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IS THE SEVERITY OF SARS COV2 INFECTION DEPENDENT ON THE PATIENT`S GENDER?

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ABSTRACT

Objective: The COVID 19 pandemic has been the biggest health problem in the last 2 years, exerting huge pressure on the global healthcare system. Studies showed a predisposition in men to develop more severe forms, with a higher mortality rate, in comparison to women. Also, men infected with SARS CoV2 would be at higher risk of hospitalization in acute intensive care units (ICU) with complications that could lead to death

Methods: We conducted a retrospective cross-sectional study that included 177 hospitalized patients in a time frame of 18 months with SARS CoV2 infection confirmed by RT PCR testing in the Pneumology Department of the Clinical Hospital of Pneumophtisiology of Constanta, Romania. The information needed to conduct the study was gathered from the patient's general clinical observation sheet and included: the smoker/ non-smoker status of the patient, age, symptoms associated with COVID19 infection, biological data, form of disease, treatment administered during hospitalization.

Results: The study group included 177 patients, 42% of whom were women (82) and 54% were men (95), suggesting a higher incidence of SARS CoV2 infection in males. The most dominant symptom was cough in 62% cases of women and 56% cases of men. Females had a higher incidence of anosmia (11%) and ageusia (2%) compared to males (anosmia, ageuzia-1%). A higher predominance of women developing moderate forms compared to males. Severe forms were found in 22% of cases in women and 23% in men.

Conclusions: It is inconclusive if male patients show a more severe evolution of COVID19 infection compared to females. Women have shown a predisposition to symptoms such as ageusia, anosmia and a more severe inflammatory syndrome

Keywords: SARS-COV2, symptomatology, gender

Introduction

The COVID 19 pandemic has been the biggest health problem in the last 2 years, exerting huge pressure on the global healthcare system. Due to increased mortality and morbidity among the infected, researchers heavily mobilized to highlight the risk factors that may influence the prognosis of the disease and the need for effective treatment.

Since the beginning of the pandemic, studies have been made on the influence of certain factors in the evolution of the disease. One of those conducted in Wuhan, China showed a predisposition in men to develop more severe forms, with a higher mortality rate, in comparison to women. Also, men infected with SARS CoV2 would be at higher risk of hospitalization in acute intensive care units (ICU) with complications that could lead to death (1).

According to Wolfe J. et al., men present a higher risk of infection at ages over 50 years while women do so between ages 20 to 50 years. Also, for men, smoking was considered a risk factor with a lower adaptive T-cell response, while in the case of women, a more severe inflammatory

syndrome is described, caused by the release of increased amounts of proinflammatory cytokines.

It appears that testosterone plays an important role in suppressing the inflammatory response and low level of testosterone has been associated with a higher risk of ICU admission and death. On the other hand, the estrogen increases the level of nitric oxide, prostacyclins, reducing the platelets aggregation, lowers release of cytokines and plays an important role in decreasing viral replication inside cells.

Another discovery related to hormones influence in the evolution of the disease is the fact that for men, testosterone decreases the IFN-γ release, which can lead to the formation of autoantibodies for interferon (2,3).

Given the physiological differences of women's lungs compared to men, such as airway size, diaphragmatic excursion, total lung capacity, distribution of abdominal fat, it is considered that all these characteristics may affect the prognosis of patients infected with SARS CoV2.

It has been found that shorter women are more likely to receive a higher volume of oxygen during ventilation, thus demonstrating the importance of calculating oxygen requirements based on the patient's height and weight (4,5).

The most common symptoms described in both women and men with positive COVID 19 infection are fever, cough, dyspnea, headache, anosmia, ageusia, diarrhea, abdominal pain, nausea, with a higher prevalence of anosmia-type disorders and ageusia among women according to Spinato G. et al. (6).

Another important role in determining the risk of developing COVID-19 infection is gender occupations and hobbies such as smoking, with a higher prevalence in men. Another example is the habit of women to seek medical help faster, compared to men and the tendency of elderly women to isolate themselves from the rest of the population, thus reducing the degree of infection and transmission of the infection (6,7).

A study conducted by Haischer M. et al questioned the usefulness of wearing a face mask associated with frequent hand washing as a method of protection against COVID 19 infection and it has been shown that women were 50% more willing to comply with these regulations compared to men (8,9).

Considering all these studies, that are based on the importance of the patient's gender in the prognosis of COVID 19 infection, we decided to conduct a retrospective study on the differences between females and males infected with SARS CoV2 admitted to the Pulmonology Department of Clinical Hospital of Pneumophtisiology, Constanta from an biological, clinical, imaging and prognosis point of view.

Material and methods

We conducted a retrospective cross-sectional study that included 177 hospitalized patients in a time frame of 18 months with SARS CoV2 infection confirmed by RT PCR testing in the Pneumology Department of the Clinical Hospital of Pneumophtisiology of Constanta, Romania.

The inclusion criterias were: patient of 18 years or over (adults), male or female, infected with SARS-CoV2, certified by positive RT-PCR test, admitted to our hospital during March 2020 - August 2021, regardless of the presence or absence of comorbidities, and having the informed consent of the patient. Exclusion criteria included age under 18, lack of confirmation of SARS CoV2 infection by RT PCR testing, lack of informed consent of the patient.

The information needed to conduct the study was gathered from the patient's general clinical observation sheet and included: the smoker/ non-smoker status of the patient, age, symptoms associated with COVID19 infection, biological data (LDH, ESR, Fibrinogen, PCR), form of disease, treatment administered during hospitalization.

In order to classify the disease form, we used the imaging aspect of CT chest scan as follows: asymptomatic form (no changes on chest CT), mild form (1-10 points), moderate form (11-17 points), moderate-severe form (18-20 points), severe form (> 21 points).

Descriptive statistical analysis was performed using Microsoft Excel with the rendering of statistical information using tables and graphs.

Results

The study group included 177 patients, 42% of whom were women (82) and 54% were men (95), suggesting a higher incidence of SARS CoV2 infection in males *(Figure 1)*.

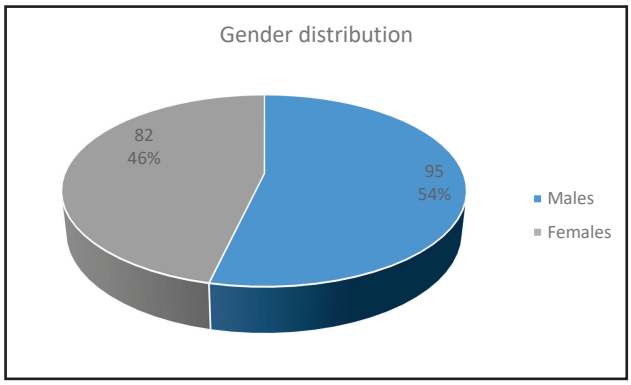


Figure 1. Distribution of patients by gender

In terms of age, the study group was divided into 8 age groups, namely: 18-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and 80-89 years. The average age in the case of females was 57 years and 54 years in males.

There is a higher incidence of SARS CoV2 infection in the 50-59 age group in both women (28%) and men (29%) (Figure 2).

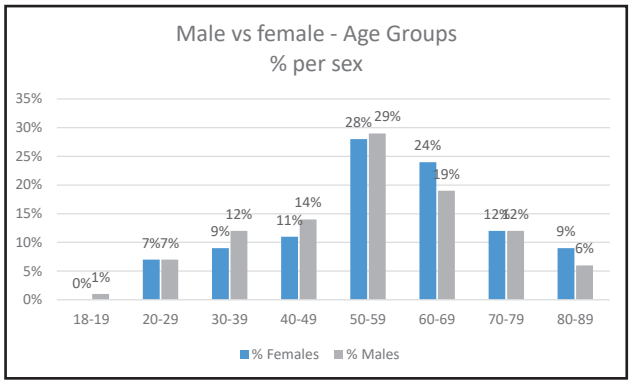


Figure 2. Incidence of SARS CoV2 infection by age groups

In terms of symptoms, the most dominant one was cough in 62% cases of women and 56% cases of men. Females had a higher incidence of anosmia (11%) and ageusia (2%) compared to males (anosmia, ageuzia-1%) (Figure 3).

Fever was more common for men (40%) than for women (35%). The least common symptom for both genders is ageusia (2% for women, 1% for men) (Figure 3).

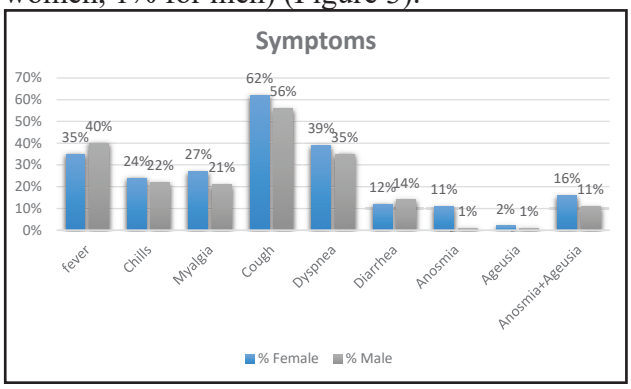


Figure 3. Incidence of symptoms per gender

In the study group, 88% of women are non-smokers (72), 10% smokers (8) and 2% ex-smokers (2). In the case of men, there is an increase in the percentage of smokers to 12% (11), 67% non-smokers (64) and a significant increase in the group of ex-smokers 21% (20) compared to the group of women.

Although approximately 21% of male patients are ex-smokers, they continue to have an additional risk of COVID 19 infection and the development of more severe forms of the disease, compared to 2% of female ex-smokers (Figure 4).

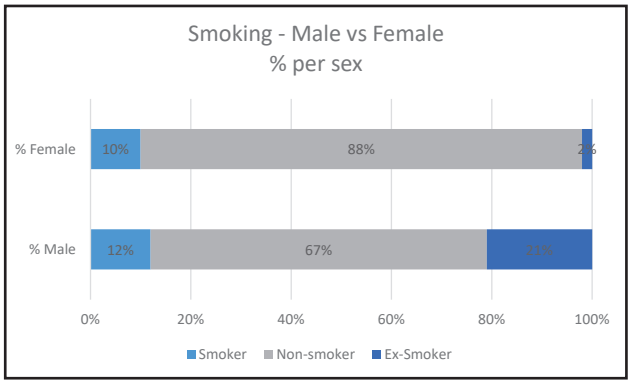


Figure 4. Incidence of smoking

There is a higher incidence of ESR growth in women (84%) compared to men (71%). In the case of Fibrinogen, it was increased in both genders (62%). Males showed a higher percentage of LDH growth (26%) compared to females (23%). C-reactive protein was found increased in 74% of males and 77% of females. (Figure 5)

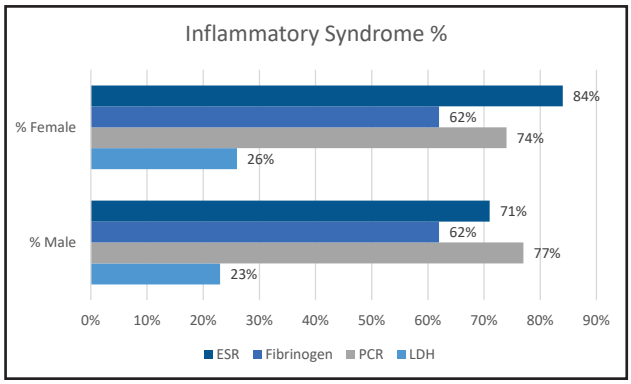


Figure 5. Inflammatory syndrome - distribution by gender

From an imaging point of view, there is a higher predominance of women developing moderate forms in a percentage of 46% compared to males (41%). Severe forms were found in 22% of cases in women and 23% in men. Mild forms were found in 22% of men and 26% of women(Figure 6).

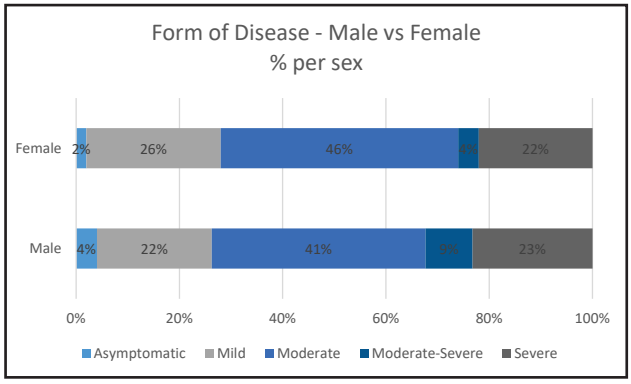


Figure 6. Form of disease based on gender

With regards to the treatment administered, the patients received therapeutic regimen according to the form of disease, symptoms and biological dynamics, indicated by national protocol in force regarding the SARS CoV2 infection.

Thus, 18% of the men included in the study required administration of Remdesivir (administered in severe forms) compared to 9% of the female group. Tocilizumab was given to 3% of men and 4% of women while Favipiravirum, indicated in mild-to-moderate forms, was administered to 42% of men and 46% of women (Figure 7).

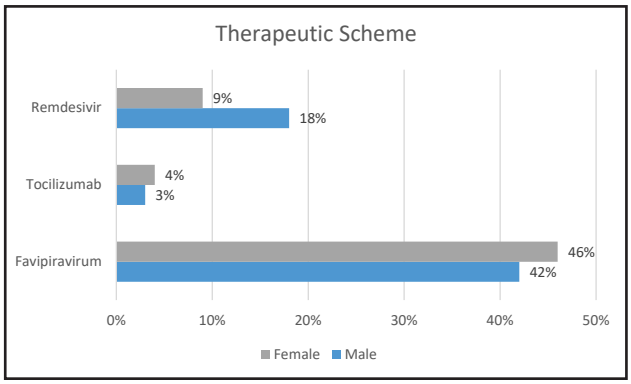


Figure 7. Treatment received per gender

In the evolution of patients, there was only one death in the male group. Also, in the case of patients declared cured, there was a higher percentage for women (26%) compared to men (14%). 8% of the males showed aggravation compared to 10% of the female group (Figure 8).

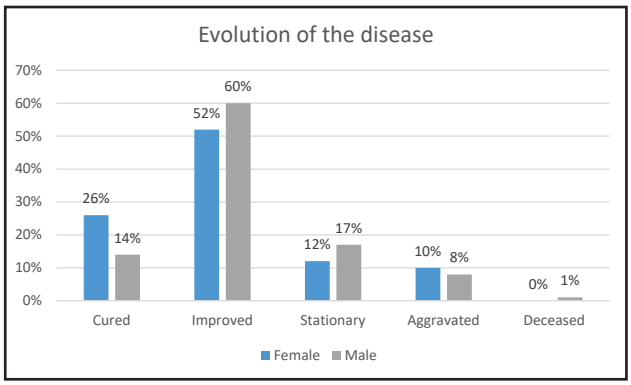


Figure 8. Evolution per gender

Discussion

The results obtained from the study on the group of patients confirmed the data in the literature according to which men are more likely to contract SARS CoV2 infection. Studies have suggested a higher predisposition to infection for men aged 50-59 years, a result also obtained in our study. For women, the study showed a higher infection rate in the 50-59 age group compared to literature data supporting a higher degree of infection in women aged 20-50 years.

Specialist studies suggest smoking as a predominant risk factor present in males, a fact demonstrated in our study group, which included 12% male smokers, 21% ex-smokers, but with a present risk of degradation due to smoking.

In terms of symptoms, as stated in the study by Spinato G. et al, women had a higher percentage of ageusia and anosmia compared to males. Fever was the predominant symptom in males (7).

Regarding the inflammatory syndrome, women had higher values of both ESR and C-reactive protein, with a gender equality in Fibrinogen`s values, as confirmed by the study by Wolfe J. et al. in which women had more severe inflammatory syndrome.

Severe forms were more developed in men, but there was no noticeable difference between the two sexes (22% in women, 23% in men), while the need for Remdesivir treatment was higher for males (18%).

The study also presented limitations, as the number of studied patients is relatively low, with an unequal distribution of sexes, as only patients admitted to our clinic for a relatively short period of time were included. Another limitation of is that the present study does not show a subsequent evolution in the dynamics of patients after an acute episode of COVID19 infection, whether or not the symptoms persisted or whether patients developed long COVID19 syndrome (10).

Conclusions

Through the analysis of the aforementioned group of patients, it is inconclusive if male patients show a more severe evolution of COVID19 infection, but their predisposition to develop more severe forms associated with risk factors such as smoking can be emphasized, along with the fact that men were the more infected of the genders. Women have shown a predisposition to symptoms such as ageusia, anosmia and a more severe inflammatory syndrome (2).

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