Impact of COVID-19 on (Non-COVID) chronic respiratory disease outcome survey in India (CCROS study)

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ABSTRACT

Background: India has high prevalence of chronic respiratory diseases, especially bronchial asthma and chronic obstructive pulmonary disease (COPD). Both of these are also recognized as risk factors for severity and poor outcome of COVID-19 disease. It is assumed that COVID-19 outbreak as well as an effective lockdown might have affected the incidence and outcome of some of these.

Methods: To substantiate above hypothesis, an online survey was mailed to 547 pulmonologists across the country; 314 (54.7%) responses were recorded in the given period. The survey included observations on incidence and outcome of common chronic respiratory diseases such as asthma, COPD and interstitial lung diseases (ILD) in predefined pre-COVID and during COVID period in a total of 24 questions.

Results: It was observed that the reduction in incidence of outpatient department cases, acute exacerbations and hospitalization for asthma, COPD and ILD was statistically significant. The outcome of acute exacerbations of these chronic respiratory diseases was analyzed in terms of discharges from hospitals after satisfactory recovery and/ or mortalities. For COPD and ILD, it was not significantly affected during the COVID period. At the same time, a relatively higher proportion of acute asthma mortality was reported. A wide variation in nebulization practices was reported during this period. The doses of inhaled corticosteroids in asthma management were not affected. A wide variety of factors including effective lockdown, better quality of air and regular use of masks were probably responsible for reduced incidence of exacerbations of these chronic respiratory diseases.

Conclusion: We conclude that while outpatient department visits, acute exacerbations and hospitalizations were significantly reduced during COVID-19 period, outcome of asthmatics was relatively unfavorable as compared to that of COPD and ILDs.

KEY WORDS: Chronic respiratory diseases, during COVID, exacerbations, pre-COVID

INTRODUCTION

It has almost been 1 year since the world is struggling with COVID-19 pandemic. India too has suffered with more than 11,733,369 cases till March 24, 2021. Overall mortality with this outbreak in India is 1.54%. On the other hand, morbidity and mortality because of common chronic respiratory diseases in India vary with the
diagnosis. Chronic obstructive pulmonary disease (COPD) is responsible for 4.55% of total disability-adjusted life years (DALYs) while asthma accounts for 1.25% of it. Interstitial lung diseases (ILDs) and sarcoidosis contribute to 0.28% of total DALYs. At the same time, COPD accounts for 9.57% of total deaths in India. Asthma and ILDs contribute to 2.12% and 0.61% of total deaths, respectively. [11]

Chronic respiratory diseases have been identified as one of the comorbidities in risk stratification for severity of COVID-19 illness and poorer outcome. The prevalence of reported respiratory comorbidities in COVID-19 in various published large series ranges from 1.5% to 17.7% for chronic pulmonary diseases (excluding asthma). [2,3] The prevalence of asthma was 14.5% in one study. [6] The reported lower prevalence of respiratory comorbidities in some of the studies is intriguing. This could be a real phenomenon, or it could be related to under-diagnosis because of lower spirometric testing.

India has observed an effective lockdown across the country from March 24, 2020, when the total number of cases was around 500. The strategy has resulted in complete shutdown of markets, travel (domestic and International) was banned, and only emergency services were continued. The culture of work from home started. All kinds of mass gatherings were strictly prohibited. Schools and colleges were closed. It has, therefore, helped not only in prevention of spread of infection at community level but also has resulted in marked improvement of air quality, limited availability of tobacco products, improvement in sanitization habits, and use of protective masks at large across the country. These have possibly resulted inadvertently in a reduction of acute episodes of common chronic respiratory illnesses such as asthma, COPD, and ILDs. Pulmonology practices have also changed across the country.

To substantiate these observations from local levels to across the country, an online survey was conducted among the pulmonologists; their perceptions and observations were recorded and analyzed.

**METHODOLOGY**

A structured questionnaire was prepared with predefined definitions of “before COVID-19” and “during COVID-19” period. It included 24 questions pertaining to prevalence, control, exacerbations, hospitalization, and outcome of asthma, COPD, and ILD during this predefined time period frame.

“Before COVID-19” period was defined as months of December 2019 and January and February 2020. “During COVID-19” was referred to as March, April, and May 2020.

The survey was mailed to 547 pulmonologists across the country on June 5, 2020. Responses received till June 15, 2020, were recorded. A total of 314 pulmonologists participated in the survey (57.4%).

The term “test for COVID” was used for reverse transcription polymerase chain reaction to detect infection with SARS-CoV-2.

The responses were tabulated and analyzed. All statistical data analyses were performed using SPSS statistical software version 23 (IBM corporation, Armonk, NY, USA).

**Observations**

**Bronchial asthma**

There were 14 questions related to bronchial asthma in this survey. These were related to asthma outpatient epidemiology, level of asthma control, severe asthma admissions, and outcome of severe asthma hospitalizations before and during COVID-19 periods. The impact of COVID-19 on nebulization practices, use of inhaled corticosteroids (ICSs) during COVID-19 period, and perceived role of lockdown on these asthma parameters were also part of the questionnaire. The proportion of the respondents varied for each of these issues. The responses were tabulated and submitted for statistical analysis [Tables 1 and 2].

**Chronic obstructive pulmonary disease**

COPD constitutes major bulk of chronic respiratory disease in India. This survey included two important aspects of COPD exacerbations in predefined before COVID-19 and during COVID-19 period. These were the estimated overall acute exacerbation hospitalizations and their outcome in terms of discharges and mortalities during these periods. The observations are projected in Table 3.

**Interstitial lung diseases**

In the past few years, ILDs are being increasingly recognized and treated among pulmonologists across the country. Although the exact incidence of ILDs cannot be figured out, its role as a risk factor for COVID-19 has not been substantiated so far. It was perceived that the number of new diagnoses and acute exacerbations was relatively low during COVID-19 period. The questionnaire in the present survey highlighted on hospitalizations because of non-COVID acute exacerbations of ILDs (AE-ILDs) and their outcome before and during COVID-19 period [Table 4].

**Respiratory comorbidities in COVID-19 patients**

The questionnaire also asked the participants on which respiratory comorbidities they came across among those tested positive for COVID-19. More than one-third responded that they came across COPD as comorbidity, and a significant number of responses also came across other respiratory comorbidities such as bronchial asthma, ILD, and tuberculosis. However, we acknowledge the bias that we only had pulmonologists as a part of this survey, and hence, this is not representative of the whole community of physicians who have managed
COVID-19 patients. The results cannot be generalized, and this gives a false sense of a high burden of respiratory comorbidities among COVID-19 patients. Since this was a part of the questionnaire, the received responses are tabulated in Table 5. It would be interesting to see how the numbers projected here compare with a nationwide data of COVID-19 as a whole.

**DISCUSSION**

COVID era, bronchial asthma, and chronic obstructive pulmonary disease

The severity of SARS-CoV-2 infection in the background of chronic respiratory disease may be greater. Effects of altered immune responses elicited in chronic respiratory diseases, especially asthma, and a protective effect of ICSs may be responsible for lower infection rates as observed in various published data till now. The American Association of Asthma, Allergy, and Immunology and several other lung diseases organizations including GOLD have reiterated that these patients should continue with their current treatment, because any exacerbations in the present scenario may lead to hospital visits and hospitalization, thus exposing them to possible SARS-CoV-2 infections. Keeping these facts in mind, we followed the practices of pulmonologists across the country, their perceived impact on common chronic respiratory diseases, and the consequent changes in treatment practices.

Our survey revealed that 50% of the participating pulmonologists (159/314; 50.6%) used to see more than six patients of bronchial asthma per day in their daily practices before COVID-19, and the numbers declined dramatically during the pandemic (10.36%). Fifty-two (17%) of the pulmonologists reported that they did not see a single patient of bronchial asthma during COVID-19 outbreak, while 213 (71.23%) reported that they attended between 1–5 patients per day. This decline in numbers was statistically significant (Chi-square = 242.51; $P < 0.0001$). Similarly, acute severe asthma admissions were also significantly less during COVID-19 period, and this was also statistically significant. At the same time, we could interpret that there were relatively more number of asthmatics who were either poorly controlled or had adverse outcome in terms of mortality during the COVID period, these differences were statistically significant [Table 1].

**Table 1: Asthma epidemiology, level of control, and acute severe asthma incidence in predefined before and during COVID-19 period**

| Average number of bronchial asthma seen in OPD per day | Before COVID-19 (314; 100%) | During COVID-19 (299; 95.22%) | $\chi^2$ | $P$ |
|-------------------------------------------------------|-----------------------------|-------------------------------|---------|-----|
| 0                                                     | 0                           | 52 (17.39)                    | 242.51  | <0.0001 |
| 1-5                                                   | 91 (28.98)                  | 213 (71.23)                   |         | Significant |
| 6-10                                                  | 114 (36.3)                  | 22 (7.35)                     |         | Significant |
| 11-15                                                 | 45 (14.33)                  | 9 (3.01)                      |         | Significant |
| >15                                                   | 64 (20.38)                  | 3 (1)                         |         | Significant |

**Level of asthma control (non-COVID)**

| Before COVID-19 (287; 91.4%) | During COVID-19 (257; 81.84%) | $\chi^2$ | $P$ |
|-------------------------------|-------------------------------|---------|-----|
| >75% well-controlled          | 150 (52.26)                   | 108 (42.02) | 16.072 | 0.0003 |
| 50%-75% well-controlled       | 116 (42.02)                  | 102 (39.08) |         | Significant |
| <50% well-controlled          | 21 (7.31)                    | 47 (18.28) |         | Significant |

**Estimated acute severe asthma admissions, non-COVID**

| Estimated acute severe asthma admissions, non-COVID (per week) | Before COVID-19 (263; 83.75%) | During COVID-19 (242; 77.07%) | $\chi^2$ | $P$ |
|---------------------------------------------------------------|-------------------------------|-------------------------------|---------|-----|
| 0                                                             | 31 (11.78)                    | 120 (49.58)                   | 88.6    | <0.0001 |
| 1-5                                                           | 186 (70.72)                  | 106 (43.80)                   |         | Significant |
| 6-10                                                          | 33 (12.54)                   | 13 (5.37)                     |         | Significant |
| >10                                                           | 13 (4.94)                    | 3 (1.24)                      |         | Significant |

**Estimated outcome of acute severe asthma (non-COVID)**

| Estimated outcome of acute severe asthma (non-COVID) | Before COVID-19 (220; 70.06%) | During COVID-19 (215; 68.24%) | $\chi^2$ | $P$ |
|-------------------------------------------------------|-------------------------------|-------------------------------|---------|-----|
| 100% discharged with good control                     | 148 (67.27)                   | 66/102* (64.70)              | 12.001  | <0.0007 |
| Mortality 1%-5%                                        | 71 (32.27)                    | 29/102* (28.43)              |         | Significant |
| Mortality 5%-10%                                       | 1 (0.45)                     | 6/102* (5.88)                |         | Significant |
| Mortality >10%                                         | 0                             | 1/102* (0.98)                |         | Significant |
| Did not have these patients                            | 0                             | 113 (52.55)                 |         | Significant |

*As 113 out of 215 pulmonologists did not have acute severe asthma admissions, the outcome analysis was done out of rest of the 102 respondents.

OPD: Outpatient department

**Table 2: Impact of corona outbreak on treatment practices in bronchial asthma during COVID-19 period**

| Parameters in question | Impact observed | n (%) |
|------------------------|-----------------|-------|
| Nebulization practices (267; 85.03%) | Not prescribed at all | 90 (33.7) |
|                        | Prescribed with individual nebulizer | 37 (13.85) |
|                        | Prescribed with individual masks | 66 (24.91) |
|                        | Used only in private/isolated rooms | 74 (27.7) |
| Use of ICS (208; 66.24%) | ICS totally withdrawn | 2 (0.96) |
|                        | Doses of ICS tapered down | 33 (15.86) |
|                        | Same doses of ICS continued | 173 (83.17) |
| Possible causes for better asthma control | Home isolation (effective lockdown) | 57 (18.15) |
|                        | Lesser air pollution | 63 (20.6) |
|                        | Away from work place | 45 (14.33) |
|                        | More compliant to treatment | 39 (12.42) |
|                        | Regular use of masks | 31 (9.87) |
|                        | All of the above | 156 (49.68) |

ICS: Inhaled corticosteroids

COVID-19 patients. The results cannot be generalized, and this gives a false sense of a high burden of respiratory comorbidities among COVID-19 patients. Since this was a part of the questionnaire, the received responses are tabulated in Table 5. It would be interesting to see how the numbers projected here compare with a nationwide data of COVID-19 as a whole.

**DISCUSSION**

COVID era, bronchial asthma, and chronic obstructive pulmonary disease

The severity of SARS-CoV-2 infection in the background of chronic respiratory disease may be greater. Effects of altered immune responses elicited in chronic respiratory
might interpret that these patients probably presented late to the specialists and therefore had a relatively poor outcome.

Nebulization practices were also observed to be changed due to the pandemic. Almost 34% of the respondents reported that they did not use nebulization during corona period, while 37 (13.85%) restricted use of a nebulizer machine to an individual patient only. A significant number of the respondents (74; 27.7%) reported that they used nebulizers only in private rooms in solitude. Almost one-fourth reported that they followed the practice of prescribing nebulizers with individual masks (66; 24.91%). According to the BTS and NICE rapid guidance, patients can continue to use their nebulizers based on the fact that aerosols come from fluid of the nebulizer and will not carry virus particles from the patients. However, personal nebulizers should be used, preferably in an open space.[6] Australian asthma manual and many others advocate against the use of nebulizers for inhaled medicines, unless unavoidable. A pressurized metered dose inhaler and spacer with or without a tightly fit face mask should be preferred instead. Under unavoidable circumstances, nebulizers should be used in isolated chambers with complete protection for staff and caregivers with personal protective equipment kits, preferably in a negative pressure chamber, if available. The nebulizers can generate aerosol droplets that can spread to several meters and remain airborne for more than 30 min.[7] Although the present survey was strictly for those who did not have COVID-related asthmatic exacerbations, still a wide variation in nebulization practices was observed. ICSs are mainstay of the treatment for bronchial asthma. A systematic review by Halpin et al.[8] clearly warns against the withdrawal of ICS during these times. At the same time, there is no clear evidence to increase the dose of ICSs at the onset of exacerbations. Following the guidelines of international societies, most of the respondents (173; 83.17%) in the present survey followed the same consensus and reported that they did not advice any change in doses of ICSs [Table 2].

Table 3: Impact of COVID-19 outbreak on chronic obstructive pulmonary disease exacerbations and outcome

| Disease entity | None | 1-5 | 6-10 | >10 |
|----------------|------|-----|------|-----|
| Before COVID-19 (195; 62.1%) | 20 (10.25) | 86 (44.1) | 39 (20) | 50 (26.6) |
| During COVID-19 (183; 58.28%) | 56 (30.60) | 100 (54.64) | 19 (10.38) | 8 (4.37) |
| \(\chi^2\) | 55.091 | Significant |

Table 4: Impact of COVID-19 outbreak on non-COVID acute exacerbations of interstitial lung disease and their outcome

| Disease entity | None | 1-5 | 6-10 | >10 |
|----------------|------|-----|------|-----|
| Before COVID-19 (194; 61.78%) | 34 (17.52) | 123 (63.40) | 26 (13.40) | 11 (5.67) |
| During COVID-19 (190; 60.50%) | 114 (60) | 70 (36.84) | 4 (2.10) | 2 (1.05) |
| \(\chi^2\) | 80.129 | Significant |

Table 5: Number of pulmonologists treated respiratory comorbidities in COVID-19 patients

| Disease entity | Number of pulmonologists reported respiratory comorbidities (%) |
|----------------|---------------------------------------------------------------|
| Bronchial asthma | 45/249 (18.07) |
| COPD | 76/204 (37.2) |
| ILD | 22/190 (11.57) |
| Tuberculosis | 31/189 (16.4) |

ILD: Interstitial lung disease, COPD: Chronic obstructive pulmonary disease
the respondents (49.68%) in this survey agreed that an effective lockdown resulting in home isolation, better air quality, away from workplace, more compliance to treatment, and regular use of masks were all responsible for better control of asthma in their patients [Table 2].

COPD is another chronic respiratory disease that has been listed as one of the comorbidities for severity of COVID-19 disease (risk of severity 63%) and poor outcome (mortality 60%). It however comes lower in the list much behind cardiovascular and endocrine comorbidities.

Respiratory viruses, though, reported as the most common cause of infectious exacerbation of asthma, about 47%–56% of COPD exacerbations are also known to occur as a result of viral infections. Given the travel restrictions and thereby limited access to specialty clinics during the pandemic, these patients were still needed to be followed closely, maybe virtually.

Our survey suggested that while 89/195 (45.6%) of the respondents reported overall six or more admissions because of acute exacerbations of COPD (AECOPD) before COVID-19 period in the emergency department, the figure fell down dramatically to 27/183 (14.75%) during COVID-19 period. 56/183 (30.60%) reported that they did not come across cases of AECOPD during COVID-19 period, while this number was 20/195 (10.25%) for before COVID-19 period. Overall difference in observations was statistically significant (Chi-square = 55.091; \( P < 0.0001 \)).

Outcome of such acute exacerbations in terms of discharges with satisfactory recovery and percentage of deaths among overall admissions of AECOPD was not statistically significant for both the periods [Table 3].

Interstitial lung disease and COVID-19
COVID-19 has also impacted key components of diagnosis and management of ILDs. Basic diagnostic workup by spirometry, imaging techniques, bronchoscopy, as well as Multidisciplinary team discussion (MDD) have all suffered during the pandemic. At the same time, limited access to medications, managing adverse drug reactions, as well as access to hospitals during acute exacerbations in this pandemic era have been the other areas of concern. There was a huge difference reported in this survey among pulmonologists in their ILD practices. While 123/194 (63.4%) respondents reported that they had come across at least 1–5 exacerbations of ILD before COVID-19 period, this figure fell down dramatically to 70/190 (36.84%) during COVID-19 period. At the same time, 37/194 (19%) reported their AE-ILD admissions 6 or more before COVID-19 period while it was only 6/190 (3.15%) during COVID-19 period. The differences were statistically significant (Chi-square value 80.129; \( P < 0.0001 \)). Outcome differences in terms of discharges with satisfactory recovery or mortalities among hospitalized patients were not statistically significant in the two periods.

Overall, we could interpret that while number of outpatient department visits, acute exacerbations, and hospitalizations because of these were significantly reduced during COVID-19 period, outcome of asthmatics was relatively unfavorable as compared to COPD and ILDs.

Limitations
1. Since the outbreak is still going on, reaching its peak, with the process of unlock under way, the figures and ratio may change. The observations must strictly be read in context with the defined period of this survey
2. The figures pointed out are those perceived by the pulmonologists and are not the exact figures. However, these figures definitely outline the prevailing trends across the country
3. The projected figures are the perception of pulmonologists and do not include internists who also treat a lot of chronic respiratory diseases.

CONCLUSION
This survey has resulted in few important conclusions for non-COVID chronic respiratory diseases in India. It was probably an effective lockdown resulting in a relatively clean environment along with regular use of masks outdoors. The result was a reduced asthma outpatient visits as well as reduced hospitalizations because of acute severe asthma. Same pattern was also observed for COPD and ILDs. While COVID-19 period did not significantly affect the outcome of COPD and ILD exacerbations, the outcome of asthmatics was adversely affected. Interestingly, consistent with global opinion, the pulmonologists in India also continued with the same dose of inhaled steroids in asthma during the pandemic.

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Conflicts of interest
There are no conflicts of interest.

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