



## Perspectives in vaccines, immune response, therapeutic interventions and COVID-19

## ARTICLE INFO

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The Coronavirus Disease 2019 (COVID-19) pandemic caused by SARS-CoV-2 has inevitably marked the 21st century based on its impact on morbidity and mortality worldwide. At the same time, the emergence of COVID-19 evoked an unprecedented research burst in the quest of deciphering its pathophysiologic mechanisms, and developing effective preventive and therapeutic strategies. In this special issue, a collection of articles are presented exploring various aspects of COVID-19 infection including risk factors, vaccines and potential complications, therapeutic options and implications in clinical practice.

Early evidence from the first year of the pandemic has highlighted that diabetes mellitus and obesity are important risk factors for SARS-CoV-2 infection and are related to adverse outcomes [1,2]. The high prevalence of obesity, which is characterized by adipose tissue dysregulation, and is accompanied by metabolic, nutritional and immune system derangement, has played a pivotal role in COVID-19 impact [3–7]. Additionally, obesity is related to multiple comorbidities such as metabolic syndrome, endocrine disorders, cardiovascular and autoimmune diseases and cancer, increasing further the risk for severe COVID-19 [8–18]. Likewise, diabetes is related to obesity, showing an increasing incidence while it increases the susceptibility to SARS-CoV-2 infection and serious complications [2,19–23]. In this context, Abbasi and colleagues focused on the mechanisms of COVID-19 pneumonia, prevention and treatment in patients with diabetes, reviewing recent findings [24]. Furthermore, Junapudi and colleagues nicely summarized the effects of COVID-19 on the cardiovascular system and analyzed the potential association between common cardiovascular drugs and susceptibility to COVID-19 as well as the cardiovascular effects of drugs used to treat COVID-19 [25].

Nutrition is important for health and may influence immunity by multiple mechanisms. For example, vitamin D deficiency has been implicated in viral infections as well as COVID-19 [4,26]. Bhatti and Mindikoglu summarized scientific evidence on the beneficial effects of

dawn to sunset fasting on the immune system with regard to COVID-19 [27]. In this intriguing comprehensive review, the authors presented current findings supporting the anti-inflammatory effects, the reduction of oxidative stress, the increased autophagy, the enhanced immunity, the improvement of metabolic syndrome components, and the remodeling of the gut microbiome after implementing dawn to sunset fasting, which is a common fasting practice during Ramadan [27].

The most impactful research evolution to contain the COVID-19 pandemic was undoubtedly the development of vaccines, deploying novel technologies and vaccine platforms. However, the massive vaccination of the world population had multiple implications, facing challenges due to the disparities in availability, the variability in immune responses and efficacy in specific populations, but also raising concerns due to potential serious complications [28–30]. Tavilani and colleagues presented important considerations regarding the safety of COVID-19 vaccines, the efficacy against new variants, challenges in distribution, disparities in availability, gender and race related differences, and implications in special populations such as children and pregnant women [31]. Tsilingiris and colleagues focused on vaccine induced thrombotic thrombocytopenia (VITT), which is a rare but serious complication of the adenoviral vector vaccines against SARS-CoV-2. In their brief review, the authors presented an analysis of potential underlying mechanisms, the clinical and epidemiologic features and also the current evidence-based recommendations on diagnosis and treatment of VITT [32]. In a mini-review, Fragkou and Dimopoulou presented current evidence regarding serious complications of the currently available COVID-19 vaccines, emphasizing the possible pathogenetic mechanisms and their incidence [33]. The authors concluded that serious complications such as anaphylaxis, vaccine-induced thrombotic thrombocytopenia, myopericarditis and Guillain-Barré syndrome are rare, and vaccination is safe for all age and sex groups with a favorable benefit-risk ratio. Furthermore, Tsilingiris's

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group critically discussed the possible implications of the lipid nanoparticle sheath of certain COVID-19 vaccines in the pathogenesis of vaccine-induced myocarditis [34]. Vallianou et al. presented a case of herpes zoster after mRNA vaccination against SARS-CoV-2 in a previously vaccinated with a live attenuated zoster vaccine immunocompetent adult [35]. Also, Siolos and colleagues reported two cases of thyroiditis after vaccination against SARS-CoV-2 [36]. The authors commented that molecular mimicry or vaccine adjuvants may be the responsible mechanism behind subacute thyroiditis, which is a rare complication of vaccines against SARS-CoV-2. Finally, in a comprehensive review Amanatidou and colleagues analyzed the causes and clinical importance of COVID-19 breakthrough infections after vaccination as well as challenges and perspectives [37].

Recent research has made significant progress in elucidating a plethora of pathophysiologic mechanisms of COVID-19 infection, which has revealed as not merely a respiratory infection but rather a multi-system disease with various complications [38,39]. Furthermore, the inflammatory response during COVID-19 may be characterized as a cytokine storm that is associated with sepsis and septic shock [40,41]. In light of this evidence, it is imperative to understand the mechanisms underlying COVID-19 and its differences with sepsis due to other pathogens. In this context, much research has been conducted on biomarkers in sepsis and biomarkers in severe COVID-19 [42–48]. Accordingly, new treatments as well as repurposed drugs have been proposed and tested against COVID-19 [49–52]. Vallianou and colleagues reviewed current and under development drugs for the treatment of COVID-19, also presenting the future perspectives for new drugs from the study of various therapeutic targets [53]. This study is complemented by the review of Ayele and colleagues who nicely summarized repurposed drugs against COVID-19, novel therapeutic targets, vaccines, as well as herbal medicines used in the prevention and treatment of COVID-19 [54]. In addition, Kifle provided current evidence regarding the role of Bruton's tyrosine kinase (BTK) inhibitors in the treatment of COVID-19 [55] BTK inhibitors used in the treatment of certain hematologic malignancies, target a wide range of pro-inflammatory signaling pathways. In this narrative review, the author outlined experimental and clinical evidence supporting the anti-inflammatory and protective effects of BTK inhibitors against lung injury during COVID-19 [55].

During the pandemic, there was a renewed interest for nutraceuticals, mainly due to the lack of specific treatment. Due to their anti-inflammatory and antiviral actions, many dietary supplements and herbal medicines have been proposed either for prophylaxis against SARS-CoV-2 infection or for alleviation of symptoms of COVID-19 [56, 57]. Demeke and colleagues provided an update on the immunomodulatory effects of various herbal medicines, highlighting their anti-inflammatory and immune-boosting effects as well as their antiviral actions specific to SARS-CoV-2 replication and entry into host cells [58]. The authors argued that herbal medicines may have potential beneficial effects as preventive and adjunct treatment in COVID-19. Furthermore, Mentis and co-workers critically discussed evidence supporting potential anti-inflammatory and immune-promoting properties of saffron and analyzed its mechanisms of action related to COVID-19 [59]. In a systematic review, Aucoin and colleagues thoroughly examined human, animal, and cell culture studies on the effect of Echinacea supplementation on cytokine levels, with the aim to identify a possible role in COVID-19 related cytokine storm [60]. The authors concluded that the majority of studies support the anti-inflammatory effects of Echinacea supplementation, expressed as decreased levels of the pro-inflammatory cytokines (IL-6, IL-8, TNF) and increased levels of the anti-inflammatory cytokine IL-10 and interferon, with possible clinical implications in the management of COVID-19.

The impact of the COVID-19 pandemic in public health has been remarkable. Patients with COVID-19 occupied the vast majority of hospital beds worldwide, presenting an important barrier for all patients with other medical problems to access medical services. Furthermore, quarantine measures imposed more barriers, while other strategies were

employed to accommodate patients' medical needs such as telemedicine and remote monitoring using novel technologies [61]. Although SARS-CoV-2 may involve almost every organ, there were a significant number of patients with specific chronic problems unrelated to COVID-19, who faced difficulties to access medical services [62]. In a mini-review, Syriga and colleagues studied the effect of the COVID-19 pandemic and the lockdown policies on the attendance and clinical outcomes of patients with ophthalmic diseases [63]. The authors found that there was a reduction in the number of appointments, cancellations of non-emergency conditions and delays of surgical interventions leading to suspension and delay in the diagnosis and management of ophthalmologic conditions worldwide with a negative impact in terms of visual outcomes.

In conclusion, this collection of articles will provide valuable resources to researchers interested in COVID-19 covering a wide range of aspects from pathogenesis, vaccines and current treatment options to the role of diet and nutraceuticals as well as future therapeutic targets.

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The author has no conflicts of interest to declare that are relevant to the content of this article.

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