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Differential IFN genes expression in the upper airways of children and adults

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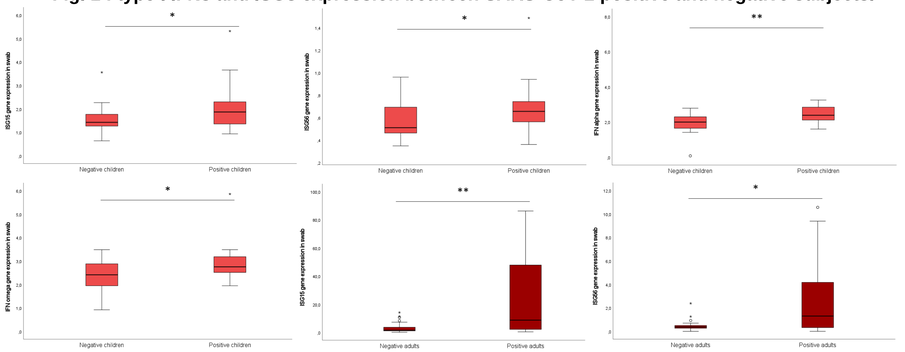
BACKGROUND

An older age, male sex and the presence of comorbidities have been identified as risk factors predisposing to severe COVID-19. Children generally develop a mild disease after SARS-CoV-2 infection. In this context mucosal response may have a key role limiting viral infection to upper airways, resulting in mild symptoms. Indeed, it has been shown (Loske J al., 2021) that higher basal expression of relevant pattern recognition receptors in children may result in a stronger early innate antiviral than in adults. However, how the early interferon (IFN) response differs from that in adults and the role of type-III IFN in these infections is not fully characterized. Hence, we aimed to investigate the expression of several IFN-related genes in nasopharyngeal (NP) cells from children and adults with asymptomatic or mild COVID-19, not requiring hospitalization.

METHODS

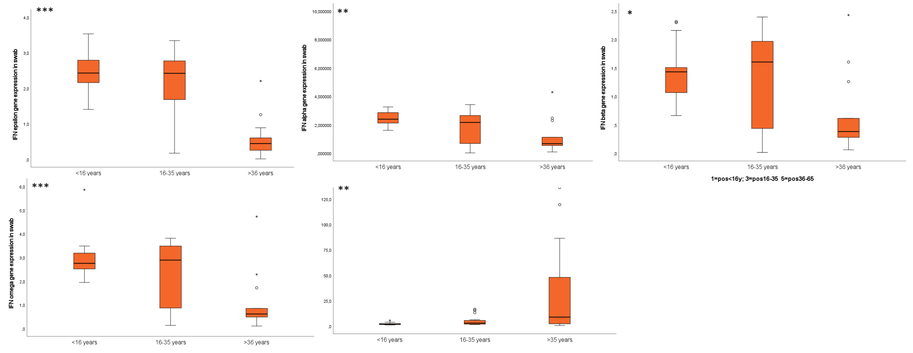
Children and adults attending emergency departments (ED) of Sapienza University Hospital, to perform SARS-CoV-2 molecular tests, were enrolled from November 2020 to February 2021, after informed consent was obtained. RNA from residual NP swabs was purified and quantified and a total of 200 ng were reverse transcribed. Gene expression of genes coding for type I and III IFNs and for the well-known markers of IFNs' activation, ISG15 and ISG56, was measured by exonuclease-based Real time PCR assays with relative quantification to the invariant gene GUS (the 2−ΔCt method). Statistical analysis were performed using SPSS software.

Fig. 1 : type I IFNs and ISGs expression between SARS-CoV-2 positive and negative subjects.



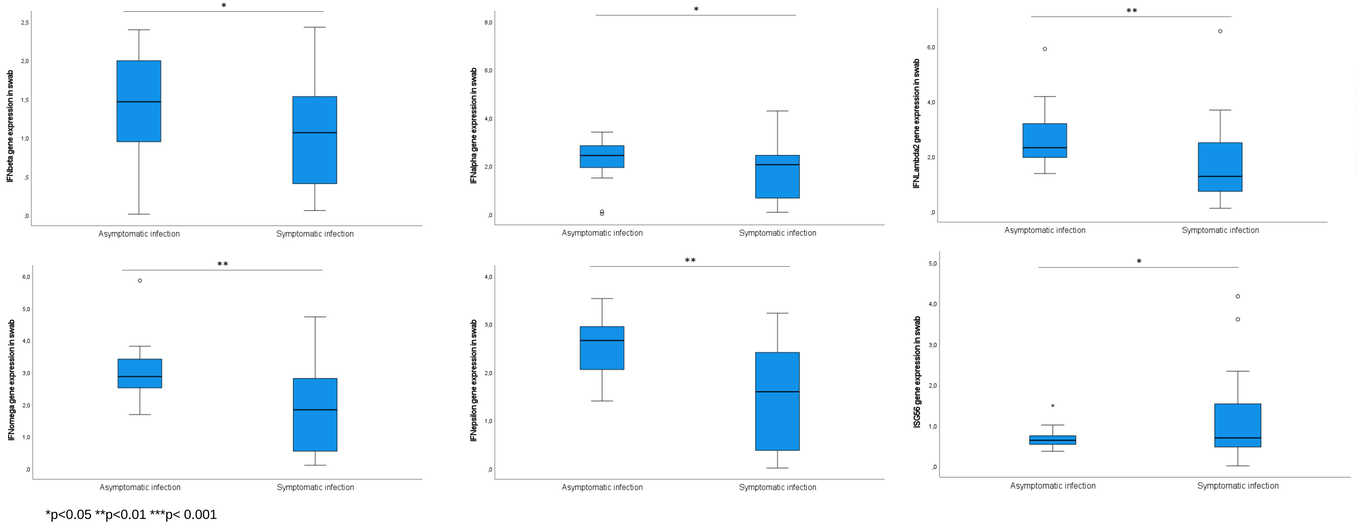
*p<0.05 **p<0.01 ***p< 0.001

Fig. 2 : type I and III IFNs and ISGs expression in SARS-CoV-2 positive between age groups.



*p<0.05 **p<0.01 ***p< 0.001

Fig. : type I and III IFNs and ISGs expression in symptomatic and asymptomatic infections.



*p<0.05 **p<0.01 ***p< 0.001

RESULTS

Residual NP cells from a total of 132 children and adults were included in the study; 56 had SARS-CoV-2 positive results and 76 resulted negative. The expression of all tested genes showed a moderate significant inverse correlation with age, with the exception of ISG15. Participants were further stratified in age groups (< 16; 16-35; 36-65 years) resulting in: 25 SARS-CoV-2 negative and 26-positive children; 14 SARS-CoV-2 negative and 16-positive young adults and 37 SARS-CoV-2 negative and 14-positive adults. In SARS-CoV-2 negative samples, higher levels of all study genes were found in children, while significantly decreasing in young and elderly adults (p<0.05). Positive children showed higher expression of ISG15, ISG56, IFN alpha and IFN omega (p=0.035, p=0.011, p=0.002 and p=0.027 respectively), with respect to negative children (Fig.1). We observed the same trend (Fig.1) in adults for ISG15 and ISG56 expression (p=0.004 and p=0.012 respectively). Among SARS-CoV-2 positive samples (Fig. 2), those from children showed significantly higher levels of IFN alpha, IFN beta, IFN omega IFN epsilon and of IFN lambda2 whereas ISG15 was far more elevated in adults (p=0.002, p=0.013, p<0.001, p<0.001, p<0.001 and p=0.005 respectively). Moreover, 64.4% of children and 44.8% of the adolescents reported asymptomatic infection, while all adults reported mild symptoms. Level of and of IFN alpha, IFN beta, IFN omega IFN epsilon and IFN lambda2, were significantly higher in individuals with no symptoms (Fig.3), whereas ISG15 was elevated in those with a mild COVID-19 (p=0.023, p=0.046, p=0.001, p=0.001, p=0.009 and p=0.047).

CONCLUSIONS

Our results showed a different expression of type I and III IFNs and some ISGs in NP swabs among SARS-CoV-2 positive subjects. We found higher expression of IFNs in younger children and in the asymptomatic infection, while ISG15 showed the opposite trend. The higher baseline expression of IFN-related genes in children may prompt a quicker activation of the IFN response after SARS-CoV-2 infection and contribute to effective control of viral replication; the higher ISG activation in adults may be caused by the inflammatory response and associated to COVID-19 symptoms given that ISGs expression is not only activated by IFN pathway.