**Background:**

The emergence of novel SARS-CoV-2 variants of concern (VOCs) has altered the epidemiology and clinical characteristics of COVID-19.

This study aims to describe the changes in COVID-19 manifestations in outpatients children and adolescents during the Parental, Delta, and Omicron eras.

**Methods:**

Single-center, prospective, observational study was conducted on 0-20 year old individuals attending the Department of Women’s and Children’s Health, University Hospital of Padua between March 2020 to December 2022 (Fig.1).

Variables were summarized as counts and percentages or median and interquartile range (IQR), as appropriate, stratified by VOCs. Chi-squared or Fisher exact test and Wilcoxon’s test were used for categorical and continuous variables, respectively.

**Results:**

A total of 509 COVID-19 cases were studied (Fig.2):

- 234 (46%) females, median age of 8 years (IQR 4.38-11.53)
- 23 (4.5%) were vaccinated

Results showed an increasing trend in the incidence of fever and upper respiratory tract symptoms /e.g. rhinitis, cough, and sore throat) from Wild-type to Omicron waves (Fig.3).

**Symptoms differed with age:** fever, rhinitis, and skin rashes were higher in infants/toddlers; conversely, asthenia and headache were more frequent in children aged >5 years (Fig.4).

**Conclusions:**

The clinical manifestations of COVID-19 in children varied by age and viral variants, with Omicron being more likely to be associated with upper respiratory symptoms. Further population-based studies are needed to validate these findings, and active surveillance is essential for assessing the severity of future virus variants.

**Additional key information:**

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