Research Article

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The Relation between Diabetes and the Severity of Pneumonia, Clinical Research Article

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Abstract

This article aimed to evaluate the relation between diabetes and the severity of pneumonia by determining the proportion of diabetes type 2 in patients with pneumonia, identifying characteristics of diabetes such as duration of infection and complications associated with the disease and identifying poor outcomes of pneumonia such as the admission in the intensive care unit indication and the need for ventilation and finally to determine the relation between the severity of pneumonia, poor outcomes and diabetes.

Keywords: Pneumonia; Diabetes; Mortality; Severity; Relation; Hospitalization; Ventilation

Introduction

Diabetes mellitus, characterized primarily by hyperglycemia and resulting in significant metabolic disturbances, poses challenges in early detection. However, timely screening and intervention can effectively mitigate complications and manage the condition. According to the international diabetes federation, projections indicate a staggering 537 million individuals will be affected by diabetes in 2021, with a potential increase of 19.7% by 2030. Consequently, it is anticipated that over 10% of the global population will be afflicted by diabetes in the coming years [1].

This chronic ailment, characterized by a significant disease burden, can be categorized into Type 1 Diabetes Mellitus (T1DM), Type 2 Diabetes Mellitus (T2DM), Gestational Diabetes Mellitus (GDM) and other types of diabetes [2]. T1DM arises from the autoimmune-mediated impairment of insulin-producing beta cells, leading to diminished or absent insulin secretion. Additionally, scholarly investigations have posited that the inability of beta cells to undergo regeneration constitutes the fundamental etiology of T1DM [3].

T1DM, being a prototypical polygenic genetic disorder, is presently postulated to involve the involvement of determinants located at the DRB1, DQA1 and DQB1 loci on chromosome 6p21 [4]. Furthermore, it was observed that the abundance of phylum *Bacteroidetes* was elevated in individuals diagnosed with T1DM and the administration of probiotics led to a reduction in insulin needs among children with T1DM [5,6].

These findings suggest a potential association between bacterial presence and the pathogenesis of T1DM. Despite the presence of shared symptoms between T2DM and T1DM, the pathogenesis of T2DM distinguishes itself by exhibiting cellular insensitivity to insulin and inadequate insulin production by beta cells, resulting in an inability to meet the body's demand through feedback regulation [1]. The etiology of Type 2 Diabetes Mellitus (T2DM) is characterized by a heightened complexity, owing to the robust genetic correlation between the MTNR1B rs10830963 G allele and T2DM [7].

In addition, several research studies have revealed that the salivary microorganisms *Firmicutes, Lactobacillus, Veillonela* and *Tannerella forsythia* are enriched in patients with T2DM, obesity and cardiovascular disease [8-10]. Consequently, it can be inferred that the development of T2DM is influenced not only by genetic factors but also by external bacterial. Glucose intolerance during pregnancy is commonly identified as Gestational Diabetes Mellitus (GDM) [11]. While GDM typically resolves postpartum, it elevates the risk of developing Type 2 Diabetes Mellitus (T2DM) after delivery [12]. Furthermore, the emergence of GDM is linked to factors, such as age, body weight, polycystic ovary syndrome and a familial predisposition to

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diabetes [13]. Other types of diabetes refer to specific types of diabetes that are caused by various factors, such as monogenic diabetes syndromes, diseases affecting the exocrine pancreas and diabetes induced by drugs or chemicals [2].

The development of diabetes is commonly associated with both genetic factors and the external environment. It has been observed that individuals with diabetes who also have a *Klebsiella pneumoniae* infection experience a higher occurrence of sepsis and invasive infections. Furthermore, *Klebsiella pneumoniae* has been found to thrive in high glucose environments, resulting in elevated expression of the regulator of mucoid phenotype A (rmpA) and outer membrane protein A (ompA) genes in hyper-virulent *Klebsiella Pneumoniae* (hvKP). Consequently, this upregulation contributes to enhanced resistance against the immune system via the cyclic Adenosine Monophosphate (cAMP) signaling pathway [14].

These observational studies provide preliminary evidence on potential exposure factors associated with bacterial pneumonia in individuals with diabetes. In previous observational studies, the presence of reverse causality has posed a challenge, rendering it arduous to ascertain a causal association between bacterial pneumonia and diabetes. However, the Magnetic Resonance (MR) research approach employs genetic variation as an instrumental variable, wherein the allocation of genes to individuals occurs randomly before birth, thereby circumventing the influence of confounding factors and reverse causality.

Method and Materials

We identified "Al-Mouwasat University Hospital in Damascus, Syria" as the institute where we could collect samples from patients admitted to the hospital's respiratory disease department, so we created an automated inventory that we printed it and filled up with results, findings and important information for patient records. We archived the results by Microsoft Excel 2019 and we used the Statistical Package for Social Sciences (SPSS) 26th version for data analysis.

The study was conducted on all diabetic patients who attended the department of respiratory diseases at Al-Mouwasat University Hospital in Damascus, Syria, after obtaining informed consent where a prospective study was conducted. We determine the severity of pneumonia using the CURB-65 scale and we determine diabetes based on medical history and the result of laboratory testing and other data we have from patient records.

Exclusion criteria patients with uncertain diagnosis of diabetes, patients with serious hepatic, renal and hematologic disease and patients with previous chronic pulmonary disease which can effect the values independently of the effects of pneumonia and diabetes.

We used chi-Square test to determine whether there is a relation between two descriptive variables and we used Analysis of Variance (ANOVA) to determine whether there is a statistically significant difference between the categories.

We identifying the statistical level of 0.05 as a value to estimate the results, so if the P-value is higher than 0.05 we don't accept the result as a significant difference, but if the P-value is less than 0.05 we accept the result as a significant difference.

Results

Descriptive analysis of study variables

The study sample consisted of 213 patients with pneumonia. From the demographic data we found that the gender percentages of patients were 54.9% for males and 45.1% for females and more than half of sample (52.1%) were old people (65 years old or older). The majority of the participants (65.3%) were of smokers, while the proportion of those who consumed alcohol was lower (7.5%) and the majority of the participants were from Damascus governorate (49.8%) and Damascus countryside (42.3%). Regarding the diabetes criteria 5.6% of participants was found to have diabetes type I and 32.9% type II diabetes, as for the duration of type II diabetes, 34.3% of them have been effected around 20-30 years ago and 31.4% around 15-20 years ago and the most common complications were renal failure (18.3%) and heart failure (13.1%).

For pulmonary manifestations, productive cough (84.5%) and dyspnea (93.9%) were the most common. Regarding the results of pneumonia, more than half of sample (53.5%) were admitted to the respiratory department, while 46.5% required admission to Intensive Care Unite (ICU) and 68.1% were placed on oxygen and 31% shewed pulmonary complications. The mortality rate was 30.5% and regarding the CURP-65 scale had been found that 38.5% of participants have a score of 3 or higher indicating the severity of their condition **(Table 1)**.

Table 1: Sample characteristics N=213 (%).

Demographic data		
Sex	Males	117 (54.9%)
	Females	96 (45.1%)

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Age	<30 years	31 (14.6%)
	30-64 years	71 (33.3%)
	≥ 65 years	111 (52.1%)
Smoking	Yes	139 (65.3%)
	No	74 (34.7%)
Alcohol	Yes	16 (7.5%)
	No	197 (92.5%)
Region	Damascus	106 (49.8%)
	Damascus countryside	90 (42.3%)
	Other	17 (8%)
Diabetes diagnostic criteria		
Patient with diabetes type I	Yes	12 (5.6%)
	No	201 (94.4%)
Patient with diabetes type II	Yes	70 (32.9%)
	No	143 (67.1%)
Duration of diabetes type II (N=70)	<10 years	16 (22.9%)
	10-15 years	8 (11.4%)
	15-20 years	22 (31.4%)
	20-30 years	24 (34.3%)
Complications	Renal failure	39 (18.3%)
	Cardiac failure	28 (13.1%)
	Diabetic retinopathy	4 (1.9%)
	Diabetic neuropathy	10 (4.7%)
	Diabetic foot	12 (5.6%)
Pneumonia characteristics		
Pneumonia manifestations		
Productive cough	180 (84.5%)	
Fever	106 (49.8%)	
Wheeze	14 (6.6%)	
Dyspnea	200 (93.9%)	
Chest pain	64 (30%)	
Dry sough	20 (9.4%)	
Cyanosis	50 (23.5%)	
Consciousness impairment	70 (32.9%)	
Septic shock	22 (10.9%)	
Pneumonia result		
Type of hospital admission	The division	114 (53.5%)
	ICU	99 (46.5%)
Treatment	Mask	53 (24.9%)
	NIV	45 (21.1%)
	Mechanical ventilation	48 (22.5%)
	Medical treatment	67 (31.5%)
Need for oxygen	Yes	145 (68.1%)
	No	68 (31.9%)
Pneumonia complication	Yes	66 (31%)
	No	147 (69%)
CURP-65	0 or 1	88 (41.3%)

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	2	43 (20.2%)
	≥ 3	82 (38.5%)
Mortality	Yes	65 (30.5)
	No	148 (69.5)

Semantic analysis

The relation between diabetes and the average duration of hospitalization: There were no significant differences in the duration of hospitalization in patients with pneumonia associated with type II diabetes and patients without diabetes in the same category of people **(Table 2)**.

Table 2: Statistically significant relation.

Diabetes type II	Hospitalization duration in days (average value)	Mean square	Eta	P-value
Yes	5,34	0.009	0.001	0.98*
No	4.33	-	-	-
Note: *Statistically significant relation (P<0.005) not verified.				

The relation between type admission and diabetes in patient with pneumonia: By studying the relation between type II diabetes and type of admission in patient with pneumonia we found that most patients with type II diabetes (~69%) were admitted to Intensive Care Unit (ICU) compared to those without diabetes, where most of them (~64%) were admitted to the respiratory department with a statistical significant different (P<0.05), in addition, patients with type II diabetes were four times more likely to be admitted to the ICU **(Figure 1 and Table 3)**.

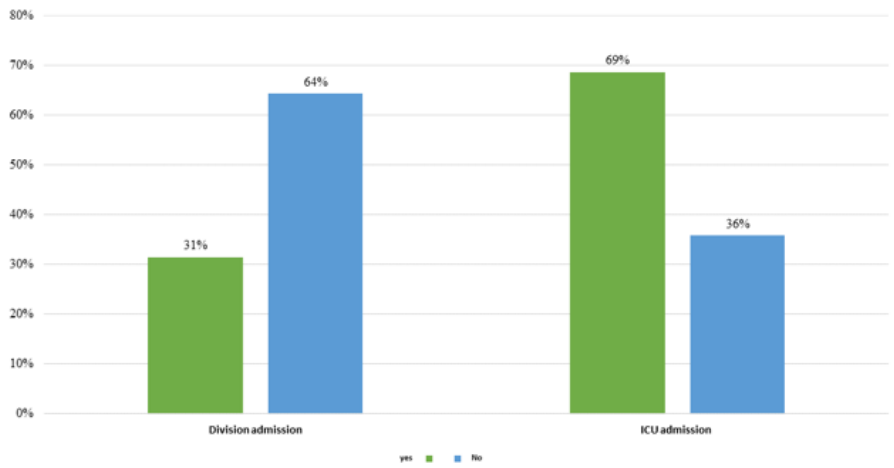

Figure 1: The relation between the type of hospital admission and diabetes type II in patients with pneumonia.

Table 3: differences in hospital admission type between diabetic and non-diabetic patients with pneumonia N=213 (%).

Admission type	Diabetes type II		Odds ratio and confidence interval or CI 95%	P-Value
	Yes	No		
Department admission	22 (31.4%)	92 (64.3%)	3.93 (2.13–7.24)	<0.001*
ICU admission	48 (68.6%)	51 (35.7%)	-	-
Total	70	143	-	-
Note: *Statistically significant relation (P<0.05) verified.				

The relation between the treatment method and diabetes in pneumonia patients and oxygen requirements: We studied the relation between having type II diabetes and the need to oxygen versus the need

for medication treatment in patient with pneumonia and we found that most diabetic patient needed oxygen in the treatment of pneumonia by 90% of cases, compared to 57% among non-diabetic patients with a statistically significant differences at high level (P<0.001), in addition the odds ratio of required oxygen in patients with pneumonia and type II diabetes were about 7 times higher than in people without type II diabetes **(Figure 2 and Table 4)**.

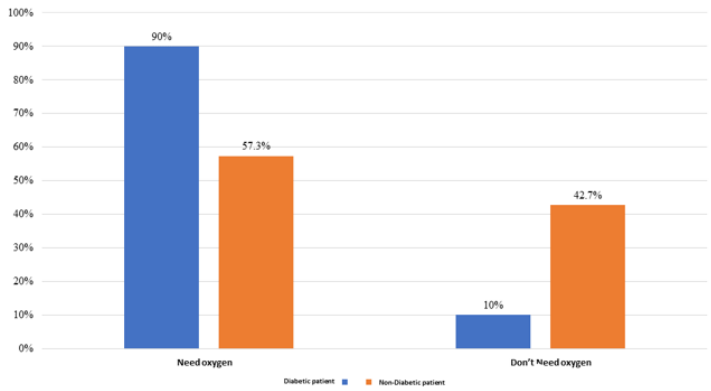

Figure 2: The relation between type II diabetes and the need for oxygen versus the need for medication treatment in patients with pneumonia.

Table 4: differences in oxygen requirements between diabetic and non-diabetic pneumonia patients N=213 (%).

Ventilation required	Diabetes type II		Odds ratio and confidence interval or CI 95%	P-value
	Yes	No		
No	7 (10)	61 (42.7)	6.69 (2.86–15.63)	<0.001*
Yes	63 (90)	82 (57.3)	-	-
Total	70	143	-	-
Note: *Statistically significant relation (P<0.05) verified.				

The difference between ventilation methods: We studied the relation between type II diabetes and the method of ventilation in patients with pneumonia who required ventilation, we found that most patients with type II diabetes required mechanical ventilation (46%) and a smaller percentage required Non-Invasive Ventilation (NIV) (~32%), compared to those without type II diabetes, most of whom required non-invasive methods, 47% were placed on a mask and approximately 30% were placed on a non-invasive ventilation, with a statistically significant difference (P<0.05) **(Figure 3 and Table 5)**.

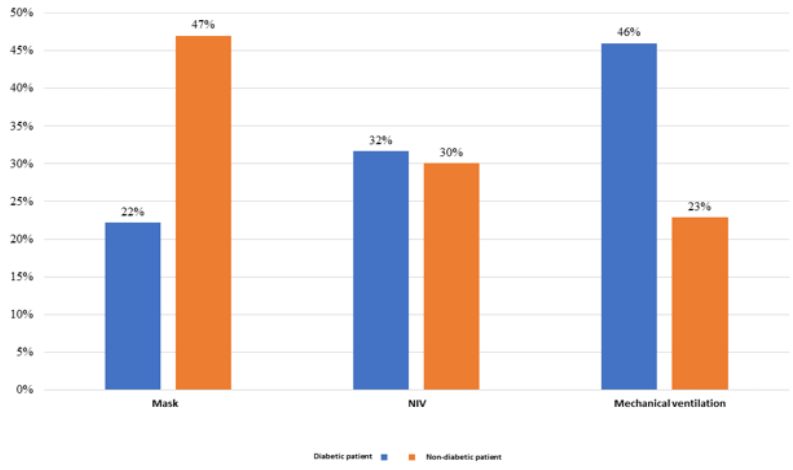

Figure 3: Difference between diabetic and non-diabetic pneumonia patients in ventilation methods.

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Table 5: Difference between diabetic and non-diabetic pneumonia patients in ventilation methods N=213 (%).

Ventilation method	Diabetes type II		Odds ratio and confidence interval or CI 95%	P-value
	Yes	No	Not applicable	0.003*
Mask	14 (22.2)	39 (47)		
NIV	20 (31.7)	25 (30.1)		
Mechanical ventilation	29 (46)	19 (22.9)		
Total	63	83		
Note: *Statistically significant relation (P<0.05) verified.				

We studied the difference between diabetic and non-diabetic pneumonia patients who required ventilation and we found that the probability of requiring g-ventilation was three timed higher with type II diabetes **(Figure 4 and Table 6).**

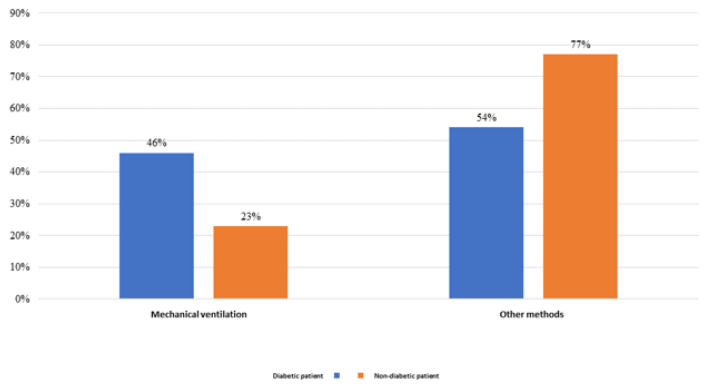

Figure 4: The difference between diabetic and non-diabetic pneumonia patients in the need for mechanical ventilation.

Table 6: Differences between diabetic and non-diabetic pneumonia patients in required ventilation N=213 (%).

Mechanical ventilation required	Diabetes type II		Odds ratio and confidence interval or CI 95%	P-value
	Yes	No		
Yes	29 (46%)	19 (22.9%)	2.87 (1.4–5.85)	0.003*
Other methods	34 (54%)	64 (77.1%)		
Total	63	83		
Note: *Statistically significant relation (P<0.05) verified.				

The relation between the mortality rate and the incidence of type II diabetes in patient with pneumonia: Nearly half of diabetic patients died from pneumonia, compared to only 24% among non-diabetic patients with a statistically significant difference (P<0.05), in addition, mortality rates due to pneumonia were 2.5 times higher in diabetic patients than non-diabetic patients **(Figure 5 and Table 7)**.

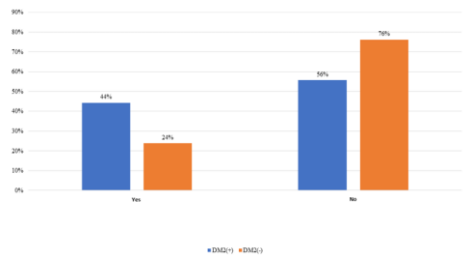

Figure 5: The difference in mortality rates between diabetic and non-diabetic patients.

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Table 7: The difference in mortality rates between diabetic and non-diabetic pneumonia patients N=213 (%).

Mortality occurrence	Diabetes type II		Odds ratio and confidence interval or CI 95%	P-value
	Yes	No		
Yes	31 (44.3%)	34 (23.8%)	2.54 (1.38–4.68)	0.002*
No	39 (55.7%)	109(76.2%)		
Total	70	143		
Note: *Statistically significant relation (P<0.05) verified.				

The relation between the severity of pneumonia according to CURP-65 scale and diabetes in pneumonia patients: We studied the differences between pneumonia patients with or without type II diabetes and we found that the proportion of patient with type II diabetes increases with the severity of pneumonia, so most patients with a severity of 0-1 on CURP-65 scale weren't diabetic patients while most patients with a severity of 3 or higher were diabetic patients and this results were statistically significant (P<0.001) **(Figure 6 and Table 8)**.

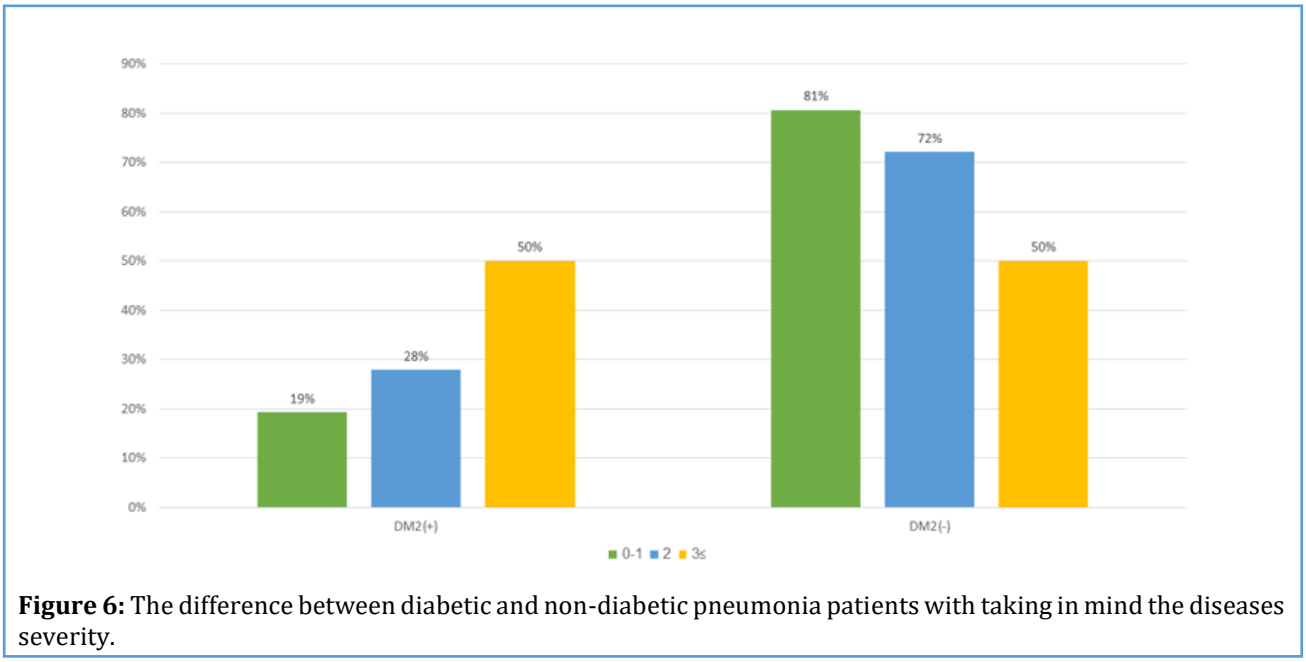

Figure 6: The difference between diabetic and non-diabetic pneumonia patients with taking in mind the diseases severity.

Table 8: The difference between pneumonia patients with or without diabetes type II with taking in mind the CRUP-65°.

Diabetes type II	CURP-65			Odds ratio and confidence interval or CI 95%	P-value
	0-1	2	≥ 3		
Yes	17 (19.3%)	12 (27.9%)	41 (50%)	Not applicable	<0.001*
No	71 (80.7%)	31 (72.1%)	41 (50%)		
Total	88	43	82		
Note: *Statistically significant relation (P<0.05) verified.					

The difference between diabetic and non-diabetic pneumonia patients in mortality rates with taking in mind the severity of pneumonia: We studied the difference between diabetic and non-diabetic pneumonia patients in mortality rates with taking in mind the severity of pneumonia and we found that there are statistically significant differences (P<0.001) in mortality rates between this two groups of

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patients. For diabetic patients, the risk of death increased significantly with increasing severity of pneumonia and the mortality rate was 6.5% for patients with severity (CURP-65=0-1) and was 9.7% for patients with severity (CURP-65=2) and 83.9% for patients with severity (CURP-65 ≥ 3). On the other hand, it was noted that the most patients with pneumonia who don't suffer from diabetes (63.3%) were in the least severe category (CURP-65=0-1), while this percentage was decreased to 21.1% and 15.6% in the most severe categories, respectively **(Figure 7 and Table 9)**.

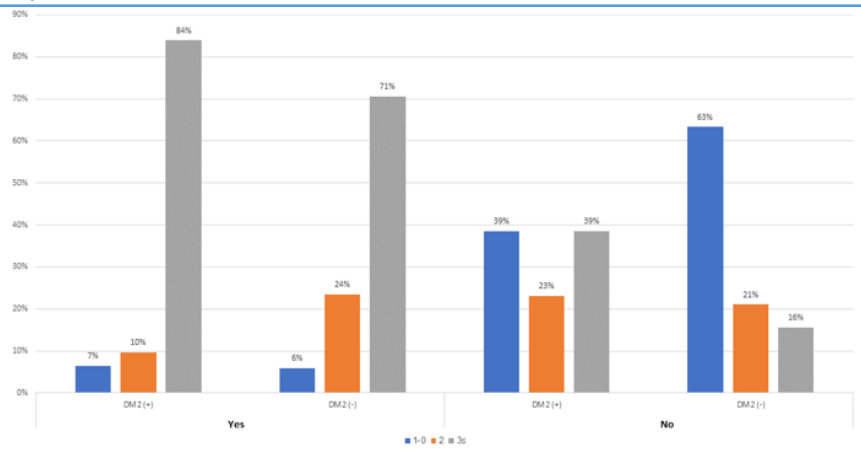

Figure 7: The difference between diabetic and non-diabetic pneumonia patients in mortality rates with taking in mind severity of pneumonia.

Table 9: The difference in mortality rates between diabetic and non-diabetic pneumonia patients, with taking in mind the severity of pneumonia N=213 (%).

Mortality occurrence	Diabetes type II	CURP-65			Total	Odds ratio and confidence interval or CI 95%	P-value
		0-1	2	≥ 3			
Yes	Yes	2 (6.5%)	3 (9.7%)	26 (83.9%)	31	Not applicable	<0.001
	No	2 (5.9%)	8 (23.5%)	24 (70.6%)	34		
No	Yes	15 (38.5%)	9 (23.1%)	15 (38.5%)	39		
	No	69 (63.3%)	23 (21.1%)	17 (15.6%)	109		
Note: *Statistically significant relation (P<0.05) verified.							

The relation between CURB-65 scale and Duration of hospitalization: We evaluated the relation between pneumonia severity and duration of hospitalization in diabetic and non-diabetic patients and found that diabetic patients tended to stay in hospital for 4.6 ± 3.4 days with CURB-65=0-1, 4.9 ± 2.5 days with CURP-65=2 and 5.7 ± 5.7 days with CURP-65 ≥ 3. In contrast, the average duration of hospital stay for non-diabetic patients was 4.9 ± 4.1 days with CURB-65=0-1, 6.1 ± 5.4 days with CURP-65=2 and 5.3 ± 4.6 days with CURP-65 ≥ 3. The statistical analysis showed that no statistically significant differences between the two groups in the average duration of hospitalization with the different levels of pneumonia severity. This result indicates that type II diabetic is associated with an increased length of hospital stay for patients with pneumonia regardless of the severity of pneumonia **(Table 10)**.

Table 10: The relation between pneumonia severity and length of hospitalization with comparison between diabetic and non-diabetic patients N=213 (%).

CURP -65	Diabetes type II	N	Mean length (in days)	F	P-value
0-1	Yes	17	4.6 (± 3.4)	0.684	0.506*

	No	71	4.9(± 4.1)		
2	Yes	12	4.9 (± 2.5)		
	No	31	6.1(± 5.4)		
≥ 3	Yes	41	5.7(± 5.7)		
	No	41	5.3(± 4.6)		
Note: *Statistical significant relation (P<0.05) not verified.					

The relation between random blood glucose and the mortality: We evaluated the relation between random blood glucose and the mortality in diabetic and non-diabetic patients with pneumonia and found that the mean random blood glucose level was 363 ± 172 mg/dL in diabetic patients who died, compared with 241±81 mg/dL in diabetic patients who still alive, while the mean random blood glucose level was 111 ± 54 mg/dL in non-diabetic patients who died compared with 133 ± 58 mg/dL in non-diabetic patients who still alive. Analysis of Variance (ANOVA) showed that these differences were statistically significant (F=15.6) and these results suggest that higher random blood glucose levels are associated with an increased risk of death (P<0.001) in the diabetic patients with pneumonia more likely than non-diabetic patients **(Figure 8 and Table 11)**.

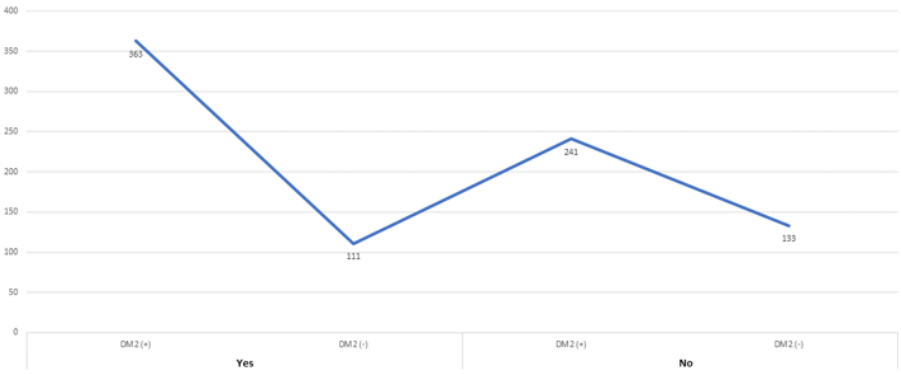

Figure 8: The relation between random blood glucose level and the mortality rates in diabetic patients.

Table 11: Variation of random blood glucose level and death occur with diabetic and non-diabetic patients.

Mortality	Diabetes type II	Mean random blood glucose	F	P-value
Yes	Yes	363 (± 172)	0.684	0.506*
	No	111 (± 54)		
No	Yes	241 (± 81)		
	No	-		
Note: *Statistical significant relation (P<0.05) not verified.				

Discussion

In our current study, we found no statistical significant difference in the length of hospitalization between diabetic and non-diabetic pneumonia patients (median days in diabetic patients 5.34 *vs.* 5.33 in non-diabetes patients. This result is consistent with the results of a Spanish study where no significant differences were found between the two groups of patients (9.78 days for diabetic patients *vs.* 9.77 days for non-diabetic patients) [15].

Oxygen requirement, the rate of need for oxygen supplementation was significantly higher in diabetic patients with pneumonia compared to non-diabetic (57% *vs.* 90%) with a statistical significant and the odds ratio was about 7 times higher, so the need for oxygen supplementation was about 7 times higher in diabetic patients with pneumonia. This findings are consistent with the Egyptian study in 2019, which reported a statistical significant difference in oxygen requirements (70% *vs.* 30%) [16]. The results in this study found that diabetic patients with pneumonia scored high score on the CURO-65 scale compared with non-diabetic patients with a statistical significant. These results are consistent with many studies that reported increased severity of infection in patients [17].

For the mortality rate, we found statistically significant differences (24% *vs.* 44%) with a mortality risk at least 2.5 times higher in diabetic patients with

pneumonia compared to non-diabetic patients. These results are consisted with two recent studies in Spain and China [15,16]. In our current study, high random blood glucose on admission was statistically significant associated with mortality in both diabetic and non-diabetic patients with a statistically significant. This result is consisted with the result in a Canadian study that found that high blood glucose level on admission associated with poor prognosis for acquired pneumonia in both diabetic and non-diabetic patients [18].

Conclusion

This study concluded that diabetic patients with pneumonia are more likely to develop the most severe scenario of disease in the term of needing to be admitted in ICU, needing oxygen supplements and needing mechanical ventilation, In addition to the severity of pneumonia and the increased mortality rate. We found a significant relation between random blood glucose on admission and death occurs in diabetic patients, so we recommend conducting more advances studies that taking in mind the risk factors associated with poor prognosis.

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