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THE EFFECT OF AGE AND SEX ON COVID-19 INFECTION SEVERITY: INSIGHTS FROM BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS IN OLDER MEN

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ABSTRACT

Background: The COVID-19 pandemic has significantly impacted global health, revealing pronounced differences in disease outcomes across various demographic groups. By analyzing biochemical and hematological parameters, we seek to gain insights into the pathophysiological processes that underpin the increased risk faced by older individuals and men and to identify potential biomarkers that could guide clinical management and therapeutic strategies.
Objective: This study aimed to investigate the effects of age and gender on COVID-19 infection severity by analyzing biochemical and hematological parameters in older men.
Materials and Methods: A retrospective analysis was conducted on 422 COVID-19 patients (230 survivors, 192 non-survivors) admitted to a tertiary care center in South India between 2020 and 2021. Key parameters including D-Dimer, Creatinine, LDH, Ferritin, CRP, Platelet Count, Absolute Neutrophil Count, and Absolute Lymphocyte Count were analyzed. The study compared these parameters across age groups, genders, and between survivors and non-survivors.
Results: The mean age of non-survivors (60.91±13.82 years) was significantly higher than survivors (47.55±19.75 years). Males constituted 63.5% of total cases and had a higher proportion among non-survivors (69.3%) compared to survivors (58.7%). Older survivors showed significantly higher levels of D-Dimer, Ferritin, and CRP. In non-survivors, most parameters did not differ significantly between age groups. Gender-specific differences were observed in several parameters, with males showing elevated levels of certain biomarkers in both survivor and non-survivor groups.
Conclusion: The study confirms that older age and male gender are associated with increased COVID-19 severity and mortality. Specific biochemical and hematological parameters, particularly in older individuals and males, may serve as important indicators for disease progression and outcome. These findings emphasize the need for age and gender-specific approaches in COVID-19 management and prognosis.
Keywords: COVID-19 severity, Age factors, Gender differences, Biochemical markers.

INTRODUCTION

On January 30, 2020, the World Health Organization's International Health Regulations Emergency Committee declared the outbreak a "public health emergency of international concern," followed by a declaration of COVID-19 as a pandemic on March 11.[1]

The virus is transmitted efficiently between humans via aerosolized particles. The definitive reservoir for the infection remains unidentified. While a considerable portion of the population may remain asymptomatic, there are cases in which individuals progressively deteriorate, leading to severe illness and potentially death.[2,3]

Several studies indicate that older adults and men are at a higher risk of developing severe disease, with some patients succumbing to their illness. The COVID-19 pandemic has profoundly influenced global health, highlighting significant disparities in disease outcomes among various demographic groups. Age has emerged as a critical determinant affecting the severity and mortality associated with COVID-19 infection. Research consistently demonstrates that older adults endure a disproportionate burden of severe illness and mortality linked to the virus. This increased susceptibility among the elderly has generated considerable interest in elucidating the underlying mechanisms that contribute to their heightened vulnerability.[4-8]

Biochemical and hematological parameters play a crucial role in elucidating why older individuals are more severely affected by COVID-19. Biochemical markers, such as inflammatory cytokines and acute phase reactants, often exhibit altered levels in older adults, potentially reflecting an exaggerated inflammatory response. Similarly, hematological parameters, including lymphocyte counts and coagulation profiles, frequently demonstrate deviations that may contribute to adverse clinical outcomes in this age group. This research paper aims to investigate how biochemical and hematological parameters influence the severity of COVID-19 infection in older adults. By analyzing these parameters, we seek to gain insights into the pathophysiological mechanisms that underpin the increased risk faced by older individuals and to identify potential biomarkers that could guide clinical management and therapeutic strategies. Understanding these factors is essential for improving outcomes and developing targeted interventions for the elderly population, who continue to be disproportionately affected by the ongoing pandemic.

Aims and Objectives

1. To evaluate how biochemical and hematological parameters differ among various age groups in COVID-19 patients, and to assess these differences between 38 survivors and non-survivors.
2. To analyze the variations in biochemical and hematological parameters across different gender groups in COVID-19 patients, and to compare these parameters 41 between survivors and non-survivors.

Inclusion Criteria

COVID-19 Positive Cases: All patients who were confirmed to be COVID-19 positive through a reliable diagnostic method (e.g., RT-PCR or rapid antigen tests) during the study period (2020-2021).

Age and Gender: Patients of all ages (pediatric, adult, and geriatric) and both genders (male and female) were included in the study.

Inpatients: All patients admitted to the tertiary care center during the specified study period for management of COVID-19.

Duration of Study: COVID-19 cases diagnosed and treated between 2020 and 2021.

Exclusion Criteria

Non-COVID-19 Positive Cases: Patients who were admitted with symptoms similar to COVID-19 but later found to be negative for the virus.

Incomplete Data: Cases where crucial clinical data or medical records were missing or incomplete.

Patients Transferred to Other Centers: Patients who were transferred to other hospitals before receiving final treatment or discharge.

MATERIALS AND METHODS

We conducted a retrospective study of important COVID-19 parameters with respect to age and gender in both surviving and non-surviving groups for a duration of one year between 2020 and 2021 in the tertiary care center of the hilly region in South India.

All the COVID-19-positive cases between 2020 and 2021 are included in the study. Information was collected from the hospital's digital storage sources for all the confirmed COVID-19 cases and were divided into two groups namely: surviving and non-surviving groups.

C-reactive protein (CRP) was assessed by Enzyme-Linked Immunosorbent Assay (ELISA) using a Roche Cobas c502 analyzer. D-Dimer was assessed by Immunoassay
using a Siemens Dimension EXL analyzer. Lactate Dehydrogenase (LDH) was assessed by Spectrophotometric assay using a Roche Cobas c311 analyzer. Serum ferritin was assessed by Chemiluminescent Immunoassay using a Roche Elecsys 2010 analyzer. Hematological parameters were measured using a Sysmex XN 1000 hematology
analyzer. Data on key COVID-19 parameters, including D-Dimer, Creatinine, LDH, Ferritin, CRP, Platelet Count, Absolute Neutrophil Count (ANC), and Absolute Lymphocyte Count (ALC), were collected. Additionally, important hematological ratios such as Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR),

and Systemic Inflammatory Index (SII) were calculated. The results were then compiled 61 and tabulated.

Statistical Package for Social Sciences [SPSS] for Windows, Version 22.0. Released in 2013. Armonk, NY: IBM Corp., was used to perform statistical analyses.

Descriptive analysis includes expressing all the explanatory and outcomes variables in terms of frequency and proportions for categorical variables and mean and standard deviation for continuous variables.

Inferential Statistics

The Mann Whitney test was used to compare the mean values of different study parameters between Survivors and non-survivors. Similar comparisons were performed based on the age and gender of study patients.

ROC analysis was performed on different study parameters to determine the cut-off between survivors and non-survivors.

The level of significance [P-Value] was set at $P<0.05$.

Ethical committee approval for the study was taken from the Institutional Ethics Committee of Kodagu Institute of Medical Sciences, Madikeri, with IEC number KoIMS/IEC/20/20-21.

RESULTS

Our study included 422 cases, of which 230 (54.5%) were Covid-19-positive surviving cases and 192 (45.5%) were Covid-19-positive non-surviving patients. [Table 1]

Table 1: Distribution of study patients based on their Survival Status

Distribution of study patients based on their Survival Status			
Variable	**Category**	**n**	**%**
Survival Status	Survivors	230	54.5%
	Nonsurvivors	192	45.5%

Age-wise distribution (Table 2)

The majority of patients are between 41 and 80 years old, with the largest group being 61-80 years old (37.9%). A significant proportion of patients are in the 41-60 years range (32.9%). Younger patients (≤ 20 years) and those older than 80 years are less common, constituting 5.0% and 3.1% of the total population, respectively.

The mean age of the study population is 53.63 years, indicating that the average patient is middle-aged. The median age is 55 years, which is close to the mean, suggesting a relatively symmetric age distribution. The age range from 3 to 94 years highlights the wide span of ages in the study population, encompassing both very young and elderly patients.

Table 2: Age-wise distribution of study patients

Age-wise distribution of study patients			
Variable	**Category**	**n**	**%**
Age	≤ 20 yrs.	21	5.0%
	21-40 yrs.	89	21.1%
	41-60 yrs.	139	32.9%
	61-80 yrs.	160	37.9%
	> 80 yrs.	13	3.1%
	Total	422	100.0%
		Mean	SD
	Mean	53.63	18.53
	Median	55	
	Range	03 - 94	

Gender-wise distribution of cases (Table 3): 63.5% of the cases were males and 36.5% of the cases were females.

Table 3: Gender-wise distribution of study patients

Gender-wise distribution of study patients			
Variable	**Category**	**n**	**%**
Gender	Males	268	63.5%
	Females	154	36.5%

Distribution of cases according to surviving and non-surviving status (Table 4): Out of 422 cases, 54.5% were survivors and 45.5% were non-survivors.

Table 4: Age and gender distribution between Survivors & Non-survivors

Age and gender distribution between Survivors & Non-survivors						
Variable	**Category**	**Survivors**		**Non-Survivors**		**P-Value**
		Mean	**SD**	**Mean**	**SD**	
Age in years	Mean &	47.55	19.75	60.91	13.82	<0.001*[a]

	SD					
	Range	03 - 94		20- 92		
		n	%	n	%	
Sex	Males	135	58.7%	133	69.3%	0.03*[b]
	Females	95	41.3%	59	30.7%	

Age: The mean age was 47.55±19.75 years for the survivor group and 60.91±13.82 years for the non-survivor group. The difference was statistically significant at < 0.001. The average age of non-survivors is significantly higher than that of survivors. This indicates that older age is associated with a higher risk of mortality from COVID-19. The wide age range in both groups shows that the disease affects individuals across a broad spectrum of ages, but the mean age difference highlights a trend where older individuals are more likely to succumb to the disease.

Gender: Among the survivors 58.7% were males and 41.3 % were females Among non survivors 69.3% were males and 30.7% were females. The gender distribution shows a higher proportion of males among non-survivors compared to surviving. This suggests that males may have a higher risk of mortality from COVID-19 compared to females. The statistically significant p-value indicates that this gender disparity is unlikely to be due to chance.

Age-wise comparison of mean values of study parameters among Survivors (Table 5):

Among survivors, several parameters showed significant age-related differences:

- **D-Dimer, Ferritin, and CRP** were significantly higher in the older age group (>55 years).
- **Creatinine** was significantly lower in the older age group, though this may reflect a different pattern of kidney function rather than disease severity.
- **LDH** and **Platelet Count** exhibited significant differences as well, with the older group showing different levels compared to the younger survivors.

Table 5: Age-wise comparison of mean values of study parameters among Survivors and Nonsurvivors using the Mann Whitney Test

Age-wise comparison of mean values of study parameters among Survivors and Non-Survivors using the Mann Whitney Test							
Parameters	**Age**	**Survivor**			**Non-survivor**		
		Mean	**SD**	**P-Value**	**Mean**	**SD**	**P-Value**
D-dimer (mg/ml DDU)	≤ 55 yrs.	1266.82	9032.12		2263.14	3937.66	
				0.005*			0.60
	> 55 yrs.	3108.11	16157.96		1904.52	2943.16	
Creatinine	≤ 55 yrs.	2.17	6.83		2.46	3.56	
(mg/dl)				<0.001*			0.29
	> 55 yrs.	1.38	0.60		3.95	20.76	
LDH	≤ 55 yrs.	586.89	575.49		991.86	550.05	
(IU/L)				0.04*			0.77
	> 55 yrs.	578.94	280.56		967.49	495.02	
Ferritin	≤ 55 yrs.	257.02	402.36		1077.21	1215.19	
(ng/ml)				0.003*			0.26
	> 55 yrs.	374.88	604.50		920.61	983.18	
NLR	≤ 55 yrs.	6.17	9.17	0.37	18.22	18.69	0.61
	> 55 yrs.	6.52	7.80		19.68	27.84	
PLR	≤ 55 yrs.	235.92	185.35		451.78	322.81	
				0.70			0.34
	> 55 yrs.	225.20	160.80		428.74	412.85	
SII	≤ 55 yrs.	14.47	21.84		35.29	31.43	
				0.60			0.21
	> 55 yrs.	12.84	14.59		40.44	70.64	
ANC	≤ 55 yrs.	5209.79	2963.28		7834.33	3945.14	
(cells/mcL)				0.70			0.88
	> 55 yrs.	5189.66	2543.48		7712.89	4032.45	
ALC	≤ 55 yrs.	1381.82	738.35		768.66	705.01	
(cells/mcL)				0.29			0.58
	> 55 yrs.	1281.61	721.68		731.20	572.97	
Platelet	≤ 55 yrs.	2.47	0.99		2.14	0.76	
(cells/mcL)				0.001*			0.06
	> 55 yrs.	2.13	1.00		1.94	0.79	
CRP	≤ 55 yrs.	40.13	65.94		106.74	95.24	
(mg/dl)				0.04*			0.57
	> 55 yrs.	94.05	112.66		114.30	81.49	

In our study, we observed that the standard deviation is larger than the mean. The standard deviation is a measure of how spread out a set of data is, while the mean is the center of the distribution. A large standard deviation means the data is spread out, while a small standard deviation means the data is clustered around the mean.

For nonsurvivors, there were no significant differences between the younger and older age groups for most parameters, except for D-Dimer and Platelet Count, where trends were observed but not statistically significant.

These results underscore that age-related differences are more pronounced in certain biomarkers among survivors, reflecting a potential impact of age on disease severity and progression.

Genderwise comparison of mean values of study parameters among Survivors and Nonsurvivors using the Mann Whitney Test (Table 6):

For males, significant differences were observed in creatinine, ferritin, NLR, ALC, and platelet count between survivors and nonsurvivors. In females, significant differences were noted in creatinine, ALC, and platelet count. Both genders showed a trend where non-survivors had elevated ferritin levels and reduced ALC and platelet counts compared to survivors, indicating potential markers of poor prognosis. The results suggest that while some parameters are consistently indicative of severity across genders, others may vary, emphasizing the need for gender-specific considerations in COVID-19 management and prognosis.

Table 6: Genderwise comparison of mean values of study parameters among Survivors and Non-Survivors using Mann Whitney Test

Genderwise comparison of mean values of study parameters among Survivors and Non-Survivors using Mann Whitney Test							
Parameters	**Gender**	**Survivor**			**Non-survivor**		
		Mean	**SD**	**P-Value**	**Mean**	**SD**	**P-Value**
D-dimer	Males	3097.82	15897.82		2386.84	3648.45	
(mg/ml DDU)				0.21			0.09
	Females	360.73	259.33		1195.20	2197.55	
Creatinine	Males	2.16	5.62		4.23	20.27	
(mg/dl)				<0.001*			<0.001*
	Females	0.98	0.23		1.61	1.89	
LDH (IU/L)	Males	593.88	475.50	0.21	968.83	511.14	0.84
	Females	564.00	413.60		992.82	523.86	
Ferritin (ng/ml)	Males	395.32	578.39	<0.001*	1056.39	1137.62	0.13
	Females	146.79	222.64		786.49	870.53	
NLR	Males	6.75	9.99	0.19	21.66	28.46	0.01*
	Females	5.65	6.31		13.54	12.93	
PLR	Males	225.16	170.05	0.63	460.02	428.74	0.52
	Females	241.39	185.05		384.40	247.01	
SII	Males	14.04	22.03	0.75	42.73	69.64	0.38
	Females	13.59	15.01		29.41	25.49	
ANC	Males	5208.89	2720.20		7990.23	4028.91	
(cells/mcL)				0.62			0.20
	Females	5192.63	2938.64		7225.60	3889.99	
ALC (cells/mcL)	Males	1300.00	716.44		697.74	623.83	
				0.21			0.007*
	Females	1406.32	753.26		849.15	605.54	
Platelet (cells/mcL)	Males	2.24	1.12	0.009*	1.90	0.73	0.006*
	Females	2.48	0.80		2.26	0.84	
CRP (mg/dl)	Males	76.22	101.41	0.72	117.27	93.53	0.43
	Females	52.17	86.00		98.72	66.58	

A large standard deviation shows that data points vary widely from the mean, often seen in datasets with both low and high extremes.

DISCUSSIONS

COVID-19 has had a profound impact globally, affecting millions and altering lives indefinitely. The disease has disproportionately affected certain groups, leading to severe and often fatal outcomes. Our study, which explored the impact of age and gender on COVID-19 severity and mortality, aligns with and extends previous research findings.

Age and Severity

Our study confirms that older age is a significant risk factor for severe COVID-19 outcomes, consistent with findings from previous research. Data from Table 2 shows that the majority of patients were in the middle-aged to elderly categories, with a notable concentration in the 61-80 years age group. This distribution reflects the heightened vulnerability of older adults to severe COVID-19, corroborating findings by Jian-Min Jin

et al,[4] who observed increased mortality rates among older populations.

Similarly, Savitesh Kushwaha et al,[5] reported higher infection and mortality rates among older individuals, which is consistent with our study's observation that non survivors had a significantly higher mean age compared to survivors.

This trend highlights the broader impact of age on COVID-19 outcomes, emphasizing the importance of targeted interventions for older patients.

In our study, the mean age of survivors was 47.55±19.75 years, whereas non-survivors had a significantly higher mean age of 60.91±13.82 years ($p < 0.001$). This significant age difference underlines the elevated risk older patients face, consistent with the trend observed in earlier research. However, once the disease progresses to a severe stage, biochemical and hematological parameters did not show significant differences between older and younger non-survivors. This finding suggests that while age is a crucial factor in disease progression, biochemical parameters may not differ significantly in severe

cases regardless of age, echoing the conclusions of Federico Raimondi et al,[6] and Hiroki Ueyama et al.[7]

Gender Differences

Our findings also support the notion that gender plays a crucial role in COVID-19 outcomes. Table 4 highlights that males constituted 63.5% of the total cases, and a higher proportion of non-survivors were male (69.3%) compared to survivors (58.7%), with a statistically significant p-value of 0.03. This observation aligns with the conclusions of Jian-Min Jin et al,[4] and Savitesh Kushwaha et al,[5] who found that males were more susceptible to severe COVID-19 and had higher mortality rates.

Jian-Min Jin et al,[4] reported that men had a 2.4 times higher mortality rate from COVID-19 compared to women, a finding that is consistent with our study's results. Moreover, our study found that males exhibited significantly higher levels of certain biomarkers, such as Creatinine, Ferritin, and Platelet Count, in both survivor and non survivor groups. This supports the findings of Federico Raimondi et al,[6] and Hiroki Ueyama et al,[7] who noted that males are more likely to develop severe infections, though there was no significant difference in mortality between genders once severe disease occurred. All these studies had in common the conclusion that men and the older population were more at risk in susceptibility and mortality in Covid-19 infection.[4-8]

Liao et al. found that elevated D-dimer, CRP, and other inflammatory markers correlated with severe outcomes. Our study also identified these parameters as significant in assessing progression in both survivors and non-survivors, particularly noting their elevated levels in older populations with mild to moderate COVID-19.[9]

Ramos-Peñafiel highlighted the prognostic value of NLR in severe cases. Our study also observed the significance of NLR in male patients with severe outcomes, aligning with the idea that higher NLR can indicate a worse prognosis. While our study focused on individual parameters such as creatinine, ferritin, and thrombocytopenia, the findings on NLR complement our observations of how certain hematological markers are critical for assessing disease severity and progression.[10]

Our study's focus on parameters such as D-dimer, CRP, ferritin, and creatinine aligns with Shang et al.'s emphasis on using clinical parameters to predict severity. Our results support their findings by showing that these markers are significantly elevated in non survivors compared to survivors. Shang et al. found that parameters could predict severity across different demographics.[11]

Underlying Factors

The increased susceptibility of males and older individuals to severe COVID-19 outcomes can be attributed to various factors. The ACE2 receptor serves as the entry point for the SARS-CoV-2 virus into host cells, has been linked to susceptibility. Some studies suggest that males may have higher levels of ACE2 receptors, potentially increasing their risk of infection and severe outcomes. Men often have higher risky lifestyle factors such as smoking and alcoholism, which may also contribute to increased susceptibility and severity.[12,13] As individuals age, their immune system undergoes changes that reduce its effectiveness. This process, known as immunosenescence, results in a less robust response to infections, including COVID-19. Older adults have a diminished ability to produce new immune cells and to mount effective responses against pathogens. Older adults are more likely to have chronic health conditions such as hypertension, diabetes, cardiovascular diseases, and chronic respiratory conditions, which can exacerbate the severity of COVID-19. These comorbidities can impair the body's ability to cope with the infection and contribute to more severe outcomes.[14]

Hormonal differences between males and females, particularly levels of sex hormones like testosterone and estrogen, may influence the severity of COVID-19. For instance, testosterone has been associated with increased inflammation and immune responses, which might contribute to more severe disease outcomes in males. Conversely, estrogen is thought to have protective effects and may contribute to a less severe response in females.[15]

Generally, females have stronger innate and adaptive immune responses compared to males. This can lead to a better ability to control infections and mount an effective immune response. However, this heightened immune response can also sometimes lead to more severe autoimmune reactions.[16]

In summary, our study reinforces the importance of considering age and gender when evaluating COVID-19 risk and outcomes. The higher risk for severe disease and mortality among older adults and males is well-documented in our findings and aligns

with previous research. This underscores the need for targeted strategies to address the specific vulnerabilities of these groups, optimizing care and potentially improving outcomes for affected patients.

CONCLUSION

Older age and male gender are associated with increased mortality and severity, supported by elevated levels of specific biomarkers. These findings align with previous research but also provide new insights into the nuanced ways in which age and gender interact with biochemical and immunological parameters.

Among survivors, monitoring biomarkers such as D-Dimer, CRP, Ferritin, and Platelet Count is critical for assessing the severity and progression of COVID-19 in older individuals, particularly in those with mild to moderate disease. For men: Elevated creatinine, thrombocytopenia, ferritin, NLR, and ALC are crucial indicators of disease progression in both mild and severe cases, requiring careful monitoring and potentially more aggressive treatment approaches. This suggests that age and gender-specific thresholds for these biomarkers might be important for assessing disease severity, and predicting outcomes and can aid in developing targeted interventions, and improving patient outcomes. and emphasizes the need for further studies to explore these factors in greater detail.

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REFERENCES

1. Shereen MA, Khan S, Kazmi A, et al . COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res. 2020; 24: 91-98.
2. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. Eurosurveillance. 2020;25(4).
3. Parry J. China coronavirus: Cases surge as official admits human-to-human transmission. British Medical Journal Publishing Group; 2020.
4. Jin JM, Bai P, He W, et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Front Public Health.2020 ; 8:152.
5. Kushwaha S, Khanna P, Rajagopal V, et al. Biological attributes of age and gender variations in Indian COVID-19 cases: A retrospective data analysis. Clin Epidemiol Glob Health. 2021; 11:100788.
6. Raimondi F, Novelli L, Ghirardi A, et al. HPG23 Covid-19 Study Group. Covid-19 and gender: lower rate but same mortality of severe disease in women-an observational study. BMC Pulm Med. 2021; 21(1):96.
7. Ueyama H, Kuno T, Takagi H, et al . Gender Difference Is Associated With Severity of Coronavirus Disease 2019 Infection: An Insight From a Meta-Analysis. Crit Care Explor. 2020; 2(6): e0148.
8. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 271 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive 272 study. Lancet. 2020; 395(10223):507-13.
9. Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, et al. Haematological characteristics
10. and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. The Lancet Haematology 2020; 7:671–8.
11. 10.Ramos-Peñafiel CO, Santos-González B, Flores-López EN, Galván-Flores F, Hernández-Vázquez L, Santoyo-Sánchez A, et al. Usefulness of the neutrophil-to-
12. lymphocyte, monocyte-to-lymphocyte and lymphocyte-to-platelet ratios for the prognosis of COVID-19-associated complications. Gaceta medica de Mexico 2020; 156:405–11.
13. 11.Shang W, Dong J, Ren Y, Tian M, Li W, Hu J, et al. The value of clinical parameters in predicting the severity of COVID-19. Journal of medical virology 2020; 92:2188–92.
14. 12.Hamzelou J. Does a cell protein explain covid-19 severity?. New Sci. 2020; 246(3277):9.
15. 13.Bwire GM. Coronavirus: Why Men are More Vulnerable to Covid-19 Than Women?. SN Compr Clin Med. 2020; 2(7):874- 6.
16. 14.Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis. BMC Geriatrics. 2021;21(1).
17. 15.Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Seminars in Immunopathology. 2017;39(5):529–39.
18. 16.Klein SL, Flanagan KL. Sex differences in immune responses. Nature Reviews Immunology, 2016;16(10), 626-638.