



## A STUDY ON RESPIRATORY PROBLEMS AND PULMONARY FUNCTION TEST ABNORMALITIES IN CHILDREN AFTER COVID-19 ILLNESS

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**ABSTRACT** **Context:** Children account for 1-5% of diagnosed COVID-19 cases however, many infected asymptomatic children may go undiagnosed without population screening. Even though the severity of disease in children is mild to moderate, the risk of long-term effects on respiratory health especially in children with comorbidities cannot be ruled out. **Aims:** To evaluate respiratory problems and pulmonary function test abnormalities in children after COVID-19 infection. **Methods And Material:** The study had 86 individuals, 52 of whom were male and 34 of whom were female, with ages ranging from 6 to 18 years. The respiratory issues that each child's parents experienced both during and at least six month after their COVID-19 illness and recovery were enquired about. The American Thoracic Society (ATS) spirometry guidelines were adhered to, and computerized spirometry devices (RMS Helios 702 spirometer) were utilized for the investigation. Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), FEV1/FVC, Peak expiratory flow rate (PEF), and forced expiratory flow between 25% and 75% expired volume (FEF25-75) were the spirometry variables that were measured. The 6-MWT was carried out in compliance with ATS recommendations, and the outcomes were documented and compared to expected normal values. **Results:** Post covid respiratory problems were present in up to 67.3% of symptomatic and 25.8% of asymptomatic children which includes respiratory symptoms in 52.3%, abnormal chest x-ray findings in 16.3%, abnormalities in 6-MWT results in 29.1% cases. **Conclusions:** To conclude that covid-19 illness is generally less severe in majority of children still it was associated with significant post covid respiratory problems and pulmonary function abnormalities in our study. Therefore, all cases of covid-19 illness should undergo long term follow up by regular clinical examination, 6-MWT and pulmonary function test for early detection of post covid respiratory morbidities.

**KEYWORDS :** SARS COV-2-Severe Acute Respiratory Syndrome Corona Virus-2 infection, 6-MWT(SIX MINUTE WALK TEST), Pulmonary function test

### INTRODUCTION:

Corona virus disease-19 (COVID-19) is a viral pandemic that was started in China and spread throughout the world. It is caused by Ribonucleic Acid (RNA) virus, Severe Acute Respiratory Syndrome Corona Virus-2 (SARS COV-2). The virus affects the upper respiratory tract, causes pneumonia and transmits easily from human to human. After outbreak of COVID-19 in China and its potential of rapid spread throughout the country and subsequently to other countries World Health Organization (WHO) declared it as a global health emergency on 31 January 2020; subsequently, on 11 March 2020, they declared it a pandemic situation.<sup>[1]</sup> Children account for 1-5% of diagnosed COVID-19 cases however, many infected asymptomatic children may go undiagnosed without population screening.<sup>[2]</sup> Paediatric COVID-19 infection is comparatively mild and children are reported to have a better prognosis. Mortality in children is quite rare.<sup>[3]</sup> The clinical features, disease course and outcome in children appear significantly milder compared to older people. The clinical characteristics of COVID-19 infection in children is highly wavering, and still there is dearth of information from developing countries, except for China. Associated comorbidities in children with COVID-19 were reported in 100% patients from China but in 83% of those in United States (US) and Canadian intensive care units. Despite scarce evidence in children, increasing reports have emerged that long-term adverse outcomes are frequently encountered in adults related to COVID 19 following resolution of acute illness. A noteworthy facet of the SARS-CoV-2 pandemic is that children are found to be less affected, thus, less studied aspect of COVID-19 pandemic. However, children as a vulnerable group pose unique challenges, both diagnostically and therapeutically, during the unprecedented pandemic.<sup>[4]</sup> Even though the severity of disease in children is mild to moderate, the risk of long-term effects on respiratory health especially in children with comorbidities cannot be ruled out. Thus, it is important to study the long-term effects of SARS-CoV-2 infection on the Pulmonary Function Test (PFT) in children because even minimally symptomatic children may have objective abnormalities post recovery from acute COVID-19. Previous studies have reported that even among young adults aged 18–34 years with no chronic comorbidities, approximately

one in five had not achieved their usual state of health 14–21 days after acute stage of infection. “Long COVID” is defined by the National Institute of Health and Care Excellence as symptoms that persistent beyond four weeks, and distinguishes between ongoing symptomatic COVID-19 as signs and symptoms of COVID-19 from four to twelve weeks and post-COVID-19 syndrome as signs and symptoms that continue for more than twelve weeks.<sup>[5]</sup> There is currently a paucity of literature describing such post-acute symptoms in paediatric patients with COVID-19 and its long-term sequelae on pulmonary health. In this review, the present study was done with the purpose to evaluate respiratory problems and pulmonary function test abnormalities in children after COVID-19 infection.

### Subjects And Methods:

An institutional Ethics committee approval was obtained for this study. It's a prospective cross-sectional study. Children with COVID-19-related illnesses between the ages of 6 and 18 who were either RT-PCR positive or SARS CoV-2 antibody positive were included at least six month after recovery as the study population. Individuals needing mechanical ventilation, Patients with a past medical history of respiratory system trauma, chronic respiratory illness, cardiovascular disease cases that have been diagnosed, such as congenital heart disorders, cases of neurological illnesses or muscle abnormalities, such as Duchene muscular dystrophy, as well as patients with any kind of chest wall deformity were excluded from the study.

The study had 86 individuals, 52 of whom were male and 34 of whom were female, with ages ranging from 6 to 18 years. All patients had detailed clinical history, examination and treatment received. A survey was conducted to gather data on the age and gender of the participants as well as their anthropometric, imaging (chest x-ray) and spirometric parameters. The respiratory issues that each child's parents experienced both during and after their COVID-19 illness and recovery were enquired about. The American Thoracic Society (ATS) spirometry guidelines were adhered to, and computerized spirometry devices (RMS Helios 702 spirometer) were utilized for the investigation.<sup>[6]</sup> An experienced physician oversaw the process. The

nose clip was used to compress the nose during the procedure, which was done while the patient was seated. Three maneuvers at the very least and eight at the very most were carried out. Graphs of spirometry were examined and Evaluations were conducted on the ATS/ERS task force 2005 standardization guidelines' acceptability, repeatability, and reproducibility criteria. Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), FEV1/FVC, Peak expiratory flow rate (PEF), and forced expiratory flow between 25% and 75% expired volume (FEF25-75) were the spirometry variables that were measured. The 6-MWT was carried out in compliance with ATS recommendations, and the outcomes were documented and compared to expected normal values.

#### Statistical Methods:

The Qualitative data was analysed using Chi-square test/ Mann Whitney U test. Quantitative data was expressed as mean  $\pm$  standard deviation and analyzed using Student's t test/ Mann Whitney U test. A p value of  $<0.05$  was considered significant. The data analysis was done using SPSS20 software.

#### RESULTS:

Of the 86 children, 34 (39.5%) each belonged to the 6–10 and 11–15-year age groups, respectively, and the remaining 18 (20.9%) to the 16–18-year age group. The children had a mean age of  $11.86 \pm 3.68$  years. The mean height of the children in our study was  $133.66 \pm 15.42$  cm, and their mean weight was  $34.05 \pm 12.87$  kg. Of the 86 patients in our study, the majority (54.7%;  $n=47$ ) presented with history of fever. Other complaints included respiratory symptoms (34.9%), gastrointestinal symptoms (14%;  $n=12$ ); and other symptoms (11.6%;  $n=10$ ) such as body aches and rashes in 34.9% of the children.

As per severity of covid-19 illness in children, nearly half of the children in the current study (54.7%, 47/86) had mild sickness. One child (1.2%) had severe COVID-19 disease, seven (8.1%) had moderate illness, and around one-third (36%, 31/86) of the children were asymptomatic. In our study, the most common post-covid respiratory problems were cough and difficulty breathing during exertion, affecting 23 (26.7%) of the children, followed by chest pain in 11 (12.8%) and breathing difficulty during rest in 6 (7%) of the children. Nearly half of the children (47.7%, 41/86) had no post-covid respiratory problems. 76 children (88.4%) in the current study experienced less than three episodes of post-COVID respiratory infections and rest 10 children (11.6%) experienced three or more episodes of post-COVID respiratory infections. On evaluation of requirement of post-COVID hospitalizations, 60.5% of the children in our study did not require hospitalization, 33.7% of the children required hospitalization once, 3.5% required hospitalization twice, and 2.3% required hospitalization three times. Nine children (10.5%) had restricted air entry and bilateral wheeze, four children (4.7%) exhibited basal crepitations, and the majority of the 73 (84.9%) children in our research who received a respiratory examination at the time of enrolment had no notable findings.

In our study, the majority of the 72 children (83.7%) who had a post-covid chest x-ray showed no abnormalities. Six children (7%), had bilateral haziness over lower lobes, 5 (5.8%) children had bilateral patchy infiltration, 1 (1.2%) child had bilateral lower lobe consolidation, bilateral lower lobe consolidation with pleural effusion and bilateral middle lobe consolidation each.

The majority of the children (60.5%) in our study had normal post-covid PFT, 17 (19.8%) had mild restriction, 12 (14%) had moderate restriction, 2 (2.3%) had mild restriction with an obstructive pattern, 2 (2.3%) had moderate obstruction, and 1 (1.2%) had moderate restriction with an obstructive pattern.

In our research, the most frequent finding of post-covid 6-MWT in 13 (15.1%) children was chest discomfort, which was followed by fatigue in 11 (12.8%), dyspnea in 8 (9.3%), and myalgia in 7 (8.1%) children. The remaining had normal post-covid 6-MWT.

In our study, the Mean value of FVC was  $83.59 \pm 18.72$  (50-151), FEV1 was  $95.51 \pm 27.88$  (55-277), FEV1/FVC was  $114.63 \pm 17.96$  (79-231), PEFR was  $100.41 \pm 23.91$  (49-203), and FEF25-75 was  $78.43 \pm 14.75$  (67-112). In our study, 67.3% ( $n=37$ ) symptomatic and 8 (25.8%) asymptomatic children during covid-19 illness presented with post covid respiratory problems while 18 (32.7%) symptomatic and 23 (74.2%) asymptomatic children during covid-19 illness did not

have any post covid respiratory problems. Association of presenting symptoms during covid-19 illness with post covid respiratory problems was found to be statistically significant ( $p$  value  $< 0.001$ ).

Two thirds (65.5%) of the children in our study who were symptomatic during the COVID-19 illness had normal post-illness PFT readings, while nearly one third (34.5%) had abnormal results. Throughout the post-COVID-19 period, nearly half (48.4%) of the children who were asymptomatic throughout the illness had abnormal PFT readings, whereas the other half (51.6%) had normal results. The correlation between presenting symptoms during the COVID-19 pandemic and post-pandemic PFT readings was determined to be statistically non-significant ( $p$  value  $> 0.05$ ). (Table-1)

**Table1- Relation Of Post Covid PFT Indices With Presenting Symptoms During Covid-19 Illness-**

| Post covid<br>PFT indices | Covid-19 symptoms during<br>illness |       |                       |       | Test of significance             |
|---------------------------|-------------------------------------|-------|-----------------------|-------|----------------------------------|
|                           | Asymptomatic<br>(n=31)              |       | Symptomatic<br>(n=55) |       |                                  |
|                           | Mean                                | SD    | Mean                  | SD    |                                  |
| FVC                       | 89.68                               | 13.86 | 80.16                 | 20.29 | t=2.328,Df=84,p<br>value= 0.022  |
| FEV1                      | 101.03                              | 34.4  | 92.4                  | 23.22 | t=1.385,Df=84,<br>p value=0.170  |
| FEV1/FVC                  | 112.29                              | 24.54 | 115.95                | 12.97 | t=0.906,Df=84,<br>p value=0.367  |
| PEFR                      | 101.06                              | 23.74 | 100.04                | 24.21 | t=0.189,Df=84,<br>p value =0.851 |
| FEF25-75                  | 84.19                               | 10.74 | 75.18                 | 15.76 | t=2.831,Df=84,<br>p value=0.006  |

FVC=Forced Vital Capacity FEV1=Forced Expiratory Volume In 1 Second PEFR=Peak Expiratory Flow Rate FEF= Forced Expiratory Flow

In our study, among the symptomatic children during covid-19 illness, 8 (14.5%) children had abnormal and 47 (85.5%) had normal chest x-ray findings during post covid period. Among asymptomatic children during covid-19 illness, 6 (19.4%) had abnormal and 25 (80.6%) had normal post covid chest x-ray findings. Association of presenting symptoms during covid-19 illness with post covid chest x-ray findings was found to be statistically insignificant ( $p$  value  $> 0.05$ )

In our study, among children with post covid respiratory problems, almost three fourth (73.3%) had abnormal and about one fourth (26.7%) had normal post covid PFT findings while among children with no post covid respiratory problems, only one (2.4%) had abnormal and rest (97.6%) had normal post covid PFT findings. Association of post covid PFT finding abnormalities with post covid respiratory problems was found to be statistically significant ( $p$  value  $< 0.001$ ). (Table-2)

**Table 2- Relation Of Post Covid PFT Indices With Post Covid Respiratory Problems**

| PFT indices | Post covid respiratory problems |       |               |       | Test of significance             |
|-------------|---------------------------------|-------|---------------|-------|----------------------------------|
|             | Absent(n=41)                    |       | Present(n=45) |       |                                  |
|             | Mean                            | SD    | Mean          | SD    |                                  |
| FVC         | 96.07                           | 13.84 | 72.22         | 15.02 | t=7.635,Df=84,<br>p value<0.001  |
| FEV1        | 107.63                          | 32.04 | 84.47         | 17.52 | t=4.210,Df=84,<br>p value<0.001  |
| FEV1/FVC    | 111.17                          | 20.63 | 117.78        | 14.65 | t=1.724,Df=84,<br>p value=0.08   |
| PEFR        | 99.37                           | 22.87 | 101.36        | 25.04 | t=0.384,Df=84,<br>p value=0.0702 |
| FEF25-75    | 83.71                           | 12.07 | 73.61         | 15.44 | t=3.355,Df=84,<br>p value=0.001  |

FVC=Forced Vital Capacity FEV1=Forced Expiratory Volume In 1 Second PEFR=Peak Expiratory Flow Rate FEF= Forced Expiratory Flow

In our study, among the children with post covid respiratory problems, 21 (46.7%) had abnormal and 24 (53.3%) had normal post covid 6 minutes' walk test while 4 (9.8%) children with no post covid respiratory problems had abnormal and 37 (90.2%) had normal post covid 6 minutes' walk test. Association of abnormal post covid 6

minutes' walk test with post covid respiratory problems was found to be statistically significant (p value<0.001)

In our study, among the children with post covid respiratory problems, 14(31.1%) had abnormal and 31(68.9%) had normal post covid chest x-ray findings while none of the child with no post covid respiratory problems had abnormal post covid chest x-ray findings. Association of post covid chest x-ray abnormalities with post covid respiratory problems was found to be statistically significant (p value<0.001). In our study, among the children with normal chest x-ray, 21(29.2%) had abnormal and 51(70.8%) had normal PFT findings while most 13(92.9%) of the children with abnormal chest x-ray had abnormal and 1(7.1%) had normal PFT results during post covid period. Association of chest x-ray abnormalities with abnormal PFT findings during post covid period was found to be statistically significant (p value<0.001). (Table-3)

**Table 3- Relation Of PFT Indices With Chest X-ray Findings In Post Covid Period**

| PFT indices | Chest x-ray findings |       |                |       | Test of significance           |
|-------------|----------------------|-------|----------------|-------|--------------------------------|
|             | NAD(n=72)            |       | Abnormal(n=14) |       |                                |
|             | Mean                 | SD    | Mean           | SD    |                                |
| FVC         | 87.88                | 16.91 | 61.57          | 10.33 | t=5.605,Df=84<br>p value<0.001 |
| FEV1        | 99.15                | 28.75 | 76.79          | 10.84 | t=2.860,Df=84<br>p value=0.005 |
| FEV1/FVC    | 112.54               | 17.52 | 125.36         | 16.83 | t=2.519,Df=84<br>p value=0.014 |
| PEFR        | 100.81               | 23.91 | 98.36          | 24.7  | t=0.349,Df=84<br>p value=0.728 |
| FEF25-75    | 78.91                | 15.31 | 75.93          | 11.57 | t=0.690,Df=84<br>p value=0.492 |

FVC=Forced Vital Capacity FEV1=Forced Expiratory Volume In 1 Second PEFR=Peak Expiratory Flow Rate FEF= Forced Expiratory Flow

In our study, among the children with normal chest x-ray, 12(16.7%) had abnormal and 60(83.3%) had normal 6-MWT while most 13(92.9%) of the children with abnormal chest x-ray had abnormal 6-MWT and 1(7.1%) had normal 6-MWT during post covid period. Association of chest x-ray abnormalities with abnormal 6-MWT during post covid period was found to be statistically significant (p value<0.001).

In our study, among the children with abnormal PFT findings, half (50%) had abnormal and half (50%) had normal 6-MWT while, among the children with normal PFT findings only 8 (15.4%) children had abnormal and 44(84.6%) had normal 6-MWT during post covid period. Association of abnormal PFT findings with abnormal 6-MWT during post covid period was found to be statistically significant (p value<0.001).

In our study, among patients with normal post covid 6-MWT (n=61), the mean value of FVC was  $87.66 \pm 14.9$ , FEV1 was  $97 \pm 18.25$ , FEV1/FVC was  $110.9 \pm 10.92$ , PEFR was  $97.51 \pm 15.38$  and was  $79.81 \pm 15.94$  for FEF25-75. Among patients with abnormal post covid 6-MWT (n=25), the mean value of FVC was  $73.68 \pm 23.29$ , FEV1 was  $91.88 \pm 43.61$ , FEV1/FVC was  $123.72 \pm 26.87$ , PEFR was  $107.48 \pm 36.88$  and was  $75.04 \pm 10.9$  for FEF25-75. The mean FVC of cases having abnormal post covid 6-MWT was significantly lower (p=0.001), while FEV1/FVC ratio was significantly higher in those cases (p=0.002).

## DISCUSSION:

This study was conducted to evaluate respiratory problems and pulmonary function test abnormalities in children after the covid-19 illness. The majority of the patients, in our study, belonged to the age group of 6-15 years, constituting about 79% of the patients. It was comparable to the study conducted by Dobkin et al.<sup>[7]</sup> where the age range was 4-19 years. In the study conducted by Oztruk et al.<sup>[8]</sup> and Ipek et al.<sup>[9]</sup> the age range was 5-18 years.

The symptomatology in our study is comparable to that conducted by Fang et al.<sup>[29]</sup> where fever constituted 57.9%, cough 39.9%, diarrhoea and/or vomiting 10.6%, whereas less frequent symptoms included stuffy nose, coryza, sneezing, headache, dizziness, malaise, myalgia, and sore throat. In contrast, the study conducted by Sman et al.<sup>[11]</sup>

demonstrated tiredness as the most common reported symptom in 46%, followed by fever in 42%. In comparison of the severity of COVID illness with the Fang et al.<sup>[10]</sup> study, moderate COVID-19 was 45.9%, mild 41.9%, severe (0.2%), and critical (0.8%), while 11.2% of children were totally asymptomatic. (Our study showed 54.7% of children had a mild illness, 8.1% had a moderate illness, and 1.2% had a severe COVID-19 illness, while 36% were asymptomatic.).

In our study, 61.6% of children required treatment; out of which 50% received only symptomatic treatment, 11.6% were given antibiotic therapy, 11.6% children needed oxygen therapy, and 5.8% required steroid therapy, while 38.4% required no treatment. This was similar to the study conducted by Banerjee et al.<sup>[12]</sup> where active management was required in eleven (26.8%) patients, 14.63% of mildly symptomatic children were treated with nasal drops and antihistamines, 7.3% needed oxygen inhalation, and 2.43% required a high flow nasal cannula (HFNC) and 2.43% mechanical ventilation.

On comparison of post COVID respiratory problems, our study showed, breathing difficulty on exertion and cough in 26.7% of children, followed by chest pain in 12.8%, and 7% of children had breathing difficulty at rest, while almost half (47.7%) of children had no post-covid respiratory problems. This was comparable to a study conducted by Oztruk et al.<sup>[8]</sup> where persistent respiratory symptoms were found to be present in 14 (28%) patients; common symptoms were dyspnea (35.7%), exertional dyspnea (35.7%), dry cough (21.4%), and chest pain and tightness (21.4%). In the study conducted by Dolezolavet al.<sup>[13]</sup> the dominant symptoms were exertional dyspnoea in 76.9% and chronic cough (48.7%), while dyspnoea at rest (30.8%) and chest pain (17.9%).

In our study, on respiratory system examination at the time of enrolment, 15.2 % had abnormal auscultatory findings, which is comparable to the study conducted by Dobkin et al.<sup>[7]</sup> (6.9% vs. 15.2%). In our study, on evaluation of post- COVID x rays, 7% of children had bilateral haziness over the lower lobes, 5.8% of children had bilateral patchy infiltration, 1.2% of children had bilateral lower lobe consolidation, bilateral lower lobe consolidation with pleural effusion, and bilateral middle lobe consolidation each. This was in contrast with the study conducted by Fang et al.<sup>[10]</sup> where 63.3% had a ground-glass or interstitial infiltration appearance, 1.9% had increased lung markings, and 34.8% had no radiological abnormality. In our study, 60.5% of children had normal PFT and 39.5% had significance in PFT findings; out of which 50% had mild restriction, followed by moderate restriction in 35.3% of children, 5.9% had mild restriction with obstructive pattern, 5.9% children had moderate obstruction and 2.9% children had moderate restriction with an obstructive pattern. This was in contrast with the study conducted by Dobkin et al.<sup>[7]</sup> where obstructive ventilatory defects were present in 10.7% of patients with restrictive ventilatory defects. A study by Oztruk et al.<sup>[8]</sup> where 6% had obstructive deficit and 2% patient had restrictive deficit.

In our study, chest pain was the most common finding of 6-MWT in 15.1% of children, followed by fatigue in 12.8% of children, dyspnoea in 9.3% of children, and myalgia in 8.1% of children. The normal finding of 6-MWT was present in 70.9% of children. This was in contrast with the study conducted by Dobkin et al.<sup>[7]</sup> where exercise intolerance on a 6 MWT was observed in 66.7% of participants.

Our study showed a significant association between the presenting symptoms during COVID-19 illness and post covid respiratory problems (p value<0.001).

On comparison of PFT variables, in the Dobkin et al. study, the FEV1, FVC, FEV1/FVC, FEF25-75 were  $107 \pm 12$ ,  $110 \pm 16$ ,  $86 \pm 8\%$  and  $100 \pm 23$ , respectively.<sup>[7]</sup>

## CONCLUSION:

In our study, we concluded that COVID-19 disease was linked to significant post-infection respiratory difficulties and abnormalities in pulmonary function, even though it is often less severe in the majority of children. In the post-covid era, even children with asymptomatic COVID-19 disease showed abnormal PFT in 48.4% of cases, abnormal 6-MWT in 25.8% of cases, and respiratory issues in 25.8% of cases. In order to detect post-COVID respiratory morbidities early on, all cases of COVID-19 disease should receive long-term follow-up that includes routine clinical examinations, 6-MWTs, and pulmonary function tests.

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