



LONG TERM TELEPHONIC REVIEW OF RTPCR/RAT POSITIVE COVID 19 CHILDREN - A PROSPECTIVE OBSERVATIONAL STUDY

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(ABSTRACT) **Objective-** To identify the long term sequelae following RTPCR/ RAT positive COVID 19 in children of age group < 20 years periodically over 3 years. **Design-** Prospective Observation Study. **Participants-** 273 children diagnosed with RT PCR/ RAT positive COVID 19 at Bapuji Child Health Institute and Research Centre, Davanagere, Karnataka in the first 5 months of 2021. **Intervention-** Telephonic review as a follow up done in July 2021, January 2022 and in October 2023 via a questionnaire designed to ask primary care givers. **Outcome Measured-** The follow up interview documented present status of the child, any symptoms (persisting or newly developed), further hospital admissions, vaccination status, morbidity, mortality and reoccurrence of COVID 19 in the children as well as the family. **Results-** Of our 273 patients, 71% had contracted the virus from family members in their vicinity who had COVID19, 5% necessitated admission and a mortality rate of 1% was identified. Children had minimal persisting effects, and majority of them returned to good health. The common sequelae noted were repeated episodes of URTI, hair loss, body weight changes and anosmia. A paradigm shift was noted in the vaccination status between first and third review, with >90% vaccination completion in both parents and children by 2023.

KEYWORDS : Telephonic review, COVID19, parents

INTRODUCTION:

SARS CoV2 virus took the world by a storm when it presented as a novel infection causing severe pneumonia in December 2019. The disease waxed and waned over the course of the next two years, majorly affecting the adult population with reduced incidence and severity in children and adolescents. (1)

COVID 19 has varied presentation in children ranging from asymptomatic cases, or symptomatic cases which are mild and can be treated on OPD basis to severe respiratory distress which required ICU admission and respiratory support. The pandemic has also resulted in the emergence of a new entity called multisystem inflammatory syndrome in children (MIS-C), presenting at about 2-4 weeks after acute SARS-CoV-2 infection. (2)

Common symptoms of SARS-CoV-2 infection, commonly referred to as coronavirus disease 2019 (COVID-19), include shortness of breath, fever, cough, sore throat, malaise, myalgia, anorexia, nausea, diarrhoea, anosmia, and ageusia (1).

Persistent symptoms after COVID-19 have multiple names including "post-COVID conditions," "long-COVID," "long-haul COVID," "post-acute COVID-19," "long-term effects of COVID," and "chronic COVID." (3).

The World Health Organisation (WHO) developed a clinical case definition of post-COVID-19 conditions, including persistent, relapsing or new symptoms beyond 12 weeks after infection (4). Two years have elapsed since the zenith of this ailment, it becomes imperative to undertake a comprehensive analysis of the enduring implications it may have on children and adolescents, in long term. While several studies have been conducted in adults, none have yet yielded findings from a follow up spanning the period of 2 years within this specific demographic.

This study aims to add to the limited available data regarding the prolonged effects of COVID 19 on children diagnosed at a tertiary care hospital in Davanagere through a prospective study done as standardized telephonic reviews at three intervals over a period of 3 years.

METHODOLOGY:

This is a prospective observational study of children (< 20 years) diagnosed at Bapuji Child Health Institute, Davanagere, Karnataka with COVID 19 in the year of 2021 in the first wave of the pandemic. All of these children had either Reverse Transcriptase PCR or Rapid Antigen Test positive for SARS CoV2. They were under home isolation as per National Guidelines and did not require in patient care. Subsequent to the completion of home isolation period, a telephonic review with standardized questions was conducted by a team

comprising paediatric doctors and residents of the hospital. Of 273 children with COVID 19, follow up interview was done thrice, initially in July 2021 followed by a subsequent round in January 2022 culminating with the last follow up in October 2023, after an average period of 2.5 years. A total of 224, 144 and 102 children could be contacted for primary, secondary and tertiary reviews respectively. (Flowchart 1). The questions were asked to the primary care givers, parents in most cases or close relatives otherwise. In the first telephonic review, demographics, method of testing for COVID 19, and pertinent blood investigations were documented. Concurrently, present condition and any persisting/ newly developed symptoms that transpired between discharge and subsequent follow up were ascertained. The second follow up done was at the eight-month mark post discharge, to know the present health status and overall well-being of the children. In the follow up done in 2023, 2.5 years since the admission, it delved deeper into the potential impact on multiple systems; neurological, gastrointestinal, respiratory, cardiovascular manifestations, behavioural changes etc. to uncover any intricate interplay or lingering effects that may have manifested over time. The details of the symptoms are given in Table 1. At the end of the first and the third reviews, the vaccination status of the child and family, and any further detected cases of COVID 19 in the family or reinfection with COVID 19, hospital stay and readmissions was documented.

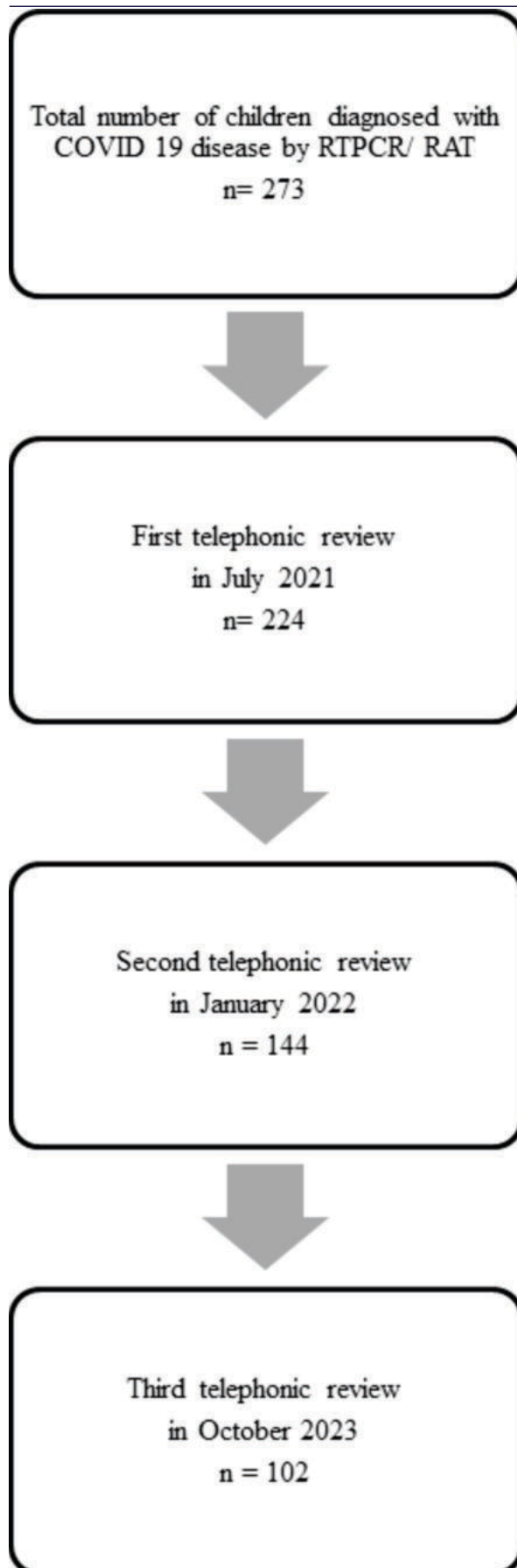
RESULTS:

FIRST TELEPHONIC REVIEW - JULY 2021:

The review primarily focused on collection of basic demographic details like age, gender, educational status along with the method of testing (RTPCR or RAT), contact with COVID 19, any familial loss due to COVID 19, repeated hospital visits and new symptoms as mentioned in the table. Data regarding the vaccination status of the family members was collected (as vaccination for children was not widely used at that point of time) which will be discussed below.

During this review, a cohort of 224 children were contacted out of which 206 (92%) were diagnosed by RT PCR and 18 children (7%) by RAT. A subset comprising six children had both RTPCR and RAT positive for SARS CoV2. (Table 2). A pivotal parameter under scrutiny was identification of the source of COVID 19 for these children during the lock down period. To elucidate this, comprehensive data pertaining to exposure to COVID 19 within the family was collected. it was noted that 161 (71.8%) of these children were living in close contact with a primary diagnosed case of COVID 19, majority of whom were parents or first degree relatives. (Table 3)

On enquiring regarding persisting or newly developed symptoms, 4 children had persistent fever and 3 children had pain abdomen, all of which were treated on OPD basis as mentioned in Table 4.



Flowchart 1: COVID 19 Positive Children Followed Up By Telephonic Reviews.

TABLE 2: DEMOGRAPHIC DATA

AGE	<2 YEARS: 21 2-10 YEARS: 61 11-20 YEARS: 142
GENDER	MALE: 124 FEMALE: 100
COVID TESTING	RTPCR POSITIVE: 206 RAT POSITIVE: 18 BOTH POSITIVE: 6

TABLE 3: COVID 19 HISTORY

DURING 1ST REVIEW:	
HISTORY OF CONTACT WITH COVID 19 PATIENTS	YES: 161 NO: 63
LOSS OF FAMILY MEMBER DUE TO COVID 19	24
DURING 3RD REVIEW:	
RECURRENCE OF COVID	IN SELF: 0 IN FAMILY MEMBERS: 5

TABLE 4: STATUS OF THE CHILD (DURING 1ST REVIEW)

FEVER	4
VOMITING	NONE
PAIN ABDOMEN	3
CONVULSIONS	NONE
ALTERED SENSORIUM	NONE
RECENT BEHAVIOURAL CHANGES	1 (Increased Gadget Use)

It was also essential to understand if any child deteriorated during home isolation and required hospital stay/ repeated hospital visits, details enumerated in Table 5. Our study show that of these children, 77 (34%) visited the hospital once where 31 children were treated on OPD basis for symptoms of fever and URTI and 26 came for follow up as advised during testing period and were reported to be of good health. 14 (5%) children necessitated admission, of which 2 were admitted for isolation purposes, one was a known case of Beta Thalassemia came for routine blood transfusion, two for surgical reasons, and eight of these children had worsening of symptoms (breathing difficulties, fever, persistent cough, lethargy) and required admission for an average period of 5-7 days. It is affirming to note that all the children who required admission recovered well and currently maintain good health with an exception of one child who succumbed to severe disease progression during hospital stay.

TABLE 5: REPEAT HOSPITAL VISITS

DURING 1ST REVIEW	1ST VISIT: 77 Reasons: FOLLOW UP: 26 FEVER/COLD/COUGH: 31 OTHER SYMPTOMS: 3 COVID TESTING: 3 ADMISSION: 14
	2ND VISIT: 7 Reasons: OPD VISIT FOR FEVER: 3 LOSS OF APPETITE: 1 FOLLOW UP: 3
	3RD VISIT: 1 Reasons: FOLLOW UP: 1

SECOND TELEPHONIC REVIEW- JANUARY 2022:

The second review was conducted 7 months post diagnosis of COVID 19, where mainly the general well being of the child was inquired. A total of 144 children were contacted, of which 140 (97%) were of good health with no complaints, and 4 (3%) had symptoms of URTI but otherwise well. No other major differences from the first review was noted during this period. (Table 6)

TABLE 6: 2ND REVIEW	NO OF CHILDREN
NO OF CHILDREN CONTACTED	144
WELL CHILDREN	140
UNWELL CHILDREN (URT)	4

THIRD TELEPHONIC REVIEW- OCTOBER 2023:

The final follow up was done 2.5 years later in October 2023 by the doctors at BCHI and RC, this was a more extensive review which covered multiple parameters ranging from recurrence of COVID 19, COVID vaccination status of child and family, to long term symptoms like body weight changes, hair loss, loss of appetite; all of which is mentioned in Table 7. A total of 102 children could be contacted. 5 children had history of recurrence of COVID 19 in the family, but no children had any further episodes of diagnosed COVID 19.

Table 7 : Questions Asked During The Third Telephonic Review Done In October 2023.

SYSTEM	MANIFESTATIONS
RESPIRATORY	Chest pain Recurrent URTI/ LRTI symptoms - persistence of cough/ cold Exercise Intolerance Difficulty in breathing Loss of smell
CARDIOVASCULAR	Palpitations Chest Tightness
NEUROLOGICAL	Headache Sleep Difficulties Tremors
BEHAVIOURAL	School Performance Any cognitive difficulties Sudden behavioural/ mood changes
GASTROINTESTINAL	Vomiting/ nausea Diarrhoea Constipation Pain Abdomen Loss of appetite
MISCELLANEOUS	Body weight changes Hair loss

The parents of these children were asked regarding the school performance, and 65% of them reported good performance whereas 30% and 5% felt it has deteriorated post COVID with average performance and below average performance respectively. Two of the major symptoms that had developed in the Post COVID era were body weight changes and hair loss. 10 children have weight gain issues and have faced difficulties in maintaining their BMIs, and 3 children have had loss of weight following the illness. Hair loss was noted in 10 (10%) of the children during the third review. Apart from this, 21% of parents gave history that their child has developed episodes of URTI following COVID 19 and required multiple visits to the OPD for the same. (Table 8). The reasons for the same has been discussed below.

TABLE 8: STATUS OF CHILD (DURING 3 RD REVIEW)	NO OF CHILDREN
SCHOOL PERFORMANCE	GOOD: 66 AVERAGE: 31 BELOW AVERAGE: 5
BEHAVIOURAL CHANGES	4
HAIR LOSS	10
BODY WEIGHT CHANGES	WEIGHT LOSS: 3 WEIGHT GAIN: 10
LOSS OF SMELL	4
LOSS OF APPETITE	1
REPEATED URTI	22

COVID 19 Vaccination Status:

In all 3 telephonic reviews that were conducted, the vaccination status of the child and the family were undertaken. In the first review, children were yet to be widely vaccinated in the country, 81 (36%) of the families had not yet received vaccination, 78 (34%) children's parents had received at least one dose, and 63 (28%) families had parents who had completed both doses of the vaccine. A paradigm shift was evident by the third review after 2.5 years when 99% of children had received the vaccination and 95% of the families had completed both doses of the vaccination as well. (Table 9).

DEATHS:

Given that our study mainly encompassed children with mild to asymptomatic diseases, four deaths were observed in our cohort. One child died during hospital stay, another passed away 3 days post diagnosis during home isolation. The third death was attributed to a newly diagnosed cardiac condition 4 months post diagnosis, while the

cause of the fourth death remains unknown. No further evidences were available to ascertain the exact cause of death except the knowledge of the parents. (Table 10)

Table 9: Covid Vaccination Status	No Of Children
1ST REVIEW (n= 224)	
VACCINATION STATUS	NOT VACCINATED: 81 FAMILIES VACCINATED: SELF: 2 FAMILY- 2 DOSES RECIEVED: 63 1 DOSE RECIEVED: 78
3 RD REVIEW (n=102)	
VACCINATION STATUS	SELF: 101 FAMILY: 99

TABLE 10: DEATHS	NO OF CHILDREN
1ST REVIEW	3 children CAUSES: 1- During hospital stay 1- Cause unknown 1- 3 days post diagnosis
2ND REVIEW	1 child CAUSE: 1 - Newly diagnosed ?cardiac condition

DISCUSSION:

The impacts of the coronavirus disease pandemic, have been pervasive across the world. (5) Over time COVID 19 has been widely studied in both adults and children, to know the epidemiology, the spectrum of symptoms and the immediate complications. The disease per say has rampantly affected adults, children have accounted for a minority of infections at the population level but the delta and omicron variants have proved considerably more adept at infecting children than previous variants. (6) (7) An Indian Council of Medical Research survey conducted in December 2020 and January 2021 showed that the percentage of infected children in the age group of 10-17 years was around 25%, the same as adults (8). But almost 90% of infections in children are mild/asymptomatic. This indicates that while children are contracting the virus similarly as adults, they tend to not get the severe form. As per data gathered in the initial two waves, even severe COVID infections in children are less inclined to necessitate intensive care unit management. (9).

They are usually affected by contact with infected adults via respiratory droplets but further spread from children has contributed minimally for the epidemic itself. This can be reasoned with the fact that children remained in lockdown during this period and had limited exposure to the outside world in contradiction to adults. Initially with the increase in the vaccination rate in adults, there appeared to be a shift in the infection frequency towards children. (10). Our study also indicates that these children continued to remain asymptomatic or recovered with mild disease, and only 5% required hospital admissions, which was due to deterioration of symptoms, but all children had a smooth uneventful hospital stay. Children produce more interferons at the mucosal surface, which rapidly alert the immune system at the first sign of infection, making it harder for the virus to penetrate the body. (11) They are also thought to have a faster innate immune response, because their T cells are mostly untrained, giving them a greater capacity to respond to novel viruses. Most children are also much less autoantibodies in their blood, which target the body's own cells and actively disable interferons, hindering the body's capability to fend off viruses (12). There is recent data that shows that the severity and mortality of COVID 19 is different between High income and LMICs, though limited. (13).

Though multiple studies have been done worldwide to study the effects of the disease, it is essential to understand the prolonged effects of this virus on children as to date, the potential range of signs and symptoms following the illness and their frequency of occurrence in children and adolescents remains unclear (14). These are defined as Long Covid or Post Covid by WHO which mainly concentrates on the 3 to 6 weeks period following the acute infection. As of September 2023, more than 300 children in Davanagere have tested positive for COVID 19 (SARS CoV2), our study mainly focuses on children who have been diagnosed with COVID 19 and have undergone home isolation due to

mild or asymptomatic disease. The idea behind this study is a triphasic approach to provide a comprehensive understanding of their general well being, to ensure regular follow up and to identify any short or long term complications of the disease over a period of 2.5 years.

71% of our study population acquired the disease from close contact to a proven case of COVID 19, and the evidence indicated a discernable discrepancy in the severity of COVID 19 between adults and children, as the disease presented far worse in adults as 24 of these children have lost a family member due to the disease itself while they presented with minimal or no symptoms. Interestingly, 8 children required admission for worsening of symptoms and were recovered well, while the rest of the cohort returned to normal health following home isolation.

Though multiple studies identified symptoms associated to long-COVID, such as mood, fatigue, sleep disorders, orthostatic intolerance, decreased concentration, confusion, memory loss, balance problems, exercise intolerance, hyperhidrosis, blurred vision, body temperature dysregulation, dysfunction on heart, rate variability and palpitations, constipation or diarrhea, and dysphagia as the most common complaints, our cohort showed body weight changes and recurrent URTI as the main findings. (15) Obesity, or unable to gain weight and decline in academic performance which was also observed could be attributed to prolonged lock down, online teaching, increased use of gadgets and reduced physical activity, ie., due to psychosocial factors than the disease itself. Parents of 4 children noted that their children have developed some behavioural changes over the last 2.5 years like increased gadget use, anxiety, excessive sleepiness. Some symptoms that were studied extensively in adults like anosmia were noted in four children of our cohort.

Concerning age, most of the studies did not discriminate between children (<12-year-old) and adolescents. Given that the risk increases with age, there is a need for future studies to stratify by age. In addition, the evaluation of self-reporting symptoms can be significantly biased by age as younger children might not be able to express their emotional and functional status relevant to post-COVID-19 adequately. Further studies targeting age groups are required. (16)

Our study also highlights the reach of vaccination in the country among the pediatric age group, which has yielded highly positive results in both the children and their families underlining a significant stride in the immunization efforts which has been successful.

CONCLUSION:

The focus of COVID 19 has been on the severe aspects of the diseases from pneumonia, respiratory failure to MISC-C, this study highlights the outcome of children with minimal disease of COVID 19 and the long-term sequelae of the same. Majority of our children have remained in good health, indicating that the outcome with mild or moderate disease is promising. But this also emphasizes on the need to understand the disease depth and to remain vigilant to design further guidelines regarding clinical management, follow up and rehabilitation of these children.

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REFERENCES

1. Borrelli M, Corcione A, Castellano F, Fiori Nastro F, Santamaria F. Coronavirus disease 2019 in children. *Front Pediatr*. 2021;9: 668484. <https://doi.org/10.3389/fped.2021.668484>.
2. Godfred-Cato S, Bryant B, Leung J. COVID-19-associated multisystem inflammatory syndrome in children—United States, March–July 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:1074–1080.
3. Thallapureddy K, Thallapureddy K, Zerda E, Suresh N, Kamat D, Rajasekaran K, Moreira A. Long-Term Complications of COVID-19 Infection in Adolescents and Children. *Curr Pediatr Rep*. 2022;10(1):11–17. doi: 10.1007/s40124-021-00260-x. Epub 2022 Feb 1. PMID: 35127274; PMCID: PMC8803461.
4. World Health Organization (WHO) Clinical Case Definition Working Group on Post COVID-19 Condition. WHO; 2021. [(accessed on 22 October 2021)]. A Clinical Case Definition of Post COVID-19 Condition by a Delphi Consensus, 6 October 2021.
5. World Health Organization. Weekly Epidemiological Update on COVID-19: Edition 50. Geneva/CMR sero survey: One in five Indians exposed to Covid-19. Accessed 23 June, 2021. Available from: <https://www.bbc.com/news/world-asia-india-55945382>: WHO; 2021.
6. Williams PCM, Howard-Jones AR, Hsu P et al. SARS-CoV-2 in children: Spectrum of

disease, transmission and immunopathological underpinnings. *Pathology* 2020; 52: 801–8.

7. Cox D. What do we know about covid-19 and children? *BMJ* 2023; 380 :p21 doi:10.1136/bmj.p21
8. ICMR sero survey: One in five Indians exposed to Covid-19. Accessed 23 June, 2021. Available from: <https://www.bbc.com/news/world-asia-india-55945382>
9. The pandemic and India's children, Piyush Gupta, <https://www.indianpediatrics.net/july2021/july-607-608.htm>
10. Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: Demographics, risk of hospital admission, and vaccine effectiveness. *Lancet* 2021; 397: 2461–2.
11. Peeples L. Understanding Kids and COVID. *Proc Natl Acad Sci U S A* 2022;119:e2203753119. doi:10.1073/pnas.2203753119 pmid:3531614
12. Mallapaty S. Kids and covid: why young immune systems are still on top. *Nature*. Sep 2021. <https://www.nature.com/articles/d41586-021-02423-8>
13. Gupta, Vidushi et al. Severity and mortality associated with COVID-19 among children hospitalised in tertiary care centres in India: a cohort study, *The Lancet Regional Health - Southeast Asia*, Volume 13, 100203
14. Bialek, S. et al. Coronavirus disease 2019 in Children—United States, February 12–April 2, 2020. *Morb. Mortal Wkly. Rep*. 69, 422–426. <https://doi.org/10.15585/mmwr.mm6914e4> (2020).
15. Dotan, A., David, P., Arnheim, D. & Shoenfeld, Y. The autonomic aspects of the post-COVID19 syndrome. *Autoimmun. Rev*. 21, 103071. <https://doi.org/10.1016/j.autrev.2022.103071> (2022).
16. Lopez-Leon, S., Wegman-Ostrosky, T., Ayuzo del Valle, N.C. et al. Long-COVID in children and adolescents: a systematic review and meta-analyses. *Sci Rep* 12, 9950 (2022). <https://doi.org/10.1038/s41598-022-13495-5>.