WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 23, 889-910. Research Article ISSN 2277–7105

ASSESSMENT AND MANAGEMENT OF RISK FACTORS IN RESPIRATORY TRACT INFECTION - A PROSPECTIVE OBSERVATIONAL STUDY

Yathiraj K. M.* and Mahadevamma L.

Department of Pharmacy Practice, East West College of Pharmacy, Bengaluru, Karnataka, India.

Article Received on
11 October 2024,

Revised on 01 Nov. 2024,
Accepted on 21 Nov. 2024

DOI: 10.20959/wjpr202423-34633

***Corresponding Author**
Yathiraj K. M.
Department of Pharmacy Practice, East West College of Pharmacy, Bengaluru, Karnataka, India.

ABSTRACT

Inflammation of the lung parenchyma is referred to as pneumonia. The likelihood of infection rises as a result of pneumonia risk factors. Around the world, it is significant source of mortality and morbidity. The present study was carried out to assess the risk factors and variables for effective management of risk factors for Respiratory Tract Infections (RTI). This was a prospective and observational study in which 110 subjects were enrolled based on study the criteria in Sagar Hospital, the data collected was assessed and evaluated by suitable statistical method. In this study the prevalence of males (70.1%) is more than females and a greater number of patients were identified in the age group of 60-90 years. The common risk factors observed were smoking (12.7%), alcoholism (7.3%) and age group of 60-90 years (15.5%). The variables used were PaO_2 and $PaCO_2$. These parameters were chosen as they are likely to show abnormalities during respiratory tract infection. Most common respiratory pathogen found was *Streptococcus pneumoniae* and the common antibiotics used were Cefoperazone+Sulbactam[20] and Piperacillin+Tazobactam with Azithromycin,[31] Remidesivir and Pipercilline+Tazobactam.[17] The study was concluded with an understanding of risk factors that helped to identify individuals who have more chance of developing the disease, which helps to lower the respiratory infection related morbidity and mortality rates by administering appropriate antimicrobial regimen along with patient counseling, regarding lifestyle modification, dietary approaches and other precautions to be taken. This study provides

valuable laboratory data to monitor the status of antimicrobial usage among respiratory pathogens and improve treatment recommendations in a hospital.

KEYWORDS: Respiratory Tract Infection, Risk factors, PaO_2, PCO_2, Antibiotics.

INTRODUCTION

Respiratory tract infections (RTIs) is defined as any infections in the parts of the body involved in breathing, such as the sinuses, throat, airways or lungs.[1] RTI are of 2 types - Upper respiratory tract infections (URTI) and lower respiratory tract infections (LRTI), Upper respiratory tract infections (URTIs) include common cold, sinusitis, pharyngitis/tonsillitis epiglottitis and laryngotracheitis and (LRTIs) are Bronchitis, Bronchiolitis, Chest Infection Pneumonia.[2] Causative agents of (LRTIs) are viral or bacterial. Viruses cause most cases of bronchitis and bronchiolitis.[3,4] Many factors, including environmental contaminants and autoimmune diseases, as well as infection, may cause pneumonia. The various infectious agents that cause pneumonia are categorized in many ways for purpose of laboratory testing, epidemiologic study and choice of therapy.[5]

The present study was carried out to assess the risk factors and variables for effective management of risk factors for Respiratory Tract Infections (RTI). This was a prospective and observational study in which 110 subjects were enrolled based on study the criteria in Sagar Hospital, the data collected was assessed and evaluated by suitable statistical method.

Methodology

Study site

The study was conducted in the General Medicine and Pulmonology department of Sagar Hospital, Bengaluru.

Study design

A Prospective and Observational study.

Sample size

A total of 110 patients from the General Medicine and Pulmonology department of Sagar Hospital, who satisfied the study criteria and consented to participate and included for the study.

Study period

The study was conducted over a period of 06 months starting from February 2022 to July 2022.

Ethical approval

Ethical committee clearance has been obtained by the Institutional Ethical Committee of Sagar Hospitals.

Study criteria

Inclusion criteria

- Patient Infected with Respiratory Tract Infection
- Patient of age 5 to 90 years

Exclusion criteria

- Newborn
- Neonate
- Infant
- Lactating and Pregnancy Women

Materials

Data Collection Form

Patient Consent Form

Source of data

Patient Case Note

Treatment Chart

Laboratory Reports

Study procedure

Patient enrolment

Patients with RTI and who were admitted to the General Medicine and Pulmonology department of Sagar Multi Speciality Hospital in Bengaluru during the study period were screened for different risk factors and treatment approach based on the inclusion and exclusion criteria. Patient who met all the criteria and who consented for the study were enrolled for the study.

Methods of data collection

Patients with RTI admitted to the General Medicine and Pulmonology department of Sagar Hospitals in Bengaluru- during the study period- were screened for the risk factors and treatment pattern in adult RTI patients. Those who met the study criteria were enrolled for the study. Follow-ups were carried from the day of admission to the day of discharge of the enrolled patients. After the diagnosis was confirmed by the physician, relevant and necessary baseline information such as the socio-demographic details of the patient and details on the visit for the treatment was obtained from patient case notes. To assess the risk factors demographic details like age, gender, past medical history, past medication history, social history was collected from patient case note. To assess the treatment pattern, therapeutic data like drug name and drug class from the patient case file was evaluated. Treatment pattern was assessed with the help of laboratory variables like sputum test, total leukocyte count, erythrocyte sedimentation rate, partial pressure of oxygen, partial pressure of carbon dioxide, X ray or CT scan, which were collected in a suitably designed data collection form. To assess the outcome of therapy, duration of hospital stay was evaluated from patient case note. The data was evaluated with suitable statistical method.

RESULTS

Table 1: Subject distribution for gender.

Gender	Frequency in no. (110)	Percentage (%)
Female	45	40.9
Male	65	59.1
Total	110	100.0

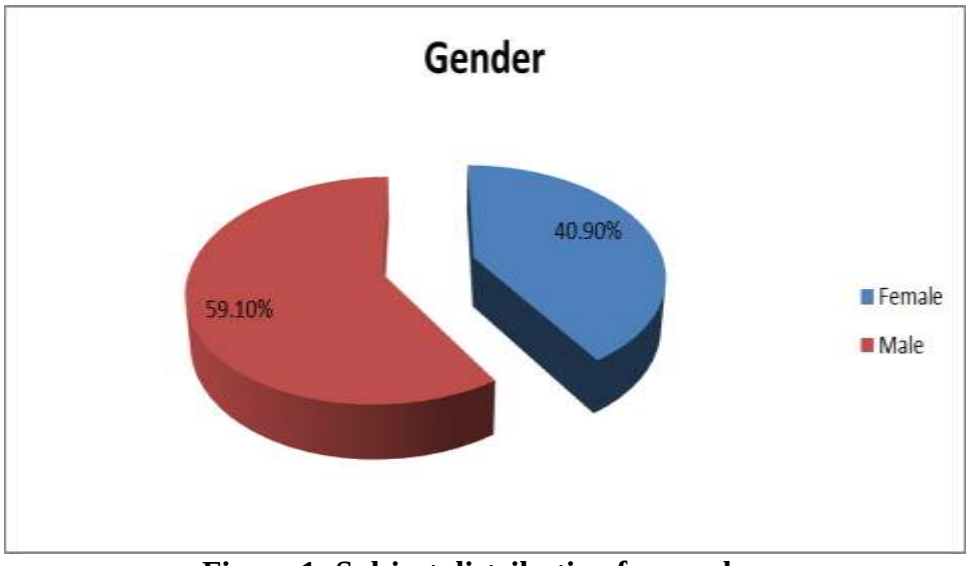


Figure 1: Subject distribution for gender.

The study Subjects were distributed based on the gender. In the total population, the male gender was found to be predominant 65(59.10%) then the female gender 45(40.90%).

Table 2: Subject distribution of the study on population.

Age (in years)	Frequency in no. (110)	Percentage (%)
Child Age 5-12	2	1.8
Young Age 15-20	3	2.7
Adult Age 21-29	6	5.5
Middle Age 30-59	35	31.8
Geriatric Age 60-90	64	58.2
Total	110	100

From the distribution table of subjects based on their age groups, a greater number of patients were identified in the age group of 60-90 years -64 (58.2%) and the least was found in the age group of 5-12 years 2 (1.8%).

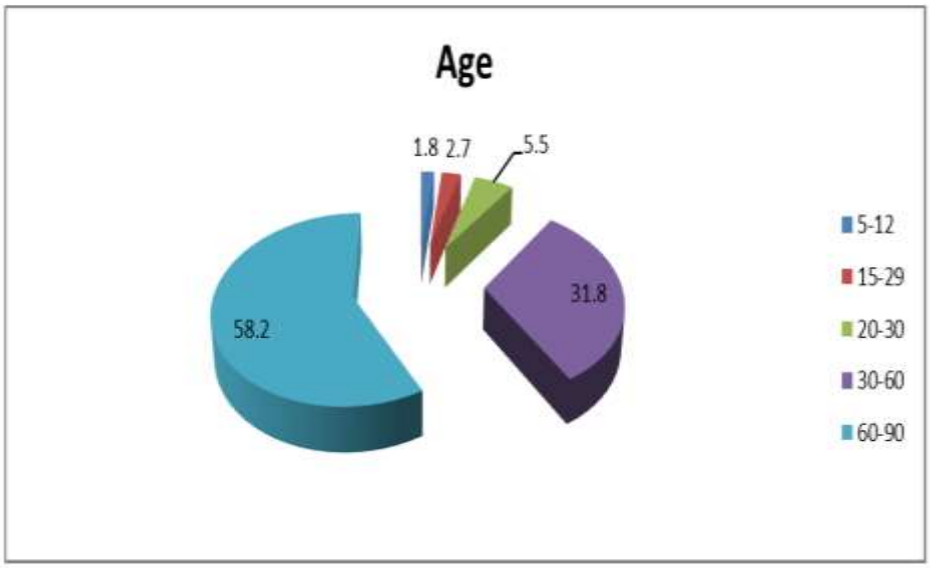


Figure 2: Subject distribution of the study on population.

Table 3: Subject distribution based on Age and Social History (Smoking).

Age interval	Smoking		Total
	No	Yes	
5-12	2	0	2
	1.8%	0.0%	1.8%
12-20	3	0	3
	2.7%	0.0%	2.7%
20-30	6	0	6
	5.5%	0.0%	5.5%
30-60	32	3	35
	29.1%	2.7%	31.8%

60-90	53	11	64
	48.2%	10.0%	58.2%
Total	96	14	110
	87.3%	12.7%	100.0%

Chi-square statistic=3.295, p-value=0.510 (not significant)

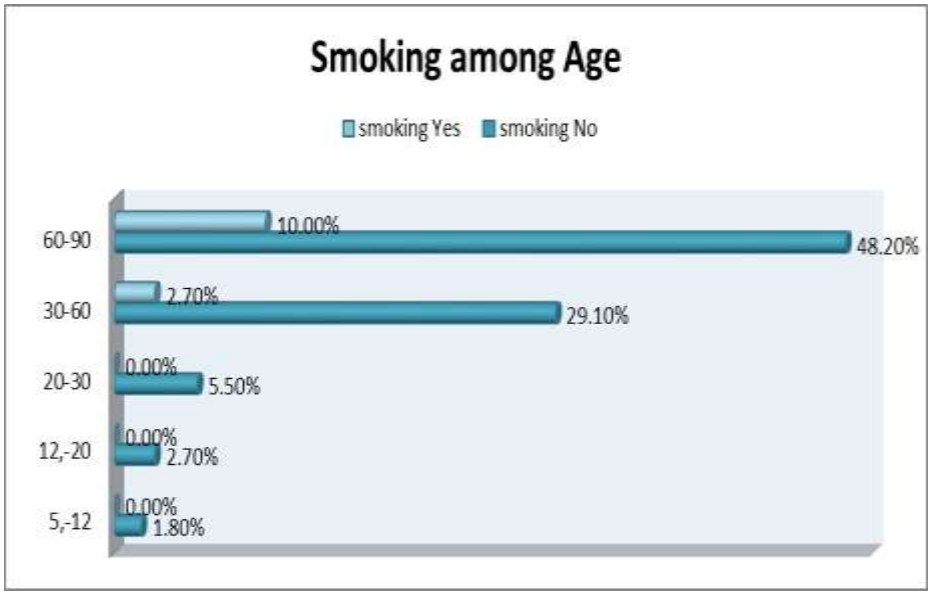


Figure 3: Subject distribution based on Age and Social History (Smoking).

From the distribution table of subjects based on age and smoking, higher number of patients 11 (10%) were found in the age group of 60-90 years and least number of patients 03(2.7%) were found in the age group of 30-60 (2.7%).

Table 4: Subject distribution based on Partial Pressure of Oxygen.

	Partial Pressure of Oxygen before Treatment		**Partial Pressure of Oxygen after Treatment**	
	Patients with Normal PaO2	**Patients with abnormal PaO2**	**Patients with Normal PaO2**	**Patients with abnormal PaO2**
	69	41	110	00
	62.7%	37.3%	100%	00%
Total	110		110	
	100%		100%	

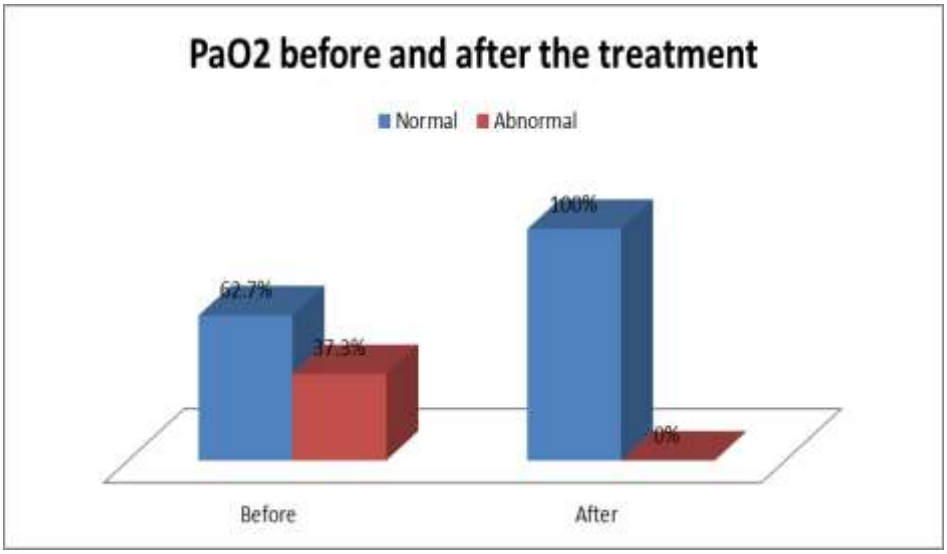


Figure 4: Subject distribution based on partial pressure of oxygen.

In our study, out of 110 patients, 41(37.3%) patients who had their partial pressure of oxygen in abnormal range before treatment and (100%) had their partial pressure of oxygen corrected after treatment.

Table 5: Subject distribution based on partial pressure of carbon dioxide.

	Partial Pressure of carbon dioxide before Treatment		Partial Pressure of carbon dioxide after Treatment	
	Patients with Normal PaCO2	Patients with abnormal PaCO2	Patients with Normal PaCO2	Patients with abnormal PaCO2
	70	40	110	00
	63.6%	36.4%	100%	00%
Total	110		110	
	100%		100%	

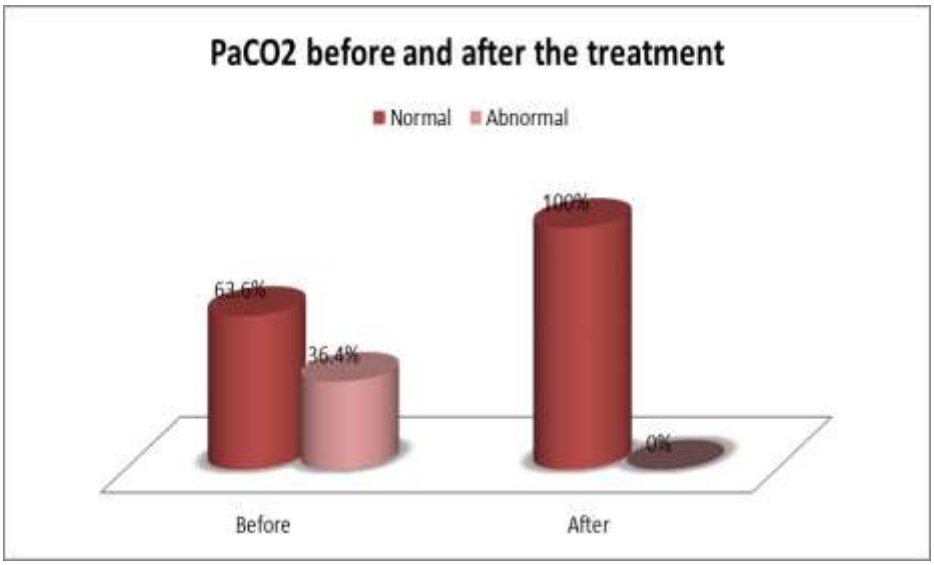


Figure 5: Subject distribution based on partial pressure of carbon dioxide.

In this study, out of 110 patients, 40 (36.4%) patients who had their partial pressure of carbon dioxide abnormal range before treatment were brought to normal with treatment.

Table 6: Subject distribution based on disease.

Disease Names	Frequency	Percent
Nil	3	2.7
URTI	2	1.8
LRTI	23	20.9
ASTHMA	12	10.9
Bronchitis	2	1.8
COPD	12	10.9
Respiratory type 2	1	.9
Respiratory type 1	1	.9
TB	1	.9
Covid-19 pneumonia	25	22.7
Pneumonia	10	9.1
LRTI & Covid-19 pneumonia	5	4.5
LRTI & TB	2	1.8
LRTI & COPD & Pneumonia	1	.9
LRTI & Pneumonia	1	.9
COPD & Respiratory 2	2	1.8
LRTI & Respiratory 1	1	.9
LRTI & COPD	2	1.8
LRTI & Respiratory 2 & Covid-19 Pneumonia	1	.9
LRTI & COPD & Respiratory 1	1	.9
COPD & Respiratory 2	1	.9
COPD & Covid-19 Pneumonia	1	.9
Total	110	100.0

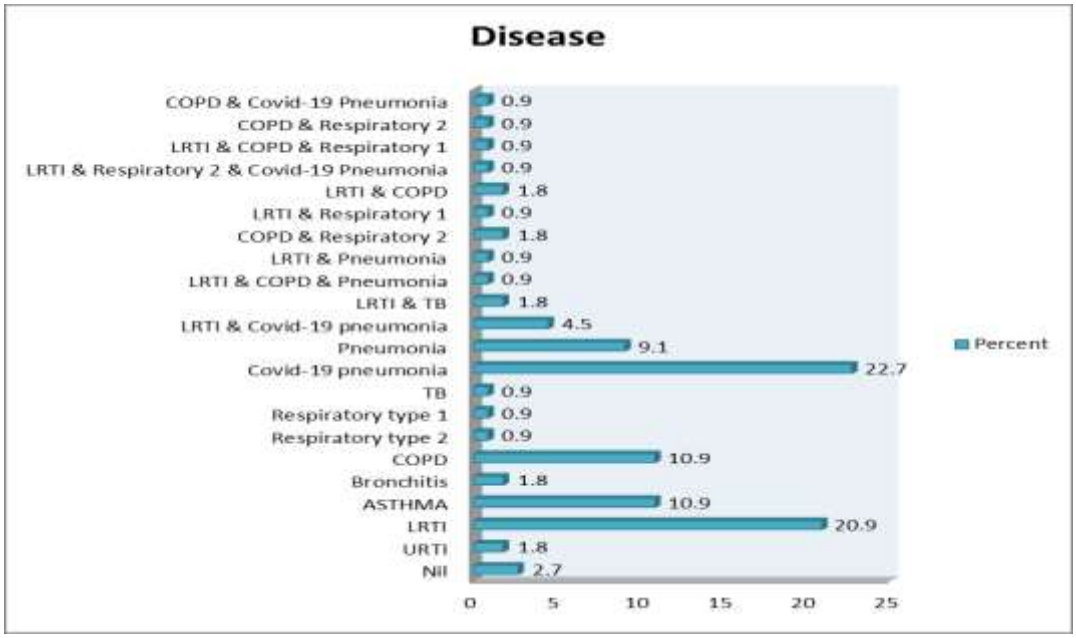
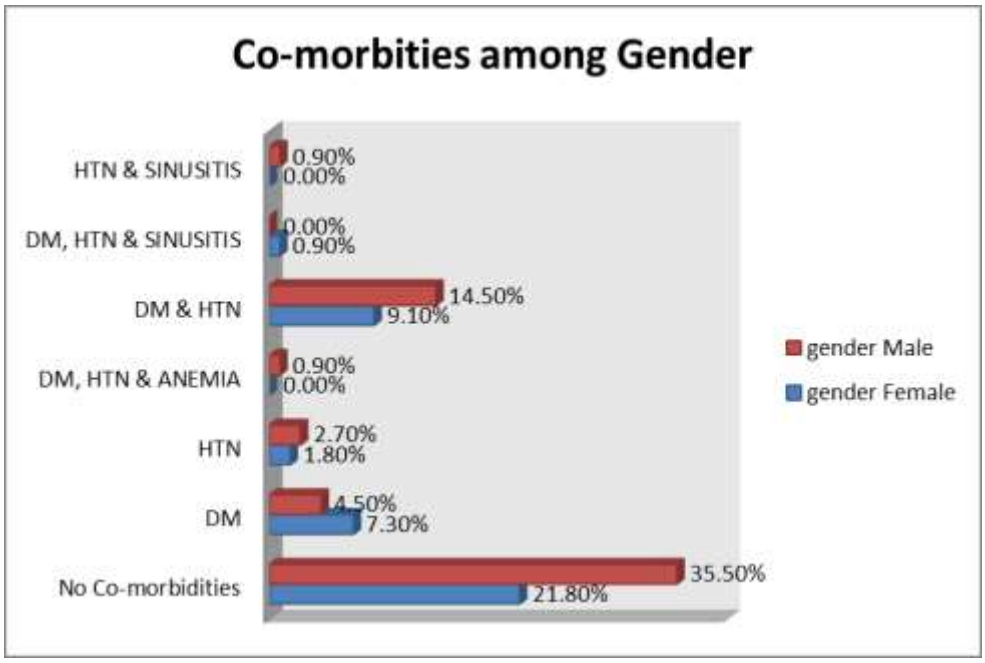


Figure 6: Subject distribution based on disease.

From the distribution table based on Disease, a higher number of patients are seen to present in Covid pneumonia 25 (22.7%) and Second highest is lower respiratory tract infection 23 (20.9%), the 3rd highest is COPD and Asthma with 12 (10.9%), the fourth highest is pneumonia, 10(9.1%), and fifth highest is upper respiratory tract infection and bronchitis with 2 (1.8%), patient.

Table 7: Subject Distribution Based on Co-Morbidities.

Co-morbidities	Gender		Total
	Female	Male	
No Co-morbidities	24	39	63
	21.8%	35.5%	57.3%
DM	8	5	13
	7.3%	4.5%	11.8%
HTN	2	3	5
	1.8%	2.7%	4.5%
DM, HTN & ANEMIA	0	1	1
	0.0%	0.9%	0.9%
DM & HTN	10	16	26
	9.1%	14.5%	23.6%
DM, HTN & SINUSITIS	1	0	1
	0.9%	0.0%	0.9%
HTN & SINUSITIS	0	1	1
	0.0%	0.9%	0.9%
Total	45	65	110
	40.9%	59.1%	100.0%



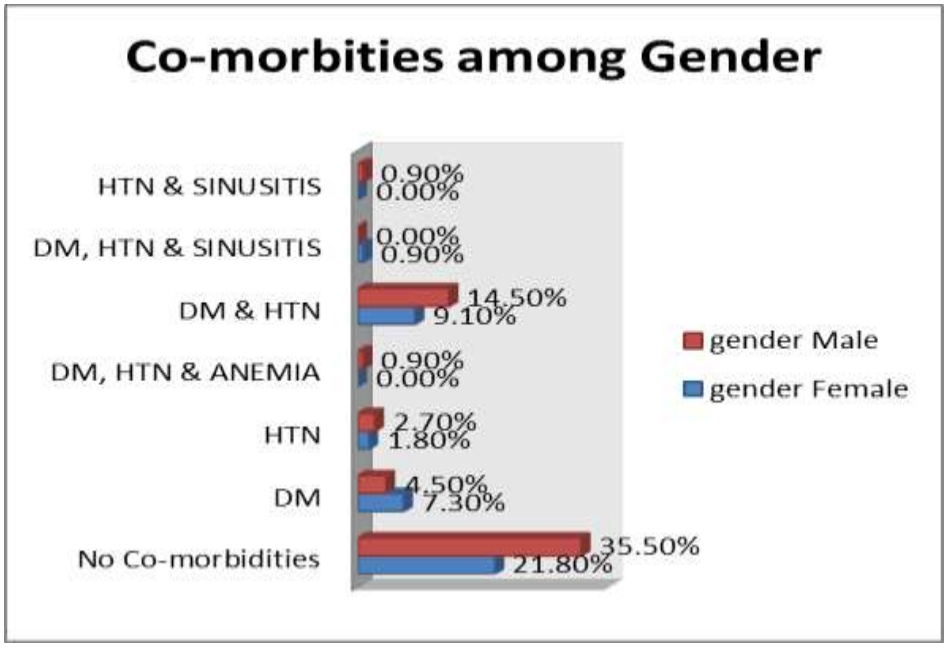


Figure 7: Subject Distribution Based on Co-Morbidities.

From the distribution table based on co- morbidities, a higher number of diseases are present in diabetes mellitus 13 (11.8%), followed by Hypertension 5 (4.5%), Sinusitis and Anemia 1 (0.9%).

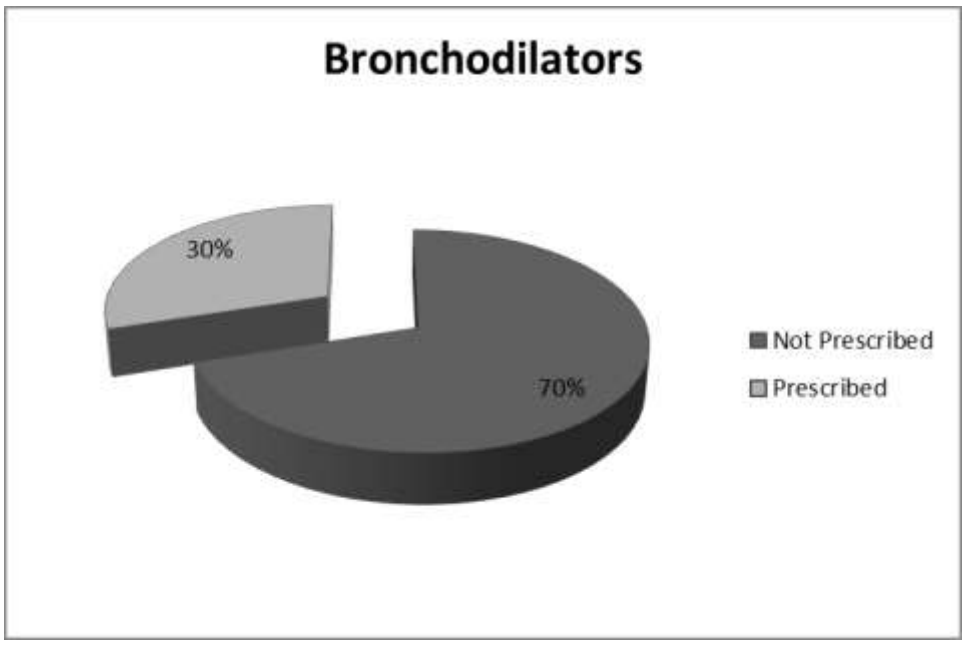


Figure 8: Subject distribution based on prescription of bronchodilators.

In the present study, bronchodilators were not prescribed for a majority of population.

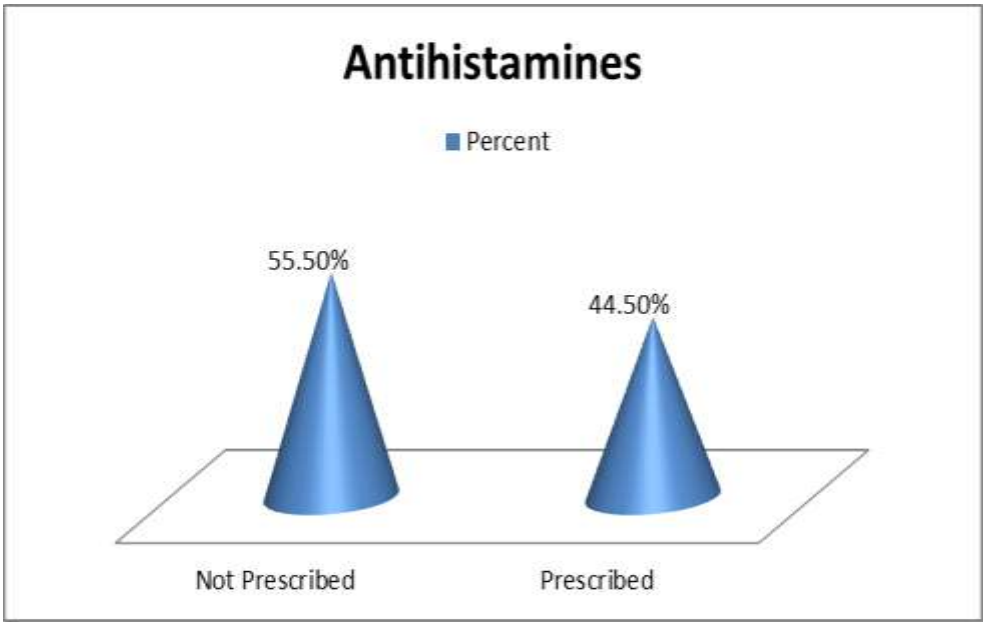


Figure 9: Subject distribution based on prescription of antihistamines.

In the present study, antihistamines were not prescribed for majority of patients.

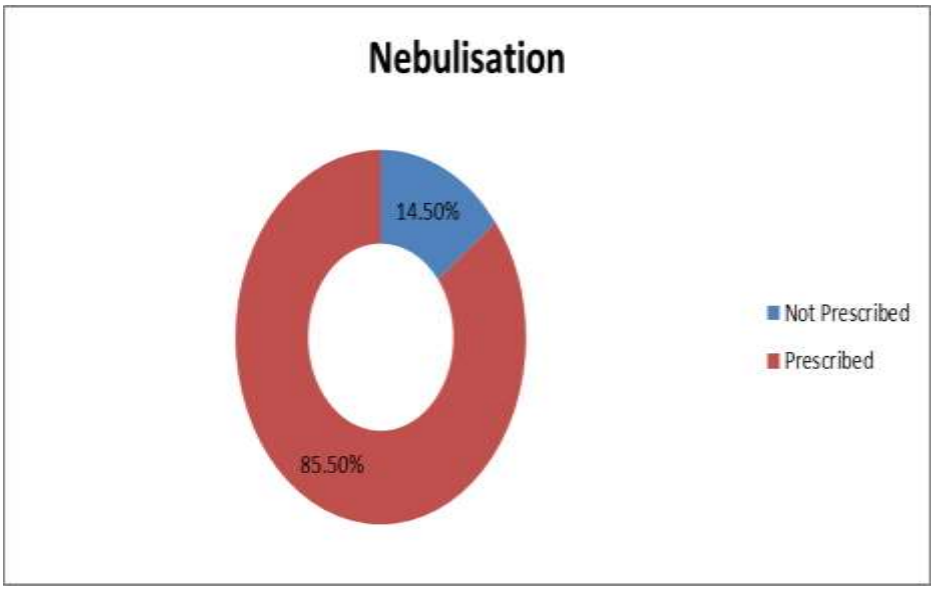


Figure 10: Subject Distribution based on prescription of nebulisation.

In the present study, nebulization was prescribed for majority of patients.

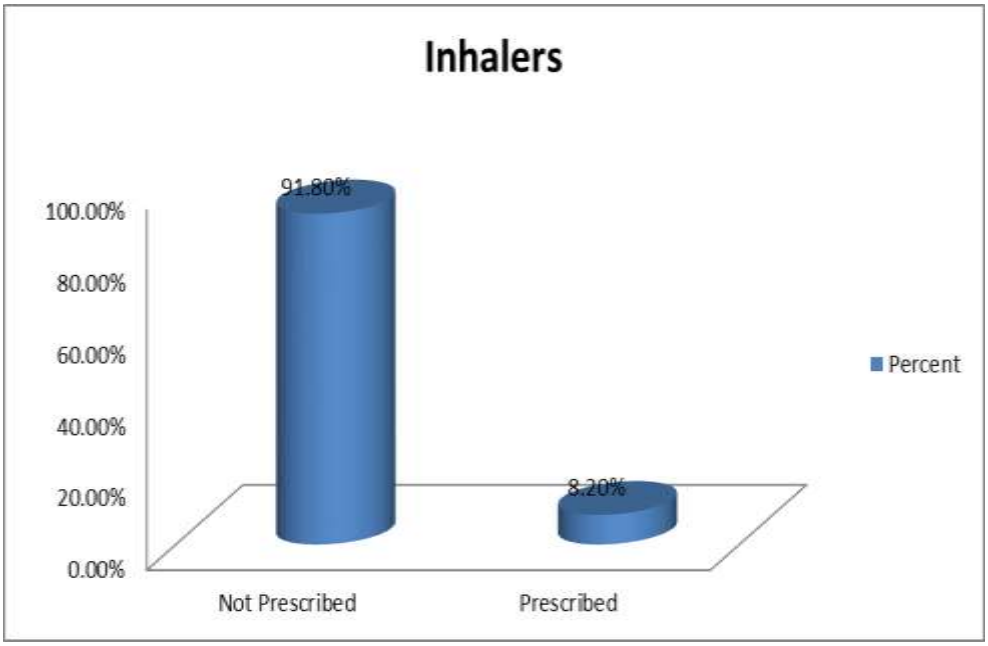


Figure 11: Subject Distribution based on prescription of Inhalers.

In the present study, Inhalers were not prescribed for majority of patients.

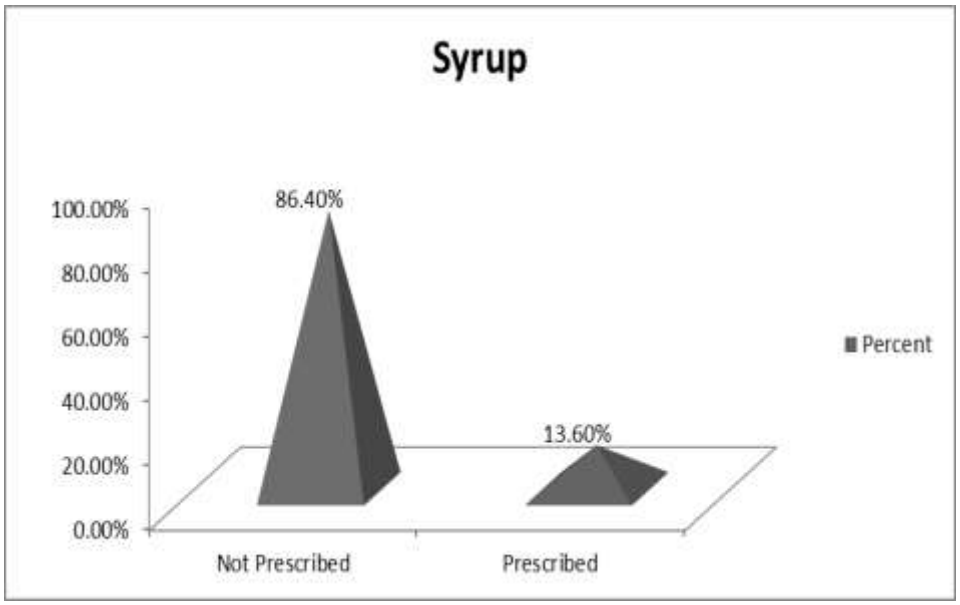


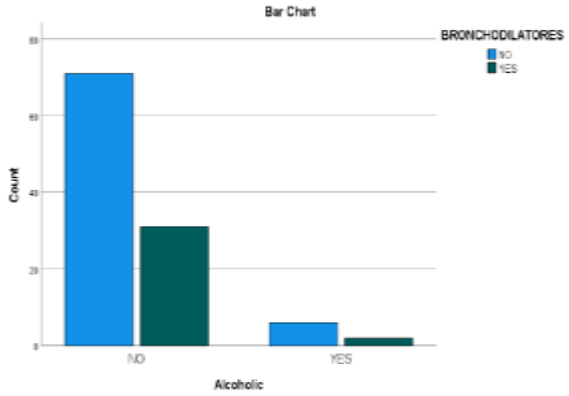
Figure 12: Subject distribution based on prescription of syrups.

In the present study, syrups were not prescribed for majority of patients.

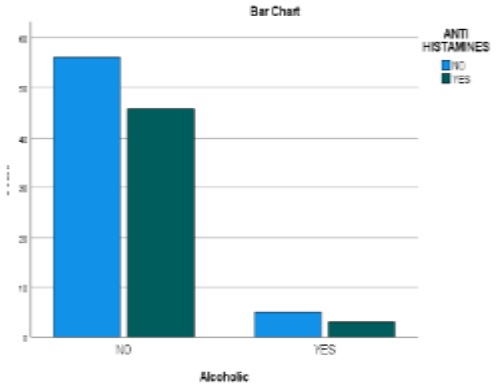
Below table gives the details of patient distribution according to the prescription of Bronchodilators in alcholers. Using chi-square test it is estimated that, the odds of prescribing Bronchodilators among alcoholic patients is increased by 1.335 times compared with nonalcoholic patients and it is found to have nosignificants ($p>0.05$)

Table 8: Patient distribution according to the prescription of Bronchodilators in alcoholics.

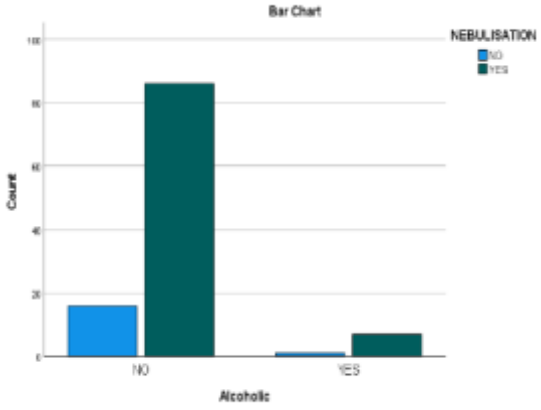
Alcoholic	Bronchodilatores		Total	Odds ratio	Significance
	NO	YES			
NO	71	31	102	Odds Ratio = 1.335 (0.250 - 6.849)	p-value = 0.749 (NS)
	64.5%	28.2%	92.7%		
YES	6	2	8		
	5.5%	1.8%	7.3%		
Total	77	33	110		
	70.0%	30.0%	100.0%		



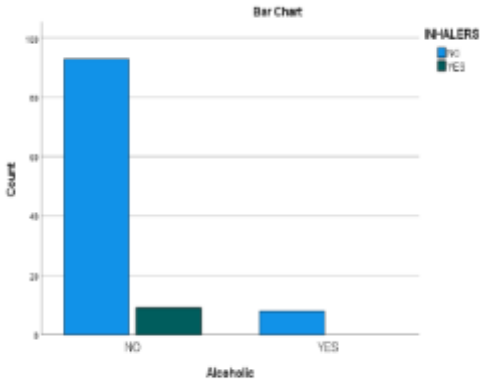
(A)



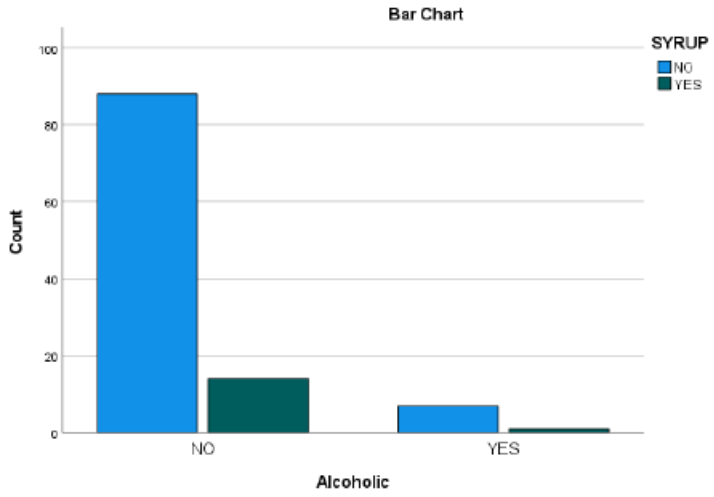
(B)



(C)



(D)



(E)

Figure 13: Patient distribution according to the prescription of (A) Bronchodilators, (B) Antihistamines, (C) Nebulisation, (D) Inhalers & (E) Syrups in alcoholics.

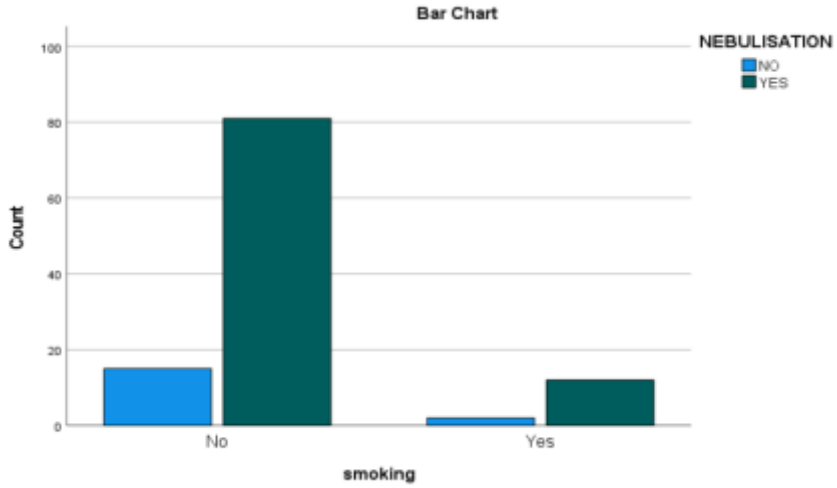


Figure 14: Patient distribution according to the prescription of nebulisation.

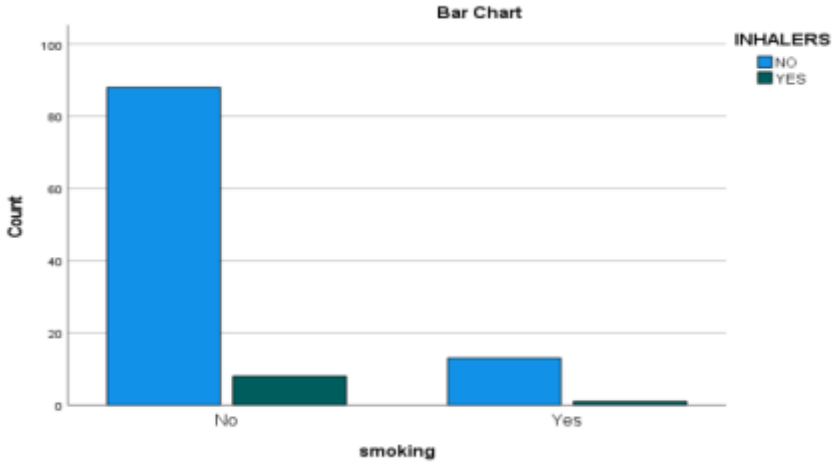


Figure 15: Patient distribution according to the prescription of inhalers.

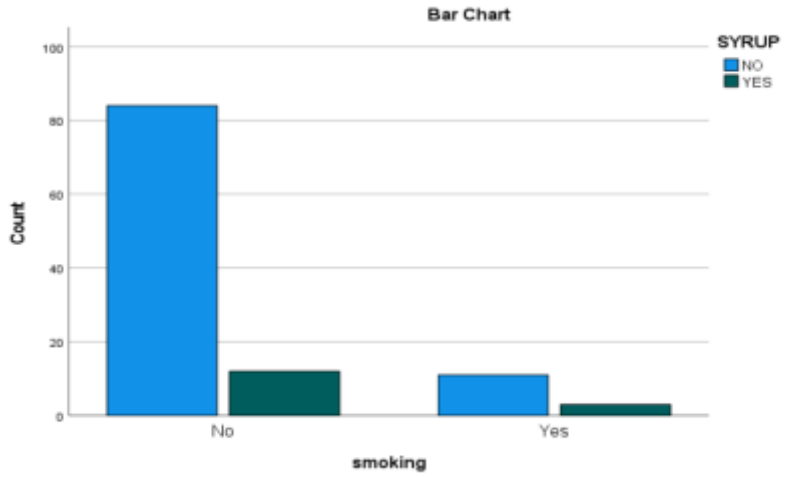


Figure 16: Patient distribution according to the prescription of syrups.

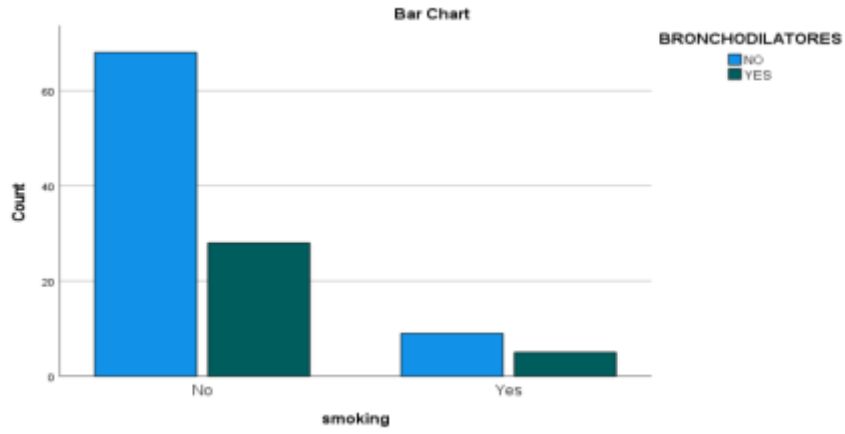


Figure 17: Patient distribution according to the prescription of bronchodilators.

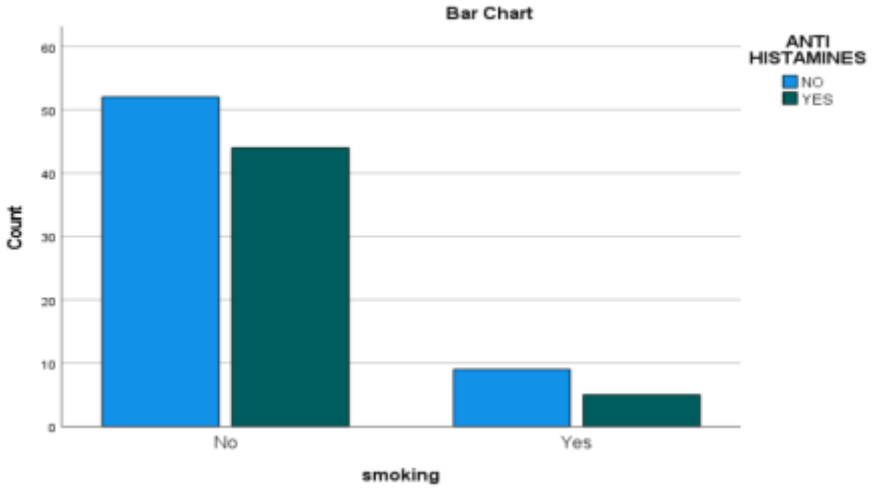


Figure 18: Patient distribution according to the prescription of Antihistamines

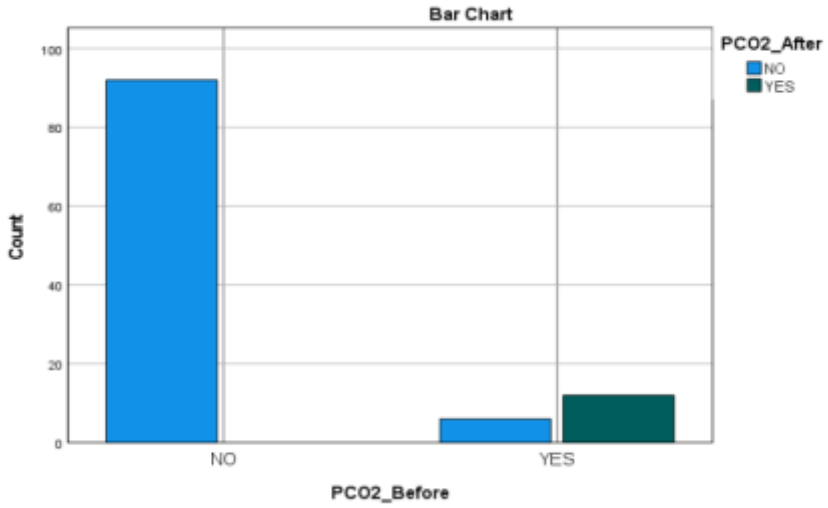


Figure 19: Effect of various treatments on PCO2.

DISCUSSION

A prospective study was conducted on the patients who were diagnosed with Respiratory tract infection in the department of General Medicine and Pulmonology in Sagar Hospital, Bengaluru. The patients were enrolled on the basis of complaints related to respiratory tract infection and analyzed for the risk factors and drugs prescribed.

Gender

In the current study, a total of 110 patients were involved out of which 45 were females and 65 were males giving 40.9% and 59.1% respectively. This represents that male predominated over females in pneumonia. This is due to the lack of estrogen, a sex hormone that can boost the immune system and also due to lifestyle, behavioural pattern such as smoking and alcoholism in males. Similar findings were found in the study conducted by Zhiping Yang, Yuh Ching T Huang and Henry Koziel, where males were more exposed to respiratory tract infection.[6,7]

Age

The age distribution of the study population showed 1.8% of patients belong to the age group of 5-12 years, 2.7% in the age group of 15-20 years, 5.5% in the age group of 21-29 years 31.8% in the age group of 30-59 years and 58.2% in the age group of 60-90. This implies that higher incidence of pneumonia were found in the age group 60-90 years because of weakened immune system, chronic medical conditions such as diabetes, COPD, asthma that increases the risk of developing respiratory infection. Their muscles too are weakened to clear secretions from lungs resulting in infections. Similar findings were found in the study

conducted by Bilal Bin Abdulla, Mohammed Zoheb and Syed Mustafa, where patients between 60-65years are more with pneumonia.[8]

Age and Alcohol consumption

In our study, we found that 1.8% patients belonging to the age group of 30-60years and 5.5% patients belonging to the age group of 60-90 years consume alcohol. This implies that age group of 60-90 years may have more chance of developing pneumonia as alcohol consumption interferes with the functioning of alveolar macrophages which is the first line defense in lung cellular immunity. Similar findings were found in the study conducted by Samantha M and Joseph H Sisson.[9]

Age and Smoking

In our study, we observed that 2.7% patients belonging to the age group of 30-60 years and 10.0% patients belonging to the age group 60-90 years are smokers. This implies that patients belonging to the age group of 60-90 years have more chance of developing respiratory tract infection as the large amount of free radicals in cigarette smoke can damage the alveolar epithelial cells leading to pneumonia and COPD. Similar findings were found in the study conducted by Chen Jiang, Qiong Chen and Mingxuan Xie.[10]

Gender and Alcohol consumption

The distribution of subjects based on the gender and alcohol consumption which show that 7(6.4%) of males and 01 (0.9%) female consumes alcohol. This implies that males are at more chance of developing pneumonia than females as alcohol consumption interferes with the functioning of alveolar macrophages which is the first line defense in lung cellular immunity.

Gender and Smoking

The distribution of subjects based on the gender and smoking which show that 14 (12.7%) males and 0 (0.0%) females are smokers. This indicates that males are at more risk of developing pneumonia then females as the large amount of free radicals in cigarette smoke can damage the alveolar epithelial cells leading to pneumonia, COPD, Respiratory tract infection.

Risk factors

The risk factors for respiratory tract infection show that alcoholics are found to have 3 times more chance of developing respiratory tract infection than non-alcoholics followed by the age group 60-90 years with more chance and smokers more chance of getting respiratory infection. This implies that alcoholics followed by age group of 60- 90 years and smokers are at more risk of developing respiratory infection.[11]

Partial pressure of oxygen Before and After treatment

Distribution of subjects based on Partial Pressure of Oxygen before and after treatment, which showed that before treatment 69 (62.7%) patients had their Partial Pressure of Oxygen in abnormal range and after treatment only patients had their Partial Pressure of Oxygen in abnormal range. This implies that after treatment there is significant improvement in ventilation, since alveolus is responsible for supplying oxygen to blood.

Partial pressure of carbon dioxide Before and After treatment

Distribution of subjects based on Partial Pressure of Carbon Dioxide before and after treatment, which showed that before treatment 70 (63.6%) patients had their Partial Pressure of Carbon Dioxide in abnormal range and after treatment only patients had their Partial Pressure of Carbon Dioxide in abnormal range. This implies that there is significant improvement in ventilation, since Partial Pressure of Carbon Dioxide accounts for alveolar ventilation within the lungs.

Based on the disease condition

Distribution of subjects based on disease condition of covid-19 pneumonia (22.7%). Lower respiratory tract infection (20.9%) Chronic obstructive pulmonary and Asthma (10.9), Respiratory failure type1 and 2.and tuberculosis is (9.1%).[12]

Based on co – Morbidities condition

Distribution of subjects based on disease condition the highest number in diabetes mellitus the males 5 (7.3%), and females 8 (4.5%), Secondary highest number is hypertension the males 3 (2.7%), and females 2 (1.8%), third highest number is sinusitis and anemia 2 (1.8%).

Antibiotics used in respiratory tract infection

Distribution of subjects according to antibiotics used in respiratory tract infection which shows that patient was treated with cefoperazone+sulbactam and patients and drug was given

20 patients. Combination of pipericillin+tazobactam and azithromycin was given to 31 patients and Remidesivir and pipercilline+tazobactamto 17 patients. From the study it was found that cefoperazone+sulbactam was the most commonly prescribed antibiotic as it has broad spectrum activity against both gram-positive and gram-negative organisms and piperacillin+tazobactam with azithromycin was found to be the most commonly prescribed combination therapy as it is the first line treatment for patients infected with streptococcus pneumoniae.

Bronchodilators used in respiratory tract infection

The distribution of subjects based on the bronchodilators used in Respiratory tract infection which shows that patients were treated with ipratropium bromide+levosalbutamol, formoterol fumarate, budesonide, theophylline, Acebrophylline. From the study it was found that ipratropium bromide+levoslabutamol, budesonide was the most commonly prescribed bronchodilator as both of them shows bronchodilation which accounts for asynergistic effect.[13,14] Similar findings were found in the study conducted

Antihistamine used in respiratory tract infection

The distribution of subjects based on the antihistamines used in Respiratory tract infection shows that patients were treated with Fexofinidine, Montelukast sodium, levocitrizine and patients treated with any antihistamines (44.5%) agents.

Nebulization used in respiratory tract infection

The distribution of subjects based on the nebulization used in respiratory tract infection which shown that patients were treated with most in the bronchodialators and steroids this drugs more frequently used in respiratory tract infection prescribed bronchodilator as both of them shows bronchodilation which accounts for asynergistic effect. Similar findings were found in the study conducted.

Inhalers used in respiratory tract infection

The distribution of subjects based on inhalers used in respiratory tract infection (8.2%) prescribed in study.

Syrups used in respiratory tract infection

The distribution of subjects based on syrups used in respiratory tract infection (8.2%), prescribed in study.

Outcome in relation to gender

In the study 45 females and males 65 were treated for respiratory infection, based on laboratory data as partial pressure of oxygen and partial pressure of carbon dioxide have shown response of before and after treatment patients have shown partial response. Patients were treated for respiratory infection this implies that a greater number of patients with partial response were found to be males and females patients enrolled in the study.

Outcome in relation to age

In the study 45 females and males 65 were treated for respiratory infection, on age based child age 5-12, young age 15,20, adult age 21-29, middle age 30-59, geriatric age 60-90, of based on laboratory data as partial pressure of oxygen and partial pressure of carbon dioxide have shown response of before and after treatment patients have shown partial response. Patients were treated for respiratory infection this implies that a greater number of patients with partial response after the treatment were found to be males and females patients enrolled in the study.

CONCLUSION

The study shows the detailed in formation of the risk factors and treatment used for RTI patients. Patient characteristics were assessed and evaluated. In this study the prevalence of males is more than females due to lack of estrogen, lifestyle behavioural pattern such as smoking and alcoholism in males. Study showed that, pneumonia in accordance with age, a greater number of patients were identified at the age group 60-90 years because of the weakened immune system. The common risk factors observed were alcoholism (6.4%), smoking (12.7%) and age group of 60-90 years (5.5%) as alcohol consumption interferes with the functioning of alveolar macrophages and free radicals in cigarette smoke can damage alveolar epithelial cells leading to respiratory infection.

The patients were evaluated and diagnosed on the basis of commonly observed symptoms of respiratory infection and laboratory values such as, PaO_2, $PaCO_2$ and C-Reactive Proteins (CRP). These parameters were chosen as they are likely to show abnormalities during RTI. The patients on admission were managed with commonly prescribed antibiotics therapy and bronchodilators, antihistamines, nebulization, inhalers, syrups. They were also advised to follow appropriate diet and lifestyle modification. During the course of hospital admission on the basis of total subjects were treated with Cefoperazone-sulbactam 20 patients and oseltamivir 7 patients, carbapneam 5 patients, meropenem 4 patients were treated and

combination therapy piperacillin-tazobactam with azithromycin.31, and resmidesivir and pipercillin+tazobactam 17 patients were given and bronchodilator are given (30%), anti histamime (44.5%), nebulization (85.5%), inhalers are given (8.2%), syrup (13.6%), Study revealed that the treatment used in RTI was effective since the outcome indicates that, a majority of patients has shown partial response and a least number of patients has not shown complete response.

The study concluded that understanding the risk factors have helped to identify individuals who have more chance of developing the disease and respiratory infection related morbidity and mortality rates, by counseling the patient regarding lifestyle modification, dietary approaches and other precautions to be taken. It also aids the clinical pharmacists in improving their knowledge and providing better counseling to the patients and outcome of the disease was also evaluated to assess effectiveness of treatment and improve the quality of life.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. Graffunder EM, Preston KE, Evans AM, Venezia RA. Risk factors associated with extended-spectrum β-lactamase-producing organisms at a tertiary care hospital. Recent AdvAntiinfect Drug Discov. [cited 2022 Aug], 2005; 1, 56(1): 139-45.
2. Raman G, Avendano EE, Chan J, Merchant S, Puzniak L. Risk factors for hospitalized patients with resistant or multidrug-resistant Pseudomonas aeruginosa infections: a systematic review and meta-analysis. [Internet]. Antimicrobial Resistance & Infection Control. [cited 2022 Aug 2], 2018; 7(1): 1-4.
3. Walter EB, Talaat KR, Sabharwal C, Gurtman A, Lockhart S, Paulsen GC, Barnett ED, Muñoz FM, Maldonado Y, Pahud BA, Domachowske JB. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. [Internet]NPJ Aging. [cited 2022 Aug5], 2022; 6, 386(1): 35-46.
4. Km R, Gupta V, Ahmad S, Ranhotra S, Issrani R, Prabhu N. Assessment of anemia as a risk factor for acute lower respiratory tract infections in children: a case-control study. [Internet]. Clin Med Pediatr. [cited 2022 june2], 2015; 12, 4(2-3): 149-53.
5. Behairy OG, Mohammad OI, Elshaer OS. Iron-deficiency anemia as a risk factor for acute lower respiratory tract infections in children younger than 5 years. [Internet].

Egyptian Journal of Bronchology. [cited 2022 june3], 2018; 12(3): 352.

6. Steinman MA, Landefeld CS, Gonzales R. Predictors of broad-spectrum antibiotic prescribing for acute respiratory tract infections in adult primary care. [Internet]. JAMA Health Forum.[cited 2022 june5], 2003; 12, 289(6): 719-25.
7. Stone S, Gonzales R, Maselli J, Lowenstein SR. Antibiotic prescribing for patients with colds, upper respiratory tract infections, and bronchitis: a national study of hospital-based emergency departments. [Internet].J Am CollEmerg Physicians Open. [cited 2022 june10], 2000; 1, 36(4): 320-7.
8. Tchatchouang S, Nzouankeu A, Kenmoe S, Ngando L, Penlap V, Fonkoua MC, Pefura-Yone EW, NjouomR.Bacterialaetiologies of lower respiratory tract infections among adults in Yaoundé, Cameroon. [Internet]. Biomed Clin Anal. [cited 2022 July3], 2019; 17: 2019. Available from: https://www.hindawi.com/journals/bmri/2019/4834396/
9. Bradburne A.F., Bynoe M.L., Tyrrell D.A. Effects of a “new” human respiratory virus in volunteers. [Internet]. BMJ. [cited 2022 July5], 1967; 3: 767–769.
10. Greenberg SB, Allen M, Wilson J, Atmar RL. Respiratory viral infections in adults with and without chronic obstructive pulmonary disease. [Internet].American Lung Association. [cited 2022 July10], 2000; 1, 162(1): 167-73.
11. Raherison C, Poirier R, Daurès JP, Romand P, Grignet JP, Arsac P, Tartavel JM, Touron D, Taytard A. Lower respiratory tract infections in adults: non-antibiotic prescriptions by GPs. [Internet]. RespirMedi. [cited 2022 July15], 2003; 1, 97(9): 995-1000.
12. van der Meer V, Neven AK, van den Broek PJ, Assendelft WJ. Diagnostic value of C reactive protein in infections of the lower respiratory tract: systematic review. [Internet]. Bmj. [cited 2022 July18], 2005; 30, 331(7507): 26.
13. Garbino J, Gerbase MW, Wunderli W, Kolarova L, Nicod LP, Rochat T, Kaiser L. Respiratory viruses and severe lower respiratory tract complications in hospitalized patients. [Internet]. Chest. [cited 2022 July], 2004; 1, 125(3): 1033-9.
14. Nyquist AC, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. [Internet].JAMA Health Forum. [cited 2022 Aug18], 1998; 18, 279(11): 875-7.