Prevalence of Respiratory Complications In Covid-19 Patients

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Abstracts: Background & Objective: In 2019 COVID-19 virus was emerged from China which was then declared a pandemic by WHO. This virus affects different organs of the body and causes some serious complications mainly affecting the respiratory system. The main objective of this research was to find out the prevalence of respiratory complications in patients with COVID-19. Methodology: A cross-sectional survey was conducted on patients with COVID-19 to find out the prevalence of respiratory complications in people. A sample size of 200 participants was selected using the non-probability convenience technique. The duration of the study was 6 months i.e., April to September 2021. Data was collected from Public sector hospitals situated in Rawalpindi and Islamabad in the form of hard copies. The tools used for the data collection were the CAP scale, MMRC scale for dyspnea, and CAT scale. The collected data was analyzed using SPSS Statistics V23.0. Results: Out of 200 participants, 111(55.5%) were male and 89 (44.5%) were females. The mean values of Community-acquired pneumonia (CAP) scale, Modified Medical Research Council (MMRC) scale for dyspnea and COPD Assessment Test (CAT) scale are 48.3, 3.02 and 26.09. Out of 200 participants Dyspnea was prevalent in 77.5% of people, Pneumonia was prevalent in 68% of people and COPD was prevalent in 56% of people. The P value for the three groups including CAP, MMRC and CAT is less than 0.05 (P < 0.05) which indicates that results are statistically significant. Conclusion: The findings indicate that there is a prevalence of Respiratory complications in COVID-19 Patients. Results are statistically significant as P value is P < 0.05

Keywords: COVID-19, Pneumonia, COPD, and Dyspnea.

1. INTRODUCTION

In December 2019, a new virus instigated a disease outbreak in Wuhan, China which is named as corona virus 2019 (COVID-19). COVID-19 caused hazardous infectious diseases throughout the world. This virus affects different organs most importantly the respiratory system. The human-to-human transmission was considered a major source for the outspread of this virus. It was then declared as a pandemic by World Health Organization (WHO). [1]

This virus is impacting a very large population being reported as of 13 July 2021 there have been **186,821,815** confirmed cases including **4,038,342** fatalities globally and **976,867** confirmed cases including **976,867** fatalities in Pakistan.

There are two modes of transmission of the corona virus, direct and indirect. Human to human transmission occurs via direct contact or through droplets that are spread by coughing, sneezing from an infected individual. Whereas indirect transmission occurs through fomites and aerosols. [2]

Symptoms of COVID-19 infection appear after an incubation period of approximately 5 days. COVID-19 causes systemic disorders including respiratory disorders. Respiratory disorders include rhinorrhea, sneezing, sore throat, pneumonia, ground-glass opacities, and respiratory distress syndrome. Other clinical findings of respiratory

symptoms include hypoxemia which is manifested as dyspnea. It can also lead to other respiratory problems like respiratory failure, COPD and ARDS. [3]

The first step in viral infection is the binding of receptor by host cell followed by fusion within the cell membrane. Lung epithelial cells are the primary target of the virus. Virus enter into the host cell through ACE2 receptor. SARS CoV2 binds with the part of the Renin-Angiotensin System which is called as Angiotensin converting enzyme 2. Afterward the activation of RAS, the kidneys start their production of renin by juxtaglomerular apparatus. With the help of angiotensin converting enzyme, the renin starts to convert angiotensinogen into angiotensin1 and then into angiotensin 2. ACE 2 releases various vasoactive anti-inflammatory peptides which are used by the COVID-19 to enter the kidney, endothelial, heart, intestine and alveolar host cell. [4]

COVID-19 virus when reaches the lungs, the immune system starts fighting against the invading virus. The invasion of virus leads to the inflammation of the alveoli which results in Pneumonia and hypoxemia. [5]

The purpose of conducting this research study is to summarize the huge available data on respiratory disorders (Pneumonia, COPD and Dyspnea) of human health due to COVID-19. So, this study will help in finding the prevalence of respiratory complications in patients with COVI-19 through conducting surveys and by using standards questionnaires (mMRC, CAT and CAP) and getting responses from different stakeholders. This study will help in evaluating the prevalence of respiratory complications in patients with COVID-19.

1.1. Significance and Rationale

As COVID-19 has hit the world as a pandemic, there's a dire need to carry out researches on its outcomes. As COVID-19 has an adverse effect on different organs of the body, most importantly the respiratory system. So, it was very important to find out the prevalence of Respiratory complications in COVID-19 patients. This study aims to evaluate the prevalence of respiratory comorbidities which occurs as a manifestation of COVID-19. This study will help the people by providing them the knowledge regarding the respiratory complications which occur as a consequence of COVID-19, so that new treatment protocols can be discovered to help out the people.

1.2. AIM OF STUDY

This study aims to evaluate the prevalence of Respiratory complications caused by COVID-19 by identifying the severity of complications

1.3. OBJECTIVES

- To evaluate prevalence of respiratory complications caused by COVID-19

- To study the relationship, if any between pneumonia, dyspnea and COPD in patients with COVID-19

- To determine the associated symptoms which occur as a manifestation of COVID-19.

2. LITERATURE REVIEW

Koichi Yuki et al. published an article on 20th April 2020 which states that In December 2019, a new virus emerged from Wuhan, China. Which can be transmitted from one person to another and is known as the Corona virus (COVID-19). This human-to-human transmission played a major role in its outbreak. And it was declared a pandemic by WORLD HEALTH ORGANIZATION (WHO). This virus cause's series of respiratory complications in addition to that it involves other organs of the body. As this virus affects the respiratory system, it shows symptoms like fever, dry cough and dyspnea. And it also displays non respiratory symptoms including myalgia, headache, diarrhoea, weakness etc. This disease can get worse and can lead to death. [1]

Mary Kathryn Bohn, et al. conducted a study which was published on 12 Aug. 2020 describes structural composition. It states that SARS CoV 2 comprises of 4 structural glycoproteins including spike (S), membrane (M), envelope (E) and nucleocapsid (N). N, M and E proteins are considered critical for viral release and assembling whereas for viral binding the required protein is S and also this spike is responsible for the entry into host cell. Fusion between virus and cell membrane, enables the entry of the virus into the cell. S protein is essential for the binding of SARS CoV and host cell. [6]

Yang j. et al. conducted a study to evaluate the prevalence of comorbidities in COVID-19 which concludes that the most predominant symptoms of COVID-19 include fever, cough, fatigue, and dyspnea. And most prevalent comorbidities include respiratory system diseases and cardiovascular diseases. [7]

Pauline Vetter et al. conducted research that was published on 17th April 2020. This case series states non respiratory symptoms. So, the symptoms of GIT system manifests as diarrhoea, vomiting etc. Symptoms of the neurological system manifests as loss of perception of taste and smell, ischemic or haemorrhagic stroke, dizziness, altered mental state and Guillain-Barre syndrome. Cardiovascular events associated with corona virus include myocardial injury, cardiac arrhythmias, myocarditis, myopericarditis etc. Ocular manifestations include cconjunctival hyperemia, chemosis, and increased secretions in ear. [8]

Nascimento Conde et al. conducted a research in 2020 which states that corona virus is an enveloped RNA virus with glycoprotein spikes present on its envelop. COVID-19 virus binds to angiotensin converting enzyme 2 receptors of host cell to invade ciliated epithelial cells of respiratory tract which result in an inflammatory response that leads to respiratory complications. And thus, leading to improper or no gaseous exchange which results in serious complications. [9]

Nanshan chen et al. conducted a study which was published on 29th January 2020 which illustrates that polymerase chain reaction (PCR) test and sputum culture test is used to detect the virus in the human body. This retrospective study also concluded that smokers and old age patients are more prone to severe complications caused by COVID-19. [10]

Anat Ratnovsky et al. published an article in 2008 which concludes that Respiratory system is considered to be the requisite organ of human body as it takes part in gaseous exchange which is going on between alveolar sacs and pulmonary circulation. The respiratory system comprises of upper and lower respiratory tract, through which oxygen is supplied to the whole body to keep it functional. As lungs are known as passive extensible organs of the body, so during the gaseous exchange, the diameter of lungs changes along with the thoracic cavity to accommodate inhalation and exhalation. [11]

Pneumonia is an infection of lungs which result from the build-up of fluid or pus in the alveoli. Virend k. somer et al. published an article on September 30, 2020 in which it was concluded that COVID-19 causes pneumonia by replicating in the respiratory tract and alveoli which causes an autoimmune response leading to a cytokine storm which results in inflammation. The inflammation and reduced surfactant production increase the lungs consolidation and hypoxia. [5]

Jose Augusto Barreto-Filho et al. conducted a research which was published on October 8, 2020 which concluded that patients with COVID-19, pneumonia had peculiar blunted dyspnea in hypoxemic respiratory failure. Sensations of dyspnea is a defence response during hypoxemia. Other factors responsible for dyspnea include hypercapnia, increase sense of effort and dynamic compression. Hypoxemia stimulates the chemoreceptors in carotid and aortic bodies. And the sensory information reaches the brain stem through vagus and glossopharyngeal nerves which increases the breathing activity. [12]

Abdul Manan Baig et al. conducted a research on the title of "Computing the effects of SARS-CoV-2 on respiratory regulatory mechanisms in COVID-19". This research was published online on 29 June 2020. In his research he reported that advanced coronavirus can cause severe alveolar damage and pneumonia. Consolidation of lungs has been established which can cause hypoxemic respiratory failure. COVID-19 can cause damage to
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multiple organs including the central nervous system, which regulates the breathing process. This research supports that corona virus can invade in CNS areas like brain stem and disturb normal breathing process which is controlled by brainstem. [13]

Li Shi and Ying Wang et al conducted a systemic review and meta-analysis on the title of "Risk factor of critical & mortal COVID-19 cases". The paper was published on 13th May 2020 in the journal of infection. Their results concluded that there is negative association between fever and COVID-19 progression. While there is positive association between progression of COVID-19 and dyspnea. According to their research dyspnea instead of fever is indicator of poor outcome in COVID-19 patients. [14]

Jiang xie et al. conducted research on the Association between hypoxemia and mortality in patients with COVID-19 which was published on 11th April 2020 which concludes that low oxygen saturation which is caused by the reduced oxygen supply to the blood is an independent source of mortality in patients. He concluded that patients with > 90% blood oxygen saturation have more likely chance to survive but the patients with <90% blood oxygen saturation have less likely chance to survive. [15]

Claire Launois et al. conducted a research which supports that mMRC scale might be an easy and useful tool to access dyspnea. Hence the modified Medical Research Council scale (mMRC) is largely used for the assessment of dyspnea.[16]

Janice M. Leung et al. conducted their study on the topic "COVID-19 and COPD". Which was accepted on 2nd June 2020. It states that the COPD patients are more susceptible to viral aggravations. As COPD patient have increased pulmonary expression for ACE 2 receptor which helps the virus to easily enter into the cells. COPD patients also have endothelial cells dysfunction which results in worst outcomes of COVID-19 including high mortality rate. [17]

Amy Attaway et al. in a peer review about "Management of patient with COPD during the COVID-19 pandemic" which was published on 13th April 2020 concluded that management of COPD with COVID-19 permits the usual treatment with corticosteroids and antimicrobial agents. Patients of Chronic obstructive pulmonary disease and Corona virus infection that treats their disease while staying at home should use nebulizers that evade the viral aerosolization, self-isolate themselves and they should sanitize the room surfaces on regular basis. [18]

Enya Daynes et al. conducted a study which was published on November, which explains that symptom of COPD can be assessed by COPD Assessment test (CAT). This scale consists of 8 items with each item comprises of 5 points, and a total score of 40. Total CAT score > 10 were reported in more than half of COVID-19 patients having any previous secondary lung disease. CAT can not only be used for diagnosis but also to assess severity of disease and also use to guide management. [19]

Cristina Stasi et al. published an article on Treatment of COVID-19 which states that till the treatment of COVID-19 was not formed, some classes of drugs were used in order to decrease the severity of the disease. Involving antiviral agents which prevents the replication of the virus by inactivating the proteases, inflammation inhibitors, heparins and hyper immune immunoglobulins. [20]

Deivendran Kalirathinam et al. published a narrative review on physiotherapy management in COVID-19 which was approved on 21st may 2020. This review illustrates that physiotherapy also plays and important role in the management of COVID-19. Involving the exercises like respiratory muscle training, airway clearance exercises, and exercises for strengthening and reconditioning of weak muscles can play a vital role for significant health outcomes in COVID-19 patients. [21]

Parisa Ghelichkhani et al. published an article on 11th April 2020 which states that prone positioning can aid the patient in improving the ventilation. The prone position can help the patient by increasing the end-expiratory lung volume, chest wall elasticity, improving the tidal volume and by decreasing the alveolar shunt. The patients with severe hypoxia can get a relief by adopting this position. [22]

3. RESEARCH METHODOLOGY:

A descriptive cross-sectional survey was conducted from April to September 2021 in twin cities (Rawalpindi and Islamabad) of Pakistan to evaluate the prevalence of respiratory complications in COVID-19 patients.

3.1. Study Design

This study was a cross sectional descriptive survey.

3.2. Setting

The data was collected from Public sector hospitals having separate COVID-19 care wards and quarantine facilities. Data was collected from the hospitals mentioned below

    i.   Combined Military Hospital (CMH), Rawalpindi

    ii.   Benazir Bhutto Hospital (BBH), Rawalpindi

    iii.   Pakistan Institute of Medical Sciences (PIMS), Islamabad

3.3. Study Population

COVID-19 patients of Rawalpindi and Islamabad were taken as the study population.

3.4. Duration of Study

The duration of study was 6 months after the approval of the synopsis.

3.5. Sample Size

The sample size for this study was 200 (n = 200) was taken using WHO calculator

3.6. Sampling Technique

Non probability convenience sampling technique was used.

3.7. Inclusion Criteria

- Patients who are diagnosed with COVID-19.

- Patients between age group of 20 years to 60 years.

- Both genders (male and female) are included in this research.

- Individual who doesn't have any respiratory complications before COVID-19 attack.

3.8. Exclusion Criteria

- Patient having any secondary lung complications i.e., lung carcinoma before COVID-19 attack will be excluded from this research.

- Patients diagnosed with any psychiatric disorder will be excluded from this research.

3.9. Instrument

The data was collected by using 3 standard questionnaires including Modified Medical Research Council scale, Community acquired pneumonia scale, COPD assessment Test scale. The mMRC consists of 5 grades from grade 0 to grade 4, to assess the degree of baseline functional disability due to dyspnea. CAT consists of 8 items with each item comprises of 5 points, and a total score of 40 and it is used in patients diagnosed with COPD to assess the progression of lung disease and decline in functional status. And the CAP consists of 18 items and it is used to assess the severity of symptoms in pneumonia.

4. RESULTS

A total of 200 participants with active COVID-19 virus fulfilling exclusion and inclusion criteria were enrolled in this study. Out of 200 participants, 111(55.5%) were male and 89 (44.5%) were females as shown in figure
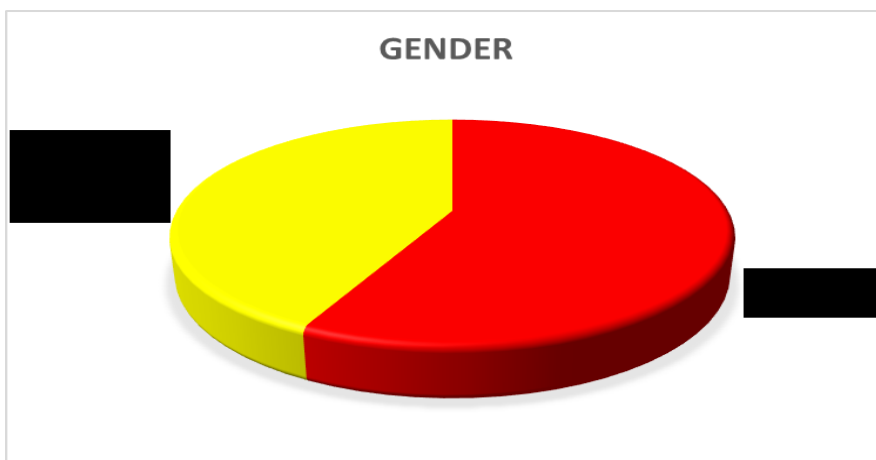
Figure 1: Pie chart showing Gender distribution in N= 200 participants

The 1 standard questionnaire which were used to find out the prevalence of respiratory complications in COVID-19 patients were CAP (community acquired pneumonia scale), MMRC (modified medical research council for dyspnea scale) and CAT (COPD assessment test scale) which represents Pneumonia, Dyspnea and COPD. Their mean, median, standard deviation and prevalence are mentioned in table 4.1.

Table 2: Descriptive Statistics of Pneumonia, Dyspnea & COPD

	Mean	Median	Std. Deviation	Percentages
Pneumonia	48.3	48	7.679	68%
Dyspnea	3.02	3	0.859	77.5%
COPD	26.09	26	6.075	56%

To compare categorical outcomes; Chi square test was applied at 5% level (P value less than 0.05 significant). So, three variables were compared which were CAP, CAT and MMRC. The P values are mentioned in the description of the charts

Table 3: Chi Square interpretation showing *P* value of CAP, MMRC & CAT

CROSSTABULATION	*P* VALUE
CAP & MMRC	0.011
CAP & CAT	0.001
CAT & MMRC	0.003

The figure represents the correlation between the 3 scales including Community Acquired Pneumonia (CAP) scale, Modified Medical Research Council (MMRC) scale for dyspnea and COPD assessment test (CAT) scale. The *P* values of these 3 scales are 0.011, 0.001 & 0.003 which shows positive association between these scales. As *P* < 0.05 this represents that the results are statistically significant.

Table 4: Descriptive Statistics of associated symptoms which comes as a manifestation of COVID-19

Variables	Mean	Median	Std. Deviation
Cough	3.47	3	0.934
Dyspnea	3.31	3	1.009
Muscle Pain	3.64	4	1.018
Fatigue	3.72	4	0.984
Headache	3.23	3	1.114
Diarrhoea	2.01	2	1.197
Vomiting	1.88	2	1.254
Nausea	2.41	2	1.112

Mean, Median and St. Deviation of associated symptoms are mentioned above in the table 4.3
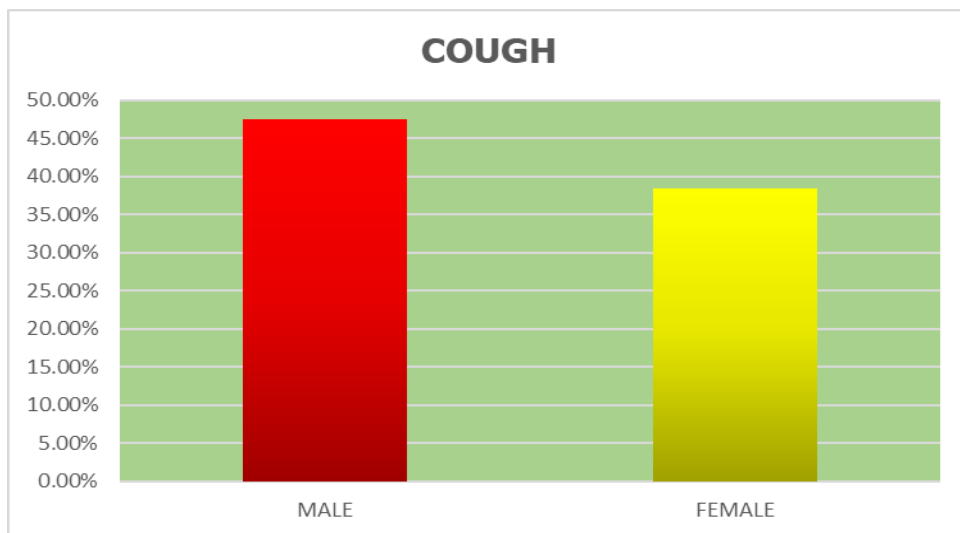

Figure 2: Showing Gender distribution of participants presented with cough.

Cough is the major symptom which comes as a manifestation of COVID-19. Among total number of participants, 85% are presented with cough out of which 46.5% are males and 38.5% are females.
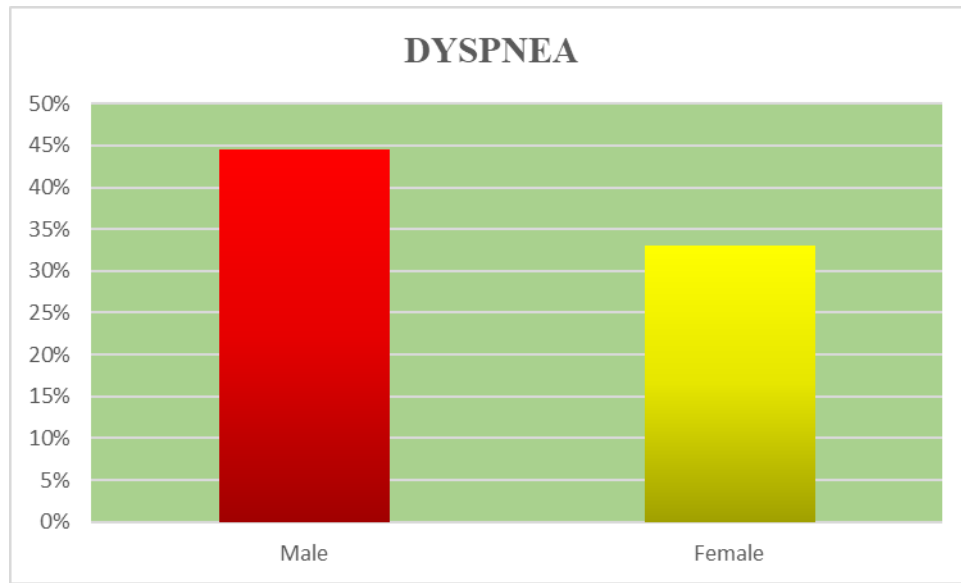

Figure 2: Showing Gender distribution of participants presented with dyspnea

Dyspnea is the one of the major symptoms which comes as a manifestation of COVID-19. Among 200 participants 77.5% presented with dyspnea out of which 44.5% are male and 33% are females.
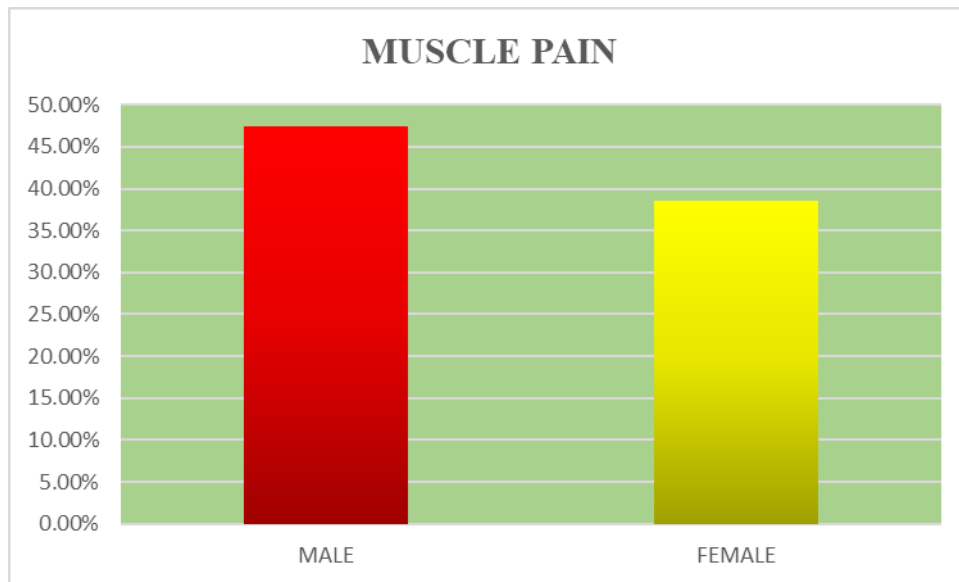

Figure 5: Showing Gender Distribution of participants presented with muscle pain

Muscle pain is another major symptom associated with COVID-19. Among 200 participants 86% were presented with muscle pain out of which 47.5% are males and 38.5% are females.
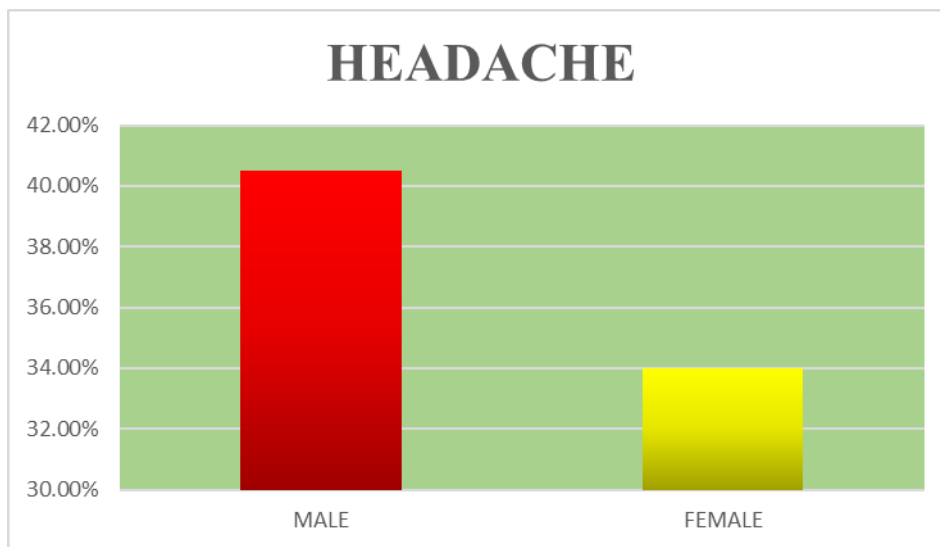
Figure 3: Showing Gender Distribution of participants presented with muscle pain

Headache is an associated symptom which comes as a manifestation of COVID-19. Among 200 participants 74.5% out of which 40.50% are males and 34% are females.
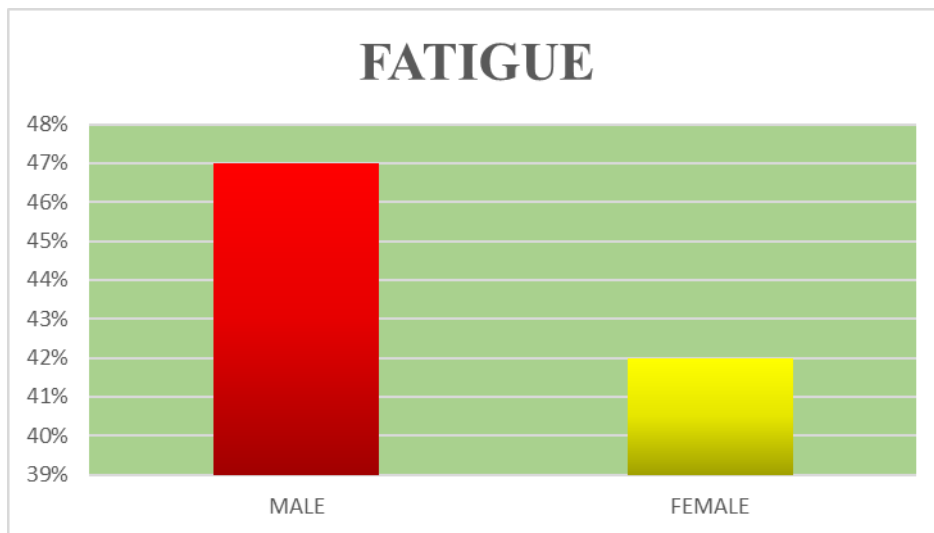

Figure 4: Showing Gender distribution of participants presented with fatigue

This figure (6) indicates the presence of fatigue in COVID-19 patients. Among 200 participants 89% of people were presented with fatigue out of which 47% are males and 42% are females.

Figure (7, 8, 9) shows the involvement of GIT system in patients with COVID-19.
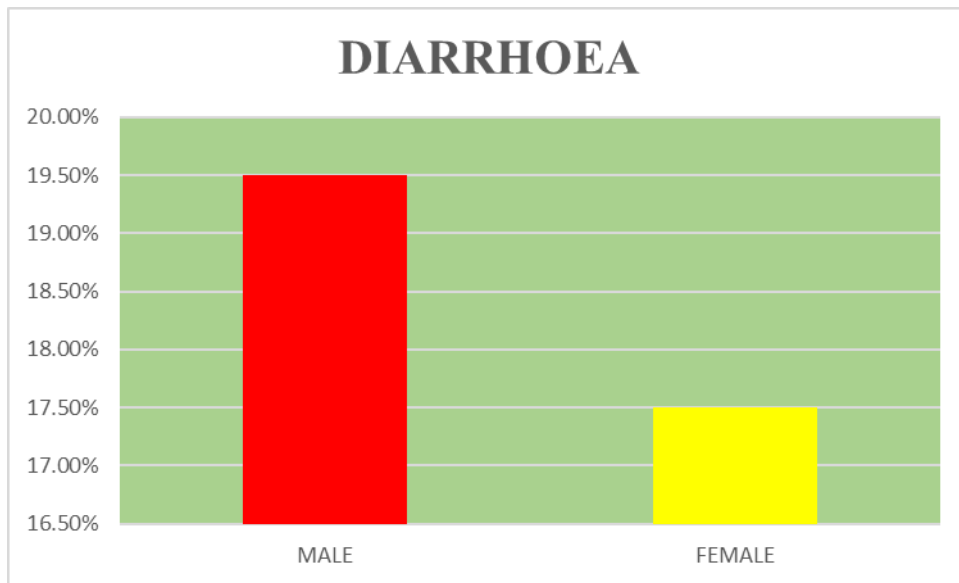
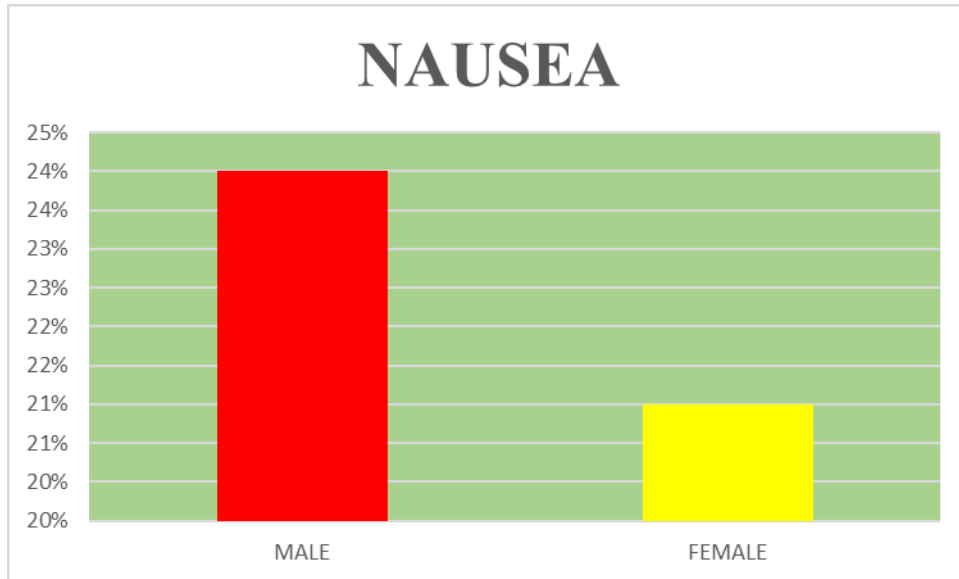**Figure 5:** Showing Gender distribution of participants presented with diarrhoea

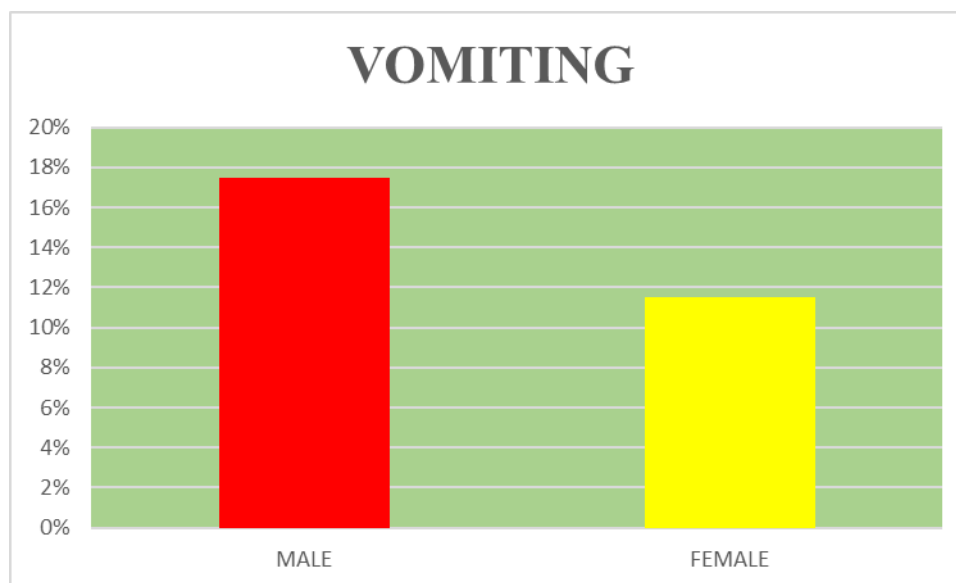**Figure 6:** Showing Gender distribution of participants presented with nausea

Figure 7: Showing Gender distribution of participants presented with vomiting

Among 200 participants 37% are presented with diarrhoea, 45% are presented with nausea and 29% are presented with vomiting as a manifestation of COVID-19.

5. DISCUSSION

The current study was conducted to evaluate rhe prevalence of respiratory complications in COVID-19 patients. According to this study different respiratory complications including pneumonia, dyspnea & COPD with some associated complications occur as a manifestation of COVID-19.

According to research by Jian-Min et al which studied the Gender differences in patients with COVID-19, men with COVID-19 are more prone to complications as compared to women independent of age. The main purpose of this study was to compare the severity and complications between males & females. For their study they have extracted data from 1- case series of 43 hospitalized patients. In their results male cases were more severe than females (P= 0.035).[23] Our study states the similar outcomes by showing dominancy of males over females. Out of 200 participants 55.5% are male and 44.5% are females.

A study was conducted by Virend k. somer et al in which they concluded that COVID-19 causes pneumonia. This study was conducted on 140 patients that were admitted due to COVID-19 in Wuhan, China. Their results showed that hallmark of COVID-19 morbidity is pneumonia.[5] Our study concluded similar results by declaring that COVID-19 can cause pneumonia.

A systematic review and meta-analysis was conducted by Li Shi and Ying Wang et al to investigate the risk factors of critical and mortal COVID-19 cases. Statistical analysis indicated that there was a positive association between dyspnea or shortness of breath with progression of COVID-19 (P<0.00001).[14] Similar to that, this study concluded that dyspnea is one of the major symptoms that arises in patients with COVID-19. As per statistical results out of 200 patients 77.5% were reported with dyspnea.

Another study was carried out on march 2020 by Shao Chung Chung et al. in which they investigated/ reported the very first novel COVID-19 pneumonia (NCP) case which concluded the major symptoms of the ongoing disease. In accordance to reports COUGH, FEVER & DYSPNEA were the main symptoms. Hence this study is positively associated to current study, as it concludes that dyspnea and cough are the major symptoms seen in COVID-19.[24] As per statistical results of this study out of 200 patients 85% were reported with cough and 77.5% were reported with shortness of breath.

Another research was carried out by Bertran Recasens et al on "the lack of dyspnea in COVID-19 patients: another neurological conundrum?" This research suggested that absence of dyspnea is one of the relevant features of COVID-19. In Wuhan a cohort study was conducted which showed that 62.4% of severe cases and 46.3% of other cases (ventilated, intubated or dead) even didn't present dyspnea.[25] But our study shows contrary results as it concludes that dyspnea is associated with COVID-19.

A systematic review by Eduardo et al. was conducted on the title of "asthma and COPD in hospitalized COVID-19 patients. This systematic review was conducted to analyze the presence of comorbidities and risk factors in patients with COVID-19. They concluded that only 1.5% of patients had respiratory diseases. In critical care units only 4% had COPD but asthma figure was so low.[26] Similarly, by the help of CAT scale this research concluded that COPD occurs as a comorbidity with COVID-19.

Louis Poncet-megemont et, al highlighted the major prevalence of headache in post COVID-19 patients. Out of 139 patients 59% patients reported headaches.[27] Another research was conducted by Hayrunnisa Bolay on COVID-19 is a real Headache! And concluded that along other major COVID-19 manifestations headache is also rapidly increasing symptom, about 6-10% patients report headache as symptom of COVID-19. [28] Our study concludes that headache is common in COVID-19 patients out of 200 people 74.5% people reported headache as a symptom.

A systematic review and Meta-analysis were carried out on January 06th, 2021 by the SUBASH GHIMIRE et al. in their study they reported that the diarrhoea is linked with increased severity of disease in COVID-19. Initially, the COVID-19 disease was defined only by the presence of respiratory complications and respiratory symptoms but now it is well studied and after the number of evidences it is cleared that there is involvement of multiple systems. Gastrointestinal system involvement has been identified by this study and also this study reported that the gastrointestinal systems can also be the lone presenting symptoms in the COVID-19 patients. Out of 38 studies with 8407 number of participants, 15.47 % patients were presented with at least one Gastro Intestinal symptom. The prevalence of diarrhoea was 11.52% and prevalence of nausea/vomiting is 7.53%..[29] Similarly, the current study states that there is involvement of gastrointestinal system in COVID-19 and as per statistical results out of 200 patients 37% are presented with diarrhoea, 45 % are presented with nausea and 29% of patients are presented with vomiting.

A meta-analysis conducted by Yang j. et al assessed the prevalence of comorbidities in COVID-19 patients which concluded that the most was fever, followed by cough, fatigue and dyspnea[7]. Similarly, this research also concluded that the major symptoms of COVID-19include cough (85%), dyspnea (77.5%) and fatigue (89%).

6. LIMITATIONS OF STUDY

There were various limitations in this study. The sample size was small and hence cannot be generalized throughout the country. The data was collected from Rawalpindi and Islamabad only but Pakistan is a diverse country and each region has its own statistics. The study was quantitative and gave us a quantitative analysis, if it was combined with qualitative analysis, it would have given more valuable findings.

CONCLUSION & RECOMMENDATIONS

Conclusion

This study concluded that there is prevalence of respiratory complications in patients with COVID-19. According to the results the major conditions which occurs as a consequence of COVID-19 are Dyspnea, Pneumonia and COPD. Out of 200 participants Dyspnea was prevalent in 77.5% of people, Pneumonia was prevalent in 68% of people and COPD was prevalent in 56% of people. The major symptoms which comes as a manifestation of COVID-19 are Cough, shortness of breath, fatigue, muscle pain etc. These symptoms occurred more in males as compared to females. The P value was $P < 0.05$ which shows that the results are statistically significant.

Recommendations

- The sample size of this study was only 200. Thus, an increase in sample size will help in generalization of the study.

- This research was conducted only in Rawalpindi and Islamabad but efforts can be made to generalize the findings throughout the world.

- As this study was focused only upon the respiratory complications in COVID-19. So, more researches should be conducted to find the manifestations of COVID-19 in other body systems.

- Both qualitative and quantitative analysis can be used to enhance the findings.

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