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COVID-19 impact on women on both sides of the frontline – the American College of Cardiology Women in Cardiology Section's International Working Group perspective

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SUMMARY

At the beginning of the SARS Co V2 (COVID-19) pandemic, women worldwide represented the majority of health care workers.

As part of the fight against the pandemic, women health care workers became a part of the significant frontline response.

This led to unique challenges that affected women physicians as well as the women patients they were taking care of. The American College of Cardiology Women in Cardiology International Working Group set up a webinar to discuss the challenges being faced by women physicians and women patients in various parts of the world and look towards finding possible solutions for these issues in a webinar themed "WIC Global Perspectives: COVID-19."

Keywords: COVID-19; pandemic; sex differences; pregnancy; women in cardiology; discrimination

INTRODUCTION

The American College of Cardiology's Women in Cardiology (WIC) section was established in 1996 aiming to support female members advance their careers. Irrelevant of parity achieved at medical schools' graduation level, the percentage of women opting for cardiology remained low, prompting the WIC Section and its Leadership Council to strive to recruit more women both nationally and internationally [1, 2]. In 2018, the ACC WIC International Working Group (WG) was launched. Its first meeting gathered over 50 WIC from 30 countries during the European Society of Cardiology annual meeting, after a year of diligent fieldwork aimed to define its agenda. The WG's scope was set to globally promote #EquityBasedMeritocracy - hashtag coined by its founding Chair, Dr. Biljana Parapid – for WIC trained in the United States who either returned to their home institutions outside the USA or opted practicing elsewhere, and also to give an opportunity and facilitate early career cardiologists worldwide to find a mentor and build a collaboration (Figure 1). First speed mentorship table was held only two months later, during the ACC Middle East annual meeting in Jeddah hosted by Dr. Mirvat Alasnag. Medical students, trainees, adult and pediatric cardiologists equally, as well as cardiac surgeons, who were wholeheartedly supported by their male mentors and colleagues, participated in fruitful discussion with all ACC WIC faculty who joined (Figure 2) [3].

The ACC WIC International WG endeavored throughout 2019 to promote education and grew its global membership particularly through social media, which became the silver lining of the 2019/2020 SARS-CoV2 pandemic. As women worldwide turned into key frontline workers in part due to initial mis-perception that they are less prone to SARS-CoV2 infection, ACC worked diligently across its sections to maintain its core values present in times of adversity. Simultaneously, the ACC WIC Leadership Council worked closely with the ACC WIC International WG and in response to the concerns raised by women physicians, opted to address issues linked both to women's health and women's battling adversity both as doctors and members of the academic community.

At the same time, the UN Women's report stated disturbing statistics hallmarking a setback in achieved gender equality so far due to Received • Примљено:

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Figure 1. The ACC WIC International WG Launch (Aug 26, 2018);

top row, ACC WIC International WG Launch, meeting wrap up (left to right): Drs. Martha Gulati (USA), Sharon Mulvaugh (Canada), Biljana Parapid (Serbia), Denisa Muraru (Italy), Hariette van Spall (Canada), Ami Bhatt (USA), Fina Mauri Fere (Spain), Mirvat Alasnag (KSA), Ing Han Lin (Singapoor), Angela Maas (the Netherlands), Alexandra Frogoudaki (Greece), Janneke Wittekoek (the Netherlands), Bharati Shivalkar (Belgium), Toniya Singh (USA), Cara Hendry (UK), Hannah Sinclair (UK), Khalida Soomro (Pakistan);

lower row left, ACC WIC Leadership presence at ESC 2018 (left to right): Drs. Ami Bhatt (ACC MA Chapter WIC delegate), Biljana Parapid (ACC WIC Leadership Council member, ACC WIC International Working Group founding Chair), Toniya Singh (ACC WIC Leadership Council Chair elect), Mary Norine – Minnow Walsh (ACC President), Mirvat Alasnag (ACC Interventional Cardiology Council member);

lower row right ACC WIC International WG Launch, beginning of the meeting: Drs. Jelena Nedeljković (Serbia), Mirvat Alasnag (KSA), Angela Maas (the Netherlands), Janneke Wittekoek (the Netherlands), Bharati Shivalkar (Belgium), Toniya Singh (USA), Alexandra Frogoudaki (Greece), Martha Gulati (USA), Lia Crotti (Italy), Ing Han Lin (Singapore), Biljana Parapid (Serbia), and Silvia Castelleti (Italy)



Figure 2. The ACC WIC International WG Speed Mentoring Tables (Oct 26, 2018) with Drs. Mirvat Alasnag (KSA), Alison Bailey (USA), Biykem Bozkurt (USA), Dipti Itchhaporia (USA), Roxana Mehran (USA), Biljana Parapid (Serbia), and Nireen Okasha (Egypt)



Figure 3. The ACC WIC International WG webinar (Jun 08, 2020) entitled "Women in Cardiology Global Perspectives: COVID-19" organized under the auspices of the WIC Leadership Council Chaired by Drs. Mirvat Alasnag (KSA) and Biljana Parapid (Serbia) with keynote speakers Drs. Shrilla Banerjee (UK), Manal Alasnag (KSA), Sondos Samargandy (KSA), and Sharonne N. Hayes (USA)

pandemic [4]. The "WIC Global Perspectives: COVID-19" webinar held on June 8, 2020 gathered experts in the field (Figure 3) who drafted this brief report aiming to distribute better the messages shared with the audience [5].

SEX DISPARITY IN MORTALITY FROM COVID-19 INFECTION

Historically, male sex has been associated with worse clinical outcomes in previous pandemics, infections, and famine. The epidemics due to coronaviruses (severe acute respiratory syndrome or SARS virus and the Middle Eastern Respiratory Syndrome (MERS) resulted in case fatality rates of 21.9% in males and 13.2% in females [6, 7].

In the majority of countries that have submitted disaggregated data to the World Health Organization – data broken down by sex difference and not just total infection and mortality figures – the infection rate in men is 50% of total, but male mortality varies from between 50% and up to 75% of total mortality [4].

Preliminary Wuhan data showed rates of infection in males ranging 51–66.7% and mortality rates of 2.8% in men *vs.* 1.7% in women, equating to just under a 2:1 mortality ratio for male:female [8, 9]. Italians report 58% of the infected population to be male, who also carried 70% of the COVID-19 related deaths [10].

Yet, global healthcare workforce is dominated by women where up to 85% of nurses in Europe and the Americas are female, as are 46–53% of physicians, which explains why 75% of COVID-19 confirmed infections among healthcare workers were women [4].

Still, the issue of mortality remained, which is explained by critical immune-modulating genes location on the X-chromosome, and in particular the gene that codes for the TLR-7 protein, which is of paramount importance in the detection of single-stranded RNA viruses, such as the coronaviruses [11]. Additionally, while one X-chromosome is usually inactivated in each female cell, the gene coding the TLR-7 protein somehow escapes this inactivation, meaning that women produce more of this protective protein and hence amplify the immune response to COVID-19 [12].

Estrogen provides a protective role, which regulates and makes the response to COVID-19 infection more appropriate. The ACE-2 receptor (with its gene also on the X-chromosome) is used as the portal of entry by the virus. After entry into the cell, the virus causes a downregulation of the ACE-2 receptor. Estrogen opposes this action and also directly suppresses viral replication to provide a two-pronged defense against COVID-19 [13, 14].

When we look into sex as a risk factor, men are known to adhere to hygiene principles less and ask for help later for classical risk factors whose burden is more prominent [13, 15]. Our Chinese colleagues have shown that men with SARS-CoV2 infection carry additional viral and bacterial infections [8].

Therefore, in summary, infection rates in the general population are similar between males and females; however, in healthcare, due to the fact that a significant part of the work force is female, there is a higher incidence of infections in females. Mortality rates, though, remained much higher in males, as a result of sex- and gender-based factors. Sex-disaggregated data are essential to understand variations in risk, infection, and disease.

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JOURNEY WITH HIGH-RISK PREGNANCY DURING COVID-19 PANDEMIC

Some of the most vulnerable patients in an overwhelmed healthcare system during a pandemic are the patients with high-risk pregnancies and their babies. Even in tertiary care facilities and during non-pandemic times, these cases are challenging. For each case, the interplay between maternal and fetal factors requires understanding, risk assessment, and meticulous planning for the delivery of comprehensive multidisciplinary healthcare [16, 17].

Pregnant women seem to have the same risk of becoming infected with COVID-19 as women who are not pregnant [16, 17, 18]. However, from historic data of other viral illnesses and recent pandemics, once infected, pregnant women have a high risk of severe infection. There are reports of increased rates of preterm deliveries and stillbirths in addition to maternal respiratory complications and maternal mortality [18, 19]. The WHO-China Joint Mission on Coronavirus Disease 2019 reported on a cohort of 147 COVID-19 PCR-positive pregnant patients. One percent developed critical illness requiring mechanical ventilation for respiratory failure with or without organ support in the intensive care [20].

Delayed recognition and obstacles to access healthcare are well-recognized causes for an increase in both maternal and fetal mortality rates [21]. Moreover, the physiological changes that occur during pregnancy mimic early presentations of both cardiac and respiratory disease. It is well established that during pregnancy, oxygen consumption increased by up to 30%. To meet demands, cardiac output increases. Hence, it is not uncommon to see tachycardia and shortness of breath at rest during pregnancy. As the pregnancy progresses, there may be basal lung atelectasis [17]. This makes visual triaging very tricky, especially if it is done virtually as is often the case in the current pandemic.

The American College of Obstetricians and Gynecologists developed a risk assessment pathway for pregnant outpatients with suspected or confirmed COVID-19. Such efforts ensure that appropriate channeling of patients into needed healthcare services is done in a timely manner for each case [22]. Peripartum management checklists have also been developed by many centers to outline the preplanned multidisciplinary care needed for women with COVID-19. These checklists identify where the patient will be admitted and the teams that need to be activated upon admission of the patient. Details of the intrapartum management and postpartum management for the mother are charted. Similarly, for the newborn, the care plan includes the clinical samples to be taken as well as the timing of theses samples [23].

Early testing may lead to false positive results due to contamination with maternal fluids. For this reason, the Centers for Disease Control and Prevention recommends testing all neonates born to women confirmed or suspected at the age of 24 hours. If initial results are negative, testing is repeated at 48 hours of age using nasopharyngeal, oropharyngeal, or nasal swabs for RT-PCR [18]. For research

purposes, there are centers that take samples from amniotic fluid, umbilical cord, placenta, and rectal swabs for the neonate.

A systematic review of COVID-19 in newborns reported a very small number of COVID PCR-positive cases. There were no adverse perinatal outcomes found and most had no or mild symptoms. Studies that tested breast milk reported negative COVID results [24]. The virion has been seen on electron microscopy of placental tissue. However, there is much uncertainty regarding vertical transmission. Therefore, based on current literature, there is no evidence to support the absolute contraindication of breastfeeding nor temporary separation of mothers from their newborn. Caution must be advised due to the risk of direct postnatal droplet transmission. Most centers are using shared decision-making between the mother and the clinical team on a case-by-case basis with the option of expressed breast milk [18].

Another challenge during this pandemic is the newborn with congenital heart disease. The British Congenital Cardiac Association has listed the high-risk groups and included single ventricle patients and all infants less than 12 months of age. For those already on medications, such as ace-inhibitors and aspirin, they recommend continuing mediations. For those who need interventions, most hospitals are restructuring their pathways to accommodate the most urgent cases. Minimal interventions are favored and case-by-case plans are made as institutions face these uncharted waters. The learning curve has been steep. But the silver lining of this pandemic has been the support of colleagues across the world in sharing experiences and our agility to reshape and restructure our services.

COVID-19 AND FAMILY CHALLENGES FOR WORKING WOMEN

The World Health Organization has expressed concerns about the COVID-19 pandemic' mental health and psychosocial ramifications generally [25]. A total of 68.7% of frontline medical staff who were women reported a feeling of anxiety regarding their safety and the safety of their families among the participants [26]. Women are less likely to have access to personal protective equipment or correctly sized equipment. Therefore, the effects of this crisis on working women are substantial, and its long-term consequences from depression, suicide, possible self-harm and mood-related issues are genuine and concerning.

During the pandemic, the closedown of schools and daycare centers have shifted the burden of care and schooling of children to working mothers [27].

In response to these challenging times, healthcare establishments are modifying work arrangements to be more flexible with opportunities for both men and women to work from home. Strict infection control guidelines and specialized fitting protected equipment have started to be implemented. Appreciation and acknowledgement of health staff drive and effort by hospital managements and governments, in addition to providing onsite and online

Awareness & Solutions

- ✓ Look to Covid19 pandemic induced crisis as an opportunity to reduce/eliminate gender disparities, barriers and deep-seated biases
- Acknowledge systematic differences in WIC's abilities to fully contribute (eg. caregiving, pregnancy)
- ✓ Datal
 - Assess compensation and other gaps and disparities
 - Assess both leading (publications, grant submissions) and trailing (grants, promotions) indicators
- ✓ Create (new?) infrastructures to allow for women to more fully participate
- ✓ Stop or extend tenure clocks
- Challenge fundamental evaluation systems and resource allocation mechanisms and take into account the inequities in labor distribution for women and other minorities.

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Figure 4. Awareness and solutions for academic advancement during COVID-19 pandemic

psychological support, will help decrease the psychological toll of this pandemic on working women. There is a slow shift in what used to be the social norms, with more men participating in the domestic chores and child care in an equal partnership in these difficult times.

On the bright side, communities have come together to help and support working mothers offering help in child-care and house chores. Additionally, this has led to an open dialogue that has shed light on the unequal distribution of domestic chores, which has led to a discussion on social norms related to this. Thus, it became more acceptable to share domestic responsibilities among men and women, especially in dual-career houses brought to by the social, health and economic demand of COVID-19 crises. Furthermore, many working establishments came to adjust their regulation and schemes allowing remote working and outsourcing, which will improve the balance between work and home that many women are striving to achieve.

COVID-19 AND LOST OPPORTUNITIES FOR WOMEN

Women in medicine, particularly in academic medicine, have disproportionately been adversely affected by the COVID-19 pandemic, all but reversing recent gains. Even before the pandemic, women vs. men cardiologists in the United States faced barriers – importantly, more responsibility for housework, childcare, and supervising family activities [1]. At work, women cardiologists experience more discrimination and higher burnout rates [1, 28], are less likely to participate in research and receive less encouragement to do so, while at the same time perform more service work ("office housework"), diverting energy and time from activities that drive career advancement. These

factors contribute to women cardiologists holding fewer leadership roles and academic promotions and working for substantially lower pay for similar work [29].

The pandemic has further exacerbated domestic workloads, particularly among those with school-age children, threatening to widen the gender academic productivity divide. Women have experienced challenges in academic productivity as COVID-19 has resulted in less direct/onsite work and more remote work. In contrast, academic productivity for men, who are on average less responsible for childcare, may have benefitted. Supporting this hypothesis is evidence that pre-prints and manuscript submissions by women have declined, while increasing/stable among men, with the greatest declines in medicine and among first-author submissions by women (Figure 4) [30]. Lack of face-to-face work means that women and minorities, who previously had less access to informal mentoring and coaching, are now truly "on their own." Younger female cardiologists, already disadvantaged, are also at risk for being disproportionately affected by the many cancelled meetings and lost speaking opportunities - important in and of themselves, but also for networking, since women tend to be less well known.

Finally, in the COVID-19 era, the work is fundamentally different. In-person inequities are heightened with remote work. If it was difficult to be recognized when physically present at a meeting, video meetings render women even less "visible" – and "Zoom fatigue" is real. Women working directly on COVID-19-related science are less likely to be authors [31], cited, or featured in media stories [32, 33], and when featured, often are not afforded their professional title of "Dr." when men are afforded theirs [34]. Taken together, if nothing is done to support women cardiologists at home and at work, these factors are likely to delay academic

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promotions and leadership opportunities, and to lead to more women leaving the cardiology workforce altogether.

The pandemic will subside, but without action these inequities will not, and progress made in advancing women in cardiology will be reversed. We must use this crisis as an opportunity to reduce and/or eliminate gender disparities, barriers, and deep-seated biases. We must challenge the fundamental evaluation systems and resource allocation mechanisms and fully take into account the inequities in labor distribution for women and other minorities. We must acknowledge and address the systematic differences in women cardiologists' ability to fully contribute (e.g. caregiving, pregnancy). Data are needed on compensation, leading (publications, grant submissions) and trailing (grants, promotions) indicators in order to create infrastructures that will allow women to more fully participate and succeed.

CONCLUSION

From the beginning of the SARS-CoV2 pandemic, the world has seen an unprecedented healthcare crisis and also its finest moment in social solidarity and bridging gaps of care and need for all the sick and disadvantaged. Women physicians already suffering biases in both clinical

and academic settings are at a higher risk of losing the ground they have gained so far. While looking for solutions, their unique circumstance should be taken into account. Flexibility in work and academic production will go a long way in mitigating these issues. Continuing to work on maintaining a strong network of mentors and sponsors through events such as these by the ACC WIC International Work Group helps us stay connected and work toward actionable solutions.

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Conflict of interest: None declared.

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Утицај инфекције *COVID-*19 на жене са обе стране прве линије фронта – становиште Интернационалне радне групе Секције за жене кардиологе Америчког колеџа кардиолога

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САЖЕТАК

На почетку пандемије SARS CoV2 (COVID-19) жене широм света представљале су већину здравствених радника. У склопу борбе са пандемијом, жене здравствени радници постале су значајан део снага прве линије одбране. Ово је довело до јединствених изазова који погађају жене као лекаре и жене које оне збрињавају. Интернационална радна група Секције жена кардиолога Америчког колеџа карди-

олога организовала је вебинар како би размотрила изазове са којима се суочавају жене лекари и жене пацијенти широм света и покушала да пронађе могућа решења за ове проблеме кроз вебинар насловљен "Глобалне перспективе жена кардиолога: COVID-19".

Кључне речи: *COVID*-19; пандемија; сексуалне разлике; трудноћа; жене у кардиологији; дискриминација