Case Report

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Acute hypothermia in a patient with COVID-19: a case report and summary of the evidence

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Introduction and importance: SARS-COV-2 has many presenting signs including a number of typical and atypical symptoms. However, having the enormous capacity of mutation, the virus is changing its genetic pattern continuously, giving rise to newer and rarer manifestations. Here, the authors report a case of adult COVID-19 along with features of hypothermia which is relatively rare and has future implications in clinical perspective.

Case presentation: The patient presented with hypothermia and indicative symptoms of COVID-19 during admission. Comorbidities were assessed, potential differentials were ruled out thorough appropriate clinical examination and investigations. Insulation with a blanket and room heater was used to stabilize the normal body temperature (98.6°F) in the hospital setting, during this period vitals (Blood pressure, Pulse rate and oxygen saturation) were assessed regularly. On the sixth day of hospital admission, he was discharged from the hospital with advice.

Clinical discussion: COVID-19 virus can enter into brain through olfactory tract and may cause dysfunction in the medial preoptic area of the hypothalamus containing warm sensitive neurons directly or via cytokine-induced release of prostaglandin E2 from endothelial cells, which acts through a paracrine mechanism that may provoke hypothermia in our case.

Conclusions: This case highlights a rare presentation of COVID-19 infection that has not been thoroughly explored. The authors believe the case report holds particular importance especially in dealing with COVID-19 cases in both clinical and home settings.

Keywords: Case Report, COVID-19, hypothermia, SARS-CoV-2, temperature, viral infections

Introduction

COVID-19 is a newly emerged coronavirus which is spread primarily through droplets of saliva or discharge from the nose when an infected person coughs and sneezes. The WHO reported that all people can be affected by COVID-19 which may cause fever, dry cough, tiredness (most common symptoms), body ache, sore throat, conjunctivitis, diarrhoea, loss of taste or smell sensation and chest pain (less common and serious symptoms) and along with other clinical symptoms, fever, cough and myalgia are the main clinical symptoms according to meta-analysis[1].

HIGHLIGHTS

- Novel hypothermic presentation of COVID-19 infection.
- Hypothermia can be an emerging emergency in COVID-19.
- Temperature Dysregulation is still uncharted territory for COVID-19 variants.

Hypothermia (decreased core body temperature below 95°F) is a rare condition reported to be associated with COVID-19[2]. Factors, such as exposure to extreme cold, alcohol use, hypoglycemia, poor clothing, extreme age, and chronic medical conditions (hypothyroidism and sepsis), may trigger hypothermia[2,3]. A study mentioned that every year, ~1500 people die due to hypothermia in the United States[4,5], which is less common in a country like Bangladesh due to its humid and warm climate. Older people may harbour the potential for developing hypothermia during a COVID-19 infection although it is still illusive. Therefore, it is necessary to depict the relationship between hypothermia and COVID-19. We believe the reported case will highlight and address the knowledge gap for clinicians, proving helpful for clinical management of hypothermia during COVID-19.

Case presentation

A 28-year-old man with bronchial asthma visited to the outdoor patient department with history of fever (axillary temperature was 100.5°F, measured by contact digital thermometer). He had experienced generalized weakness for 5 days, shortness of breath

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for 1 day and feeling of severe cold for the last 2 days. He did not have a dry cough, sore throat, loss of smell and taste, headache, body ache, abdominal pain, diarrhoea, burning micturition, or any other bleeding manifestation. Following the initial symptoms, he visited the nearest healthcare centre where an real-time polymerase chain reaction (RT-PCR) for COVID-19 test was performed on nasopharyngeal swab, confirming a positive result. and found positive. The patient had a history of bronchial asthma with adequate control but no history of chest pain, palpitations, orthopnea or paroxysmal nocturnal dyspnoea. On inquiry, he gave no current use of smoking or alcoholism except a history of smoking 5–6 years back. He also added that, he had no professional, personal, accidental or outdoor activities related to exposure to cold environment and he had no history of prolong standing in cold environment or wind chills and wearing of wet clothes. With all of the complaints above, the patient got himself admitted into the hospital.

During admission, the conscious and oriented patient had a pulse of 85 beats/min, blood pressure (BP) of 110/80 mm (Hg), respiratory rate (RR) of 20 breaths/min, oral temperature of 94.5°F which was measured three times at 5 min interval by contact digital thermometer (Getwell Digital Thermometer) and every time, it was constant. His oxygen saturation (SpO2) was 97% in room air. After resuscitation, the patient was moved to the COVID-19 isolation cabin at the hospital, insulated with a warming blanket, and advised to undergo laboratory and radiological investigations. Oral temperature was recorded three times per using a digital contact thermometer, and vitals were also assessed daily for follow-up.

On laboratory investigations, the haematological and biochemical report for the blood and urine tests showed no abnormalities. Renal and liver function test, coagulation profile and immunological tests were also normal. The serum creatinine level was 0.41 mg/dl and Serum sodium, potassium, chloride, and bicarbonate was 137, 3.66, 104 and 20 mmol/l, respectively, with an Anion gap 16.66 mmol/l. SGPT was 44 U/l, and serum bilirubin was 1.21 mg/dl (Table 1). To exclude a hypothalamic lesion that may be responsible for decreased body temperature, an MRI of the brain was performed and found no abnormalities. Serum procalcitonin (0.01 μmol/l), C-reactive protein (1 mg/dl), erythrocyte sedimentation rate (ESR) (22 mm/1st h) and D-dimer (250 μg/l FEU), were within the physiological limit (Table 1). However, in our patient, hypothermia was observed during the conservative treatment while staying at home and after admitting into hospital. The temperature was assessed at morning (9 am), afternoon (2.30 pm), and night (11 pm) on each day which as, respectively, 97°F, 95°F, 95°F on day 1, 97°F, 97°F, 96.5°F on day 2; 96°F, 97°F, 98°F on day 3, on day 4 it was 98°F, 98°F, 98.6°F and on day 5 it was 98°F, 98.2°F, 98.6°F and on day 6 (morning), the temperature was 98.6 °F and the patient was thermally stable. The pulse rate and blood pressure were within the physiological limit throughout the entire follow-up period though the blood pressure was initially swinging but the patient was hemodynamically stable after fourth day following admission (Fig. 1B). The oxygen saturation was assessed daily during the follow-up period and it was found normal (Fig. 1C). In our case, there were no classical symptoms of cardiac chest pain, basal crackles, and oedema was not noted anywhere during the follow-up period. The electrocardiogram (ECG) findings as well as chest X-ray findings were also normal. So, the patient was diagnosed as a case of COVID-19 pneumonia with hypothermia with a history of bronchial asthma. The patient was treated with Inj. Ceftriaxone and Inj. Remdesivir, Inj. Enoxaparin sodium, and intravenous administration of Dexamethasone sodium phosphate according to his body weight for 5 days. Oral levofloxacin and other symptomatic drugs were also used based on best clinical judgement. A consecutive 5-day follow-up was performed which showed that the patient was hypothermic up to the third day of follow-up. On the fourth day, the patient was almost thermostable and recovered completely from temperature instability. On the fifth day of admission. All vitals gradually improved and found within physiological limit in subsequent follow-up.

Table 1

Laboratory investigations of the patient

Name of the investigation	Unit	Result value	Reference value (adult male)
Total red blood cell	/μl	6.3×10^6	4.5–5.5
Haemoglobin	gm/dl	12.2	13–18
Haematocrit	%	38.7	40–54
Mean corpuscular volume	fl	61.9	76–94
Mean corpuscular haemoglobin	pg	19.5	27–32
Mean corpuscular haemoglobin concentration	gm/dl	31.5	31–35
Red cell distribution width	%	14.8	11–14
Total platelet count	/μl	210×10^3	$150–450\times10^3$
Total white blood cell count	/μl	6.3×10^3	4–11
Neutrophil	%	85.8	40–75
Lymphocyte	%	10.9	20–50
Monocyte	%	2.5	2–10
Eosinophil	%	0	1–6
Basophil	%	0	< 0.1
Immunoglobin E (IgE)	%	0.8	0–0.6
Erythrocyte sedimentation rate	mm/1st hour	22	< 29
C-reactive protein	mg/l	1	< 5
S. Sodium (Na +)	mmol/l	137	136–145
S. Potassium (K +)	mmol/l	3.66	3.5–5.1
S. Chlorine (Cl −)	mmol/l	104	98–107
S. bicarbonate (HCO3 −)	mmol/l	20	21–24
Anion gap	mmol/l	16.06	21–31
S. Procalcitonin	mmol/l	0.01	< 0.1
S. Bilirubin	mg/dl	1.2	0.3–1.2
Serum glutamic pyruvic transferase	U/l	44	upto 55
S. Creatinine	mg/dl	0.41	0.72–1.25
estimated glomerular filtration rate	ml/min/ $1.73m^2$	> 60	> 55 (normal)
D-dimer	μg/l FEU	250	0–550
Thyroid stimulating hormone	μlU/ml	1.15	0.35–4.94
S. Ferritin	μg/l	378	20–300
Blood for culture and sensitivity	No growth of microorganism		

Discussion

COVID-19 mainly affects the respiratory system and may manifest complications, such as- pneumonia, hypoxemic respiratory failure/acute respiratory distress syndrome (ARDS), diffuse alveolar damage and fibrosis. It also causes cardiovascular system (CVS) complications, that is myocardial injury, myocarditis, acute myocardial infarction, heart failure, dysrhythmias, and

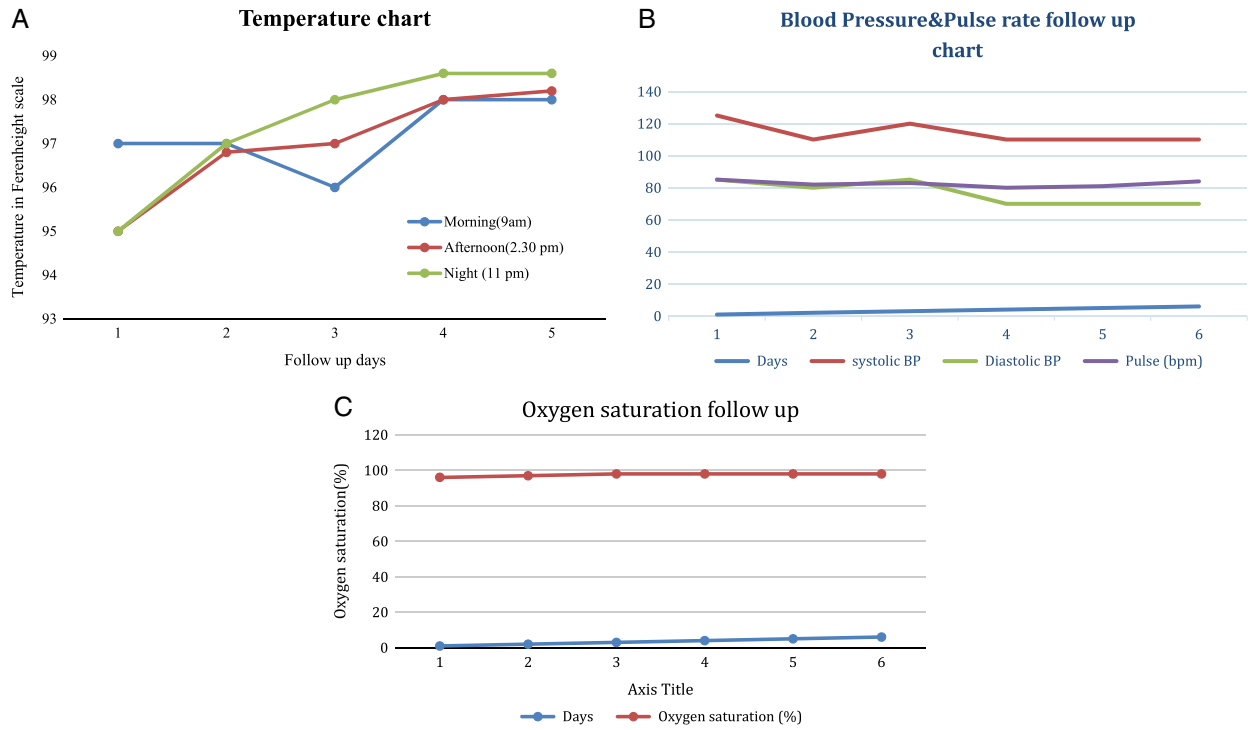

Figure 1. (A) Follow-up temperature values from admission. (B) Follow-up blood pressure and pulse rate from admission. (C) Follow-up oxygen saturation from admission. BP, blood pressure.

venous thromboembolic events[6]; hepatic complications, that is liver injury through systemic inflammatory response syndrome (SIRS), cytokine storms, ischaemia-reperfusion injury, and even hepatocytes can be attacked directly by underlying liver disease via ACE2[7]; renal complications, including worsening of preexisting chronic kidney disease (CKD) and end-stage kidney disease and acute kidney injury[8]; neurological complications, including encephalopathy, encephalitis, stroke, epileptic seizures, rhabdomyolysis, Guillain–Barre Syndrome, and haemorrhagic encephalitis[9]; thromboembolic complications[10], venous thromboembolism, disseminated intravascular coagulation (DIC), and thrombosis[11]. In our case, there were no classical symptoms of cardiac chest pain, no basal crackles or oedema. ECG findings, as well as chest X-ray findings, exclude cardiac complications. The serum creatinine level, estimated glomerular filtration rate, and serum electrolyte findings suggested no renal complications. Serum glutamic pyruvic transferase and serum bilirubin indicate no hepatic complications. MRI of the brain revealed no abnormalities, and the procalcitonin as well as c-reactive protein and ESR (22 mm/1st h) were also normal, which suggested no neural complications or systemic inflammatory storms. The D-dimer level of the patient was within the normal range, suggesting no thromboembolic complications. However, our patient experienced a feeling of cold during conservative COVID-19 treatment at home. After admission to the hospital, the temperature was assessed in the morning (9 am), afternoon (2.30 pm), and night (11 pm), which was fluctuating during the follow-up period. This course of thermostatic imbalance during COVID-19 may provide new insight into the correlation of hypothermia and COVID-19 infections. A few studies have reported on this new insight, addressing mild hypothermia as a life-saving therapeutic in the case of critically ill ventilated patients with ARDS and refractory hypoxaemia[12]. However, the HRCT findings of our patient showed no abnormality, SpO_2 was consistently greater than 95%, the inflammatory biomarkers (C-reactive protein, procalcitonin, and ferritin) level were within the physiological limit, and the patient's history does not support the development of ARDS or refractory hypoxaemia. Apart from this, our patient exhibit a neutrophil level 85% and lymphocyte level 10.9%, resulting a low NLR. A higher NLR may be associated with the severity of COVID progression in the human body[13]. However, the exact mechanism of hypothermia in COVID-19 patients is not well understood yet, acute hypothermia was observed in a patient with covid-19 even without fever in a study[2]. A hypothesis suggests that there is a chance of SARS-CoV-2 entering into the central nervous system through direct invasion or reactive inflammation with olfactory tracts as a port of entry. In central nervous system (CNS), hypothalamus and its surrounding regions have some special proteins such as—angiotensin converting enzyme (ACE), transmembrane proteinase,serine-2 and all of these mediate the entry of SARS-CoV-2 and our case supports this hypothesis, indicating that COVID-19 may cause dysfunction in the medial preoptic area of the hypothalamus containing warm sensitive neurons directly or via cytokine-induced release of prostaglandin E2 from endothelial cells, which acts through a paracrine mechanism that may provoke hypothermia in our case[14]. Similarly, the ability of human corona virus to affect the CNS after inhalation in mice in 2004 was reported by St Jean[15] where viral antigens were detected in olfactory bulb upon infection 3 days later, absence of virus in perivascular blood cells or any other part of brain. In our case, the patient had no history of alcohol, barbiturate, or benzodiazepine intake, the patients was not in the category of extreme age group, he had no history of exposure to cold environment, no history of

prolonged starvation or excessive workload or taking excessive amount of anti-diabetic drug, the patient did not complain any history of cold intolerance, constipation, husky voice and weight gain. MRI findings did not indicate haemorrhagic or ischaemic stroke, ECG findings did not support ventricular tachycardia or ventricular fibrillation. Sepsis and hypothyroidism could be important possible reasons of hypothermia in our case but, the blood culture was negative, predicting that no bacterial/fungal infection related to our case that could be a potential risk for sepsis. Thyroid stimulating hormone was normal in this case, which scuppers the chance of hypothermia development due to hypothyroidism. So, in this case, hypothermia may be a potential factor related to COVID-19 as it has strong potential to enter into CNS via olfactory bulb[15], and if kept unmanaged, death may result from cardiovascular complications, including atrial and ventricular arrhythmia, asystole, and ventricular fibrillation, along with progressive depression of CNS activity.

Conclusions

Our study highlights the potential relationship between hypothermia and COVID-19, However, hypothermia associated with COVID-19 has not been addressed clearly anywhere, and there is no indication or management protocol for hypothermia in hospital or domestic settings in the "National COVID-19 Guidelines of Bangladesh". Therefore, the present study aims to bring attention to clinical significance of this uncommon condition (hypothermia) of COVID-19 infection for clinicians and policymakers.

Limitation

Due to social constraints and conventional clinical practices in temperature measurement of patients seeking healthcare attention at hospitals of Bangladesh, the rectal core temperature was not assessed for during diagnosis of hypothermia. Additionally, the acceptable margin of error for digital contact thermometer as specified by manufacturer company was not known to authors.

Ethics approval and consent to participate

Informed written consent was taken from the participant.

Consent for publication

The author agreed to publish the article by written consent.

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Author contribution

Conceptualization: A.S.J. Formal analysis: A.S.J., M.R. Investigation: A.S.J., A.B.M.K.H., J.H. Methodology: A.S.J., A.B.M.K.H., J.H. Resources: A.S.J., A.B.M.K.H., J.H. Supervision: A.B.M.K.H., J.H., M.R. Writing—original draft: A.S.J., M.R. Writing—review and editing: A.S.J., M.R.

Conflicts of interest disclosure

The authors declare that they have no competing interest.

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Availability of data and material

Data and materials will be available based upon reasonable request to corresponding author.

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My paper was not invited by-review.

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