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CASE REPORT

PERSISTENT HICCUPS IN MEN WITH COVID 19: TWO CASES FROM NIGERIA

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ABSTRACT

Hiccups are defined as extraordinary type of respiratory movement involving a sudden inspiration (intake of air) due to an involuntary contraction of the diaphragm accompanied by closure of the glottis (the vocal apparatus of the larynx). The abrupt inspiration is the result of a sudden contraction of the diaphragm. The classification of hiccups is by their duration. Acute hiccups are of less than 48 hours duration, persistent last over 2 days, and intractable last over a month.

It is a rare but distinct chemosensory presentation of COVID 19 disease and seldomly reported from Africa. We report 2 cases of persistent hiccups in Nigerian men with RT-PCR positive cases of mild COVID-19 disease. Both men (aged 59, 63 years) had associated fever, anosmia and ageusia, with hiccups onset 2-4 days after COVID- 19 diagnosis, and in one case it persisted for 10 days, including for 3 days after SARS-CoV-2 negativity.

Keywords: Hiccups, COVID-19 signs, Nigeria, SARS-CoV-2

INTRODUCTION

Hiccups (singultus) are generated by a reflex arc with phrenic (C3-C5), Vagus and intercostal sympathetic afferents (T6- T12) with central integration at spinal cord C3-C5, and medulla oblongata Dopaminergic neurons, close to the respiratory center and reticular formation, causing efferent phrenic (C3-C5) motor diaphragmatic contractions **[1].** Here we report on two cases of Hiccups seen in COVID-19 patients in Abuja, Nigeria.

Case 1: A 59-year-old man with fever (38^{o}C), headache, cough, dyspnea seen at the Gwagwalada -Abuja quarantine center, who later tested positive for Corona virus disease (COVID -19)by Reverse transcriptase polymerase chain reaction (Rt-PCR) after 3 days of mild illness based on the Sp02 criteria. The RT -PCR test was undertaken at National Center for Disease Control (NCDC) National Reference Laboratory, Gaduwa, Abuja. Hiccups onset was on the 4th day of SARS-CoV-2 positivity, the frequency was roughly 20/minute and lasting a total of 10 days. The hiccups was associated with anosmia/ageusia, anorexia , insomnia, and exacerbated by eating or drinking. The patient received azithromycin, zinc, vitamin D initially . Ivermectin 12mg daily for 5 days was later added, starting after the 2nd day of PCR positive test, after which remarkable clinical improvement occurred, but the hiccups persisted. This constitutes standard of care in Nigeria. The pulse oximetry (SpO2%) was initially 97 and serum creatinine (1.1 mg/dl) and hepatic enzymes were normal .Chlorpromazine 50mg-daily for 3 days was administered to treat the hiccups, but it did not exert any benefit. Patient was not tried on Metoclopramide. Four days after ivermectin dosing commenced, the patient tested negative to SARS-CoV-2 by repeat RT-PCR. He was afebrile, and with SP02% of 99, but the hiccups continued until 3 days after his SARS-CoV-2 PCR negativity. After stoppage of his treatment (he was on ivermectin for five days) and viral clearance at home, his residual symptoms were arthralgia, myalgia and forgetfulness. (Table 1)

Table 1. Table of Laboratory results with reference values.

Case 1	Lab Parameter	Finding	Reference values
	SpO2%	97%	
	Serum creatinine	1.1 mg/dl	
	Liver enzymes		
	ALT Alanine Aminotransferase	34 i.u./l	15-45 i.u/l
	AST Aspartate Transaminase	29i.u.	15-42i.u./l
	Serum Creatinine	93	70-110 umol/l
	Serum Albumin	42	35-50g/l
	Globulin	27g/l	20-40 g/l
	Platelet count	215 x10^{9}/l	100-400 x 10^{9}/l

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Case 2. A 63-year-old man with hiccups of more than 4 days duration, with onset after RT-PCR SARS-CoV -2 positivity. He had mild COVID- 19, with fever, cough anosmia/ageusia. The hiccups frequency was about 1-5 /minute and caused insomnia. He received Vitamin D, azithromycin, Vitamin C but was yet to receive ivermectin, which was not preferred by the attending physician. He self-discharged against medical advice without conversion and was lost to follow up. He promised to seek medical treatment elsewhere. Both cases were seen between December 2020 and February 2021.

DISCUSSION

Persistent hiccups (> 48 hours) has recently been reported atypically in COVID-19 patients [2, 3,4,5.] In the case reported by Prince et al[2] , hiccups was in fact the only presenting symptom. Only a routine X-ray and CT scan showed typical ground glass opacities in the lungs. This suggests that hiccups can be the first presenting sign, and clinicians in the COVID 19 era must have a high index of suspicion in that regard. In the case reported by Bakheet et al, the patient also had fever and sore throat as part of the presenting symptoms. Equally, CT scans revealed typical ground glass appearance and a bloated abdomen. There was no case of hiccups in patients recruited to our recent controlled study of ivermectin in COVID-19 patients seen from May to November in Lagos, Nigeria[6].

Although, racial differences in chemosensory symptoms of COVID-19 are reported globally[7], our new cases which are the first to be published in black Africans, indicate that persistent hiccups is a differential diagnostic symptom for COVID-19 in Nigerians. Both cases were men, aged about 60 years, with hiccups onset after SARS-CoV-2 positivity. Both had fever, cough and associated anosmia/ ageusia with hiccups, indicative of SARS-CoV-2 neurotropism and chemosensory loss. One patient had normal biochemical hepatic and renal functions with persistent and frequent hiccups lasting 10 days, but with no major arterial hypoxemia. His SPO2% was 99 on recovery at home. Significantly, he regained smell and taste sense before , but his hiccups continued for 3 days after SARS-CoV-2 RT- PCR negativity, and he had residual symptoms of arthralgia, myalgia, and amnesia

Since hiccups was not reported in the initial wave of COVID -19, It is not clear if this symptom is SARS -CoV-2-variant-dependent.

CONCLUSION

Persistent hiccups should be sought as COVID-19 chemosensory symptom, in patients suspected of COVID-19 in the tropics, and older men may be more susceptible.

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