J Nepal Health Res Counc 2024 Oct.-Dec.;22 (65): 756-763

Clinical Profile of Metabolic Derangements in Patients with Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Saroj Babu Aryal,[1] Akriti Panthi,[2] Nadira Aryal,[3] Bijay Risal[3]

[1]Institute of Medicine, Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, [2]Department of Community Medicine, Kathmandu Medical College, Kathmandu Nepal, [3]Department of Internal Medicine Christiana Care Christiana Hospital Ogletown Stanton Rd, Newark, Delaware USA.

ABSTRACT

Background: Chronic obstructive pulmonary disease is defined as a preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation attributable to airway accompanied by alveolar abnormalities elicited by significant exposure to noxious particles or gases. Stress hormone is involved in proclivity towards causation of hyperglycemia and hyponatremia in COPD.

Methods: This study is an analytical cross sectional single center study that was carried out in Tribhuvan University Teaching Hospital. Specimens were processed as per the guidelines of Standard Operating Procedure (SOP) of Biochemistry laboratory of Tribhuvan University Teaching Hospital.

Results: In this study of 138 patients with acute exacerbation of COPD, the mean age was (71.88±9.771) years with higher prevalence in the age group between 70-80 years of age. Females (65.2%) outnumbered males and 71.7% came from outside the Kathmandu valley. Hyponatremia was observed in sodium levels with 51.4% below normal with majority of patient's possessing mixed acid-base disorders (58.7%). Most of thepatients 76.5% received general care with a mean hospital stay of 8.7 days. Statistical analysis revealed significant associations between care type, geographical distribution (p=0.026) and duration of stay with care type (p=0.0001). No significant associations were found regarding gender, glucose, sodium, potassium levels and age with duration of stay.

Conclusions: Factors such as age, gender, and glycemic status did not significantly affect the type of care or duration of hospital stay, geographical location emerged as a significant determinant, with patients from outside the Kathmandu valley more likely to receive general care. Despite the prevalence of electrolyte imbalances and acid-base disorders, these biochemical factors showed no substantial impact on clinical outcomes, suggesting that other factors may play a more significant role in duration of stay.

Keywords: Acid-base imbalance; biochemistry; glucose; potassium; pulmonary.

INTRODUCTION

Patients presents with acute exacerbation of chronic obstructive pulmonary disease (COPD) are approximately 1.3 times per year.[1] According to the World Health Organization, fifth leading cause of death in 2002 was COPD. There is an estimation of increase in deaths by more than 30% in the next 10 years. By the time of 2030, COPD will be the third leading cause of death across the globe.[2]

Studies primarily focused on evaluating the association between metabolic disturbances (hyperglycemia, dyselectrolytemia) and the duration of hospital stay as a surrogate marker of clinical outcome. The observed correlations between specific metabolic abnormalities and prolonged hospitalization provide valuable insights into potential prognostic indicators in COPD exacerbation.[3,4]

The primary aim of this study was to investigate the status of hyperglycemia, dyselectrolytemia and acid base disorder among patients with acute exacerbation of COPD admitted to Tribhuvan University Teaching hospital and their clinical

Correspondence: Dr Saroj Babu Aryal, Institute of Medicine, Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, Kathmandu, Nepal. Email: sarojstep3@gmail.com, Phone: +9779865603208.

outcome particularly focused on duration of stay.

METHODS

The study was an analytical cross-sectional study carried out in Tribhuvan University Teaching Hospital with 138 particpants. Patients diagnosed with Acute Exacerbation of COPD admitted to the Department of Pulmonology of TUTH were taken as study participants. Non-probability sampling method was used for data collection after ethical clearance being taken from IRC Ref No (115080/081). Patients diagnosed with type 1 and type 2 Diabetes, CKD, heart failure, chronic liver disease, patients on diuretics were excluded. Data were collected using questionnaire following informed written and verbal consent. Venous sample of random blood glucose, sodium and potassium were taken in gel tube vial as well as arterial blood for pH, pCo2, po2, and HCO3 were taken in 3ml of heparinized syringe during the time of admission. In laboratory sodium and potassium were estimated by ion selective electrode method. Glucose was estimated by hexokinase method. Calibration and quality control of analytes were done routinely to get precise and accurate results. The variable required for the study were noted in pro-forma and were entered in the MS excel and analyzed using SPSS version 26. Descriptive statistics of various parameters with mean, median and standard deviation were calculated. The level of confidence was set to be at 95% with the level of significance of less or equal to 0.05. Chi-square, man-whitney, U test, kolmogorovsmirnov and co-relation test were applied to the variable to get the result.

RESULTS

Out of 138 study participants, there were 90 females and 48 males. Female were 65.2% among the study participants. Distribution of age with their percentage is allocated in figure 1.

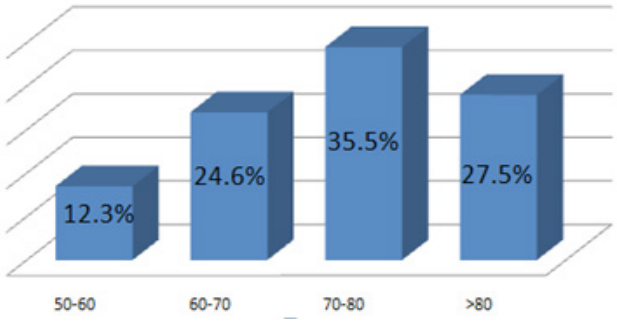

Figure 1. Distribution of Age.

28.3% of study participants were from inside the valley and 71.7% of study participants were from outside the valley. Patient having acid base disorder is described in figure 2.

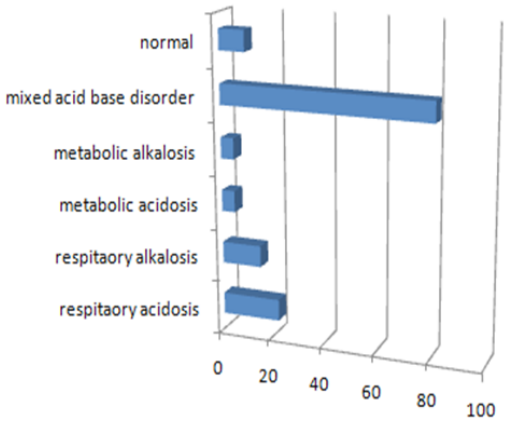

Figure 2. Acid base disorder in AECOPD.

Patients having RBS less than 7.8 mmol/L were 100 as compared to patient having RBS more than 7.8mmol/L were 38. In terms of percentage 72.5% had glucose level less than 7.8mmol/L and 27.5% had glucose above the 7.8 mmol/L. Mean random blood Glucose (RBS) was (6.9± 2.1) median being 6.6. Maximum blood glucose recorded was of 17.1mmol/L along with minimal value of 2.4mmol/L.

Patients having sodium less than 135 meq/L were 71 while patients having sodium more than 135 meq/L were 67. In terms of percentage, 51.4% had sodium level less than 135 meq/L in contrast to 48.6% patients with sodium level above the 135 meq/L. Mean sodium was (133.43±5.04) with median 134. Maximum sodium recorded was 143 and minimal was 113.

Patients with potassium less than 3.5 meq/L were 18 and patients with potassium more than 3.5 meq/L were 120. In terms of percentage 13% had potassium level less than 3.5 meq/L as compared to 87% had blood potassium level above the 3.5 meq/L. Mean potassium was (4.113±0.6) along with median 4.1. Maximum potassium recorded was of 6.1 and minimal value was 2.1

Patients who received general care in the TUTH were 106 while patients who received crital care in the TUTH were 32. Hence 76.5% were in the general care in contrast to 23.2% of patients who were in critical care. Therefore, mean duration of stay of was (8.70±4.92) while median was 7.0. Minimum duration of hospital stay for the patients was 2 and maximum length of stay for patients was 28.

Table 1. association of Variables (gender, geographical distribution, glucose, sodium, potassium and care obtained) with duration of stay.

	Male/female	N	Median(Q1, Q3)	*p-value*
Duration of Stay	Female	90	7(5,10)	
	Male	48	8(6, 11.75)	0.245[a]
Association between geographical distribution with duration of stay				
	address	N	Median(Q1, Q3)	*p-value*
Duration of stay	Kathmandu valley	39	8(5,12)	
	Outside valley	99	7(5,10)	0.582[a]
Association between glucose with duration of stay				
	glucose	N	Median(Q1, Q3)	*p-value*
Duration of stay	<7.8mmol/L	100	7(5,10)	0.061[a]
	>7.8mmol/L	38	9(5,13)	
Association between sodium with duration of stay				
	sodium	N	Median(Q1, Q3)	*p-value*
Duration of stay	<135 meq/L	71	8(6,11)	0.357[a]
	>135meq/L	67	7(5,11)	
Association between potassium with duration of stay				
	potassium	N	Median(Q1, Q3)	*p-value*
Duration of stay	<3.5 meq/L	18	7(5,10)	0.827[a]
	>3.5meq/L	120	7.5(5.25,11)	
Association of care obtained with duration of stay				
	Care obtained	N	Median(Q1, Q3)	*p-value*
Duration of stay	General care	106	7(5,9.25)	<0.001*[a]
	Critical care	32	11(7.25, 13)	

[a] Mann-Whitney U test

*Significant

Table 2. association between different age group with duration of stay.

Age group	N	Mean	Std. Deviatian	Std error	Median(Q1, Q3)	p
50-60	17	9.41	4.5	1.09	8(6,12)	0.843[b]
60-70	34	8.94	5.3	0.91	8(5.75,11.25)	
70-80	49	8.43	4.1	0.59	7(6, 10.50)	
>80	38	8.53	5.7	0.92	7(4.75, 10.25)	
Total	138	8.70	4.9	0.41		

[b] kolmogorovsmirnov test

Table3. Association of acid base disorder of AECOPD patients with duration of stay.

Parameter	Mean	Median	p
Respiratory acidosis	7.82 ± 6.15	6.5	
Respiratory alkalosis	10.4 ± 6.09	10	
metabolic acidosis	8.8 ± 2.68	9	
metabolic alkalosis	6.6 ± 1.82	6	0.241[c]
Mixed	8.91 ± 4.69	8	
Normal	7.4 ± 3.34	6.5	
Total	8.7 ± 4.94	7	

[c] kruskal-wallis test

Table 4. spearman Correlation between various parameter.

		duration of stay	Age	pH	CO2	o2	HCO3	rbs	na	k
N		138	138	138	138	138	138	138	138	138
duration of stay	Correlation Coefficient	1.000	-0.114	-0.005	0.146	0.098	0.159	0.033	-0.080	0.040
	Sig. (2-tailed)		0.182	0.953	0.088	0.254	0.063	0.698	0.352	0.645
Age	Correlation Coefficient	-0.114	1.000	.168*	-.303**	-0.082	-.246**	0.061	-0.081	-0.150
	Sig. (2-tailed)	0.182		0.049	0.000	0.340	0.004	0.477	0.342	0.079
pH	Correlation Coefficient	-0.005	.168*	1.000	-.573**	-0.115	-0.112	-0.097	-0.014	-.499**
	Sig. (2-tailed)	0.953	0.049		0.000	0.180	0.190	0.259	0.868	0.000
CO2	Correlation Coefficient	0.146	-.303**	-.573**	1.000	-0.056	.818**	0.066	0.021	.238**
	Sig. (2-tailed)	0.088	0.000	0.000		0.515	0.000	0.441	0.805	0.005
o2	Correlation Coefficient	0.098	-0.082	-0.115	-0.056	1.000	-0.128	0.075	0.114	0.074
	Sig. (2-tailed)	0.254	0.340	0.180	0.515		0.135	0.381	0.183	0.391
HCO3	Correlation Coefficient	0.159	-.246**	-0.112	.818**	-0.128	1.000	-0.025	0.005	0.015
	Sig. (2-tailed)	0.063	0.004	0.190	0.000	0.135		0.773	0.956	0.865
rbs	Correlation Coefficient	0.033	0.061	-0.097	0.066	0.075	-0.025	1.000	-0.144	0.019
	Sig. (2-tailed)	0.698	0.477	0.259	0.441	0.381	0.773		0.091	0.829
na	Correlation Coefficient	-0.080	-0.081	-0.014	0.021	0.114	0.005	-0.144	1.000	-0.148
	Sig. (2-tailed)	0.352	0.342	0.868	0.805	0.183	0.956	0.091		0.084
k	Correlation Coefficient	0.040	-0.150	-.499**	.238**	0.074	0.015	0.019	-0.148	1.000
	Sig. (2-tailed)	0.645	0.079	0.000	0.005	0.391	0.865	0.829	0.084	

DISCUSSION

The main aim of this study was to investigate the status of hyperglycemia, dyselectrolytemia and acid base disorder among patients with acute exacerbation of COPD admitted to Tribhuvan University Teaching hospitaland their clinical outcome. In clinical outcome duration of stay in the hospital was focused while clinical findings and other variables were excluded. The findings from this study provide valuable insights into this complex relationship. This discussion section contextualizes the study's findings within the broader landscape of COPD management and patient care.

Das et al. and Garcia Sanz et al. found significant metabolic disturbances, such as hyperglycemia and acid-base disorders, during COPD exacerbations. These findings highlight the systemic nature of exacerbations and the need for comprehensive patient assessment inorder to improve management strategy.[4,5]

The study by Dhimal et al. found a higher prevalence of COPD among participants aged 60 and above, particularly in males and mainly from Karnali province. Das et al. reported average serum sodium and potassium levels in COPD patients (133 ± 6.86) meq/l and (3.39 ± 0.96) meq/l, respectively. Baker et al. analyzed blood glucose levels in 193 participants, divulging 72% participants with blood glucose level >6.1 mmol/l and 11% with accompanying levels >11.1 mmol/l, with a median concentration of 7.0 mmol/l. Additionally, Claudio Terzano et al. reported mixed acid-base disorders during acute COPD exacerbations.[5-8]

Our study included participants aged 50 to 92, with a mean age of (71.88±9.7) predominantly in the 70-80 age group.Out of 138 participants, 90 were females, indicating a higher impact of acute COPD exacerbations amongst women. Notably, 71.7% of patients were from outside the Kathmandu valley. The mean glucose level was (6.9±2.1), mean sodium was (133.43±5), and mean potassium was (4.1±0.6), with mixed acid-base disorders beingquite common during acute exacerbations.

Mizock BA et al. stated that hyperglycemia can lead to several adverse effects, including osmotic diuresis, fluid and electrolyte imbalances, hyperosmolar nonketotic diabeticcoma, and impaired immune function which increases susceptibility to infections. Studies suggest that this heightened infection risk is linked to decreased cellular immune function, particularly impaired activity of polymorphonuclear leukocytes. Research in diabetic animals has shown that poor glucose control results in reduced phagocytic activity and increased vulnerability to infection. Consequently, hyperglycemia is an independent predictor of morbidity and mortality in various acute conditions including acute coronary syndrome and community-acquired pneumonia whereby glucose level above 14 mmol/l during admission is associated with poor outcome.[9-14]

Butler et al. and Jafar et al. explored the link between metabolic disturbances, particularly hyperglycemia, and duration of hospital stay as a marker of clinical outcome in COPD exacerbations. These findings suggest that hyperglycemia is a significant predictor of longer hospital stays emphasizing the importance of glycemic control. While this focuses on length of stay providing insights for resource utilization, healthcare planning and future research should include additional outcome measures for more comprehensive understanding. McAlister et al. found that patients with admission glucose levels >11 mmol/L encountered 73% higher mortality risk and 52% higher risk of in-hospital complications compared to those with levels <6.1 mmol/L, underscoring the serious implications of hyperglycemia in clinical settings.[1,3,15]

Our study produced contrasting results compared to existing literature. Among 100 patients with glucose levels <7.8 mmol/L, the mean hospital stay was (7.9±3.8) days. In contrast, 38 patients with glucose levels >7.8 mmol/L had a longer mean stay of (10.58±6.6) days. The Mann-Whitney U test yielded a value of 0.061 (p>0.05), indicating no significant difference between the two groups.

The global prevalence of COPD rose by 5.9% from 1990 to 2017 leading to at least 2.9 million deaths annually.[16]

Prognostic factors for patients experiencing acute exacerbations of chronic obstructive pulmonary disease (AECOPD) include baseline disease severity, frequency and severity of previous exacerbations, age, comorbidities, and prior admission rates for AECOPD. Additionally, physiological and laboratory parameters such as lung functions, respiratory rate at admission, hypoxemia, and hypercapnia also play a critical role in determining outcomes.[17]

Approximately 15% of patients with (COPD) experience anacute exacerbations that necessitate hospitalization, resulting in increased medical resource utilization and costs. A study by Jeffrey et al. involving 139 COPD patients with respiratory failure found that arterial hydrogen ion concentration is a significant prognostic indicator for survival in this population.[18,19]

Identifying metabolic disturbances as common comorbidities in COPD exacerbation patients is crucial for healthcare providers, as addressing these issues early can improve outcomes. Effective management should include optimizing glycemic control, correcting electrolyte imbalances, and managing acid-base disturbances. In Nepal, geographical challenges, including rugged terrain and natural disasters, complicate healthcare access and contribute to a high prevalence of chronic non-communicable diseases, as highlighted by.[6]

The Government of Nepal must prioritize the urgent management of non-communicable diseases to improve public health and avoid financial crises. Effective programs for prevention and control are essential, and the findings of recent studies can inform updates to national action plans and budgets. For instance, research by Umiperez et al. revealed that patients with newly diagnosed hyperglycemia had a mean age of 59, which is significantly younger than known diabetics and normoglycemic patients, with no notable differences in gender, hospital stay length, or ICU admissions among these groups.[6,20]

Our study analyzed 138 patients, revealing that 28.3% were from the Kathmandu valley, with 23.6% receiving general care and 43.8% critical care. In contrast, 71.7% were from outside the valley, predominantly admitted to general care (76.4%) rather than critical care (56.3%). A significant geographical difference was noted (p=0.026), underscoring the need for improved healthcare infrastructure both within and outside the valley. It emphasizes the importance of enhancing healthcare infrastructure both within and outside the valley, likely to address disparities in healthcare access, delivery, or outcomes. Age did not significantly affect hospital stay duration across groups, with mean stays ranging from (8.43±4.1) to (9.41±4.5) days, contrasting with other studies that defined prolonged stays as over 3 days. The median stay in this study was 6 days, aligning with typical lengths reported in the literature.

In contrast to a Spanish study where over 90% of patients were male, our study found that more than half of the AECOPD population were female. While previous studies did not establish a significant relationship between gender and length of stay, our findings indicated that females had a mean hospital stay of (8.40±4.8) days, compared to (9.27±5.0) days for males.[21,22] However, the Man-Whitney U test showed no significant difference (p=0.245), suggesting that gender did not significantly influence the duration of hospital stay in our sample.

García-Sanz et al. found that hyponatremia was linked to longer hospital stay in AECOPD patients but our study did not support this association.[4] Out of 138 patients, 71 had sodium levels below 135 mEq/L, with a mean hospital stay of (8.87±4.6) days, while 67 patients had levels above 135 mEq/L, with a mean stay of (8.52±5.2) days. The Man-Whitney U test indicated no significant difference between the two groups (p=0.357), suggesting that sodium levels did not significantly affect the duration of hospital stay.

Most patients in our study exhibited mixed acid-base disorders, which are increasingly common due to high rates of comorbidities and multidrug therapies especially among critically ill and elderly populations. Acidosis can lead to serious complications such as myocardial depression, arrhythmias, and hypotension while hypercapnic acidosis weakens respiratory muscles and promotes inflammation and cachexia. Additionally, it affects renal blood flow and activates several hormonal systems. Terzano et al. noted that mixed acid-base disorders in hypercapnic COPD exacerbations are associated with a greater need for non-invasive ventilation and longer treatment durations.[8,23]

The limitation of study indicates that the factors such as glucose levels, gender, electrolyte status, and age are relevant and posess direct influence on hospital outcomes which may be influenced by other clinical variables as they were not statistically significant in relation to duration of stay. For the better assessment of the effects of hyperglycemia, dyselectrolytemia, and acid-base disorders, a thorough patient history is of grave importance. Additionally, to determine the prevalence of acute exacerbation of COPD across different regions of Nepal, a larger, more specific sample size from diverse geographical areas is recommended which would enhance study's reliability and validity leading to increment in generalizability while using a control groups could help to minimize confounding variables and reduce bias.

CONCLUSIONS

Overall. this study found no significant associations between age, gender, and the type of care received or the duration of stay. Gender also had no impact on care outcomes, indicating consistency across genders. However, a significant relationship (p=0.026) was observed between geographical location and care type, with patients outside the valley more likely to receive general care, possibly reflecting differences in illness severity or regional healthcare resources. Similarly, patients receiving critical care tend to stay in hospital longer compared to those with general care. In contrast, hyperglycemia, electrolyte imbalances, and mixed acid-

base disorders did not significantly affect the type of care or hospital stay duration, suggesting that other factors may be more influential in determining care outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCE

1. Jafar N, Edriss H, Islam E, Nugent K. The association between blood glucose levels and hospital outcomes in patients admitted with acute exacerbations of chronic obstructive pulmonary disease. The Southwest Respiratory and Critical Care Chronicles. 2014 Jul 10;2(7):1–11.doi: https://doi.org/10.12746/swrccc2014.0207.082

2. Islam EA, Limsuwat C, Nantsupawat T, Berdine GG, Nugent KM. The association between glucose levels and hospital outcomes in patients with acute exacerbations of chronic obstructive pulmonary disease. Ann Thorac Med. 2015;10(2):94–9. doi: https://doi.org/10.4103/1817-1737.151439

3. Butler SO, Btaiche IF, Alaniz C. Relationship Between Hyperglycemia and Infection in Critically Ill Patients. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2005;25(7):963–76. doi: https://doi.org/10.1592/phco.2005.25.7.963

4. García-Sanz MT, Martínez-Gestoso S, Calvo-Álvarez U, Doval-Oubiña L, Camba-Matos S, Rábade-Castedo C, et al. Impact of Hyponatremia on COPD Exacerbation Prognosis. JCM. 2020 Feb 12;9(2):503.doi: https://doi.org/10.3390/jcm9020503

5. Das P, Bandyopadhyay M, Baral K, Paul R, Banerjee AK. Dyselectrolytemia in Chronic Obstructive Pulmonary Diseases with acute exacerbation. Nigerian Journal of Physiological Sciences. 2010;25(1):25–7.

6. Dhimal M, Karki KB, Sharma SK, Aryal KK, Shrestha N, Poudyal A, et al. Prevalence of Selected Chronic Non-Communicable Diseases in Nepal. J Nepal Health Res Counc. 2019 Nov 14;17(3):394–401. doi: https://doi.org/10.33314/jnhrc.v17i3.2327

7. Baker EH. Hyperglycaemia is associated with poor outcomes in patients admitted to hospital with acute exacerbations of chronic obstructive pulmonary disease. Thorax. 2006 Apr 1;61(4):284–9.doi: https://doi.org/10.1136/thx.2005.051029

8. Terzano C, Di Stefano F, Conti V, Di Nicola M, Paone G, Petroianni A, et al. Mixed Acid-Base Disorders, Hydroelectrolyte Imbalance and Lactate Production in Hypercapnic Respiratory Failure: The Role of Noninvasive Ventilation. Rojas M, editor. PLoS ONE. 2012 Apr 23;7(4):e35245. doi: https://doi.org/10.1371/journal.pone.0035245

9. Mizock BA. Alterations in fuel metabolism in critical illness: hyperglycaemia. Best Practice & Research Clinical Endocrinology & Metabolism. 2001 Dec 1;15(4):533–51.doi: https://doi.org/10.1053/beem.2001.0168

10. Golden SH, Peart-Vigilance C, Kao WH, Brancati FL. Perioperative glycemic control and the risk of infectious complications in a cohort of adults with diabetes. Diabetes Care. 1999 Sep 1;22(9):1408–14. doi: https://doi.org/10.2337/diacare.22.9.1408

11. Khaodhiar L, McCowen K, Bistrian B. Perioperative hyperglycemia, infection or risk? Current Opinion in Clinical Nutrition & Metabolic Care. 1999 Jan;2(1):79. doi: https://doi.org/10.1097/00075197-199901000-00013

12. Sima AAF, O'Neill SJ, Naimark D, Yagihashi S, Klass D. Bacterial Phagocytosis and Intracellular Killing by Alveolar Macrophages in BB Rats. Diabetes. 1988 May 1;37(5):544–9. doi: https://doi.org/10.2337/diabetes.37.5.544

13. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview - The Lancet [Internet]. [cited 2024 Sep 27]. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(99)08415-9/abstract

14. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A Prediction Rule to Identify Low-Risk Patients with Community-Acquired Pneumonia. New England Journal of Medicine. 1997 Jan 23;336(4):243–50. doi: https://doi.org/10.1056/NEJM199701233360402

15. The Relation Between Hyperglycemia and Outcomes in 2,471 Patients Admitted to the Hospital with Community-Acquired Pneumonia | Diabetes Care | American Diabetes Association [Internet]. [cited 2023 Jul 27].doi: https://doi.org/10.2337/diacare.28.4.810

16. Kisa A, Disease Collaborators GCR, Soriano JB, Kendrick PJ, Vos T, Kisa S, et al. Prevalence and attributable health burden of chronicrespiratory diseases, 1990–2017: a systematic analysis forthe Global Burden of Disease Study 2017. The Lancet Respiratory Medicine [Internet]. 2020 Jun 1 [cited 2024 Sep 29]; Available from: https://oda.oslomet.no/oda-xmlui/handle/10642/8703

17. Flattet Y, Garin N, Serratrice J, Perrier A, Stirnemann J, Carballo S. Determining prognosis in acute exacerbation of COPD. International Journal of Chronic Obstructive Pulmonary Disease [Internet]. 2017 Jan 31 [cited 2024 Sep 29]; Available from: https://www.tandfonline.com/doi/abs/10.2147/COPD.S122382 doi: https://doi.org/10.2147/COPD.S122382

18. McCrory DC, Brown C, Gelfand SE, Bach PB. Management of Acute Exacerbations of COPD: A Summary and Appraisal of Published Evidence. Chest. 2001 Apr 1;119(4):1190–209.doi: https://doi.org/10.1378/chest.119.4.1190

19. Jeffrey AA, Warren PM, Flenley DC. Acute hypercapnic respiratory failure in patients with chronic obstructive lung disease: risk factors and use of guidelines for management. Thorax. 1992 Jan 1;47(1):34–40.doi: https://doi.org/10.1136/thx.47.1.34

20. Hyperglycemia: An Independent Marker of In-Hospital Mortality in Patients with Undiagnosed Diabetes | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic [Internet]. [cited 2023 Jul 27]. [Article]doi:https://doi.org/10.1210/jc.87.3.978

21. Current Opinion in Pulmonary Medicine [Internet]. [cited 2024 Sep 30]. Available from: https://journals.lww.com/co-pulmonarymedicine/abstract/2010/03000/chronic_obstructive_pulmonary_disease.6.aspx

22. Wang Y, Stavem K, Dahl FA, Humerfelt S, Haugen T. Factors associated with a prolonged length of stay after acute exacerbation of chronic obstructive pulmonary disease (AECOPD). International Journal of Chronic Obstructive Pulmonary Disease. 2014 Jan 20;9:99–105.doi: https://doi.org/10.2147/COPD.S51467

23. Bruno CM, Valenti M. Acid-Base Disorders in Patients with Chronic Obstructive Pulmonary Disease: A Pathophysiological Review. Journal of Biomedicine and Biotechnology. 2012;2012:1–8.doi: https://doi.org/10.1155/2012/915150