The lens of gender medicine on the COVID-19 front

In the age of personalised medicine, and in spite of the current law on gender medicine, there is still no widespread attention of the national and regional health system to the fact that the study of gender and gender differences even during SARS-COV-2 infection could lead to a greater appropriateness in the practice of treatment and prevention of men and women from the early stages of the clinical setting.

Epidemic-prone infectious diseases have likely accompanied humanity since prehistoric times, and already in 2007 the WHO had indicated that stratification of data by gender would help to overcome them [1] This seems to be particularly true in the case of Covid-19. While infection with SARS- CoV-2 does not seem to differ between the two genders [2] , prevalence, severity and mortality predominate in men, especially in age groups over -50 years [3],[4]. In Italy, it reported that 29% of the total number of deceased are women and that they are younger than men (median: men 82 years old, women 79 years old). In this respect, COVID-19 resembles SARS and MERS [5].

In advance of the COVID-19 pandemic, Professor Klein's group at John Hopkins University highlighted that, in general, women are less susceptible to various viral infections for both biological and social reasons. On the other hand, it has been known for many years that the immune system is different in both sexes. Different genes of inflammation and immune-related reactions that control innate and adaptive immune responses are located on the X chromosome.

So women, who have two, can activate an advantageous mosaicism. In addition, immunity and inflammation are, at least in part, controlled by sex hormones[6]. Some authors argue that the greater resistance to viral infections in women and the higher incidence and prevalence of many autoimmune diseases in women is precisely related to sex hormones. In addition, people with diabetes, high blood pressure, immunodepressed people and people with cancer have a much more severe symptom picture that often leads to a fatal outcome. To enter the cell, the virus uses the angiotensin 2 conversion enzyme (ACE2), encoded by a gene located on the X chromosome, with a mechanism to be investigated.

Until now no differences between the two sexes have been described regarding the activity of RNA polymerase and "invisible proteins" used by the virus to mask its RNA[7]. In addition, COVID-19 infection does not seem to have a negative impact on pregnancy and there is no evidence of vertical transmission . The available data do not support the elective cesarean section, the few cases of delivery in positive patients with pneumonia have been carried out for respiratory problems in labor[8] .

At the moment moment, it is well known that no specific and selective therapy is used towards COVID-19, even if a lot of fake news on the drugs are widespread. For example, the use of supplements, such as vitamin

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[1] https://www.who.int/csr/resources/publications/SexGenderInfectDis.pdf
[2] https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000180
[3] https://www.thelancet.com/journals/lanres/onlineFirst ; https://www.nejm.org/doi/full/10.1056/NEJMoa2002032
[4] https://www.epicentro.iss.it/coronavirus/bollettino/Report-COVID
[5] https://jhu.pure.elsevier.com/en/publications/the-intersection-of-sex-and-gender-in-the-treatment-of-influenza;
[6] https://doi.org/10.1016/j.redox.2020.101482
[7] https://rega.kuleuven.be/if/pdf_corona
[8] https://www.rcog.org.uk/globalassets/documents/guidelines/2020-03-26-covid19-pregnancy-guidance.pdf

C, and homeopathic remedies in prevention and therapy finds no scientific evidence. On the other hand, there is talk of the alleged worsening induced by non-steroidal anti-inflammatory drugs, in particular ibuprofen, which does not require a prescription, although the news has not been confirmed by WHO[9]. We wonder if there is a difference in adhering to the fake news about drugs and supplements, between men and women considering that their consumption is increased in women[10].

Given the several differences in the immune system, the pulmonary system and the response to drugs between men and women[11] in our opinion it seems appropriate to consider them in the design and development of anti-SARS-CoV-2 drugs as also provided for by the Italian law 3 of 2018[12].

Furthermore, it is well known that roles, relationships, norms can induce different behaviours between men/boys/elderly people compared to women/girls /elderly people. This may change vulnerability to the disease and exposure to the infectious agent, vaccinations and their adverse reactions as well as treatments and risk factors [13],[14] ,[15]. Women, for example, smoke less than men and smoking could be a risk factor for the severity and mortality of SARS-CoV-2[16] infections.

Several studies so far have shown that men are less willing (more than 30%) to consult doctors (even in the presence of obvious symptoms) and to follow healthier lifestyles[17]. It seems that the indications of this period find men and women willing to respect the rules of hygiene and behaviour in the same way. Will this encourage stable change?

Finally, we must point out that, since the start of the lockdown to date, crime, including gender-based violence, has been drastically reduced. Reports of sexual violence have fallen by 69% [18], feminicides have almost gone to zero. The reasons for this are still unknown. Perhaps it depends on the social control derived from the restrictions, the continuous presence of people in the neighboring apartments are demotivating violent behavior or, and we hope that this is not the case, women who are victims of violence are in absolute impossibility or incapacity to report those who at that time are forced to live together? Answering this question is an ethical and scientific commitment that the whole community must take on.

In the era of personalized medicine, and despite the law in force in Italy on gender medicine, there is still no widespread attention of the national and regional health system to the fact that the study of gender and sex differences even during SARS-COV-2 infection could lead to a greater appropriateness in the practice of treatment and prevention of men and women from the early stages of clinical setting.

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[9] https://www.quotidianosanita.it/scienza-e-farmaci/articolo.php?articolo_id=82754
[10] https://ec.europa.eu/eurostat/web/products-eurostat-news/-/DDN-20170505-1?inheritRedirect=true&
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