

ROLE OF INTRAVENOUS MAGNESIUM SULPHATE IN PATIENTS PRESENTING WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. Acute exacerbations of COPD (AECOPD) contribute substantially to hospital admissions and healthcare costs. Intravenous magnesium sulphate has bronchodilatory and anti-inflammatory properties and is established in acute asthma management, but its role in COPD remains controversial.

Objective: To evaluate the efficacy of intravenous magnesium sulphate as an adjunct to standard therapy in patients presenting with acute exacerbations of COPD.

Methodology: This prospective, randomized, open-label comparative clinical trial was conducted in the Accident and Emergency Department of Mayo Hospital, Lahore from 1 February 2025 to 31 May 2025. A total of 190 patients with AECOPD were enrolled using non-probability consecutive sampling and randomly allocated into two equal groups. Group A received intravenous magnesium sulphate (2 g in 100 ml normal saline over 30 minutes) along with standard therapy, while Group B received standard therapy alone. Primary outcome was rate of discharge from the emergency department within 90 minutes. Secondary outcomes included changes in FEV₁, PEF, oxygen saturation, and respiratory rate.

Results: Patients in the magnesium group achieved significantly greater improvements in lung function and clinical outcomes compared to placebo. Mean increase in FEV₁ was 296 ± 74 ml in Group A versus 130 ± 68 ml in Group B (p<0.001). PEF improved by 17.1 ± 6.3% in Group A compared to 7.6 ± 5.9% in Group B (p<0.001). Oxygen saturation increased by 6.8 ± 2.3% with magnesium versus 3.9 ± 2.5% with placebo (p<0.001). Respiratory rate decreased by 6.5 ± 2.1 breaths/min in Group A compared to 3.4 ± 2.2 breaths/min in Group B (p<0.001). Discharge within 90 minutes was achieved

in 65.3% of patients in the magnesium group versus 44.2% in the placebo group ($p=0.003$). Adverse events were minor and self-limiting, with no serious complications observed.

Conclusion: It is concluded that intravenous magnesium sulphate is a safe, effective, and inexpensive adjunct to standard therapy in acute exacerbations of COPD. Its use was associated with significant improvements in lung function, oxygenation, and discharge outcomes, suggesting potential to reduce hospitalization rates and healthcare burden

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an established disease associated with disability due to persistence and obstruction of airflow, inflammation, and structural alteration of the lungs. It is known to be one of the major morbidity and mortality causes worldwide with more than 300 million cases of COPD being recorded globally with the World Health Organization estimating three million COPD related deaths per year [1]. It is estimated that the disease will be the third major cause of death by 2030, and this is propelled by the use of tobacco, environmental pollution, occupational exposures and a rise in the aging populations [2]. In addition to death, COPD imposes a serious economic and social burden, as chronic casualties lead to several hospitalizations related to acute exacerbation resulting in higher spending on health services as well as decreasing the quality of life [3]. Acute exacerbations of COPD (AECOPD) defined as acute deterioration in respiratory symptoms that requires some other interventions are the key points of the disease progress. They enhance the rate of damage to the lung functionality, predetermine such patients to frequent stays in hospitals, and increase both short-term and long-term mortality [4]. The generally accepted management of AECOPD is bronchodilators (short-acting beta-2 (SABA) and muscarinic (SAMA) antagonists, systemic corticosteroids, antibiotics where necessary, and oxygen supplementation [5]. Although these interventions are in place, the results are mixed and there is still keen interest in the development of adjuvant treatments that can enhance the prognosis of a patient or decrease exacerbations and their severity.

Being an important intracellular cation, magnesium is found to exert its key biologic influence in the processes of neuromuscular conduction, smooth muscle relaxation, and regulation of inflammatory processes [6]. Improvements in magnitude and time, quality of life improvement, improvement in the response to the beta agonist, and the reduction of hospitalizations have been widely investigated in the administration of intravenous magnesium sulphate ($MgSO_4$) in aiding treatment of acute severe asthma, as well as the presence of bronchodilatory effects [7]. These pathways lead to the possibility of magnesium involvement in COPD, in which airway hyperresponsiveness, smooth muscle contraction, and inflammatory changes are the main characteristics of the exacerbations. The reason to its utilization is that it prevents the inflow of calcium into the airway smooth muscle cells, thereby decreasing bronchoconstriction and its antioxidant and anti-inflammatory capabilities [6][8]. However, the role played by intravenous magnesium sulphate in the treatment of COPD has remained controversial. Considering some randomized controlled trials, substantial increases in post-therapeutic parameters of lung functioning, i.e. forced expiratory volume in one second (FEV_1) and peak expiratory flow rate (PEFR), improved oxygen saturation, and higher discharge rates out of emergency departments were registered in connection to patients treated with magnesium in relation to placebo [8][9]. However, the other studies could not prove any statistically significant benefit stating that there was no difference in respiratory parameters or changes at discharge between magnesium and control groups [10][11]. The above-mentioned

inconsistencies require a further well-designed clinical trial to reveal whether magnesium sulphate is an essential part of COPD exacerbation management practices.

In low- and middle-income countries such as Pakistan where the prevalence of COPD is increasing with high prevalence rates of smoking, exposure to biomass fuels, and limited access to health care, cost-effective and easy access to treatments would have tremendous clinical and economic value [3]. The assessment of magnesium sulphate as an adjunctive treatment could thus prove to be of special interest in the alleviation of emergency care admissions, management of symptom control, and administration of resources in overwhelmed health care systems. The current study will evaluate the effectiveness of the intervention about the administration of intravenous magnesium sulphate in patients when there was an acute worsening of COPD, and the results of this study could be used in clinical practice guidelines.

Objective:

To evaluate the efficacy of intravenous magnesium sulphate as an adjunct to standard therapy in patients presenting with acute exacerbations of COPD.

Methodology

This was a prospective, randomized, open-label comparative clinical trial conducted in the Accident and Emergency Department of Mayo Hospital, Lahore, from 1 February 2025 to 31 May 2025, enrolling 190 patients with acute exacerbation of chronic obstructive pulmonary disease (COPD). Patients were recruited using non-probability consecutive sampling and randomly allocated into two equal groups of 95 each: Group A received intravenous magnesium sulphate (2 g in 100 ml of normal saline over 30 minutes) in addition to standard therapy, while Group B received standard therapy alone, serving as the placebo group. Standard therapy consisted of nasal cannula oxygen therapy (2–3 L/min), nebulization with salbutamol, ipratropium, and

beclomethasone, along with intravenous hydrocortisone (100 mg).

Inclusion Criteria

- Adults aged 30–65 years.
- Both male and female patients.
- Previously diagnosed cases of COPD confirmed by medical records.
- Patients presenting with acute exacerbation of COPD requiring hospitalization, as defined by \worsening of respiratory symptoms necessitating therapy beyond regular treatment.

Exclusion Criteria

- History of cardiac disease.
- Patients requiring immediate assisted ventilation (GCS $\leq$ 8/15).
- Patients unable to perform PEFr and FEV1 measurements.
- Prior use of magnesium-containing antacids.
- Intravenous magnesium sulphate administration within the last 24 hours.
- Hyperkalemia (serum potassium $>$ 5.5 mmol/L).
- Hypocalcemia (serum calcium $<$ 8.8 mg/dl).

Data Collection

After obtaining informed consent, baseline characteristics including age, gender, smoking status, prior inhaler therapy, socioeconomic status, presence of pets at home, residential setting (urban/rural), use of masks, and baseline dyspnea scores (Modified MRC Dyspnea Scale) were recorded. Clinical assessment included respiratory rate, oxygen saturation, Glasgow Coma Scale (GCS), arterial blood gases (PaO₂ and PaCO₂), forced expiratory volume in one second (FEV₁), and peak expiratory flow rate (PEFR%). Patients randomized to Group A received intravenous magnesium sulphate along with standard therapy, while Group B received standard therapy only. Monitoring during infusion included patellar reflex assessment at 15 and 25 minutes to detect magnesium toxicity; infusion was discontinued if reflexes were diminished. Post-therapy evaluations of respiratory rate, oxygen saturation, FEV₁, and

PEFR% were recorded at baseline, 30 minutes, 60 minutes, and 90 minutes. Discharge status from the emergency department was determined using predefined discharge criteria ($\text{SpO}_2 > 90\%$, respiratory rate $< 25/\text{min}$, no dyspnea at rest, GCS 15/15, and absence of cyanosis or respiratory failure).

Statistical Analysis

All collected data were entered into SPSS version 20 for analysis. Continuous variables, including age, BMI, respiratory rate, oxygen saturation, PaO_2 , PaCO_2 , FEV1, and PEFR%, were expressed as mean $\pm$ standard deviation (SD). Categorical variables, such as gender, smoking status, socioeconomic status, and discharge outcomes, were presented as frequencies and percentages. Within-group comparisons of baseline and post-therapy values were conducted using the paired t-test. Between-group comparisons at each time point were performed using the independent t-test for continuous

variables and chi-square or Fisher's exact test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

Results

The mean age of participants was 53.4 ± 7.2 years, with no significant difference between groups (53.8 ± 7.1 vs 53.1 ± 7.4 years, $p=0.62$). Males comprised 64.2% of the overall sample, with 66.3% in the magnesium group and 62.1% in the placebo group ($p=0.54$). The mean BMI was similar across groups (24.3 ± 3.7 vs 24.0 ± 3.5 kg/m^2 , $p=0.73$). A history of smoking was prevalent in 72.6% of participants, including 74.7% in the magnesium group and 70.5% in the placebo group ($p=0.51$). Socioeconomic and residential status were also comparable, with 44.2% of patients belonging to low-income households and 62.1% residing in urban areas. Nearly half of all patients had an MRC dyspnea score of ≥ 3 , with similar proportions between groups (45.3% vs 46.3%, $p=0.89$).

Table 1. Baseline Demographic and Clinical Characteristics of Patients (N = 190)

Characteristic	Total (N=190)	Group A: MgSO_4 (n=95)	Group B: Placebo (n=95)	p-value
Age (years), mean $\pm$ SD	53.4 ± 7.2	53.8 ± 7.1	53.1 ± 7.4	0.62
Male sex, n (%)	122 (64.2)	63 (66.3)	59 (62.1)	0.54
BMI (kg/m^2), mean $\pm$ SD	24.1 ± 3.6	24.3 ± 3.7	24.0 ± 3.5	0.73
Smoking history, n (%)	138 (72.6)	71 (74.7)	67 (70.5)	0.51
Socioeconomic status - Low, n (%)	84 (44.2)	43 (45.3)	41 (43.2)	0.77
Urban residence, n (%)	118 (62.1)	59 (62.1)	59 (62.1)	1.00
Baseline MRC Dyspnea ≥ 3 , n (%)	87 (45.8)	43 (45.3)	44 (46.3)	0.89

The mean respiratory rate was 28.4 ± 4.2 breaths per minute overall, with no significant difference between groups (28.6 ± 4.1 vs 28.2 ± 4.3 , $p=0.53$). Baseline oxygen saturation averaged $87.5 \pm 3.6\%$, being $87.7 \pm 3.5\%$ in the magnesium group and $87.3 \pm 3.7\%$ in the placebo group

($p=0.46$). Mean PaO_2 values were 64.5 ± 6.7 mmHg in the magnesium group and 63.8 ± 6.9 mmHg in the placebo group ($p=0.39$), while mean PaCO_2 levels were 54.2 ± 7.3 mmHg and Spirometry revealed low baseline lung function,

with mean FEV₁ of 828 ± 188 ml in the magnesium group and 812 ± 192 ml in the placebo group (p=0.64). Baseline PEFR was also

similar (41.6 ± 8.2% vs 41.0 ± 8.8% predicted, p=0.57).

Table 2. Baseline Physiological and Laboratory Parameters

Parameter	Total (N=190)	Group A (n=95)	Group B (n=95)	p-value
Respiratory rate (/min), mean ± SD	28.4 ± 4.2	28.6 ± 4.1	28.2 ± 4.3	0.53
SpO ₂ (%), mean ± SD	87.5 ± 3.6	87.7 ± 3.5	87.3 ± 3.7	0.46
PaO ₂ (mmHg), mean ± SD	64.1 ± 6.8	64.5 ± 6.7	63.8 ± 6.9	0.39
PaCO ₂ (mmHg), mean ± SD	53.8 ± 7.5	54.2 ± 7.3	53.5 ± 7.7	0.52
Baseline FEV ₁ (ml), mean ± SD	820 ± 190	828 ± 188	812 ± 192	0.64
Baseline PEFR (% predicted), mean ± SD	41.3 ± 8.5	41.6 ± 8.2	41.0 ± 8.8	0.57

At 90 minutes post-therapy, patients in the magnesium group showed significantly greater improvement in lung function compared to the placebo group. Mean FEV₁ increased from 828 ± 188 ml to 1124 ± 204 ml in the magnesium group, compared to an increase from 812 ± 192 ml to 942 ± 210 ml in the placebo group. The net improvement in FEV₁ was nearly twice as high with magnesium (296 ± 74 ml vs 130 ± 68 ml, p<0.001). Similarly, PEFR improved from 41.6 ±

8.2% to 58.7 ± 9.5% in the magnesium group, compared with 41.0 ± 8.8% to 48.6 ± 10.1% in the placebo group. The mean rise in PEFR was 17.1 ± 6.3% with magnesium versus 7.6 ± 5.9% with placebo, reflecting a mean difference of 9.5% (p<0.001).

Table 3. Post-Therapy Changes in Lung Function (FEV₁ and PEFR%)

Parameter	Group A: MgSO ₄ (n=95)	Group B: Placebo (n=95)	Mean Difference	p-value
FEV ₁ (ml) – Baseline	828 ± 188	812 ± 192	16	0.64
FEV ₁ (ml) – 90 min	1124 ± 204	942 ± 210	182	<0.001
Change in FEV ₁ (ml)	+296 ± 74	+130 ± 68	166	<0.001
PEFR (% predicted) – Baseline	41.6 ± 8.2	41.0 ± 8.8	0.6	0.57
PEFR (% predicted) – 90 min	58.7 ± 9.5	48.6 ± 10.1	10.1	<0.001
Change in PEFR (%)	+17.1 ± 6.3	+7.6 ± 5.9	9.5	<0.001

Marked improvements in oxygenation and respiratory rate were observed in the magnesium group compared to placebo. Mean oxygen saturation increased from $87.7 \pm 3.5\%$ to $94.5 \pm 2.8\%$ in the magnesium group, versus $87.3 \pm 3.7\%$ to $91.2 \pm 3.2\%$ in the placebo group. The net rise in SpO_2 was $6.8 \pm 2.3\%$ versus $3.9 \pm$

2.5% ($p < 0.001$). Similarly, the respiratory rate decreased more significantly in the magnesium group, falling from 28.6 ± 4.1 to 22.1 ± 3.2 breaths per minute, compared to a reduction from 28.2 ± 4.3 to 24.8 ± 3.5 in the placebo group. The mean reduction was -6.5 ± 2.1 versus -3.4 ± 2.2 breaths per minute ($p < 0.001$).

Table 4. Post-Therapy Changes in Oxygenation and Respiratory Rate

Parameter	Group A: MgSO ₄ (n=95)	Group B: Placebo (n=95)	Mean Difference	p-value	
SpO ₂ (%) – Baseline		87.7 ± 3.5	87.3 ± 3.7	0.4	0.46
SpO ₂ (%) – 90 min		94.5 ± 2.8	91.2 ± 3.2	3.3	<0.001
Change in SpO ₂ (%)		+6.8 ± 2.3	+3.9 ± 2.5	2.9	<0.001
Respiratory rate (∕min) – Baseline		28.6 ± 4.1	28.2 ± 4.3	0.4	0.53
Respiratory rate (∕min) – 90 min		22.1 ± 3.2	24.8 ± 3.5	-2.7	<0.001
Change in respiratory rate (∕min)		-6.5 ± 2.1	-3.4 ± 2.2	-3.1	<0.001

Magnesium sulphate use was associated with a significantly higher rate of early discharge from the emergency department. Within 90 minutes of treatment, 65.3% of patients in the magnesium group were discharged compared to 44.2% in the placebo group ($p = 0.003$). Conversely, hospitalization was required in only 34.7% of the

magnesium group versus 55.8% of the placebo group ($p = 0.003$). The mean duration of emergency department stay was also significantly shorter among magnesium recipients (104 ± 28 minutes vs 137 ± 32 minutes, $p < 0.001$).

Table 5. Emergency Department Discharge Outcomes

Outcome	Group A: MgSO_4 (n=95)	Group B: Placebo (n=95)	p-value
Discharged from ER within 90 min, n (%)	62 (65.3)	42 (44.2)	0.003
Required hospitalization, n (%)	33 (34.7)	53 (55.8)	0.003
Mean ER stay duration (min), mean $\pm$ SD	104 ± 28	137 ± 32	<0.001

Magnesium sulphate was generally well tolerated with no serious adverse events reported. Minor side effects included transient flushing in 7.4% of patients, mild dizziness in 5.3%, nausea or vomiting in 4.2%, and diminished reflexes in

2.1%. None of these events occurred in the placebo group except for mild dizziness (2.1%) and nausea/vomiting (3.2%).

Table 6. Adverse Events Reported During Study

Adverse Event	Group A: MgSO ₄ (n=95)	Group B: Placebo (n=95)	p-value
Transient flushing, n (%)	7 (7.4)	0 (0)	0.014
Mild dizziness, n (%)	5 (5.3)	2 (2.1)	0.24
Nausea/vomiting, n (%)	4 (4.2)	3 (3.2)	0.70
Diminished reflexes, n (%)	2 (2.1)	0 (0)	0.15
Serious adverse events, n (%)	0 (0)	0 (0)	—

Discussion

This randomized controlled trial compared the intravenous magnesium sulphate usage with subsequent augmentation of routine treatment in patients who were affected with acute exacerbation of chronic obstructive pulmonary disease. Its results proved the effectiveness of magnesium sulphate in patients showing a marked increase in lung capacity, oxygen levels and clinical condition as opposed to patients who received the regular treatment alone. The findings expose the possible clinical applicability of magnesium sulphate in faster healing and lesser cases of extended hospitalization. Both groups were also very similar in terms of the demographic characteristics as well as their smoking history and the severity of the disease at the baseline point. This was to make sure that any issues of outcome detected in the results could not be attributed to underlying imbalances. The results were also impressive concerning the improvement of lung function after treatment: the patients assigned to the magnesium group demonstrated the mean increase of FEV1 by 296 ml as opposed to 130 ml in the placebo group, whereas PEFR decreased by 17.1% as opposed to

7.6%. This supports bronchodilatory and airway-stabilizing effects of magnesium which are probably due to calcium channel blockade of airway smooth muscle and effects of anti-inflammatory responses. Other symptoms of improved parameters of pulmonary functions were also noticed and the previous studies stated that there were significant changes in FEV1 and PEFR after magnesium administration [12][13]

In addition to spirometric parameters, magnesium sulphate displayed better outcomes in the enhancement of vital signs. Magnesium produced an average response in oxygen saturation of 6.8 percent compared to 3.9 in the placebo group and respiratory rate decreased 6.5 breaths per minute compared to 3.4 in controls. These results indicate that magnesium has not only the effect of facilitating bronchodilation, but also accelerates the process of restoring the gas balance. Similar improvement in oxygenation and respiratory rates had been reported in previous studies emphasizing the role of magnesium in stabilizing an acutely decompensated patient [14][15]. The most clinically significant finding was an increased rate of discharge amongst magnesium recipients in

the course of the study. After 90 minutes, 65.3 percent of the patients in magnesium group had been fit to go home against 44.2 percent in placebo group. One-third of additional patients were not subjected to hospitalization and the average amount of time spent in emergency department was shortened by nearly 30 minutes. These results suggest that magnesium can play a role in significantly decreasing the need in healthcare service use under a resource-restricted conditions. Earlier studies have also provided results that were consistent with magnesium usage as they reported greater discharge rates and reduced emergency room stay times [16][17]. Magnesium sulphate was found to be quite safe as most of the reported adverse effects occurred only mildly and intermittently and included flushing, dizziness, nausea, and reduced reflexes. Notably, there was no extreme toxicity or life-threatening complications noticed. This is in agreement with prior studies, which have unanimously indicated that magnesium is an intervention that can be used safely under the requisite supervision [18] [19]. Magnesium is an effective treatment and its friendly safety profile has rendered it a useful adjunctive treatment in emergency care.

Such positive results notwithstanding, the outcomes of other studies have not been as encouraging [20]. There are also trials that showed no significant varying between magnesium and placebo in asthmatic subjects regarding FEV₁, oxygenation, and discharge results. Such variability in the results could be explained by different study design, different sample size, different patient population, baseline severity of the disease or use of concomitant therapies. The current study contributes to the evidence by showing consistent positive effect on various clinically relevant outcomes, which makes evident the requirement of bigger multicentric trials in order to define its role in management of COPD exacerbations. Altogether, this paper indicates that intravenous magnesium sulphate can be used effectively and safely at a low cost as an adj vain in managing acute exacerbations of COPD. It was found that its application was related to substantial advances in the lung

functioning, oxygenation, and discharge rates versus the placebo. Combined with earlier studies, the results can be interpreted suggesting that magnesium supplementation can augment the current treatment protocols and cut the healthcare burden, especially in resource-critical environments.

Conclusion

It is concluded that intravenous magnesium sulphate, when administered alongside standard therapy, provides significant clinical benefits in patients presenting with acute exacerbations of COPD. Patients receiving magnesium showed greater improvements in lung function, with mean FEV₁ and PEF_R increases substantially higher than placebo, as well as superior oxygenation and larger reductions in respiratory rate.

REFERENCES

- Mukerji, Saptarshi, Berinder Shahpuri, Bevan Clayton-Smith, Nicola Smith, Patrick Armstrong, Moira Hardy, George Marchant, and Emma Marsh. "Intravenous magnesium sulphate as an adjuvant therapy in acute exacerbations of chronic obstructive pulmonary disease: a single centre, randomised, double-blinded, parallel group, placebocontrolled trial: a pilot study." *The New Zealand Medical Journal (Online)* 128, no. 1425 (2015): 34.
- Shivanthan, Mitrakrishnan Chrishan, and Senaka Rajapakse. "Magnesium for acute exacerbation of chronic obstructive pulmonary disease: A systematic review of randomised trials." *Annals of thoracic medicine* 9, no. 2 (2014): 77-80.
- Selvam, Neethi Shelly. "A Prospective Study to Compare the Efficacy of Iv Magnesium Sulfate Infusion vs. Placebo, As an Adjuvant to Nebulized Salbutamol in Acute Exacerbations of Chronic Obstructive Pulmonary Disease." PhD diss., Rajiv Gandhi University of Health Sciences (India), 2017.

- Farid, Taimur, Abdousamad Said Omar, Sijah Varar Kandi, Soja Puthiyara Maliyekal, Tze Quan Tuen, Amrutha Thazhuthedath Vijayan, Lakshmi Sudhir Pillai et al. "Intravenous Magnesium Sulphate as an Adjuvant Therapy for Acute Exacerbations of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis." *Life* 15, no. 6 (2025): 973.
- Vafadar Moradi, Elnaz, Elham Pishbin, Seyed Reza Habibzadeh, Morteza Talebi Doluee, and Azadeh Soltanifar. "The adjunctive effect of intravenous magnesium sulfate in acute exacerbation of chronic obstructive pulmonary disease: a randomized controlled clinical trial." *Academic Emergency Medicine* 28, no. 3 (2021): 359-362.
- González, Juan Abreu, Concepción Hernández García, Pedro Abreu González, Candelaria Martín García, and Alejandro Jiménez. "Effect of intravenous magnesium sulfate on chronic obstructive pulmonary disease exacerbations requiring hospitalization: a randomized placebo-controlled trial." *Archivos de Bronconeumología ((English Edition))* 42, no. 8 (2006): 384-387.
- Edwards, Llifon, Philippa Shirtcliffe, Kirsten Wadsworth, Bridget Healy, Sarah Jefferies, Mark Weatherall, Richard Beasley, and Magnesium COPD Study Team. "Use of nebulised magnesium sulphate as an adjuvant in the treatment of acute exacerbations of COPD in adults: a randomised double-blind placebo-controlled trial." *Thorax* 68, no. 4 (2013): 338-343.
- Aziz, Hany S., Adel I. Blamoun, Mohammed K. Shubair, Mourad MF Ismail, Vincent A. DeBari, and M. Anees Khan. "Serum magnesium levels and acute exacerbation of chronic obstructive pulmonary disease: a retrospective study." *Annals of Clinical & Laboratory Science* 35, no. 4 (2005): 423-427.
- Bajracharya, Manjita, Ramesh P. Acharya, Ram P. Neupane, Rekha Sthapit, and Apurva R. Tamrakar. "Nebulized magnesium sulphate versus saline as an adjuvant in acute exacerbation of chronic obstructive pulmonary disease in a tertiary centre of Nepal: A randomized control study." *Journal of Institute of Medicine Nepal* 43, no. 1 (2021): 5-10.
- Datta, Priyanka Kumar, Ajisha Aravindan, Sayan Nath, Sumit Roy Chowdhury, and Deep Dutta. "Nebulised magnesium sulphate as an adjuvant to the treatment of acute exacerbation of COPD: A systematic review and meta-analysis of randomised controlled trials with trial sequential analysis." *Lung India* 40, no. 4 (2023): 339-348.
- Kumar, Pavan N., Amirullah Amirullah, and Deepak R. Kumar. "Association between serum magnesium levels and acute exacerbations in chronic obstructive pulmonary disease patients." *International Journal of Medicine and Health Development* 30, no. 2 (2025): 146-151.
- Bessmertny, Olga, Robert V. DiGregorio, Henry Cohen, Ellen Becker, Darrell Looney, Jonathan Golden, Lewis Kohl, and Thomas Johnson. "A randomized clinical trial of nebulized magnesium sulfate in addition to albuterol in the treatment of acute mild-to-moderate asthma exacerbations in adults." *Annals of emergency medicine* 39, no. 6 (2002): 585-591.
- Sulehria, Sohail Bashir, Hafiza Farah Masood, Muhammad Kamran Yousaf, Nasir Hussain, Masooma Batool, and Ch Adnan Ahmed Athar. "Effectiveness of Oral Magnesium in improving in-Hospital Outcome in patients presenting with Acute Exacerbation of Chronic Obstructive Pulmonary Disease." *Pakistan Journal of Medical & Health Sciences* 16, no. 10 (2022): 108-108.
- Kshirsagar, Ketan, and Virendra C. Patil. "Chronic obstructive pulmonary disease: Is serum magnesium level a risk factor for its acute exacerbation?." *Caspian journal of internal medicine* 12, no. 2 (2021): 223.

- Bhatt, Surya Prakash, Pooja Khandelwal, Sudip Nanda, Jill C. Stoltzfus, and Gloria T. Fioravanti. "Serum magnesium is an independent predictor of frequent readmissions due to acute exacerbation of chronic obstructive pulmonary disease." *Respiratory medicine* 102, no. 7 (2008): 999-1003.
- Irazuzta, Jose Enrique, and Nicolas Chiriboga. "Magnesium sulfate infusion for acute asthma in the emergency department." *Jornal de pediatria* 93, no. suppl 1 (2017): 19-25.
- Edwards, L. (2014). *Three aspects in the treatment of acute exacerbations of chronic obstructive pulmonary disease: the rôle of nebulised magnesium, the risks of oxygen and the utility of the CRB-65 score* (Doctoral dissertation, Cardiff University).
- Rowe, Brian H., Jennifer A. Bretzlaff, Chris Bourdon, Gary W. Bota, and Carlos A. Camargo Jr. "Intravenous magnesium sulfate treatment for acute asthma in the emergency department: a systematic review of the literature." *Annals of emergency medicine* 36, no. 3 (2000): 181-190.
- Silverman, Robert A., Harold Osborn, Jeffrey Runge, E. John Gallagher, William Chiang, James Feldman, Theodore Gaeta et al. "IV magnesium sulfate in the treatment of acute severe asthma: a multicenter randomized controlled trial." *Chest* 122, no. 2 (2002): 489-497.
- Singhi, Sunit. "Intravenous magnesium sulfate in acute severe asthma not responding to conventional therapy." *Indian pediatrics* (1997).