



Nicotinic acetylcholine receptors may induce urinary incontinence in patients with Covid-19

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According to the International Continence Society (ICS), urinary incontinence encompasses any complaint of involuntary urine leakage. Globally, more than 200 million women worldwide have this problem, and its prevalence varies from 2.5 to 8.70 in different regions (Islam et al., 2018). Although urinary incontinence occurs regardless of sex, its prevalence is higher in women and increases with age. It is one of the clinical manifestations of pelvic floor muscle instability, impacting over 50% of women during their lifetime (Aoki et al., 2017). Various etiologies contribute to its onset, including urinary tract or vaginal infections, constipation, medication, lower urinary tract dysfunction, etc. (McAuley et al., 2023). To our knowledge, clinicians have to consider the outbreak of COVID-19 as well.

COVID-19, caused by the acute respiratory syndrome coronavirus 2 (SARS-COV-2), presents with a spectrum of symptoms ranging from mild to severe. Approximately 14% of patients experience such as dyspnea, hypoxia, or extensive lung involvement, while 5% progress to critical symptoms like respiratory failure, shock, or multiple organ dysfunction (Wei et al., 2020). Notably, the virus can target neurons by affecting the central nervous system (CNS), potentially involving acetylcholine and nicotinic acetylcholine receptors (NACHRs) (Carod-Artal, 2020). Acetylcholine plays pivotal roles in various neurological functions and homeostasis, in-

cluding respiratory regulation (Pourfridoni et al., 2021).

Urinary continence relies on the interplay of sympathetic, parasympathetic, and somatic nerves (pudendal). In this letter to the editor, we want to consider the somatic innervation which is associated with the filling phase of the bladder (Thomas, 2011). During this phase, the guarding reflex contracts the external urethral sphincter and pelvic floor muscles via NACHRs and pudendal nerves (Vizzard, 2010). Pudendal neuropathy has been reported in viral infections such as human immunodeficiency virus and herpes zoster (Kaur and Singh, 2020). Pourfridoni et al. recently declared that in patients with COVID-19, neural damage leads to bladder and bowel incontinence due to inflammation and demyelination in the pudendal nerve (Pourfridoni et al., 2021). It is assumed that COVID-19 may interact with NACHRs, as their subunits bear similarities to COVID-19 Spike co-receptors (Dormoy et al., 2022). Therefore, we hypothesized that the occurrence of urinary disorders in patients with COVID-19 could be attributed to this interaction, because it may inhibit the voluntary contraction of the pelvic floor muscles and the external urethral sphincter through the pudendal nerve.

References

Aoki Y, Brown HW, Brubaker L, Cornu JN, Daly JO, Cartwright R. Urinary incontinence in women. *Nat. Rev. Dis.*

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- Primers 2017; 3:1-20. <https://doi.org/10.1038/nrdp.2017.42>
- Carod-Artal FJ. Neurological complications of coronavirus and COVID-19. *Rev Neurol* 2020; 70: 311-322. <https://doi.org/10.33588/rn.7009.2020179>
- Dormoy V, Perotin JM, Gosset P, Maskos U, Polette M, Deslée G. Nicotinic receptors as SARS-CoV-2 spike co-receptors? *Med Hypotheses* 2022; 158: 110741. <https://doi.org/10.1016/j.mehy.2021.110741>
- Islam RM, Bell RJ, Hossain MB, Davis SR. Types of urinary incontinence in bangladeshi women at midlife: Prevalence and risk factors. *Maturitas* 2018; 116: 18-23. <https://doi.org/10.1016/j.maturitas.2018.07.012>
- Kaur J, Singh P. Pudendal nerve entrapment syndrome. Treasure Island, FL; 2020
- McAuley JA, Mahoney AT, Austin MM. Clinical practice guidelines: rehabilitation interventions for urgency urinary incontinence, urinary urgency, and/or urinary frequency in adult women. *The Journal of Women's & Pelvic Health Physical Therapy*. 2023 Oct 1;47(4):217-36. <https://doi.org/10.1097/JWH.0000000000000286>
- Pourfridoni M, Pajokh M, Seyedi F. Bladder and bowel incontinence in COVID-19. *J Med Virol* 2021; 93: 2609-2610. <https://doi.org/10.1002/jmv.26849>
- Thomas S. Pelvic organ dysfunction in neurological disease: Clinical management and rehabilitation. *Ann Indian Acad Neurol* 2011; 14: 321-322. <https://doi.org/10.1007/s00192-011-1539-4>
- Vizzard MA. Spinal interneurons and micturition reflexes: focus on "Characterization of a spinal, urine storage reflex, inhibitory center and its regulation by 5-HT1A receptors in female cats". *Am. J. Physiol. Regul* 2010; 298: R1195-1197. <https://doi.org/10.1152/ajpregu.00127.2010>
- Wei J, Xu H, Xiong J, Shen Q, Fan B, Ye C, et al. Novel coronavirus (COVID-19) pneumonia: serial computed tomography findings. *Korean J Radiol* 2020; 21: 501-504. <https://doi.org/10.3348/kjr.2020.0112>