ORIGINAL ARTICLE

AL-ANBAR MEDICAL JOURNAL
Anb. Med. J. 18(1):43–47, 2022

Dermatological Manifestations of Patients with COVID 19: A Cross-sectional study

Iqbal G. Farhood,[1,*] Ali T. AbdulHasan,[2] Salam F. Lafta,[3] Afraa Mamoori,[4] and Fatima Al-Hasani[5]

[1] *Department of Medicine/Dermatology, College of Medicine, Al-Nahrain University. Baghdad, Iraq.*
[2] *Department of Medicine/Dermatology, College of Medicine, Kerbala University, Kerbala, Iraq.*
[3] *Al Hur Sector, Karbala Health Directorate, Kerbala, Iraq.*
[4] *Department of Pathology/ Molecular Pathology, College of Medicine, University of Babylon, Babylon, Iraq.*
[5] *Department of Medicine/Dermatology, Al-Husseini Medical City, Kerbala, Iraq.*

(Received : 1 January 2022; Accepted : 25 April 2022; First published online: 5 May 2022)

ABSTRACT

Background: A Global pandemic Coronavirus disease-19 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was isolated in December 2019 in Wuhan (China). Skin manifestations of COVID-19 disease are overlooked in the clinical approach to those suspected of this virus focusing on the pulmonary findings.
Objectives: This study aimed to describe the dermatological manifestations of COVID-19 in Iraqi patients.
Materials and methods: A cross-sectional study was carried out at general hospitals, primary care centers, and private clinics in three Iraqi cities Baghdad, Babil, and Karbala. The study covered the period from October 2020 to February 2021. Data regarding the demographic and clinical characteristics of each participant were registered. A thorough physical examination by a dermatologist was conducted for every subject. The data were entered and analyzed using SPSS version 25.
Results: One hundred COVID-19 patients with cutaneous manifestations were enrolled in this study. There were 59 females. Their ages ranged from 19-62 years. Most of the patients were from the age group $\leq$ 40 years (68). Just above half of the participants were non-healthcare workers. The highest blood group of the patients was A (45) and the least AB (11). Half of the subjects were presented within the first 7 days from the onset of the disease. Fifty-one cases were with mild disease form. In 54 patients, dermatological manifestations have appeared in the active stage of the disease. Hair loss was the commonest manifestation (30), all of them in the age group $\leq$ 40 years, and the majority of the cases (26) was affecting the female. While the least manifestation was acrocyanosis in 2 patients, both of them were male and from the age group$>$ 40 years. There were highly statistically significant differences between the skin manifestations and the age and gender (P-value = 0.000). .
Conclusion: Most of the patients were from the age group $\leq$ 40 years and female. Hair loss was the commonest skin abnormality due to COVID-19. The majority of cutaneous manifestations were started in the active phase of the infection. The age and gender determined the type of dermatological manifestations.
Keywords: COVID-19; Dermatological manifestations; Age; Gender; Multicenter study.

DOI: 10.33091/amj.2022.174530

INTRODUCTION

World Health Organization announced coronavirus 2019 disease (COVID-19) as a pandemic condition on March 11, 2020. The rapid spread of new cases of pneumonia was had been diagnosed in Wuhan, China in late December 2019. It

* Corresponding author: E-mail: driqbalderma30@gmail.com
Phone number: +9647809864746

is caused by a novel coronavirus, named SARS-CoV-2 [1]. The clinical spectrum ranges from asymptomatic to fever, dry cough, dyspnea, fatigue, diarrhea, olfactory and gustatory impairments, and even normal or leukopenia and radiographic evidence of pneumonia with ground glass appearance on CT chest [2–4]. Endocytosis or phagocytosis of the virus after attachment to the cell surface by a receptor depends on integument system impairment [5]. Infected host cell membrane expressing the surface receptors angiotensin-converting enzyme 2 (ACE2) which shows high affinity to SARS-CoV-2 protein (S). Angiotensin-converting enzyme 2 (ACE2) is found in the basal cell layer of the epidermis and hair follicles [6]. Cellular apoptosis and inflammatory cascade reaction triggered by rapid viral replication. Risks of lung injury increased with increased blood levels of cytokines and chemokine since the high production of these cytokines is responsible for the accumulation of cells and fluids (cytokine storm) [7].

There is a diversity of clinical spectrum of the novel coronavirus including dermatological manifestations [4]. There is a wide range of clinical skin manifestations due to COVID-19 including, but not exclusively, hair loss, acneform rash, vesicular rash, urticaria, petechia, etc. Despite many studies across the globe describing the skin features due to COVID-19 [8, 9], there is a paucity of investigations coming from Iraq regarding this issue. A recent study from Al Diwaniyah province, Iraq described the mucocutaneous manifestations due to this disease [10]. However, this study was conducted in a single center. Hence, this multicenter study aimed to describe the dermatological manifestations of the COVID-19 among Iraqi patients.

MATERIALS AND METHODS

A prospective cross-sectional study was carried out from October 2020 to February 2021. The patients were recruited from general hospitals, primary healthcare centers, and private clinics in 3 Iraqi cities; Baghdad, Babil, and Karbala. Proved COVID-19 subjects with real-time polymerase chain reaction (PCR) presented with dermatological manifestations from both sexes, $>$ 18 years old, and who they wish to participate in the study were enrolled in the current study. The exclusion criteria included; patients with an age $\leq$ 18 years, chronic dermatological diseases, dermatological manifestation due to other causes, and those who didnt wish to participate in the study. Data were collected regarding the demographics of the patients, cutaneous manifestations, medical history, family history of COVID-19, drug history, laboratory ndings, and treatment.

Informed consent was taken from every subject. The study was approved by the Medical Research Bioethical Committee of the University of Kerbala (reference number 25 on 24-4-2022).

All patients were examined thoroughly by a specialist doctor for cutaneous manifestations. The patients were divided into three groups regarding the treatment of the COVID-19; those who received an ordinary regimen (oral azithromycin, vitamin C, and D), others who received multiple regimens of ordinary and convalescence plasma, and the last group had received multiple regimens and steroid.

The severity of the condition was determined from the clinical symptoms and divided into mild cases (fever, cough, sore throat, malaise, headache, gastrointestinal symptoms, loss of taste and smell) without shortness of breath, or abnormal chest imaging. Moderate severity; in which there are respiratory symptoms with abnormal chest imaging, and severe cases in which there are severe respiratory symptoms that require hospital admission and intervention with abnormal chest imaging [2].

The collected data were entered and analyzed using version 25 SPSS for a window. Continuous variables were presented as mean SD. While categorical variables were presented in simple tables or figures as percentages and/or frequencies. The Chi-square test was used to compare categorical variables. A P-value of less than 0.05 was considered a statistically significant difference.

RESULTS

Out of 100 COVID-19 subjects with dermatological manifestations, there were 59 (59%) females. The age ranged from 19-62 years with a mean age of 34.25 $\pm$ 11.848 years. Most of the patients (68%) belongs to the age group $\leq$ 40 years and 53% were non-healthcare workers (Table 1).

Forty-five patients with a blood group A. Just above half of the patients were with a mild form of COVID-19. The mean duration of the dermatological manifestations was 8.11 days $\pm$ 4.311 with a range of 2-20 days. Half of the patients presented within the first 7 days of the onset of disease and 54% were in the active disease stage (Table 2).

Table 1. Demographic characteristics of the 100 COVID-19 patients with dermatological manifestations.

Variables	Frequency	Percent
Age groups per years		
$\leq$ 40	68	68.0
$>$ 40	32	32.0
Gender		
Males	41	41.0
Females	59	59.0
Occupation		
Healthcare workers	47	47.0
Non-healthcare workers	53	53.0

Table 2. Clinical characteristics of the 100 COVID-19 patients with dermatological manifestations.

Variables	Frequency	Percent
Blood groups		
A	45	45.0
B	19	19.0
AB	11	11.0
O	25	25.0
Duration per days		
$\leq$ 7	50	50.0
$>$ 7	50	50.0
Severity		
Mild	51	51.0
Moderate	45	45.0
Severe	4	4.0
Phase		
Active	54	54.0
Convalescent	12	12.0
Late	34	34.0

http://doi.org/10.33091/amj.2022.174530

The majority of the cases (60%) were taken an ordinary regimen for their disease (Figure 1).

The highest skin manifestations were hair loss (30%), all cases were in the age group ≤ 40 years. While, the lowest manifestation was acrocyanosis (2), both of them in the age group > 40 years. There was a highly statistical difference between the manifestations and the age groups (P-value = 0.000) (Figure 2).

The highest skin manifestations were hair loss (30), 26 of them in females and 4 in males. While, the lowest manifestation was acrocyanosis (2), both of them in males. There was a highly statistical difference between the manifestations and the gender (P-value = 0.000) (Figure 3).

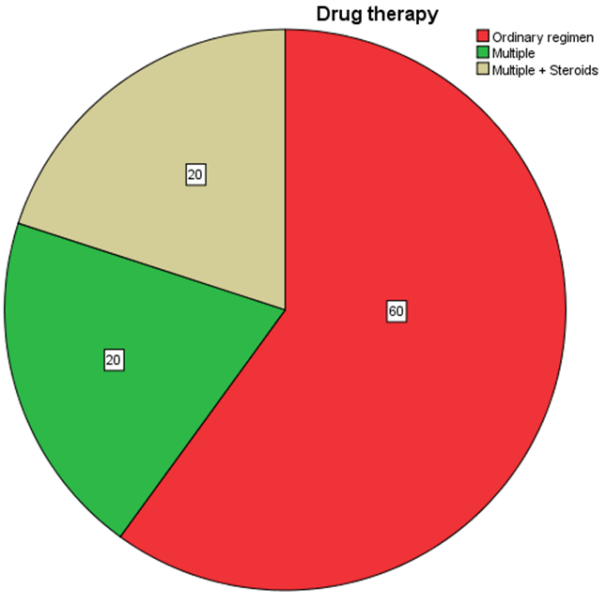

Figure 1. Drug therapy among 100 COVID -19 patients with dermatological manifestations.

DISCUSSION

The pandemic of COVID-19 affects many organs of the body including the skin, once developed may give clue to the diagnosis or arise a hint to complications. The majority of viral infections presented with an exanthem (skin rash) and, oftentimes, with enanthem (mucosal membrane involvement). These skin alterations are due to interactions with the immune system [11]. This explains the different forms of skin manifestations. Dermatologic findings may be the first signs of a viral infection, this motivates us to search for skin findings in COVID-19, which can help to take early intervention and protection [12].

COVID-19 is a pandemic condition mainly presented with cough, dyspnea, and fever. Skin symptoms occur in up to 20.4% of patients. Most studies suggest the onset of the dermatologic findings several days after the onset of respiratory symptoms; while others noted occurrence before other symptoms depending on viral load and host immune reaction [13]. In this study, we found that the majority of cutaneous manifestations were started in the active phase in 54% of the cases. This was much higher than what was reported in the previous

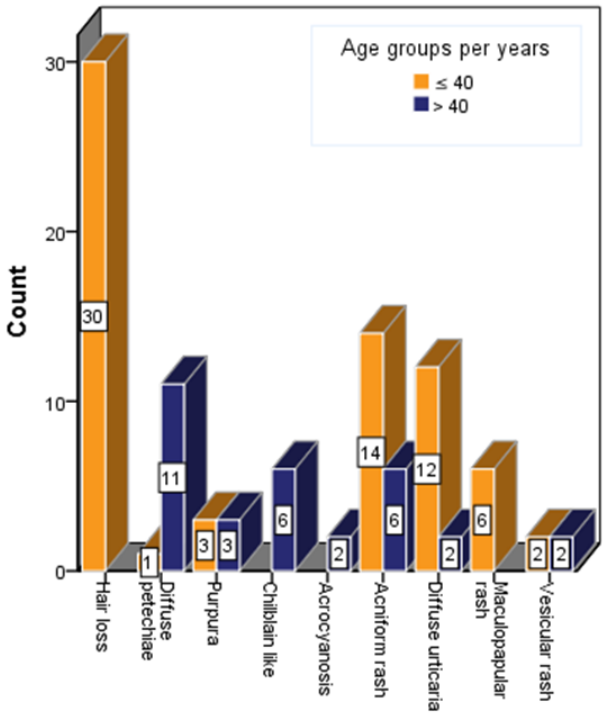

Figure 2. The distribution of the dermatological manifestations according to the age groups. P-value = 0.000.

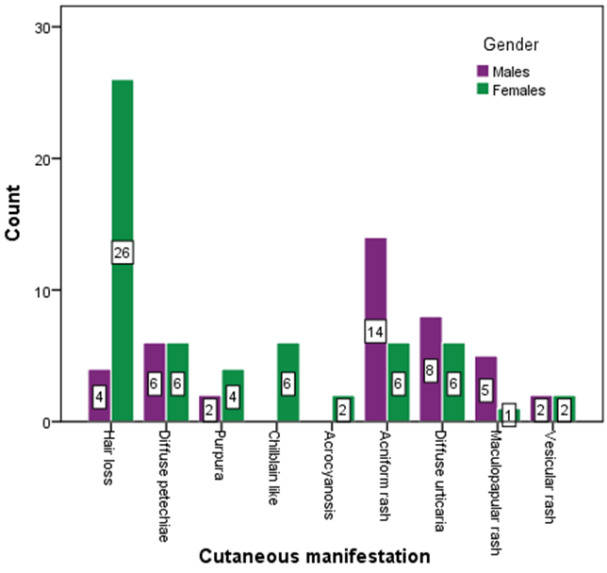

Figure 3. The distribution of the dermatological manifestations according to gender. P-value = 0.000.

study (20.4% of a group of 88 patients were featured present from the start) [[13].

In this study, the most frequently reported manifestations were hair loss which had been seen in 30 patients. Hair loss can be explained as a response to severely stressful events and fear of this life-threatening infection. This necessitates strict quarantine conditions and social isolation creating a poor psychological state and increasing psychosocial stress which is

http://doi.org/10.33091/amj.2022.174530

embodied in impaired immunity and hair loss [14]. The prevalence of female hair loss can be used as a clue against a preliminary observation of the high frequency of male pattern hair loss among admitted COVID-19 patients; suggesting androgen expression might be a clue to COVID-19 severity [15].

In this study there were 26 patients had vascular manifestations in which 12 patients had diffuse petechiae, 6 had purpura, 6 had chilblain-like lesions, and 2 patients had acrocyanosis (Figures 2 and 3). Petechiae/purpuric rash sparing mucosal membrane and palmoplantar skin and druginduced rash should be excluded [16]. Besides, Purpura was found in 6 patients. Normal vascular integrity disrupted results in vasculitic changes from direct damage of the virus to the endothelial cells or as host inflammatory responses. Mechanical cause with increased intravascular pressure from coughing also results in petechiae or purpura, although in about 10% of cases, the cause might be drug-induced, and manifests 7 to 21 days after exposure [17]. Chilblain lesion has occurred as a result of cytokine-mediated inflammatory response due to increased interferon release induced by COVID-19 [18]. Obliterative microangiopathy and coagulation abnormalities could be a possible explanations [19].

Acneiform rash was seen in 20 patients either due to the corticosteroids used in the treatment of this infection rather than as a direct effect of the viral infection, this explains its rarely reported among the literature reviewed studies [17]. We need to emphasize an important fact about drug eruptions, which is its ability to imitate most of the skin presentation, and this is an important issue that needs to be considered in differentiation between those finding that correlated with COVID-19 from those resulting from side effects of drugs [20].

Our study revealed that diffuse urticaria was presented in 14% of the patients in comparison with 16.7% of total skin manifestations [13]. It is of utmost importance to exclude urticarial druginduced rash as one of the main differential diagnoses [21].

The maculopapular rash was seen in 6 patients which is much lesser than a prior study from Spain on a large sample size (375 patients) study. The study reported that maculopapular eruptions presented in 47% of cases [22]. This difference may be attributed to the geographical differences between the two studies.

Vesicular (Chickenpoxlike) rashes appear as small monomorphic vesicles mainly on the trunk, mostly in middleaged COVID19 patients in up to 4% of cases which is less than what is reported in many studies (9%) [22–24]. Patients with papulovesicular exanthem were 34 (9%), while they were 3 out of 52 (5.8%), 1 out of 18 (5.5%), and 2 out of 53 (4%) in the cohorts published by Askin et al. [9], Recalcati [10] and De Giorgi et al. [8]. Galvn Casas et al. [22] declared that vesicular lesions tend to occur in middle-aged patients, before systemic symptoms onset in 15% of cases, and tend to be associated with intermediate COVID-19 severity. We think the differences in the frequency of vesicular rash among the various studies could be attributed either to the geographical differences or the availability of widespread testing which determines the causal effect relationship together with the observed skin manifestations during the COVID-19 pandemic.

The pathophysiology of dermatologic conditions in patients with COVID-19 may be explained as a result of complement system activation with diffuse microvascular vasculitis outcome. This explanation is supported by interstitial and perivascular neutrophilia and the deposition of complement protein in the dermal capillaries [13]. A direct effect of the virus may be another speculation based on high concentrations of lymphocytes without eosinophils [25].

The most important strength of the current study was that age and gender were factors that determine the dermatological manifestations due to COVID-19. Since the occupational gender differences make women more vulnerable to COVID-19 as two-thirds of the health and social care workforce worldwide are women as well as females tend to seek medical advice urgently more than males [26]. However, our study didnt find a cause of the significant relationship between the age of the patients and skin manifestations.

The ABO blood group has an A allele associated with an incremented risk of cardiovascular diseases when exposed to redox stresses [27]. Since the A antigen protects intercellular cell adhesion molecule 1 (ICAM1) and P-selectin from enzymatic cleavage. As inflammation increases; more leukocytes adhere to adhesion molecules and result in decreased circulation [28]. Several studies suggest that subjects with type O and Rh-negative blood were protected from a viral infection, severe illness, and mortality [29, 30]. These studies suggest that ABO blood groups affect the host's genetic susceptibility to various viral diseases and this may also apply to COVID-19. Elevation in fibrin D-dimers in patients with blood group A was detected due to pulmonary vasculopathy and coagulopathy in relevance to manifestations of respiratory failure and morbidity [31]. The present study reported that 45 patients were in blood group A, 25 O, 19 B, and 11 AB. The distribution of ABO blood groups in the general population are, 47 blood group O, 41 A, 8 B, and 4 AB. The distribution is much more different than what was reported in the current study. We can conclude from this observation that COVID-19 patients with blood group O might be protected from skin abnormalities, while subjects with other blood groups are more vulnerable to these problems. We advise further study on a large sample size to clarify this relationship between the COVID-19 patients' blood groups and the occurrence of the dermatological manifestations due to this disease.

Owing to the short period of the study, the sample size was relatively small and this is considered a limitation of the study.

CONCLUSION

Most of the patients were from the age group 40 years and female. Hair loss was the commonest skin abnormality due to COVID-19. The majority of cutaneous manifestations were started in the active phase of the infection. Age and gender can determine the type of dermatological manifestations. A blood group O in COVID-19 patients can be considered a protective factor from dermatological manifestations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

http://doi.org/10.33091/amj.2022.174530

REFERENCES

[1] A. L. Phelan, R. Katz, and L. O. Gostin. The novel coronavirus originating in Wuhan, China: challenges for global health governance. *Jama*, 323(8):709–710, 2020.

[2] X. Li, M. Geng, Y. Peng, L. Meng, and S. Lu. Molecular immune pathogenesis and diagnosis of COVID-19. *Journal of pharmaceutical analysis*, 10(2):102–108, 2020.

[3] Raid M Al-Ani. Smell and Taste Abnormalities due to COVID-19. *Al-Anbar Medical Journal*, 16(1):1–2, 2020.

[4] Hazim Ghazzay, Raid M Al-Ani, Mothana A Khalil, and Ahmed Faeq Hammad. Socio-clinical characteristics of COVID-19 disease in Anbar Governorate, Iraq. *Journal of Emergency Medicine, Trauma and Acute Care*, 2021(1):8, 2021.

[5] Christopher E M Griffiths, Jonathan Barker, Tanya O Bleiker, Robert Chalmers, and Daniel Creamer. *Rook's textbook of dermatology, 4 volume set*, volume 1. John Wiley & Sons, 2016.

[6] I Hamming, W Timens, and M L Bulthuis. Lely. AT, Navis, GJ, and van Goor, H.(2004) Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol*, 203(2):631–637.

[7] C. Huang *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, 395(10223):497–506, 2020.

[8] V. De Giorgi *et al.* Cutaneous manifestations related to coronavirus disease 2019 (COVID-19): A prospective study from China and Italy. *Journal of the American Academy of Dermatology*, 83(2):674–675, 2020.

[9] Ozge Askin, Rozerin Neval Altunkalem, Dursun Dorukhan Altinisik, Tugba Kevser Uzuncakmak, Umit Tursen, and Zekayi Kutlubay. Cutaneous manifestations in hospitalized patients diagnosed as COVID19. *Dermatologic Therapy*, 33(6):e13896, 2020.

[10] Sanaa A Bdaiwi and Resalah H Abdul-saheb. Mucocutaneous Manifestations of COVID-19 among Iraqi Patients in Al Diwaniyah Province , Iraq : Case Series Study. 2(239):239–244, 2022.

[11] Regina FölsterHolst and Hans Wolfgang Kreth. Viral exanthems in childhood. Part 3: Parainfectious exanthems and those associated with virusdrug interactions. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*, 7(6):506–510, 2009.

[12] Stephanie A Castillo, Anh Khoa Pham, and James G Dinulos. Cutaneous manifestations of systemic viral diseases in neonates: an update. *Current Opinion in Pediatrics*, 29(2):240–248, 2017.

[13] S Recalcati. Cutaneous manifestations in COVID-19: a first perspective [published online March 26, 2020]. *J Eur Acad Dermatol Venereol. doi*, 10.

[14] Dursun Turkmen, Nihal Altunisik, Serpil Sener, and Cemil Colak. Evaluation of the effects of COVID19 pandemic on hair diseases through a webbased questionnaire. *Dermatologic Therapy*, 33(6):e13923, 2020.

[15] A. Goren *et al.* A preliminary observation: Male pattern hair loss among hospitalized COVID-19 patients in Spain-A potential clue to the role of androgens in COVID-19 severity. 2020.

[16] Gerard J Nuovo, David Suster, Esmerina Tili, Hamdy Awad, and Cynthia Magro. A Standardization Protocol for the In Situ Detection of SARS-CoV2 RNA and Proteins. *Applied Immunohistochemistry & Molecular Morphology*, 30(2):83–90, 2022.

[17] Thomas P Habif. *Clinical dermatology E-book*. Elsevier Health Sciences, 2015.

[18] Z. Zhou *et al.* Heightened innate immune responses in the respiratory tract of COVID-19 patients. *Cell host & microbe*, 27(6):883–890, 2020.

[19] Gürkan Kaya, Aysin Kaya, and Jean-Hilaire Saurat. Clinical and histopathological features and potential pathological mechanisms of skin lesions in COVID-19: review of the literature. *Dermatopathology*, 7(1):3–16, 2020.

[20] Poonkiat Suchonwanit, Kanchana Leerunyakul, and Chaninan Kositkuljorn. Cutaneous manifestations in COVID-19: lessons learned from current evidence. *Journal of the American Academy of Dermatology*, 83(1):e57–e60, 2020.

[21] Chia-Yu Chu. Drug eruptions: Great imitators. *Clinics in Dermatology*, 38(2):193–207, 2020.

[22] C. Galván Casas *et al.* Classification of the cutaneous manifestations of COVID19: a rapid prospective nationwide consensus study in Spain with 375 cases. *British Journal of Dermatology*, 183(1):71–77, 2020.

[23] Uwe Wollina, Aye Serap Karada, Christopher Rowland-Payne, Anca Chiriac, and Torello Lotti. Cutaneous signs in COVID19 patients: a review. *Dermatologic therapy*, 33(5):e13549, 2020.

[24] J M Carrascosa, V Morillas, I Bielsa, and M Munera-Campos. Cutaneous manifestations in the context of SARS-CoV-2 infection (COVID-19). *Actas Dermo-Sifiliográficas (English Edition)*, 111(9):734–742, 2020.

[25] R. Gianotti *et al.* Cutaneous clinico-pathological findings in three COVID-19-positive patients observed in the metropolitan area of Milan, Italy. 2020.

[26] Tania King, Belinda Hewitt, Bradley Crammond, Georgina Sutherland, Humaira Maheen, and Anne Kavanagh. Reordering gender systems: can COVID-19 lead to improved gender equality and health? *The Lancet*, 396(10244):80–81, 2020.

[27] O Wu, N Bayoumi, M A Vickers, and PABO Clark. ABO (H) blood groups and vascular disease: a systematic review and metaanalysis. *Journal of thrombosis and haemostasis*, 6(1):62–69, 2008.

[28] G. Paré *et al.* Novel association of ABO histo-blood group antigen with soluble ICAM-1: results of a genome-wide association study of 6,578 women. *PLoS genetics*, 4(7):e1000118, 2008.

[29] Joel G Ray, Michael J Schull, Marian J Vermeulen, and Alison L Park. Association between ABO and Rh blood groups and SARS-CoV-2 infection or severe COVID-19 illness: a population-based cohort study. *Annals of internal medicine*, 174(3):308–315, 2021.

[30] J. Zhao *et al.* Relationship between the ABO blood group and the coronavirus disease 2019 (COVID-19) susceptibility. *Clinical Infectious Diseases*, 73(2):328–331, 2021.

[31] D. McGonagle, J. S. O'Donnell, K. Sharif, P. Emery, and C. Bridgewood. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. *The Lancet Rheumatology*, 2(7):e437–e445, 2020.

http://doi.org/10.33091/amj.2022.174530