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COMPARATIVE EVALUATION OF POST COVID SYNDROME IN CHILDREN AND ADULTS

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ABSTRACT

Background: While the majority of individuals recover from COVID-19 without any long-term complications, a subset of patients continues to experience persistent symptoms even after the acute phase of the illness has resolved. Extensive research has been conducted on post-COVID syndrome in adults, elucidating its prevalence, clinical characteristics, and potential mechanisms. However, limited studies have focused on the occurrence of this syndrome in children. Therefore, the objective of this study was to comprehensively evaluate and compare the clinical features and outcomes of post-COVID syndrome in both children and adults. **Aim:** This study aimed to compare and evaluate the manifestation of post-COVID syndrome in children and adults, while contrasting the available data between these two populations. **Methodology:** A retrospective and prospective cohort study was conducted over a period of six months at tertiary care hosptilals in Erode. The study included a sample of 99 individuals aged between 4 and 56 years. Statistical analysis was performed using the Chi-square test with GraphPad Prism V.9.4.1. **Results:** The findings revealed that a majority of affected individuals were children, particularly females. In contrast, no significant gender difference was observed in the development of post-COVID syndrome among adults. Interestingly, the majority of children (77.7%) received their vaccination after recovering from COVID-19, while 20% remained unvaccinated until the end of the study. These factors influenced the severity of post-COVID syndrome in children when compared to adults. **Conclusion:** In conclusion, the occurrence of post-COVID syndrome in the post-pandemic era remains comparable to previous reports. However, our study suggests a slight increase in the incidence of post-COVID syndrome in children under certain circumstances. Moreover, children appear to be more susceptible to gastrointestinal issues, cardiovascular complications, ophthalmological symptoms, and orthopedic difficulties associated with post-COVID syndrome.

KEYWORDS: Post-COVID, Vaccination, Occurance, Children, Incidence.

INTRODUCTION

Coronaviruses, including the common cold, SARS, and MERS, belong to the Coronaviridae family and are naturally transmitted between birds and animals.[1-6] Since the initial cases were identified in Wuhan, China, in December 2019, the viral illness known as coronavirus disease 2019 (COVID-19), caused by the novel coronavirus SARS-CoV-2, has resulted in significant morbidity and mortality worldwide. While most COVID-19 patients are asymptomatic or experience mild to moderate symptoms, approximately 5% to 8% develop hypoxia, bilateral lung infiltrates, and reduced lung compliance, requiring non-invasive ventilation or mechanical ventilatory support.[7] As a result of the COVID-19 pandemic, the World Health Organization declared a public health emergency, and its devastating impact extends beyond health outcomes to encompass societal and economic consequences globally.[8,9] Following the previous experience with severe acute respiratory syndrome (SARS) in 2019, post-recovery manifestations were investigated, which included chronic and persistent symptoms such as weakness, myalgia, fatigue, and depression, requiring long-term monitoring.[10] The term "post-COVID" refers to the

presence of various symptoms that persist for weeks or months after SARS-CoV-2 infection, regardless of viral status, and can be continuous or relapsing.[11,12] These symptoms may include residual acute COVID symptoms or new manifestations. Most individuals with post-COVID syndrome test negative for the virus, indicating microbiological recovery.[9] The relapsing and remitting nature of post-COVID symptoms suggest an integrative classification, including potential infection-related symptoms (up to 4-5 weeks), acute post-COVID symptoms (weeks 5-12), long post-COVID symptoms (weeks 12-24), and persistent post-COVID symptoms (lasting over 24 weeks).[13] This condition is poorly understood and affects individuals of all ages and disease severities, including younger adults, children, and those not hospitalized.[14] Existing data indicate that prolonged symptom duration is common in adults and children with both severe and non-severe COVID-19.[15] Therefore, the aim of this study is to investigate and compare the post-COVID-19 manifestations in children and adults, focusing on the range of symptoms and indicators that emerge after recovery from the disease.

MATERIALS AND METHODS

Method and methodology

This study employed a both retrospective & prospective cohort study and was conducted at tertiary care hosptilals in Erode, Tamil Nadu, India. The research was carried out over a period of six months, from March to August 2022. The sample size was determined using Raosoft with a 5% margin of error and a 95% confidence level, resulting in a calculated sample size of 103. However, a total of 99 participants were included in the study. Prior to data collection, a comprehensive literature review was conducted, and self-framed questionnaires were developed. Ethical approval was obtained from the institutional ethics committee. Both retrospective and prospective cohort studies were conducted in and around Erode, with data collection commencing in April 2022, adhering to predefined inclusion and exclusion criteria. Participant information was obtained from the Government Headquarters Hospital in Erode, and consent was obtained from adults and caregivers of children who had a history of post-COVID syndrome. The final sample consisted of 99 respondents, including 54 adults and 45 children. A comparative analysis was performed on the data collected from children and adults. Statistical analysis was conducted using the Chi-square test with GraphPad Prism V.9.4.1. The findings from the data analysis between children and adults provided conclusive insights for our study.

Inclusion and Exclusion Criteria

The inclusion criteria for this study on post-COVID syndrome encompassed both genders aged 4 to 56 years, individuals with a confirmed diagnosis of post-COVID syndrome, and their willingness to provide consent. Participants with comorbidities were included. Exclusion criteria involved infants, toddlers, geriatric individuals, and pregnant women.

RESULT

Table 1: Distribution based on gender.

Category	Gender	Respondents (%)	Total no. of respondents (n=99)
Adult	Male	27 (50.0%)	54 (54.5%)
	Female	27 (50.0%)	
Children	Male	19 (42.2%)	45 (45.5%)
	Female	26 (57.7%)	

Table 2: Relation with COVID-19.

	Total number of adults (n=54)	Total number of children (n=45)
Timeline of COVID – 19 affected patients		
2020	22 (40.7%)	29 (64.4%)
2021	21 (38.8%)	12 (26.6%)
2022	11 (20.3%)	4 (8.8%)
Vaccination status		
Single dose	3 (5.5%)	7 (15.5%)
Double dose	40 (74.0%)	29 (64.4%)
Booster dose	7 (12.9%)	-
Haven't vaccinated	4 (7.4%)	9 (20%)
Period of vaccination		
Before COVID-19 infection	16 (29.6)	1 (2.2%)
After COVID-19 infection	34 (62.2%)	35 (77.7%)
Not applicable	4 (7.4%)	9 (20%)

Table 3: Respondent's problems associated with post-COVID syndrome.

Questions	Adult (n=54)		Children (n=45)		P value
	Yes	No	Yes	No	
Did you have any gastrointestinal problems?	13 (24.0%)	41 (76.0%)	28 (62.2%)	17 (37.7%)	0.001
Did you have any Neurologic problems?	30 (55.5%)	24 (44.4%)	25 (55.5%)	20 (44.4%)	>0.999
Did you have any Cardiovascular problems?	7 (12.9%)	47 (87.1%)	8 (17.7%)	37 (82.2%)	0.5059
Did you have any Dermatological problems?	11 (20.3%)	43 (79.6%)	9 (20%)	36 (80%)	0.9635
Did you have any Hematological problems?	17 (31.4%)	37 (68.5%)	13 (28.8%)	32 (71.7%)	0.7799
Did you have any of the following COVID-related symptoms present below?	45 (83.3%)	9 (16.6%)	40 (88.8%)	5 (11.1%)	0.4296
Did you have any ophthalmological symptoms?	11 (20.3%)	43 (79.6%)	15 (33.3%)	30 (66.6%)	0.1445
Did you had any orthopedics symptoms?	29(53.7%)	25 (46.2%)	29 (64.4%)	16 (35.5%)	0.28
Did you had any previous history of respiratory diseases before COVID condition?	4 (7.4%)	50 (92.5%)	4 (8.88%)	41 (91.1%)	0.7877
Had you needed to go back to the hospital since their discharge or seek medical help/advice relating to COVID-like symptoms?	9 (16.6%)	45 (83.3%)	17 (37.7%)	28 (62.2%)	0.0175
Did you had problems with eating, drinking, or swallowing, such as coughing, choking, or avoiding certain foods or beverages?	16 (29.6%)	38 (70.3%)	14 (31.1%)	31 (68.8%)	0.8731
Did you had any diseases or disorders before COVID?	7 (12.9%)	47 (87.0%)	1 (2.2%)	44 (97.7%)	0.0509
Were there any changes in that disease or disorder after COVID?	1 (1.8%)	53 (98.1%)	1 (2.2%)	44 (97.7%)	0.8962

Table 4: Respondents had their post-COVID symptoms and their duration.

Symptoms	<1 month (potential infection-related symptoms)		1-3 months (acute post-COVID symptoms)		3-6 months (long post-COVID symptoms)		>6 months (persistent post-COVID symptoms)	
	Adult	Children	Adult	Children	Adult	Children	Adult	Children
GASTROINTESTINAL PROBLEMS								
Abdominal pain	10 (18.5%)	18(40%)	4(7.45%)	4(8.8%)	_	1(2.2%)	1(1.8%)	1(2.2%)
Constipation	5(9.2%)	4(8.8%)	1(1.8%)	_	_	_	_	_
Diarrhea	8(14.8%)	12 (26.6%)	1(1.8%)	1(2.2%)	_	_	_	_
Dysentery	4(7.4%)	2(4.4%)	_	_	_	_	_	_
Headache	16 (29.2%)	18(40%)	4(7.4%)	4(8.8%)	1(1.8%)	_	1(1.8%)	_
Migraine	6(11.1%)	2(4.4%)	2(3.7%)	1(2.2%)	_	_	1(1.8%)	_
Dizziness	11 (20.3%)	10 (22.2%)	2(3.7%)	2(4.4%)	2(3.7%)	_	_	_
Fatigue	11 (20.3%)	5 (11.1%)	3(5.5%)	2(4.4%)	2(3.7%)	_	1(1.8%)	_
CARDIOVASCULAR PROBLEM								
Chest discomfort	8 (14.8%)	6 (13.3%)	_	_	_	_	_	_
DERMATOLOGICAL PROBLEMS								
Rash	4 (7.4%)	2(4.4%)	3 (5.5%)	1 (2.2%)	_	_	_	_

Psoriasis	5 (9.2%)	1 (2.2%)	2 (3.7%)	_	_	_	_	_
Acne	4 (7.4%)	2 (4.4%)	1 (1.8%)	_	_	_	_	_
Cold sores	5 (9.2%)	2(4.4%)	3 (5.5%)	_	_	_	_	_
Dry skin	9 (16.6%)	4(8.8%)	3 (5.5%)	_	_	_	_	_
Vitiligo (loss of skin color)	6 (11.1%)	1 (2.2%)	_	_	_	_	1 (1.8%)	_
HEMATOLOGICAL PROBLEMS								
Anemia	13(24.0 %)	10(22.2%)	4(7.4%)	1 (2.2%)	_	_	2 (3.7%)	1(2.2%)
Leucopenia	4 (7.4%)	1 (2.2%)	2(3.7%)	1 (2.2%)	_	_	_	_
OPHTHALMOLOGICAL PROBLEMS								
Dry eyes	9 (16.6%)	8 (17.7%)	1(1.8%)	_	_	_	_	_
Redness of eyes	4 (7.4%)	2 (4.4%)	2(3.7%)	1 (2.2%)	_	_	_	_
Watery eyes	8 (14.8%)	1 (2.2%)	1(1.8%)	1(2.2%)	_	_	_	_
Itching of eyes	4 (7.4%)	6 (13.3%)	2(3.7%)	_	_	_	_	_
Swelling of eyes	4 (7.4%)	4 (8.8%)	1(1.8%)	_	_	_	_	_
COVID RELATED SYMPTOMS								
Fever	19 (35.1%)	1 (2.2%)	8(14.8%)	5 (11.1%)	_	_	_	1(2.2%)
Cough	24 (44.4%)	15(33.3%)	12 (22.2%)	11 (24.4%)	4 (7.4%)	1(2.2%)	1(1.8%)	1(2.2%)
Loss of taste	24 (44.4%)	23(51.1%)	10 (18.5%)	3(6.6%)	1(1.8%)	_	1(1.8%)	_
Loss of smell	22 (40.7%)	19(42.2%)	9 (16.6%)	3 (6.6%)	_	_	_	_
Stuffy nose	23 (42.5%)	12(26.6%)	6 (11.1%)	2(4.4%)	1(1.8%)	_	_	_
Runny nose	17 (31.4%)	9 (20.0%)	5 (9.2%)	_	_	_	_	_
Shortness of breath	19 (35.1%)	18(40.0%)	2 (3.7%)	5 (11.1%)	2 (3.7%)	–	_	1(2.2%)
Weight loss	12 (22.2%)	16(35.5%)	6 (11.1%)	4 (8.8%)	_	_	_	_
Excessive sweat	12 (22.2%)	9(20.0%)	4 (7.4%)	–	1 (1.8%)	–	–	–
Loss of appetite	17 (31.4%)	20(44.4%)	5(9.2%)	6 (13.3%)	3 (5.5%)	–	–	–
ORTHOPEDICS PROBLEMS								
Excessive intolerance	6 (11.1%)	5 (11.1%)	1(1.8%)	_	_	_	1(1.8%)	_
Orthostatic intolerance	6 (11.1%)	4 (8.8%)	1(1.8%)	1 (2.2%)	1 (1.8%)	–	–	–
Body pain	24(44.4 %)	15(33.3%)	5(9.2%)	8(17.7%)	2 (3.7%)	1 (2.2%)	1 (1.8%)	1(2.2%)
Joint pain	16(29.6 %)	15(33.3%)	6(11.1%)	2 (4.4%)	1 (1.8%)	–	1(1.8%)	_
Total number of symptoms that occured	36	36	33	22	12	3	11	6

DISCUSSION

A small percentage of COVID-19 patients, around 5% to 8%, experience severe respiratory symptoms such as hypoxia, bilateral lung infiltrates, and decreased lung compliance, requiring non-invasive ventilation or mechanical ventilatory support, despite the majority of

cases being asymptomatic or mild to moderate in nature.[7]

In our study, which included 99 subjects, we found no significant difference in the development of post-COVID syndrome among adult participants based on gender. However, in children, a majority of those affected were females (57.7%) (Table 1). This aligns with findings from other studies, such as the research conducted by Smane et al[15]., which demonstrated that prolonged symptom duration is common not only in adults but also among children with COVID-19. Another study by Stavem et al.[16] highlighted a higher likelihood of persistent COVID-19 symptoms in females (47%) compared to males (33%) in children. Moreover, Ludvigsson et al[17] reported a predominance of females among children with post-COVID syndrome in their case series.

Regarding the age distribution in our study, 45 respondents fell within the age group of 4-17 years, while 54 were aged 18-56 (Table 1). Notably, most children and adults in our study contracted COVID-19 in 2020 (Table 2), suggesting a peak in the outbreak during that year, potentially influenced by factors such as limited understanding of the virus's physiology, management, and the unavailability of preventive vaccinations. The World Health Organization (WHO) declared COVID-19 as a pandemic on March 11, 2020, following the emergence of the SARS-CoV-2 virus.[18]

Our study revealed that a significant proportion of both adults (77.7%) and children (62.2%) received their COVID-19 vaccines after recovering from the infection. However, a portion of the population, 20% of children and 7.4% of adults, remained unvaccinated (Table 2). The current global vaccination coverage stands at 68.3% with the lowest rates observed in low-income countries, constituting 23.3% of the population.[19] Vaccination has been recognized by the Centers for Disease Control and Prevention (CDC) as a crucial preventive measure against post-COVID syndrome.[20] However, Callaghan et al.[21] reported that there are still misconceptions and false beliefs about vaccine efficacy and safety, which can result in delays or hesitancy in vaccination efforts.

In our study, statistically significant differences (p-value = 0.001) were observed in gastrointestinal issues between children and adults, consistent with the findings of Puoti et al[22]., who highlighted the higher incidence of gastrointestinal involvement, particularly in children. Additionally, children were significantly more likely (p-value = 0.0175) than adults to seek medical advice for post-COVID symptoms (Table 3). Other studies conducted by Liu et al.[23] and Novak et al.[24] have also emphasized the need for hospitalization in children with post-COVID symptoms.

The presence of gastrointestinal symptoms in post-COVID syndrome may be attributed to the damage to the intestinal mucosal barrier and the activation of inflammatory factors. This is likely due to the interaction between angiotensin-converting enzyme 2 (ACE2) in the gastrointestinal tract and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during infection of the human body.[25] In our study, (Table 4) when comparing data from children and adults, children exhibited higher percentages of gastrointestinal issues (62.2%), cardiovascular issues (17.7%), ophthalmological symptoms (33.3%), orthopedic symptoms (64.4%), and difficulties in eating, drinking, or swallowing (31.1%). On the other hand, adults had a higher occurrence of hematological issues (31.4%). Neurological (55.5%) and dermatological issues (20%) were equally prevalent in both children and adults.

Before the onset of COVID-19, 3 individuals had respiratory issues, 2 had cardiovascular issues, 1 had gastrointestinal issues, and 1 had hematological issues. Only 1 child had a respiratory issue prior to the occurrence of COVID-19. In terms of the duration of symptoms, our study found that children (80%) were more likely to experience potential infection-related symptoms (<1 month) compared to adults (66.6%). Conversely, adults (61.11%) had a higher occurrence of acute post-COVID symptoms (1-3 months) compared to children (48.88%). For long post-COVID symptoms (3-6 months), adults (12.22%) were more affected than children (6.66%). Persistent post-COVID symptoms were also more common in adults (20.37%) than in children (13.33%). These findings indicate that adults are more susceptible to long-term symptoms compared to children. The milder nature of the disease in children and the lower occurrence of post-acute COVID-19 infection in children compared to adults have been explained in a report by Public Health Ontario.[26]

Similarly, a study conducted by Kim et al.[27] revealed that gastrointestinal problems such as abdominal pain (66.5%) and diarrhea (53.7%) were more commonly observed in children with post-COVID syndrome. Another study by Suraj et al.[28] reported that fatigue was the most prevalent post-COVID symptom, affecting approximately 80.3% of participants. Pain in joints and muscles, headaches, shortness of breath, cough, and loss of smell and taste were noted in approximately 20-34% of participants.

CONCLUSION

In conclusion, our study investigated the clinical features and outcomes of post-COVID syndrome in both children and adults. We found that the majority of children affected by post-COVID syndrome were female, while there was no significant difference in the development of post-COVID syndrome among adult genders. It was observed that gastrointestinal issues, cardiovascular issues, ophthalmological symptoms, orthopedic difficulties, and difficulties with eating, drinking, or swallowing were more prevalent in children, while adults exhibited a higher incidence of hematological issues.

Furthermore, our study revealed that the occurrence of potential infection-related symptoms was higher in children compared to adults, while adults had a higher prevalence of acute post-COVID symptoms and long-term symptoms. This finding suggests that adults may experience a more prolonged recovery phase than children. The study also highlighted the gastrointestinal symptoms observed in children, which may be attributed to the interaction between angiotensin-converting enzyme 2 (ACE2) in the gastrointestinal tract and the SARS-CoV-2 virus. Despite these important findings, our study has certain limitations. The sample size was relatively small, which may have impacted the generalizability of the results. Additionally, the reliance on self-reported symptoms without diagnostic methods introduces the possibility of recall bias and may affect the accuracy of the data. In conclusion, our study provides valuable insights into the clinical manifestations and differences in post-COVID syndrome between children and adults. These findings contribute to the growing body of knowledge on post-COVID syndrome and emphasize the need for further research with larger sample sizes and more rigorous diagnostic approaches to better understand the long-term effects of COVID-19 on different age groups.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation**.**

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LIMITATIONS

Several limitations to our study should be acknowledged. Firstly, the sample size was relatively small, making it challenging to identify a sufficient number of post-COVID syndrome patients, especially considering that the study was conducted after the COVID-19 pandemic. This limitation may have affected the generalizability of our findings to a larger population. Secondly, as a retrospective and prospective cohort study, there is a potential for recall bias among the respondents when recalling their past experiences with post-COVID syndrome. This could have influenced the accuracy and completeness of the data collected.

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