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Stressors and Hormone Levels: Predictors of COVID-19 Health Outcomes in Latine Adults

A Thesis Presented

by

Wendy Rodriguez

To the Keck Science Department

of

Claremont McKenna, Scripps, and Pitzer Colleges

In Partial Fulfillment of

The Degree of Bachelor of Arts

Senior Thesis in Biology

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ABSTRACT

The Coronavirus 2019 Disease (COVID-19) has been shown by multiple studies to have disproportionate impacts on some individuals, especially minority populations. These may be attributed to differences in biological (sex), gender, social or cultural factors. In this study, we aim to identify and investigate the gender and social predictors that may be involved in the pathogenesis of the virus and its health outcomes. To achieve this, a literature review expands on relevant topics that better contextualize COVID-19's complex nature. The potential role of hormones, estrogen, and testosterone is considered across different sexes and genders as protective agents against COVID-19. This study also describes comorbidity conditions that may further complicate COVID-19's effects on individuals. Finally, in the proposal, measurements of the Quality of Life scale, COVID-19 Severity Index, COVID-19-related stressors, and hormone levels are used to assess their association with Latine and Non-Latine individuals of different gender identities in Los Angeles County. This leads to an important aspect of this study which is to uphold the participants' individual experiences through an optional qualitative interview. Overall, this work highlights possible biological and gender-related explanations for the burdens experienced by minority groups known to be historically excluded from research.

INTRODUCTION

COVID-19 has been a concern in public health since 2020 and, ever since, there has been an interest in understanding its pervasiveness and impact. Growing areas of research on the experiences of ethnic and gender and sex minorities is crucial to understanding COVID-19 in the long term. Ethnic minorities including Black, Hispanic, and Asian American individuals have also been greatly affected by COVID-19 to the extent of reporting an increased risk of getting infected (Magesh et al., 2021). Higher mortality rates, infections, and hospitalizations during the COVID-19 pandemic have been linked to "oppressed and disenfranchised" communities (Norris and Gonzalez, 2020). Gender and sex minorities have been disproportionately affected by this global pandemic (Pharr et al., 2022). It is important to understand people with different identities and their experiences in daily life, the health care system, and scientific research. Known to be historically excluded from research and impacted by discrimination is the transgender community. In research on self-reported socioeconomic barriers and healthcare system barriers, transgender individuals have reported that access to quality healthcare is mainly impacted by providers with a lack of knowledge and competence in transgender healthcare (Safer et al., 2016). Higher mortality rates, infections, and hospitalizations during the COVID-19 pandemic have been linked to "oppressed and disenfranchised" communities (Norris and Gonzalez, 2020). Taken together, the information outlined above merits more attention on individuals of minority populations. In the proposed study, a mixed-methods approach will highlight minority experiences through the consideration of hormones, which is contextualized in detail in the paper, in health outcomes in COVID-19 potentially mediated by the quality of life and related stressors.

REVIEW

Studies of Comorbidity Conditions

An approach to better understanding the impact and responses to COVID-19 through a gender and sex lens includes investigating comorbidity conditions. A way to assess the risk of death for people with multiple conditions, the Charlson comorbidity index (CCI), categorizes risk scores as moderate to severe. Some researchers who have considered adapting the CCI for use in COVID-19 mortality risk found that the CCI score plays a predictive role in COVID-19 mortality, showing that there is a positive correlation between scores and mortality in patients (Comoglu and Kant, 2022). A retrospective study of confirmed COVID-19 patients in Spain analyzed mortality risk based on clinical and demographic factors with an emphasis on the presence of chronic diseases. Their early findings associate an increased mortality risk in women with acute myocardial infarction, coagulation, and hemorrhagic disorders (Poblador-Plou et al., 2020). Both women and men presented higher mortality with either diabetes or chronic ulcers (Poblador-Plou et al., 2020). In another, large United States cohort study, researchers evaluated sex and gender differences in comorbidities and other factors in patients infected with COVID-19. Their results yield a significantly higher count of male patients with comorbidities like hypertension and diabetes compared to their female counterparts (Kharroubi and Diab-El-Harake, 2022). The proposal to follow does not focus on the effects of comorbidities but given the findings of these studies, they are considered predictors in COVID-19 outcomes and will be recorded in this prospective study.

Sex Differences in Immune Response

Sex interactions with immunity are still not well understood but since the first months of the COVID-19 pandemic investigators began suggesting that biological and genetic differences may be at the root of disproportionate effects between males and females. Females in general are known to have stronger immune responses when compared with their counterparts (Ortona et al., 2019). In a review study of gender and sex differences, biological effects are centered on endocrinology and genetics. The impact of genetics often is intuitively linked to the X or Y chromosomes, but relevant genes for immunoregulation are located on autosomes that are gender-specific (Parsch 2007). The effects for toll-like receptors 7 (TLR7) and TLR8 in female and male responses to a measles viral infection and cytokine level were associated only with an increase in TNF α while there were no other differences in expression or response (Clifford et al., 2011). Under the hormonal influence, it has been known that females produce higher levels of antibodies than males and this reflects autoimmune diseases (Oertelt-Prigione 2012).

Sex Hormone Roles in COVID-19

Estrogen

The role of estrogens in COVID-19 has been expected to influence clinical outcomes since the beginning of the pandemic in early 2020. Estrogen can be classified into estrone, estriol, estradiol, and estetrol (Shah 2021). As part of three sex steroid hormones, estrogen (17- β estradiol, E2) has a role in the immune response to infections through antibody production. (Grandi et al., 2020). Estradiol (E2) binds to estrogen receptors $-\alpha$ or $-\beta$ at different expression levels in T cells and B cells (Grandi et al., 2020). One review study focusing on estrogens as a

protective effect in women's response to COVID-19 links E2 to the increase in expression of A Disintegrin and Metalloproteinase (ADAMs) and angiotensin-converting enzyme 2 (ACE-2) (Figure 1; Al-kuraishy et al., 2021). ADAMS and ACE-2 have been previously shown to prevent SARS-CoV-2 from entering the host cell. An increase in ADAM-17 expression mediates ACE-2 shedding which binds SARS-CoV-2 and blocks its entry (Ragia and Manolopoulos, 2020). These studies collectively record E2's protective role. A study in Italy reported that males account for 63.9% of their COVID-19-related deaths up to 2020, further alluding to the impact of sexhormone diversity on patients' susceptibility to severe health outcomes (Froldi and Dorigo, 2020). With estrogen's potential as a protective agent in COVID-19, these studies partially confirm there may be a difference in health outcomes due to gender, specifically corresponding hormone levels.

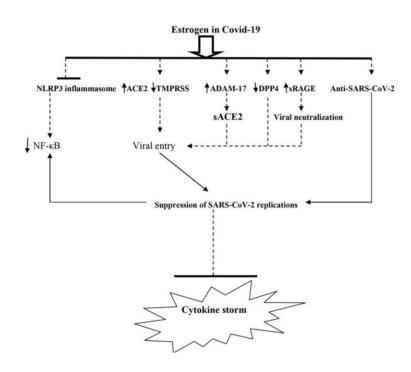


Figure 1. The proposed role of estrogen in COVID-19 as a modulator of a lung pathway (Adapted from Al-kuraishy et al., 2021).

Testosterone

In addition to estrogen, ACE-2 is also induced by testosterone. Testosterone is crucial in regulating lung inflammation and thus defends the body from pulmonary and viral infection (Alkuraishy et al., 2021). At low testosterone levels, the pulmonary-protective pathway is deregulated and exposed to viral binding by SARS-CoV-2 (Hussain et al., 2020). Despite its defensive role, during COVID-19 males have been disproportionately affected by the virus compared to females. This is important because there are sex differences in testosterone serum level; although testosterone is also secreted by females, from puberty, healthy young males show 15 times more testosterone than similar-aged females (Handelsman et al., 2018). These studies help establish the role of testosterone in the body and can help inform the interpretation of varying health outcomes.

Progesterone

Progesterone is important in females and males as a humoral steroid hormone; it indicates maturity in females and helps maintain pregnancy (Lange et al., 2007). Some patients have exhibited excessive cytokine levels also known as cytokine storm in severe COVID-19 which urges earlier recognition of this condition (Ragab et al., 2020). E2 and progesterone (P4) at high concentrations may be able to mitigate proinflammatory cytokine production, activate T cell anti-inflammatory response and antibody production to reduce the cytokine storm (Mauvais-Jarvis et al., 2020). A study with COVID-19 patients has demonstrated no significant difference in levels of progesterone compared to the non-COVID-19 group (Cai Et al., 2022). From these

studies, it seems that progesterone has an important effect but is inconclusive in its role COVID-19 infected individuals.

Clinical Studies of Sex Hormones in COVID-19

Studies of COVID-19 have reported sex differences in COVID-19 cases without considering significant physiological explanations. To address this, some studies have evaluated the effect of sex hormone levels in COVID-19 health outcomes. A retrospective cohort study of 138 patients in Italy investigated four sex hormones (testosterone, dehydroepiandrosterone, progesterone, and estradiol) in COVID-19 patients. All males were reported to have significantly lower testosterone levels irrespective of age difference while females who died or developed acute respiratory distress syndrome or severe COVID-19 did not present a significant difference (Beltrame et al., 2022). The progesterone level in males with severe COVID-19 was evidently lower compared to no statistically different progesterone levels in all females considered in the study (Beltrame et al., 2022). A study in Spain on serum testosterone levels and disease outcomes found that these markers accurately predict COVID-19 male survival (Toscano-Guerra et al., 2022). These investigators also highlight that testosterone trajectories and age are inversely related, with or without comorbid conditions, suggesting that testosterone production is dependent on age which further complicates COVID-19 recovery (Toscano-Guerra et al., 2022).

Gender-Affirming Hormone Therapy

A source of distress and conflict for some individuals is gender dysphoria. This view is defined by a discordance between biological sex (assigned at birth) and the individual's gender identity. Individuals may choose to undergo gender-affirming hormone therapy (GAHT) as an intervention to address this and improve their quality of life (QoL) (Silva et al., 2021). Through GAHT, individuals want to achieve similar sex steroid hormone concentrations to those of the gender they are affirming (Chantrapanichkul et al., 2021). Transgender women seeking GAHT normally go through estrogen therapy to reduce characteristics such as unwanted hair growth and transgender men use testosterone therapy to suppress feminine characteristics (Unger, 2016). The target hormone doses for individuals in GAHT to achieve hormone levels vary based on factors such as body mass index (Fernandez et al., 2019). From an assessment of hormone levels for transgender men, Fernandez et al. found the target testosterone range to be 320-1000 ng/dL; for transgender women, the target estradiol range is 90-200 pg/mL (Fernandez et al., 2019). As mentioned before, the receptor angiotensin-converting enzyme 2 (ACE-2) is known as the entry for the COVID-19 virus into host cells. In the context of COVID-19, a clinical study supports the potential of progesterone or estrogen+progesterone in the downregulation of ACE-2 as a protective measure for men (Masterson et al., 2021). Taken together, these studies provide insight into how hormone therapy may be a factor in COVID-19 infections.

Stress in COVID-19 Positive Individuals

COVID-19 has become a source of stress in the daily lives of individuals. Psychological stress in prior research has been shown to lead to falls in estrogen (Assad et al., 2017). Research has also suggested that testosterone is decreased under stress (Afrisham et al., 2016). The primary stress hormone in the human body is cortisol, a physiological biomarker. Cortisol indicates stress levels and can be used to measure health and wellness of the body. A clinical study that investigated the relationship between stress and infection in COVID-19 found that hospitalized patients with moderate severity of infection had higher salivary cortisol than the control group (Deneva 2022).

Through questionnaires with 221 patients (204 male identifying, 17 female identifying) confirmed with COVID-19 in Iran, individuals reported severe psychological distress (46.61%) (Moayed et al., 2021). For people that are infected or exposed to COVID-19, a quarantine period is necessary to avoid spreading COVID-19, may that be at home or in a healthcare facility. In a South Korean qualitative study, during and after the quarantine period of 932 tele-counseling COVID-19 patients, it was found through interviews that stressors were present throughout (Park et al., 2022). Stressors varied by the period of quarantine, during and after release (Table 1).

Period	Common stressors		
During the quarantine	Being diagnosed with COVID-19 Concerns about recovery from COVID-19		
	Stress related to quarantine Treatment environment issues		
	Limited information and communication		
After release from the quarantine	Reinfection or reactivation		
	Concerns about complications		
	Financial difficulties		

Table 1. The summarized results for COVID-19 stressors by period (Adapted from Park et al.,2022).

MINORITIES IN COVID-19

Research has shown minorities are greatly impacted by COVID-19 compared to non-minorities. A study based in New York City reports that Hispanic and Black people are about 1.5 times more likely to get infected with COVID-19 and 4 times more likely to get hospitalized (Li and Huang, 2022). The minority stress and intersectionality theories can help understand the disproportionate impact of poor health conditions on sexual minority groups. The minority stress theory refers to daily social situations that, over time, lead to mental health disparities (Rodriguez-Seijas et al., 2019). Latine sexual minority men in a qualitative study share experiences of increased sexual minority stress as an effect of less "identity-affirming" support which was offered through events such as LGBTQ Pride or clubs, both of which were canceled or closed due to COVID-19 stay-at-home orders (Harkness et al., 2021). Accessibility also plays a role in the quality of health such that ethnic minorities have poor access to healthcare and experience higher discrimination than white individuals (Gaia and Baboukardos, 2021). This collectively supports the need for further research on minority groups. COVID-19 has affected these groups' social life and physical/mental health.

METHODOLOGICAL APPROACH

Taking into account previous knowledge from the literature review, this study aims to investigate the impact of COVID-19 stressors and quality of life on the effect of sex hormone levels on health outcomes in Los Angeles County Latine individuals. This study will use mixed methods. Los Angeles County is a geographic area of interest because of the toll COVID-19 has had on it. This proposal consists of quantitative, qualitative, clinical, and survey methods. The results from this research will extend current data on the factors of interest in this study. Although existing research looks at these factors independently, a comprehensive approach, such as the one proposed here, acknowledges the complexity with which COVID-19 should be regarded. Data collected in this study can help inform healthcare responses to the current COVID-19 situation and other outbreaks in the future.

Participants

The participants in this proposal will consist of Latine and Non-Latine adults (N=150; ages 18-45) in Los Angeles County. This study aims to highlight minority groups with an emphasis on the Latine experience. All gender and sex identities are eligible and welcome to participate. Participants (either hospitalized or isolated) will be COVID-19 positive and will start the study in the first week of their positive status. The participants will be recruited through partnerships with local schools and volunteer work. If funding permits, an incentive in the form of a \$25 gift card will provide some compensation for their time. This will encourage retention and active participation in the measures and interviews.

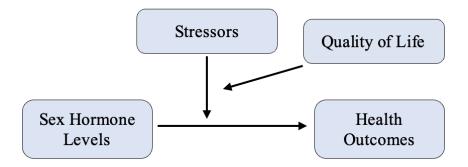


Figure 2. Double moderation model proposed for the study.

Research Team

The team will consist of researchers with different identities across sexual, gender, and ethnic identities. Individuals with a minority background are encouraged to join to increase comfort between them and the participants. Each member will provide their expertise in either medicine, biology, or public health. To support that the study will adopt a mixed-methods approach, members will receive training in conducting interviews, analysis, and patient interaction.

Procedures

For 6 months, the participants will complete the following measures in the first week of confirmed COVID-19-positive status along with hormone testing and optional one-on-one interviews. With the help of medical professionals, the participants that are hospitalized will get salivary samples taken in the mornings once a week as mental stress biomarkers for the duration of their hospitalization followed by weekly self-reported related stressors. For those participants

in isolation, stress will be qualitatively assessed through the related stressors assessment measure. This related stressors assessment will be recorded once a week for six months in the morning. To assess hormone levels, serum blood testosterone, and estrogen tests will be conducted for hospitalized individuals once every week for the duration of their stay at the hospital. Once they are released and this applies to people in isolation from the start, hormone self-administered tests will be taken once every week for six months. These steps will all be expected to take place in the mornings to account for any confounding variables such as physical activity that may influence the data. They will also be scheduled toward the end of the week, mainly, to allow for thoughtful consideration in the related stressors assessment. At the end of the study, a single 30-60-minute interview for qualitative assessment of pre-COVID-19 and post-COVID-19 experiences will be carried out.

Measures

Quality of Life

The Quality of Life Scale (QOLS) is used as a measure of an individual's well-being by comparing expectations with the realities of their experiences. QOLS (Appendix A) is used to inform and is often part of health risk assessments (Burckhardt et al., 2003). This measure will be the first one to be completed in a single seating. It is meant to represent the initial or pre-COVID-19 infection experiences of the participant. There are sixteen items with scores ranging from 7=delighted to 1=terrible. The most relevant themes that are included in this scale involve social life, financial security, work, and health.

Severity Index

The COVID-19 Severity Index (Appendix B) was developed to assess respiratory critical illness commonly associated with severe COVID-19 (Huespe et al., 2022). In the context of this study, this measure will be used to determine health conditions after diagnosis. This will be executed by a healthcare professional. There are seventeen items categorized by risk level based on the participant's score. This score is calculated by summing up the totals per row which will represent the predictive score of severity in the hospitalized participants.

Related Stressors

The related stressors measure (Appendix C) has been used to determine the impact of COVID-19 on daily life in mental health, physical health, and sleep quality (Graupensperger et al., 2023). This consists of sixteen items with a scale that ranges from 1 (Not at All) to 5 (Extremely) in response to how concerned they feel about each item. The score will be totaled for the sixteen items. A higher score will be associated with increased stress while a lower score will indicate more comfort. The scores will then be divided into low, medium, and high numbers of reports.

Considerations

To summarize the responses, average scores will be recorded for all the measures. We will also report comorbidity (if any), gender, age, setting (hospitalized or isolated), and hormone therapy (if any). For individuals that are unable to participate in any measure because of health issues, their caregiver or healthcare provider will be asked to complete it to the best of their knowledge. This becomes a potential limitation, but the best alternative to capture the participants' experience.

Hypotheses

Hypothesis 1

Latine adults with lower sex hormone levels, particularly testosterone and estrogen, will demonstrate poorer health outcomes from COVID-19 infection.

Hypothesis 2

COVID-19-related stressors, influenced by quality-of-life assessment, will have an interaction with health outcomes and ethnicity.

Hypothesis 3

There will be a significant relationship between COVID-19-related stressors, linking higher reports of stress with lower hormone levels.

Interview

Participants will have the option to take part in a 30-60-minute interview at the end of the six months in the language of their choosing if resources allow it. The purpose of these interviews is to allow the participants to express themselves about their pre-COVID-19 and post-COVID-19 experiences. Questions that will be included in the interview are: "Can you share how your life has changed, if at all, after getting infected with COVID-19?" and "What do you think about your experience with healthcare before and after knowing you were COVID-19-positive?" Other questions about their life will be asked, specifically about health care, work, and social subjects. Interviewers will be asked to show active listening skills by repeating what the participants say followed by a probing statement like "Tell me more about this experience, event, or opinion." By giving interviewers the space to talk about their experiences, this study will record a narrative and collective memory with quotes from these conversations.

Statistical Analysis

Results for this study will be analyzed using R statistical software through a multivariate modeling package. Results will be best interpreted through the multiple regression analysis of the variables of quality of life, related stressors, sex hormone levels, and health outcomes. The moderation test will be run with quality life and COVID-19-related stressors as interacting moderators, sex hormone levels as predictors, and COVID-19 health outcome as the dependent variable. In these analyses, the following will be statistically controlled for age, comorbidity, and BMI. A statistically significant result will be considered as p < 0.05.

EXPECTED RESULTS

H1: It is predicted that Latine individuals will indicate lower sex hormone levels with a statistically significant effect on COVID-19 health outcomes.

H2: It is predicted that Latine individuals will present less severity in their COVID-19 infection than Non-Latine individuals (Figure).

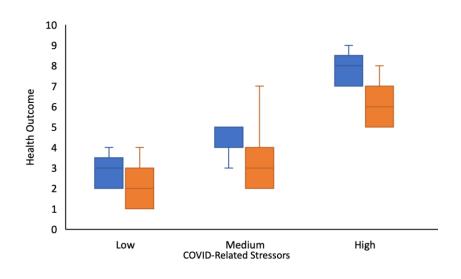


Figure 3. Health outcome vs COVID-19 Related Stressors Count in Latine (Blue) and Non-Latine individuals (Orange).

H3: It is predicted that individuals with higher reports of related stressors will have lower testosterone or estrogen levels (Figure 4; Figure 5).

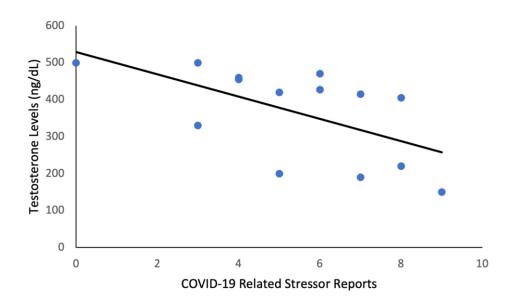


Figure 4. Relationship between COVID-19 related stressor reports and testosterone levels.

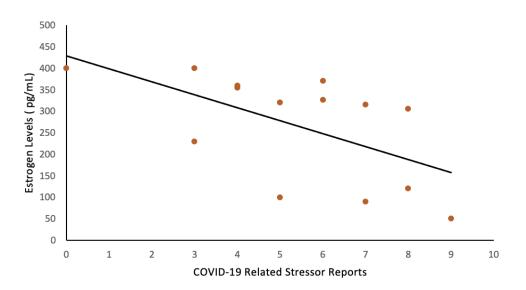


Figure 5. Relationship between COVID-19 related stressor reports and estrogen levels.

LIMITATIONS

Limitations to this research proposal should be considered in its execution and future directions. One limitation is that this study does not consider all covariates that could influence health outcomes. Possible covariates may have not been of specific interest in this study, but they were included in data collection. These include setting (hospitalized or isolated at home or other), age, or body mass index. It is important to also acknowledge COVID-19 has had a different impact on mortality and health effects by country (Pareek et al., 2020). Also, some bias may be unintentionally introduced into the results through both the team members and the participants. Team members that may resonate with participant responses, especially in interviews, might unintentionally report certain responses and leave others out in their report back. Because participants are expected to recall months of information into the past and present, their responses may be influenced by the context of the study or the inability to fully remember details.

DISCUSSION

This study is intended to better understand how stress and quality of life may be related to hormone levels and COVID-19 health outcomes in Latine Adults. In addition to contributing to scientific literature, this study aims to bring representation to historically excluded minority groups. By exploring quality of life and COVID-19-related stress as potential moderators of the relationship between hormone levels and health outcomes, this work can contribute to developing theories on the role of sex hormones. Qualitative investigation through the interview is also important in providing context to the measures and other data. It also has the potential to inspire interest and engagement in interdisciplinary investigations. Future directions from this work may include spatial or geographical considerations to acknowledge differences in healthcare access and practices, social development, and demographics. More research into gender identity and behavior is also necessary to advance knowledge about patient participation in studies.

APPENDIX

Appendix A: Quality of Life Scale (QOL)

QUALITY OF LIFE SCALE (QOL)

Please read each item and circle the number that best describes how satisfied you are at this time. Please answer each item even if you do not currently participate in an activity or have a relationship. You can be satisfied or dissatisfied with not doing the activity or having the relationship.

	Deligh	tedPleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	lUnhappy	Terrible
1.	Material comforts home, food, conveniences, financial security	6	5	4	3	2	1
2.	Health - being physically fit and vigorous 7	6	5	4	3	2	1
3.	Relationships with parents, siblings & other relatives- communicating, visiting, helping 7	6	5	4	3	2	1
4.	Having and rearing children7	6	5	4	3	2	1
5.	Close relationships with spouse or significant other	6	5	4	3	2	1
6.	Close friends7	6	5	4	3	2	1
7.	Helping and encouraging others, volunteering, giving advice7	6	5	4	3	2	1
8.	Participating in organizations and public affairs7	6	5	4	3	2	1
9.	Learning- attending school, improving understanding, getting additional knowledge 7	6	5	4	3	2	1
10.	Understanding yourself - knowing your assets and limitations - knowing what life is about 7	6	5	4	3	2	1
11.	Work - job or in home	6	5	4	3	2	1
12.	Expressing yourself creatively7	6	5	4	3	2	1
13.	Socializing - meeting other people, doing things, parties, etc	6	5	4	3	2	1
14.	Reading, listening to music, or observing entertainment	6	5	4	3	2	1
15.	Participating in active recreation 7	6	5	4	3	2	1
16.	Independence, doing for yourself7	6	5	4	3	2	1

Source: Adapted from Burckhardt et al., 2003

Appendix B: Severity Index

PARAMETERS	3	2	1	0	1	2	3
Age (years)				≤60	61-64	≥65	
Male gender			yes	no			
Heart failure			yes	no			
Chronic obstructive pulmonary disease (COPD)			yes	no			
Diabetes with end- organ damage			yes	no			
Chest x-ray				Normal or without bilateral infiltrates	Bilateral infiltrates		
Respiratory rate (breaths per minute)	≤8		9-11	12-20		21-24	≥25
SpO ₂ (%)	≤91	92-93	94-95	≥96			
SpO ₂ (%) in COPD	≤83	84-85	86-87	≥88			
Supplemental O ₂	yes			no			
Systolic BP (mmHg)	≤90			90-219			≥220
Pulse (Beats per minute)	≤40		41-50	51-90	91-110	111- 130	≥131
Temperature (°C)	≤35		35,1- 35,5	35,6-37,9	38-39	≥39,1	
Dyspnoea		yes	55,5	no			
D-Dimer(ng/ml)				≤1000	>1000		
Lymphocytes (per				≥1000	<1000	≤500	
mm) Platelets (per mm)				≥10000	<10000		

Source: Adapted from (Huespe et al., 2022)

Appendix C: COVID-19 Related Stressors Questionnaire

Perceived Stress Related to COVID-19						
	The questions in this scale ask you about your feelings and thoughts at this time during the COVID- 19, novel coronavirus pandemic. How <u>concerned</u> are you about the novel coronavirus (COVID-19)	Not at all	A little	Moderately	Quite a bit	Extremely
APSCOVID1	making you sick?	1	2	3	4	5
APSCOVID2	making your friends or family sick?					
APSCOVID3	causing you to lose your job, e.g. employer laying off?					
APSCOVID4	causing a decrease in hours for your job?					
APSCOVID5	causing you to lose your job-related benefits, e.g. health insurance, paid sick leave?					
APSCOVID6	negatively affecting your financial situation?					
APSCOVID7	causing you to not have enough food to eat ,?					
APSCOVID8	making you afraid to leave your house?					
APSCOVID9	making you feel isolated or alone?					
APSCOVID10	making you feel overwhelmed at work?					
APSCOVID11	making you feel overwhelmed with news and information?					
APSCOVID12	placing a strain on your social life?			_		
APSCOVID13	placing a strain on relationships with those you live with?					
APSCOVID14	causing your college classes to move to on-line instruction?					
APSCOVID15	affecting your ability to pay rent?					
APSCOVID16	affecting your ability to stay in school?					

Source: Adapted from Graupensperger et al., 2021

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REFERENCES

- Afrisham, R., Sadegh-Nejadi, S., SoliemaniFar, O., Kooti, W., Ashtary-Larky, D., Alamiri, F.,
 Aberomand, M., Najjar-Asl, S., & Khaneh-Keshi, A. (2016). Salivary Testosterone
 Levels Under Psychological Stress and Its Relationship with Rumination and Five
 Personality Traits in Medical Students. Psychiatry Investigation, 13(6), 637.
 https://doi.org/10.4306/pi.2016.13.6.637
- Al-kuraishy, H. M., Al-Gareeb, A. I., Faidah, H., Al-Maiahy, T. J., Cruz-Martins, N., & Batiha, G. E.-S. (2021). The Looming Effects of Estrogen in Covid-19: A Rocky Rollout.Frontiers in Nutrition, 8. https://doi.org/10.3389/fnut.2021.649128
- Al-Kuraishy, H. M., Al-Gareeb, A. I., Faidah, H., Alexiou, A., & Batiha, G. E. (2021).
 Testosterone in COVID-19: An Adversary Bane or Comrade Boon. Frontiers in cellular and infection microbiology, 11, 666987. https://doi.org/10.3389/fcimb.2021.666987
- Assad, S., Khan, H. H., Ghazanfar, H., Khan, Z. H., Mansoor, S., Rahman, M. A., Khan, G. H., Zafar, B., Tariq, U., & Assad, S. (2017). Role of Sex Hormone Levels and Psychological Stress in the Pathogenesis of Autoimmune Diseases. Cureus. https://doi.org/10.7759/cureus.1315
- Burckhardt, C. S., Anderson, K. L., Archenholtz, B., & Hägg, O. (2003). The Flanagan Quality Of Life Scale: evidence of construct validity. Health and quality of life outcomes, 1, 59. https://doi.org/10.1186/1477-7525-1-59

- Chantrapanichkul, P., Stevenson, M. O., Suppakitjanusant, P., Goodman, M., & Tangpricha, V. (2020). Serum Hormone Concentrations in Transgender Individuals Receiving Gender Affirming Hormone Therapy: A Longitudinal Retrospective Cohort Study. Endocrine Practice. https://doi.org/10.4158/ep-2020-0414
- Clifford, H. D., Yerkovich, S. T., Khoo, S.-K., Zhang, G., Upham, J. W., Le, P. N., Richmond,
 P., & Hayden, C. M. (2012). Toll-like receptor 7 and 8 polymorphisms: associations with functional effects and cellular and antibody responses to measles virus and vaccine.
 Immunogenetics, 64(3), 219–228. https://doi.org/10.1007/s00251-011-0574-0
- Deneva, T., Ianakiev, Y., & Boykinova, O. (2022). Salivary mental stress biomarkers in COVID-19 patients. Frontiers in Medicine, 9. https://doi.org/10.3389/fmed.2022.999215
- Dong, E., Du, H., & Gardner, L. (2020). Coronavirus COVID-19 global cases by Johns Hopkins CSSE. The Lancet Infectious Diseases.
- Eliane Aparecida Silva, Tayane Muniz Fighera, Martins, R., Inês, M., & Poli Mara Spritzer.
 (2021). Physical and Sociodemographic Features Associated With Quality of Life
 Among Transgender Women and Men Using Gender-Affirming Hormone Therapy.
 Frontiers in Psychiatry, 12. https://doi.org/10.3389/fpsyt.2021.621075
- Ellegren, H., & Parsch, J. (2007). The evolution of sex-biased genes and sex-biased gene expression. Nature Reviews Genetics, 8(9), 689–698. https://doi.org/10.1038/nrg2167
- Fernandez, J. D., Kendjorsky, K., Narla, A., Villasante-Tezanos, A. G., & Tannock, L. R. (2019). Assessment of Gender-Affirming Hormone Therapy Requirements. LGBT health, 6(3), 101–106. https://doi.org/10.1089/lgbt.2018.0116

- Franck Mauvais-Jarvis, Sabra L Klein, Ellis R Levin. Estradiol, Progesterone, Immunomodulation, and COVID-19 Outcomes, Endocrinology, 161(9), September 2020, bqaa127, https://doi-org.ccl.idm.oclc.org/10.1210/endocr/bqaa127
- Froldi, G., & Dorigo, P. (2020). Endothelial dysfunction in Coronavirus disease 2019 (COVID-19): Gender and age influences. Medical hypotheses, 144, 110015.
 https://doi.org/10.1016/j.mehy.2020.110015
- Gaia, S., & Baboukardos, D. (2023). Ethnic minorities, income inequalities and the COVID-19 pandemic: evidence from English local councils. Regional Studies, 1–15. https://doi.org/10.1080/00343404.2022.2157384
- Grandi, Giovanni, Fabio Facchinetti, and Johannes Bitzer. 2020. "The Gendered Impact of Coronavirus Disease (COVID-19): Do Estrogens Play a Role?" European Journal of Contraception & Reproductive Health Care 25 (3): 233–34. doi:10.1080/13625187.2020.1766017.
- Graupensperger, S., Cadigan, J. M., Einberger, C., & Lee, C. M. (2021). Multifaceted COVID-19-Related Stressors and Associations with Indices of Mental Health, Well-being, and Substance Use Among Young Adults. International Journal of Mental Health and Addiction. https://doi.org/10.1007/s11469-021-00604-0
- Handelsman, D. J., Hirschberg, A. L., & Bermon, S. (2018). Circulating Testosterone as the
 Hormonal Basis of Sex Differences in Athletic Performance. *Endocrine Reviews*, *39*(5),
 803–829. https://doi.org/10.1210/er.2018-00020

- Harkness, A., Weinstein, E. R., Atuluru, P., Hernandez Altamirano, D., Vidal, R., Rodriguez-Diaz, C. E., & Safren, S. A. (2022). Latino sexual minority men's intersectional minority stress, general stress, and coping during COVID-19: A rapid qualitative study. Journal of Gay & Lesbian Mental Health, 1–28. https://doi.org/10.1080/19359705.2021.1995096
- Huespe, I., Carboni Bisso, I., Di Stefano, S., Terrasa, S., Gemelli, N. A., & Las Heras, M.
 (2020). COVID-19 Severity Index: A predictive score for hospitalized patients. Medicina intensiva, 46(2), 98–101. Advance online publication.
 https://doi.org/10.1016/j.medin.2020.12.001
- Hussain, A. N., Hussain, F., & Hashmi, S. K. (2020). Role of testosterone in COVID-19 patients
 A double-edged sword?. Medical hypotheses, 144, 110287.
 https://doi.org/10.1016/j.mehy.2020.110287
- Kharroubi, S. A., & Diab-El-Harake, M. (2022). Sex-differences in COVID-19 diagnosis, risk factors and disease comorbidities: A large US-based cohort study. Frontiers in public health, 10, 1029190. https://doi.org/10.3389/fpubh.2022.1029190
- Lange, C. A., Gioeli, D., Hammes, S. R. & Marker, P. C. Integration of rapid signaling events with steroid hormone receptor action in breast and prostate cancer. Annu. Rev. Physiol. 69, 171–199 (2007).
- Li, R., & Huang, Y. (2022). COVID-19 pandemic and minority health disparities in New York City: A spatial and temporal perspective. Environment and Planning B: Urban Analytics and City Science, 239980832211265. https://doi.org/10.1177/23998083221126525

- Magesh, S., John, D., Li, W. T., Li, Y., Mattingly-app, A., Jain, S., Chang, E. Y., & Ongkeko,
 W. M. (2021). Disparities in COVID-19 Outcomes by Race, Ethnicity, and
 Socioeconomic Status. JAMA Network Open, 4(11), e2134147.
 https://doi.org/10.1001/jamanetworkopen.2021.34147
- Masterson, J. M., Bui, C., Zhang, Y., Yuan, X., Huynh, C., Jawanda, H., Hasan, W., Tourtellotte,
 W., Luthringer, D., & Garcia, M. M. (2021). Feminising hormone therapy reduces
 testicular ACE-2 receptor expression: Implications for treatment or prevention of
 COVID-19 infection in men. Andrologia, 53(11). https://doi.org/10.1111/and.14186
- Moayed, M.S. et al. (2021). Depression, Anxiety, and Stress Among Patients with COVID-19: A Cross-Sectional Study. In: Guest, P.C. (eds) Clinical, Biological and Molecular Aspects of COVID-19. Advances in Experimental Medicine and Biology(), vol 1321. Springer, Cham. https://doi-org.ccl.idm.oclc.org/10.1007/978-3-030-59261-5_19
- Norris, K., & Gonzalez, C. (2020). COVID-19, health disparities and the US election. EClinicalMedicine, 28. https://doi.org/10.1016/j.eclinm.2020.100617
- Oertelt-Prigione, S. (2012). The influence of sex and gender on the immune response. Autoimmunity Reviews, 11(6-7), A479-485. https://doi.org/10.1016/j.autrev.2011.11.022
- Ortona, E., Pierdominici, M., & Rider, V. (2019). Editorial: Sex Hormones and Gender Differences in Immune Responses. *Frontiers in Immunology*, 10. https://doi.org/10.3389/fimmu.2019.01076

- Pareek, M.; Bangash, M.N.; Pareek, N.; Pan, D.; Sze, S.; Minhas, J.S.; Hanif, W.; Khunti, K. Ethnicity and COVID-19: An urgent public health research priority. Lancet 2020, 395, 1421–1422.
- Park, H., Lee, N., Lee, J. H., Lee, D., Kim, K. A., Kim, H. S., Oh, E., Ha, J. H., Hyun, S. Y., Lee, J., Kim, J., Jeon, K., Kim, H. T., & Sim, M. (2022). Stress Experience of COVID-19
 Patients as Reported by Psychological Supporters in South Korea: A Qualitative Study.
 Frontiers in psychiatry, 13, 834965. https://doi.org/10.3389/fpsyt.2022.834965
- Pharr, J. R., Terry, E., Wade, A., Haboush-Deloye, A., & Marquez, E. (2022). Impact of COVID-19 on Sexual and Gender Minority Communities: Focus Group Discussions. International Journal of Environmental Research and Public Health, 20(1), 50. https://doi.org/10.3390/ijerph20010050

Poblador-Plou, B., Carmona-Pírez, J., Ioakeim-Skoufa, I., Poncel-Falcó, A., Bliek-Bueno, K.,
Cano-del Pozo, M., Gimeno-Feliú, L., González-Rubio, F., Aza-Pascual-Salcedo, M.,
Bandrés-Liso, A., Díez-Manglano, J., Marta-Moreno, J., Mucherino, S., Gimeno-Miguel,
A., & Prados-Torres, A. (2020). Baseline Chronic Comorbidity and Mortality in
Laboratory-Confirmed COVID-19 Cases: Results from the PRECOVID Study in Spain.
International Journal of Environmental Research and Public Health, 17(14), 5171.
https://doi.org/10.3390/ijerph17145171

Ragab, D., Salah Eldin, H., Taeimah, M., Khattab, R., & Salem, R. (2020). The COVID-19 Cytokine Storm; What We Know So Far. *Frontiers in Immunology*, *11*(1446). https://doi.org/10.3389/fimmu.2020.01446

- Ragia, G., & Manolopoulos, V. G. (2020). Assessing COVID-19 susceptibility through analysis of the genetic and epigenetic diversity of ACE2-mediated SARS-CoV-2 entry.
 Pharmacogenomics, 21(18), 1311–1329. https://doi.org/10.2217/pgs-2020-0092
- Raza, H.A., Sen, P., Bhatti, O.A. et al. Sex hormones, autoimmunity and gender disparity in COVID-19. Rheumatol Int 41, 1375–1386 (2021). https://doiorg.ccl.idm.oclc.org/10.1007/s00296-021-04873-9
- Rodriguez-Seijas, C., Eaton, N. R., & Pachankis, J. E. (2019). Prevalence of psychiatric disorders at the intersection of race and sexual orientation: Results from the National Epidemiologic Survey of Alcohol and Related Conditions-III. Journal of Consulting and Clinical Psychology, 87(4), 321–331. https://doi.org/10.1037/ccp0000377
- Safer, J. D., Coleman, E., Feldman, J., Garofalo, R., Hembree, W., Radix, A., & Sevelius, J. (2016). Barriers to healthcare for transgender individuals. Current opinion in endocrinology, diabetes, and obesity, 23(2), 168–171. https://doi.org/10.1097/MED.0000000000227
- Shah S. B. (2021). COVID-19 and Progesterone: Part 1. SARS-CoV-2, Progesterone and its potential clinical use. Endocrine and metabolic science, 5, 100109. https://doi.org/10.1016/j.endmts.2021.100109

- Shek, D.T.L. COVID-19 and Quality of Life: Twelve Reflections. Applied Research Quality Life 16, 1–11 (2021). https://doi-org.ccl.idm.oclc.org/10.1007/s11482-020-09898-z
- Thomas, C., Mulnick, S., Krucien, N. et al. How do study design features and participant characteristics influence willingness to participate in clinical trials? Results from a choice experiment. BMC Med Res Methodol 22, 323 (2022). https://doi.org/10.1186/s12874-022-01803-6
- Toscano-Guerra, E., Martínez-Gallo, M., Arrese-Muñoz, I. et al. Recovery of serum testosterone levels is an accurate predictor of survival from COVID-19 in male patients. BMC Med 20, 129 (2022). https://doi-org.ccl.idm.oclc.org/10.1186/s12916-022-02345-w
- Unger, C. (2016). Hormone therapy for transgender patients. Translational Andrology And Urology, 5(6), 877-884. doi:10.21037/tau.2016.09.04 [Original source: https://studycrumb.com/alphabetizer]