ORIGINAL ARTICLE

Journal of the ASEAN Federation of Endocrine Societies

Hypothalamic-Pituitary-Adrenal Axis Activity in SARS-CoV-2 Infected Noncritically Ill Hospitalized Patients

Hurjahan Banu,[1] Nusrat Sultana,[1] Md Shahed Morshed,[2] MA Hasanat,[1] Ahmed Abu Saleh,[3] Shohael Mahmud Arafat[4]

[1]*Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh*
[2]*Emergency Medical Officer, Kurmitola General Hospital, Dhaka, Bangladesh*
[3]*Department of Microbiology and Immunology, BSMMU, Shahbag, Dhaka, Bangladesh*
[4]*Department of Internal Medicine, BSMMU, Shahbag, Dhaka, Bangladesh*

Abstract

Objectives. This study determined the baseline hypothalamic-pituitary-adrenal axis hormonal levels and their associated factors in noncritically ill hospitalized patients with coronavirus disease 2019 (COVID-19).

Methodology. This cross-sectional study was carried out in 91 noncritical RT-PCR-confirmed COVID-19 patients (aged 18 to 65 years) recruited consecutively from the COVID unit of two tertiary care hospitals over a period of six months. After the screening, relevant history and physical examinations were done, and blood was drawn between 07:00 am to 09:00 am in a fasting state to measure serum cortisol and plasma adrenocorticotropic hormone (ACTH) by chemiluminescent microparticle immunoassay.

Results. Of 91 patients, 54, 26, and 11 had mild, moderate, and severe COVID-19, respectively. Median values of serum cortisol (p = 0.057) and plasma ACTH (p = 0.910) were statistically similar among the severity groups. Considering a cortisol cut-off of 276 nmol/L (<10 µg/dL), the highest percent of adrenal insufficiency was present in severe (27.3%), followed by mild (25.9%) and least in the moderate (3.8%) COVID-19 cases. Using the cortisol/ACTH ratio >15, only 6.6% had enough reserve.

Conclusions. The adrenocortical response was compromised in a significant percentage of noncritically ill hospitalized patients with COVID-19, with the highest percentage of adrenal insufficiency present in severely infected cases. The HPA axis parameters of serum cortisol, plasma ACTH and cortisol/ACTH were similar across the severity of noncritical patients with COVID-19.

Key words: hypothalamic-pituitary-adrenal axis, cortisol, ACTH, SARS-CoV-2, coronavirus disease 2019

INTRODUCTION

Cortisol and adrenocorticotrophic hormones (ACTH) are under the control of hypothalamic–pituitary–adrenal (HPA) axis that maintains the adaptive changes in metabolism, cardiovascular function, and immune-modulation.[1] Any stress can increase the secretion of cortisol hormone.[1,2] Following the severe acute respiratory syndrome coronavirus (SARS-CoV) pandemic in 2003, researchers observed that the virus may affect both the hypothalamus and pituitary glands in addition to other endocrine glands.[3,4] The genome of SARS-CoV-2 is 80% identical to that of SARS-CoV-1, and both viruses produce comparable clinical signs.[4] Angiotensin-converting enzyme 2 (ACE2) receptors are abundant in the tissues of the endocrine glands and have been identified as the domain of SARS-CoV-2 infection.[5] So, it has been proposed that SARS-CoV-2 infection might lead to hormonal problems. Specifically, the HPA axis function may be affected in two ways: (i) Directly through viral invasion and cell destruction; and (ii) Indirectly through increased cytokine production and action.[6] Furthermore, a few cases of pituitary infarction with SARS-CoV-2 infection have been reported recently.[7] The immune response and viral gene expression are responsible for the formation of viral proteins which have an impact on the HPA axis function. The adrenal glands may become temporarily or permanently dysfunctional as a result of these disease processes.[8,9] The factors that influence severity and death during the coronavirus disease 2019 (COVID-19) are still unknown.[10] This study

eISSN 2308-118x (Online)
Printed in the Philippines

Received: November 29, 2022. Accepted: January 13, 2023.
Published online first: July 3, 2023.
https://doi.org/10.15605/jafes.038.02.04

Corresponding author: Hurjahan Banu, FCPS (EM)
Medical Officer, Department of Endocrinology
Bangabandhu Sheikh Mujib Medical University
Shahbag, Dhaka-1000, Bangladesh
Tel. No.: 8612550-4, 8614545-9
Fax No.: +880-2-8624817
E-mail: dr.hurjahan_banu@yahoo.com
ORCiD: https://orcid.org/0000-0002-8115-1761

was designed to determine the baseline HPA axis hormonal levels in COVID-19 patients who were acutely unwell, as well as identify any associated factors that would have an impact on that determination.

METHODOLOGY

This cross-sectional study was done in the COVID-19 unit of two tertiary care hospitals from September 2021 to February 2022 after receiving ethical approval from the Institutional Review Board of a university. Informed written consent was taken from each participant. The sample size was calculated from a similar study taking into consideration a 95% confidence interval (Z = 1.96), the prevalence of adrenal insufficiency (p = 0.643), and a 10% margin of error (d = 0.1), and applying the following formula ($n = Z^2pq/d^2$).[11] The minimum sample size was computed at 88. The study was able to include a total of 91 noncritical adult patients aged 18 to 65 years with reverse transcription-polymerase chain reaction (RT-PCR) confirmed COVID-19 within 48 hours of viral detection. Exclusion criteria were: critical COVID-19, pregnancy, known chronic disorders affecting cortisol levels e.g., known case of Addison's disease or Cushing syndrome, chronic kidney disease, chronic liver disease, malignancy or any other diseases affecting the HPA axis, receiving steroids in any form in the last 3 months, oral contraceptive pill intake in the last 3 months and serum albumin <2.0 g/dL.

History (socio-demographic characteristics and symptoms) was taken and relevant vital signs and physical examinations (height, weight, pulse rate, respiratory rate, oxygen saturation, and blood pressure) were done. Initial investigations (complete blood count, electrolytes, C-reactive protein, and D-dimer) on admission were checked and all were recorded in a semi-structured questionnaire. To measure serum cortisol and plasma ACTH, blood was drawn by venipuncture before receiving any form of steroid between 07:00 am to 09:00 am, in a fasting state, via chemiluminescent microparticle immunoassay (Siemens, USA). For measurement of ACTH, blood was transported to the laboratory on ice and centrifuged at 4°C within 15 minutes of collection.

Diagnosis and classification of COVID-19 (mild, moderate, and severe) were done according to the World Health Organization's interim guidance (WHO, 2020).[12] To identify adrenal insufficiency (AI) during acute illness, different researchers have proposed different cut-offs for serum cortisol levels (15 μg/dL and 18 μg/dL by two authorities).[13,14] As no definite cut-off is decided, we considered 276 nmol/L (~10 μg/dL) as the cut-off for this study. To calculate the cortisol/ACTH ratio, serum cortisol (nmol/L) was divided by plasma ACTH (pg/mL converted to pmol/L by multiplying with 3.67).

Data were expressed in mean ± SD or median (inter-quartile range, IQR) or frequencies (percent, %). Association between two groups was analyzed by the independent samples t-test or Mann-Whitney U test, while Kruskal-Wallis one-way ANOVA test was employed for more than two groups. For qualitative variables, Pearson's chi-square test was done. Spearman's correlation test was done to determine the correlation of cortisol and cortisol/ACTH ratio with different clinical and biochemical variables. Statistical significance was considered with p-values below 0.05. Data were analyzed using SPSS software version 22.0.

RESULTS

Among 91 noncritical hospitalized patients with COVID-19, 37 (40.7%) were males and 54 (59.3%) were female. Fifty-four (59.3%), 26 (28.6%), and 11 (12.1%) patients had mild, moderate, and severe disease respectively. Only six participants (6.6%) had a sufficient reserve, defined as a cortisol/ACTH ratio greater than 15, 62 patients (62.81%) had a ratio between 3 and 15, and 25 patients (25.3%) had a ratio below 3.

The frequency of patients with serum cortisol <100 nmol/L, 100 to <200 nmol/L, 200 to <300 nmol/L, 300-350 nmol/L, and >550 nmol/L were seven (7.7%), four (4.4%), eight (8.8%), 41 (45.1%), and 31 (34%), respectively (Figure 1). Serum cortisol (p = 0.057), plasma ACTH (p = 0.910), and cortisol/ACTH (p = 0.206) were statistically similar across the severity of noncritical patients with COVID-19 (Table 1).

Considering the cortisol cut-off of 276 nmol/L (~10 μg/dL), a total of 18 out of the 91 patients (19.78%) had AI. When grouped according to the severity of COVID-19, 25.9% (14/54) of those with mild COVID had AI, 3.8% (1/26) in the moderate group, and 27.3% (3/11) in severe cases. The adrenal reserve was found to be similar among the study groups (p = 0.054) (Figure 2). All except one of these patients had plasma ACTH within the normal range (min: 5.1 pmol/L, max: 48.20 pmol/L, upper limit of normal: 46 pmol/L).

Using a serum cortisol cut-off of 15 μg/dL (~413.85 nmol/L), 39 (42.86%) had inadequate cortisol reserve. The patient group with the highest percentage of inadequate reserve was in the mild group (27, 50%), followed by the severe group (4, 36.4%) and, lastly, in the moderate group (8, 30.8%) of COVID-19.

Table 1. Comparison of serum cortisol, plasma ACTH levels, and Cortisol/ACTH ratio with disease severity of noncritical COVID-19 patients (n = 91)

Hormones	Reference values	Mild (n = 54)	Moderate (n = 26)	Severe (n = 11)	*p*
Serum cortisol, nmol/L	138-690	417.50 (271.55-576.30)	521.50 (376.25-769.75)	514.0 (210.50-677.0)	0.057
Plasma ACTH, pg/mL	Not detectable to 46	22.60 (15.35-32.77)	24.1 (14.25-34.50)	19.90 (13.80-37.80)	0.910
Cortisol: ACTH ratio	>15	4.45 (2.92, 6.50)	4.95 (3.92, 11.10)	3.70 (2.13, 8.40)	0.206

Kruskal Wallis one-way ANOVA test was done

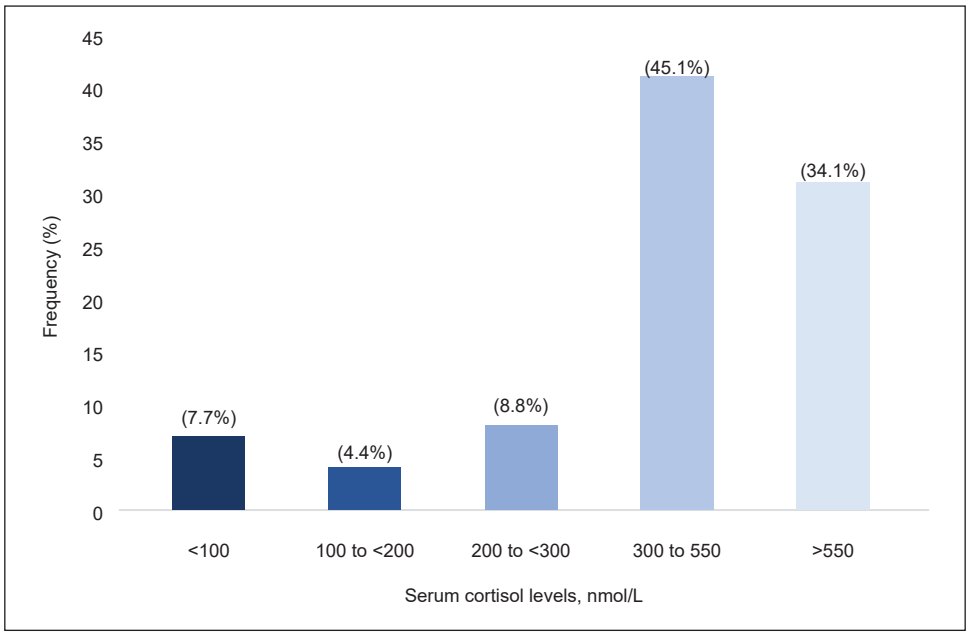
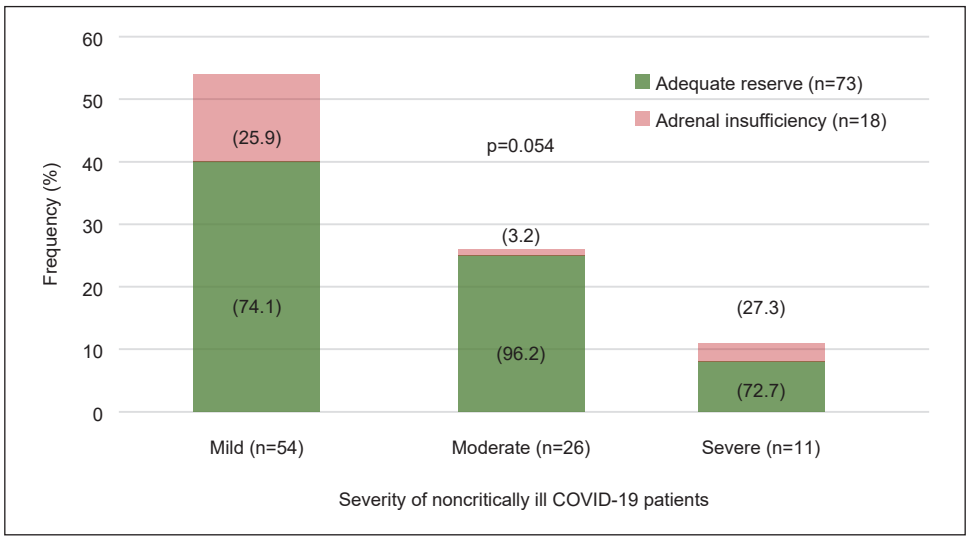


Figure 1. Stratification of the study population according to cortisol levels (n = 91).



*Cortisol reserve (cut off of 10 µg/dL = 276 nmol/L). Pearson's chi-square test was done

Figure 2. Cortisol reserve status of the study population with the severity of noncritical COVID-19 patients (n = 91).

Among all of the clinical manifestations, the prevalence of diabetes mellitus was significantly lower in patients with AI than in those with adequate cortisol reserve (11.1% vs. 47.9%, p = 0.006). The age of the participants with AI was significantly lower (40.28 ± 15.02 vs. 49.11 ± 14.52, years, p = 0.024) than those with adequate reserve. Among the different laboratory investigations, only plasma ACTH (16.59 ± 11.12 vs. 31.51 ± 23.82, pg/mL, p = 0.012) was significantly lower in patients with AI than those having adequate cortisol reserve (Table 2).

Serum cortisol had significant positive correlations with serum creatinine (r = 0.324, p = 0.018), serum ferritin (r = 0.398, p = 0.015), and plasma ACTH (r = 0.306, p = 0.003) in the study population. On the other hand, the serum cortisol/ACTH ratio had a significant negative correlation with age (r = -0.208, p = 0.048), serum creatinine (r = -0.357, p = 0.009), serum CRP (r = -0.302, p = 0.035) and serum ferritin (r = -0.528, p = 0.009) (Table 3).

DISCUSSION

The SARS-CoV-2 virus is a novel pathogen that has rapidly spread over the world since March 2020.[15] It is still unclear which factors contributed to COVID-19's severity and fatality. Unidentified primary and secondary AI may be a causative factor in the elevated fatality rates linked to COVID-19.[16] The blood cortisol cut-off in the present

Table 2. Comparison of clinical and laboratory profiles of the study population with different cortisol reserve statuses (cut-off of 10 µg/dL)

Variables	Adrenal insufficiency n = 18 (19.8%)	Adequate reserve n = 73 (80.2%)	*p*
Age, years	40.28 ± 15.02	49.11 ± 14.52	**0.024**
Sex: female	11 (61.1)	43 (58.9)	0.864
Diabetes mellitus	2 (11.1)	35 (47.9)	**0.006**
BMI, kg/m^2	22.97 ± 3.95	24.67 ± 6.31 [70]	0.282
Systolic BP, mm-Hg	124.06 ± 17.76	125.06 ± 23.58	0.874
Diastolic BP, mm-Hg	82.31 ± 10.73	79.15 ± 14.04	0.402
Neutrophil/lymphocyte ratio	3.21 (2.37-7.61) [15]	3.42 (2.17-7.91) [63]	0.712
Platelet/lymphocyte ratio	130.49 (70.34-196.01) [15]	127.83 (90.48-200.49) [63]	0.958
Na^+, mmol/L	134.0 ± 4.11 [8]	133.93 ± 6.46 [51]	0.977
S. K^+, mmol/L	4.31 ± 1.01 [8]	4.04 ± 0.81 [51]	0.401
S. ALT, U/L	51.29 ± 36.69 [7]	51.08 ± 38.14 [24]	0.990
S. Creatinine, mg/dL	0.78 ± 0.27 [8]	1.06 ± 0.47 [45]	0.107
S. CRP, mg/L	36.25 (5.53-110.55) [8]	25.0 (10.0-77.05) [41]	0.700
S. D-dimer, mg/L	0.68 (0.12-3.60) [9]	0.63 (0.21-2.81) [48]	0.895
S. Ferritin, ng/mL	274.90 (117.30-612.70) [6]	473.20 (140.0-624.40) [31]	0.615
ACTH, pg/mL	16.59 ± 11.12	31.51 ± 23.82	**0.012**

BMI (body mass index), BP (blood pressure), CRP (C-reactive protein), ACTH (adrenocorticotropic hormone)
Data were expressed in mean±SD or median (IQR) or frequency (%); [available no. in case of missing data]
Independent samples t-test or Mann-Whitney U test or Pearson's chi-square/ Fisher's exact test was done as appropriate

Table 3. Correlations of serum cortisol and cortisol/ACTH ratio with clinical and biochemical variables in the study population

Determinants of 'r'	Available no.	Cortisol		Cortisol/ACTH ratio	
		r_s	*p*	r_s	*p*
Age, years	91	0.161	0.128	-0.208	**0.048**
BMI, kg/m^2	88	-0.063	0.561	0.104	0.333
Systolic BP, mm-Hg	83	0.051	0.648	0.002	0.989
Diastolic BP, mm-Hg		-0.063	0.570	0.137	0.218
Neutrophil/lymphocyte ratio	78	0.204	0.076	0.031	0.788
Platelet/lymphocyte ratio		0.231	**0.043**	-0.012	0.916
S. Na^+, mmol/L	59	-0.083	0.531	0.176	0.181
S. K^+, mmol/L		0.028	0.831	0.082	0.539
S. ALT, U/L	31	0.228	0.218	-0.336	0.065
S. Creatinine, mg/dL	53	0.324	**0.018**	-0.357	**0.009**
S. C-reactive protein, mg/L	49	0.175	0.229	-0.302	0.035
S. D-dimer, mg/L	57	0.136	0.314	-0.009	0.948
S. Ferritin, ng/mL	37	0.398	**0.015**	-0.528	**<0.001**
P. ACTH, pg/mL	91	0.306	**0.003**	–	–

Spearman's correlation test was done

study was chosen at 276 nmol/L, whereby 18 individuals (19.78%) were diagnosed with AI. Around 25.9%, 3.8%, and 27.3% of them had mild, moderate, and severe COVID-19, respectively. There is no consensus on the diagnosis of AI in acutely ill patients and various studies used different cut-offs. An Indian cross-sectional study that used the cut-off value for blood cortisol at 138 nmol/L found that 23% of their COVID-19-affected individuals had AI and 88% had mild COVID infection.[17] If we used serum cortisol cut-off at 413.85 nmol/L, 39 (42.86%) patients in the current study showed insufficient cortisol reserve. In a comparable trial conducted in Cameroon, more than 80% of the patients exhibited an insufficient adrenal response to acute COVID-19 stress.[18] Whereas, according to Alzahrani et al., 60% of their patients had average cortisol levels below 300 nmol/L.[11]

In our study, AI was not related to the degree of severity of noncritical COVID-19 infection. Most of the studies found AI in mild cases than severely affected ones. In this study, mildly and severely affected persons with COVID-19 had nearly worse adrenal reserves than the moderately affected ones. Conventional ACTH stimulation test would have provided additional assistance in clearly recognizing AI. Kumar et al. found AI even after post-ACTH stimulation and most of their participants were mildly affected.[17]

According to one hypothesis, SARS-CoV produces an amino acid sequence that has molecular similarities with ACTH, and as a result, antibodies which developed against ACTH can inhibit the stress-induced host's cortisol response.[19] Most of our patients had plasma ACTH levels within the normal range, albeit the AI group had significantly lower levels than the normal reserve group, and showed a positive correlation with blood cortisol. This result is similar to the findings of two prior cross-sectional studies in which secondary AI was suspected.[11,18] In contrast, Gu et al., in another study, found that patients with COVID-19 had greater ACTH levels than healthy controls.[20]

The cortisol/ACTH ratio is a promising diagnostic test for primary hypoadrenalism. Lee et al. found this ratio to be safer and more convenient than the Synacthen test. They classified HPA axis status by cut-offs of 3 and 15 to define primary hypoadrenalism, secondary hypoadrenalism, and normal adrenal function respectively.[21] In the current study, more than 60% of the participants showed a cortisol/ACTH ratio between 3 and 15 indicative of secondary AI and only six persons had a ratio of more than 15. About 20% of our study participants showed baseline low serum cortisol and low normal ACTH indicating secondary AI, which is consistent with the cortisol/ACTH ratio results.

To diagnose AI, several biochemical factors are evaluated singly or in combination. Some researchers use baseline blood levels of hormones released by the adrenal cortex, whereas others use the dynamic assessment of adrenal response to typical stimuli. Among the dynamic tests, the ACTH stimulation test is commonly used. Whether the 1-μg or 250-μg ACTH stimulation test is more effective in the diagnosis of AI in non-critically ill patients is debatable.[22] We could not perform dynamic tests on any patients due to infection control precautions. However, many of our participants received steroids within a few days after being diagnosed with COVID-19, and repeat hormonal testing after recovery was difficult. Patients in the ICU were not included in our study since they had various additional confounders that may impair their adrenal function. Other limitations include the cross-sectional nature of the study design, a single measurement of ACTH, and the inability to measure cortisol binding globulin which might confound our results.

CONCLUSIONS

The absence of a significant increase in serum cortisol and low normal ACTH during acute COVID-19 infection was seen in a group of noncritically ill individuals, indicating predominant central AI. This response is not uncommon irrespective of the severity of the illness. So, the HPA axis should be evaluated on a case-to-case basis even in noncritically ill patients with COVID-19.

Acknowledgment
The authors are grateful to the Department of Microbiology and Immunology, BSMMU for the laboratory support.

Statement of Authorship
The authors certified fulfillment of ICMJE authorship criteria.

Credit Author Statement
HB: Conceptualization, Methodology, Software, Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Visualization; **NS:** Conceptualization, Methodology, Software, Investigation, Resources, Data Curation, Writing – review and editing, Visualization; **MSM:** Conceptualization, Methodology, Software, Formal analysis, Investigation, Data Curation, Writing – original draft preparation, Visualization; **MAH:** Conceptualization, Methodology, Validation, Resources, Writing – review and editing, Supervision, Project administration, Funding acquisition; **ABS:** Conceptualization, Methodology, Validation, Writing – review and editing, Supervision, Project administration, Funding acquisition; **SMA:** Conceptualization, Methodology, Validation, Investigation, Resources, Writing – review and editing, Supervision, Funding acquisition.

Author Disclosure
The authors declared no conflict of interest.

Funding Source
This work was partially funded by the University Research and Development, BSMMU.

References
1. Téblick A, Peeters B, Langouche L, Van den Berghe G. Adrenal function and dysfunction in critically ill patients. Nat Rev Endocrinol. 2019;15(7):417–27. PMID: 30850749. https://doi.org/10.1038/s41574-019-0185-7.
2. Khoo B, Boshier PR, Freethy A, et al. Redefining the stress cortisol response to surgery. Clin Endocrinol (Oxf). 2017;87(5):451–8. PMID: 28758231. https://doi.org/10.1111/cen.13439.
3. Mongioì LM, Barbagallo F, Condorelli RA, et al. Possible long-term endocrine-metabolic complications in COVID-19: Lesson from the SARS model. Endocrine. 2020;68(3):467-70. PMID: 32488837. PMCID: PMC7266418. https://doi.org/10.1007/s12020-020-02349-7.
4. Agarwal S, Agarwal SK. Endocrine changes in SARS-CoV-2 patients and lessons from SARS CoV. Postgrad Med J. 2020;96(1137):412-6. PMID: 32527756. PMCID: PMC7306278. https://doi.org/10.1136/postgradmedj-2020-137934.
5. Chappell MC. Commentary for "Endocrine significance of SARS-CoV-2's reliance on ACE2." Endocrinology. 2021;162(4):bqaa222. PMID: 33269375. PMCID: PMC7799108. https://doi.org/10.1210/endocr/bqaa222.
6. Garg MK, Gopalakrishnan M, Yadav P, Misra S. Endocrine involvement in COVID-19: Mechanisms, clinical features, and implications for care. Indian J Endocrinol Metab. 2020;24(5):381-6. PMID: 33489841. PMCID: PMC7810055. https://doi.org/10.4103/ijem.IJEM_440_20.
7. Frara S, Allora A, Castellino L, di Filippo P, Loli P, Giustina A. COVID-19 and the pituitary. Pituitary. 2021;24(3):465-81. PMID: 33939057. PMCID: PMC8089131. https://doi.org/10.1007/s11102-021-01148-1.
8. Somasundaram NP, Gunatilake SSC. Infections in endocrinology: Viruses. In: Feingold KR, Anawalt B, Boyce A, et al. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000. PMID: 33734656. Bookshelf ID: NBK568565.
9. Grassi T, Varotto E, Galassi FM. COVID-19, a viral endocrinological disease? Eur J Intern Med. 2020;77:156-7. PMID: 32571582. PMCID: PMC7274643. https://doi.org/10.1016/j.ejim.2020.06.003.
10. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19. N Engl J Med. 2021;384(8):693-704. PMID: 32678530. PMCID: PMC7383595. https://doi.org/10.1056/NEJMoa2021436.
11. Alzahrani AS, Mukhtar N, Aljomaiah A, al. The impact of COVID-19 viral infection on the hypothalamic-pituitary-adrenal axis. Endocr Pract. 2021;27(2):83-9. PMID: 33554871. PMCID: PMC7837186. https://doi.org/10.1016/j.eprac.2020.10.014.
12. World Health Organization. Clinical management of COVID-19: Interim guidance, 27 May 2020. Accessed August 2, 2022. https://apps.who.int/iris/handle/10665/332196.
13. Cooper MS, Stewart PM. Corticosteroid insufficiency in acutely ill patients. N Engl J Med. 2003;348(8):727-34. PMID: 12594318. https://doi.org/10.1056/NEJMra020529.
14. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181-247. PMID: 34599691. PMCID: PMC8486643. https://doi.org/10.1007/s00134-021-06506-y.
15. Santana MF, Borba MGS, Baía-da-Silva DC, et al. Case report: Adrenal pathology findings in severe COVID-19: an autopsy study. Am J Trop Med Hyg. 2020;103(4):1604–7. PMID: 32876012. PMCID: PMC7543860. https://doi.org/10.4269/ajtmh.20-0787.
16. Pal R. COVID-19, hypothalamo-pituitary-adrenal axis and clinical implications. Endocrine. 2020;68(2):251–2. PMID: 32346813. PMCID: PMC7186765. https://doi.org/10.1007/s12020-020-02325-1.
17. Kumar B, Gopalakrishnan M, Garg MK, et al. Endocrine dysfunction among patients with COVID-19: A single-center experience from a tertiary hospital in India. Indian J Endocrinol Metab. 2021;25(1):14-9. PMID: 34386388. PMCID: PMC8323627. https://doi.org/10.4103/ijem.IJEM_577_20.
18. Etoga MCE, Inna AH, Fokeng MG, et al. Baseline serum total cortisol during the primary coronavirus infection in the beginning

of the COVID-19 pandemic in Cameroon. Ann Endocrinol Metab. 2021;4(1):55-60. https://doi.org 10.36959/433/567.
19. Wheatland R. Molecular mimicry of ACTH in SARS – Implications for corticosteroid treatment and prophylaxis. Med Hypotheses. 2004;63(5):855–62. PMID: 15488660. PMCID: PMC7126000. https://doi.org/10.1016/j.mehy.2004.04.009.
20. Gu WT, Zhou F, Xie WQ, Wang S, Yao H, Liu YT, et al. A potential impact of SARS-CoV-2 on pituitary glands and pituitary neuroendocrine tumors. Endocrine. 2021;72(2):340–8. PMID: 33786714. PMCID: PMC8009460. https://doi.org/10.1007/s12020-021-02697-y.
21. Lee MK, Vasikaran S, Doery JC, Wijeratne N, Prentice D. Cortisol: ACTH ratio to test for primary hypoadrenalism: A pilot study. Postgrad Med J. 2013;89(1057):617-20. PMID: 23729816. https://doi.org/10.1136/postgradmedj-2012-131723.
22. Karaca Z, Lale A, Tanriverdi F, Kula M, Unluhizarci K, Kelestimur F. The comparison of low and standard dose ACTH and glucagon stimulation tests in the evaluation of hypothalamo-pituitary-adrenal axis in healthy adults. Pituitary. 2011;14(2):134-40. PMID: 21061072. https://doi.org/10.1007/s11102-010-0270-3.

JAFES

Had an intriguing discussion in Grand Rounds?
Share your Clinical Case Seminars at
JAFES@Asia.com.