

## Adolescent health issues including Precocious Puberty in Covid-19 Pandemic

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During the year 2020, the COVID-19 pandemic rapidly became a global health emergency. In order to control the spread of the novel SARS-CoV-2, many countries implemented extraordinary restrictive measures, such as a strict lockdown/MCO (movement control order) and institution closures. The pandemic had a great impact on children and adolescents' daily life, leading to sedentary lifestyle, to larger use of electronic devices and to an increase in stress-related symptoms. These changes acted as disruptors of children's normal development. Since the beginning of the pandemic, many studies reported an increase in the number of precocious puberty cases in females as well as a faster progression rate of puberty itself, compared to the pre-pandemic years. A significant increase in precocious puberty, rapidly progressive puberty and precocious menarche has been reported since the initial lockdown because of the pandemic, and this could represent a new emergency to be addressed. Covid-19 affects different persons in different ways where majority develop mild to moderate illness and recover without hospitalization and residual effects. But the adolescent health remains a worsening threat to modern society. Central precocious puberty (CPP) during Covid-19 pandemic is a global challenge to existing community as it behaves in a bewildering way with too many ongoing and residual morbidities.

It has been suggested that COVID may have a direct effect in causing Precocious Puberty. Sars-Cov2 binds ACE-II receptors that are abundant in the central nervous system, with neuronal transport, haematogenous and nasal route dissemination via the olfactory bulb, thus explaining one of the typical symptoms of anosmia. GnRH neurons in the hypothalamus share common embryonic origin with the olfactory bulb (OB): case studies have shown that few patients with recent diagnosis of precocious puberty had positive molecular diagnoses for Sars-cov2 infection, and moreover, hypo/anosmia is rare in childhood - the hypothesis of a direct effect of Sars-Cov2 as a trigger of puberty remains unlikely.

But globally lockdown was implemented with gradual relaxation in the in 2022 after widespread Covid Vaccination. This had a great impact on children and adolescents' daily life, leading to sedentary lifestyle, to larger use of electronic devices and to an increase in stress-related symptoms. These changes acted as disruptors of children's normal development. Covid -19 lockdown revealed various atypical findings includes –significant increase(CPP 2.5 fold higher in 2020-2021(5 in 100) compared to 2 in 100 in 2017-2019, P value 0.002) in rate of CPP due to various factors as higher rate of sleep disturbances, sleep breathing disorders, sleep

wave transitional disorder (SWTD), excessive somnolence, no outdoor activities, excessive consumption of junk/fast/processed food and sugar sweetened beverages and excessive exposure to blue light through online classes - all people including children & adolescents adopted significant life style changes. Changes in neurotransmitters, especially serotonin and dopamine, have been described due to increased exposure to digital device environments with reduced amount of exposure to day light and sunlight. Most alarming is the blue light from digital devices which stimulates production of cortisol, catecholamines and ghrelin (hunger hormone). The longer the exposure-the earlier the onset of puberty, children used 6-9 hours in Covid lockdown. Artificial light emitting in blue short wavelength of visible spectrum (446-482nm) has direct effect on Melatonin secretion, alertness level & cognitive performances and this effect is larger on retinal receptors. Long term exposure to blue light upsurges the incidence of CPP and has got detrimental effects on long term behavioural/psychological, sexual and eye health. The increase in BMI due to sedentary lifestyle, has paralleled an increased in indoor life which is associated also with vitamin D deficiency. Some authors found that vitamin D-deficient subjects are more likely to develop CPP. A direct effect of SARS-CoV-2 infection remains a remote hypothesis, both physical and psychological factors related to the pandemic seem to have a role in triggering GnRH pulsatile secretion leading to earlier pubertal onset. It is indeed important to stress the need to clarify the exact role of COVID-19 in early pubertal onset comparing data from all over the world; long-term comprehensive studies are also pivotal to explain whether this phenomenon will continue while we resume pre-pandemic habits. Further studies are warranted to explore whether this phenomenon is confirmed, this would allow to put in place future preventive actions for this ongoing phenomenon and to give advice for future pandemic plans. Furthermore, one needs to study whether the increased frequency of precocious puberty and menarche have psychological effects on final height, body composition, and subsequent quality of life.

Finally, until now the increase in precocious puberty has been observed in females only. It is yet unknown, but an effect in males cannot be excluded.

(Key words, Central Precocious puberty (CPP), GnRH- gonadotropin releasing hormone)