Ostracizing Children from Research in COVID-19: Is it Ethical?

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To the Editor: COVID-19 pandemic has affected all age groups including children, who comprise 2–5% of total cases, leading to significant mortality and morbidity [1]. Around 3% of the total COVID-19 deaths reported from India are in children [2]. Recently, many drugs (antivirals, steroids, and immunomodulators) are being explored in trials [3, 4]. Traditionally, the drug-trials are first conducted in adults, and if proven efficacious, children are included after a significant time gap. The potential reasoning for the exclusion of children in the initial phase is the risk of unknown adverse effects of the drug under trial and lack of an adequate number of patients for that disease. Children are particularly vulnerable due to their limited freedom and capability to make informed choices, protect themselves from the intended risk, and inability to report adverse effects like a bitter taste, smell, anxiety, palpitation, abdominal pain, etc.

However, in pandemic like COVID-19 affecting children, the exclusion from drug trials that are already being widely used in them for other indications is inappropriate and is against medical ethics [3–5]. Recently, Dexamethasone (FDA approved in children) showed a reduction in mortality in hospitalized patients with severe COVID-19 [3]. Researchers stated that the cheap and universally available dexamethasone can reduce one-third of the deaths and shall ensure universal access and equity in the care. Unfortunately, this benefit is not extended to children due to their initial exclusion, which was followed by an abrupt inclusion, detailed information of which is not yet available [3].

Despite the evidence, its use in children is limited by a lack of proven efficacy data in them. Hydroxychloroquine, which has been used off-label in children for many years in the treatment of autoimmune disorders and is studied in the non-COVID-19 clinical trial too, has shown the same exclusion in COVID-19 trial [6]. Many COVID-19 trials evaluating drugs that are widely used in pediatrics for other clinical indications also excluded children (Supplementary Table 1). The zeal for developing vaccines against SARS-CoV-2 appears paradoxical by leaving behind the vulnerable population and violates the action rule of equitable access to an intervention for a new disease.

Including children in clinical trials for newer intervention might result in better understanding of pharmacokinetics and dynamics (e.g., rapid metabolism of cyclosporin), immune response (like vaccines), unexpected responses (e.g., Grey baby syndrome in chloramphenicol), adverse drug reactions (e.g., gasping syndrome from benzyl alcohol) which might be different from the adults and can have a potential bearing over their growth (as seen with tetracycline), development, and future reproductive potential (cytotoxic therapy). If we do not recruit the children in clinical trials for COVID-19 therapy, we might end-up extrapolating data from adults and subjecting a large number of children to unknown risks, that too without monitoring.

To ensure equitable standards, regulatory bodies must ensure adequate participation of children in clinical trials [5]. Their vulnerability can be mitigated by adhering to the country-specific ethics guidelines. They should be only included in the trials that will have a direct benefit to them (holds for COVID). The research should be preferably done in the least vulnerable age-group with explicit informed consent from the parents and assent from the child. The consent and assent should clearly explain the therapy under investigation including its result in adults, potential danger to the child (including the painful procedures, amount of blood to be taken, etc), and measures in place to mitigate these risks. Involving the patient's representative bodies and pediatricians in the design of the trial and data safety monitoring bodies shall help protect the child's interests [5].

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The autonomy of children is vested in us (pediatricians), therefore ensuring justice to them by inclusion in the clinical research intended for their benefit is our responsibility.

Compliance with Ethical Standards

Conflict of Interest None.

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