella pneumoniae	3	6 %
5	Polymicrobial	3	6 %
6	Pseudomonas aeruginosa	2	4 %
7	Legionella pneumophila	1	2 %
8	Escherichia coli	1	2 %
9	Aspergillus	1	2 %

Table 16. Isolation Pattern of Microorganisms from Sputum Samples

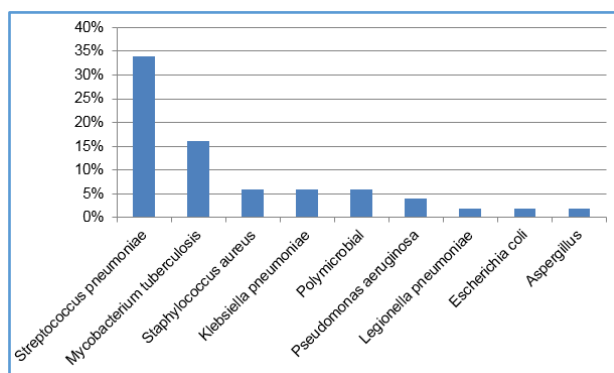


Figure 12. Isolation Pattern of Microorganisms from Sputum Samples

In our study, most common causative organism was streptococcus pneumoniae isolated in 34% of patients followed by mycobacterium tuberculosis in 16% of patients.

Serial No.	Clinical Diagnosis	Mean duration of Hospital Stay (in days)
1	Pneumonia	12.8
2	Synpneumonic effusion	14.2
3	Pleural effusion	17
4	Hydropneumothorax	17.25
5	Pneumothorax	12
6	Collapse consolidation	11

**Table 17. Clinical Diagnosis and Relation with Mean Duration of Hospital Stay**

p value = 0.175, f value =1.618 based on ANOVA.

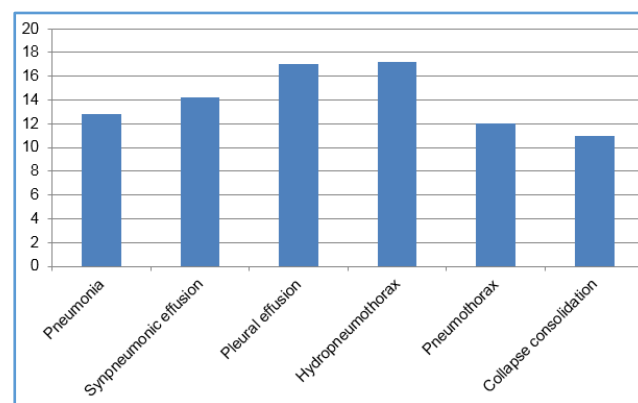


Figure 13. Clinical Diagnosis and Relation with Mean Duration of Hospital Stay

In our study, patients with hydropneumothorax had the highest mean duration of hospital stay (17.25 days) followed by patients with pleural effusion (17 days) but this association was not statistically significant.

Serial No.	Presenting Blood Sugars (mmol/L)	Mean Duration of Hospital Stay (in days)
1	5.5 – 8.3	16
2	8.4 – 11.1	14.18
3	11.2– 13.8	11.7
4	13.9 – 16.6	14.1
5	16.7 – 19.4	13.3
6	19.5 – 22.2	13.3
7	>22.2	15

**Table 18. Presenting Blood Sugars and Relation with Mean Duration of Hospital Stay**

p value = 0.823 f value =0.475 based on ANOVA.

There was no association between presenting blood sugars and mean duration of hospital stay.

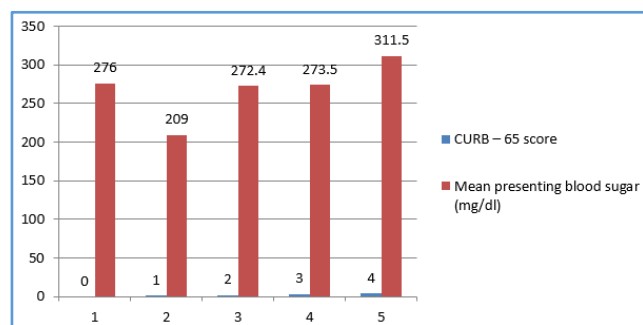
Serial No.	CURB – 65 Score	Number of Patients
1	0	2
2	1	6
3	2	15
4	3	10
5	4	7

**Table 19. Severity of Illness in Patients with Pneumonia**

Serial No.	CURB – 65 score	Mean presenting Blood Sugar – mg/dl (mmol/L)
1	0	276 (15.3)
2	1	209 (11.6)
3	2	272.4 (15.1)
4	3	273.5 (15.2)
5	4	311.5 (17.2)

**Table 20. Severity of Illness and Relation with mean Presenting Blood Sugars**

p Value = 0.496 f Value= 0.859 based on ANOVA.

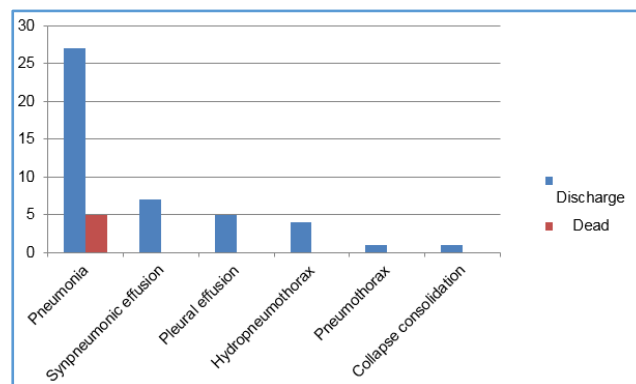


**Figure 14. Severity of Illness and Relation with Mean Presenting Blood Sugars**

Patients with more severe illness (CURB-65 scores of 3 and 4) had high mean presenting bloodsugars (273.5mg/dl and 311.5mg/dl respectively). But this association was not statistically significant.

Serial No.	Clinical Diagnosis	Discharge	Dead
1	Pneumonia	27	5
2	Synpneumonic effusion	7	0
3	Pleural effusion	5	0
4	Hydropneumothorax	4	0
5	Pneumothorax	1	0
6	Collapse consolidation	1	0

**Table 21. Clinical Diagnosis and Outcome**



**Figure 15. Clinical Diagnosis and Outcome**

Of a total of 50 patients, 45 patients got discharged and 5 patients expired. Pneumonia was the clinical diagnosis in all 5 of them.

**DISCUSSION**

Diabetes Mellitus is a common non-communicable disease in India.<sup>14</sup> Diabetic patients have been associated with increased rates of pulmonary infections compared to non-diabetic patients.<sup>15</sup>

In the current study, most frequent presenting symptoms are cough (86%) and breathlessness (86%) followed by fever (82%) and sputum production (76%). Least common respiratory symptoms are chest pain (22%) and haemoptysis (10%).

In the study of Di Yacovo et al, cough (79.5%) was the most frequent presenting symptom followed by breathlessness (64.5%), sputum production (54%) and fever (38.5%).<sup>16</sup>

Most common clinical diagnosis in the present study is pneumonia observed in 40 (80%) patients. Pleural effusion is present in 5 (10%) patients.

In the study conducted by Shruthi Bettgowda et al, pneumonia was observed in 11 (27.5%) patients out of a total of 40 patients and pleural effusion in 6(15%) patients.<sup>14</sup> In the present study, increased rate of infection is seen in patients using oral antidiabetic agents alone (72%). Similar observations were made by Shruthi et al<sup>14</sup> and Miquel Falguera et al.<sup>17</sup> They observed that the rate of infection was more in patients not on insulin therapy. According to Ooi YC et al, intensive insulin therapy and tight glyceemic control were associated with a lower risk of infection.<sup>18</sup>

Unilobar infiltration is more common than multilobar infiltration in the present study. Miquel Falguera et al made a similar observation of infiltrates.<sup>17</sup> Saibal MAA et al in their study showed that multilobar infiltrates were more common in Diabetes Mellitus patients with community acquired pneumonia compared with non-diabetic patients.<sup>19</sup>

In the present study, streptococcus pneumoniae is the most common causative organism isolated in 34% of patients and mycobacterium tuberculosis is the next common causative organism isolated in 16% of patients. In the study conducted by Di Yacovo et al, streptococcus pneumoniae was the most common organism isolated in 39% of patients.<sup>16</sup> Similar observations were made by Miquel Falguera et al.<sup>17</sup> Streptococcus pneumonia was isolated in

31% of patients in their study followed by Chlamydia pneumonia in 12% of patients.

In the current study, 45 patients got discharged without any complications and 5 patients expired. The cause of death is Tuberculosis in three patients and staphylococcal pneumonia and streptococcal pneumonia one each.

In the present study advanced age, male gender, risk factors of smoking and alcohol abuse, use of oral antidiabetic drugs and with poor drug compliance, higher CURB score and those who needed ICU admission and mechanical ventilation had high mortality.

## CONCLUSION

In this study of Diabetes Mellitus with lower respiratory tract infections, the common age group of affected individuals is between 46 - 55 years with most of them having 2 - 5 year duration of diabetes.

Increased incidence of respiratory infections is seen in male patients compared to females, probably due to habits like smoking and alcoholism and co-morbid conditions.

Respiratory infections are more in patients with poor glycemic control.

Pneumonia is the common pathology observed among respiratory infections and unilobar involvement is more common than multilobar. Streptococcus pneumoniae is the most common pathogen isolated.

Mortality is due to advanced age, increased duration of diabetes, prolonged duration of illness, poor drug compliance and increased severity of illness.

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