MEDHEALTH

LONG-COVID RESEARCH

UPDATE #2

ISSUE DATE: 17 February 2022

The aim of this series of research updates (every 4-6 weeks) is to update the MedHealth specialist doctor panel on any relevant COVID-related peer-reviewed research that is emerging. Doctors are also invited to email through any specific topic requests.

---

1. Serious complications of COVID-19 vaccines: A mini-review

Fragkou & Dimoploulou.
November 2021
Metabolism Open
Original research article; University of Athens, Greece

This article draws attention to the rare but more severe adverse reactions that are increasingly being reported globally to COVID-19 vaccinations. It distinguishes these major reactions to the usually mild side effects that are more commonly experienced (e.g. low-grade fever, pain at injection site). The rare, severe adverse reactions identified by this article include Anaphylaxis, Myopericarditis, and Guillain-Barré syndrome. Also identified was Vaccine-induced thrombotic thrombocytopenia, with a sub-condition, cerebral thrombosis, identified by other research as a specific reaction to adenoviral vector-based vaccines, e.g. AstraZeneca (Brussow, 2021)

Key things to know regarding each of these serious adverse reactions:

Anaphylaxis – usually occurs within minutes after the injection and all respond to adrenaline (median time to symptom onset = 6 minutes)

- The CDC reports 2.5 – 4.7 cases/million for Moderna and Pfizer respectively
- Common signs are urticaria, rash, angioedema, respiratory and airway obstruction symptoms and nausea

Thrombosis with Thrombocytopenia Syndrome (TTS) – first reported in a small cohort of people in the UK following AstraZeneca, but has also occurred after Johnson and Johnson (another adenoviral vector-based vaccine)

- Usually occurs within 4-42 days post vaccination; Life-threatening, often fatal
- Very rare with estimated rate of occurrence 0.73 per 100,000 individuals
- Sees the development of arterial and/or venous thrombosis (usually atypical e.g. cerebral or abdominal), low platelet count, high d-dimers, and positive antibodies for platelet factor 4 (PF4)
- Cerebral Thrombosis, subsyndrome of TTS above (see Brussow, 2021):
- Typically occurs within 2 weeks after AstraZeneca vaccination
- Young median age based on German cohort of 36 years, vast majority female
- Very serious and often fatal (6 of 11 of German & Austrian cohort died)

Myocarditis and/or pericarditis – possible causal association with COVID-19 vaccine (June 2021)

- Rate of occurrence estimated at 12.6 cases per million doses of second dose mRNA vaccine among individuals 12-39 years
- Mechanism unclear, however, possibilities are molecular mimicry of the viral spike and one of the cardiac proteins, as well as a strong immune response and a non-specific, innate inflammatory response
- Patients typically present with retrosternal chest pain, often worsened by inspiration and relieved by leaning forward; some patients develop respiratory distress as well
- Symptom onset usually within 2-3 days (Range 1-7 days) after 2nd dose mRNA vaccine
- Lab tests indicative of myocardial inflammation; abnormal electrocardiogram
- Treatment includes NSAIDS, colchicine and corticosteroids
- All reported cases have developed a non-severe disease with complete clinical recovery within 1-3 weeks post symptom onset

Guillain-Barré syndrome (GBS) – rare and associated with adenovirus vector vaccines

- Acute or subacute immune-mediated neurologic disease of peripheral nerves; median onset 13 days (range 0-75 days)
- Characterized by limb weakness, flaccid paralysis and areflexia; presents with increased CSF protein with normal cell numbers
- Rate of occurrence estimated at 7.8 cases per million doses of vaccine, which doubles for males aged 50-64 years; Median age of those affected is 57 years, 61% were male
- Typically non-fatal, with most demonstrating full clinical recovery

KEY FINDINGS AND CLINICAL RELEVANCE

- Despite these serious adverse reactions being reported, the net benefit-risk ratio remains clearly favourable towards COVID-19 vaccination for all ages and sex groups
- Adverse events to vaccines should be identified early and monitored closely
- More serious adverse reactions such as these should be promptly reported to ensure that they are collated and communicated to the medical community and other stakeholders

*Supplementary information was obtained from an additional source:
Brussow H. (2021) COVID-19: vaccination problems. Environmental Microbiology, 23(6):2878-90

2. Assessment of the further spread and potential impact of the SARS-CoV-2 Omicron variant of concern in the EU/EEA

European Centre for Disease Control (ECDC)
27 January 2022
Rapid Risk Assessment; ECDC, Stockholm

Article Significance

The Omicron COVID-19 variant is rapidly replacing the Delta variant in most EU countries, and more recently in Australia, with a sharp increase in the number of cases and an unprecedented intensity of community transmission. This triggered an assessment of the risk to public health posed by the ongoing spread of Omicron, which was carried out by the European Centre for Disease Control (ECDC).

Results overview

The report was made available in late January, 2022 with findings summarised below:

- Omicron, can to a degree, evade the protective effects of antibodies from vaccination or natural infection (depending on vaccination history and time since last vaccination / booster)
- Omicron seems less likely to lead to a severe clinical outcome that requires hospitalisation or ICU admission. Lower hospitalisation and mortality rates have been reported despite higher community levels[1]
- There are, as yet, **no data on the incidence of prolonged symptoms after COVID-19 due to Omicron**, nor whether this differs from the incidence and experience of post-COVID syndrome or Long-COVID resulting from earlier variants
- There is emerging evidence that there is a higher likelihood of being asymptomic if infected with Omicron compared with earlier variants, and of a higher number of infections in those of younger adult age groups
- The number of cases amongst older people has been increasing – hence **we may see a delayed increase in severe cases and deaths**; modelling analyses suggest that people older than 60 are expected to for the majority of hospital admissions, and people older than 80 may constitute the majority of Omicron-related mortalities
- Vaccination status continues to play a significant role in protecting against severe clinical outcomes
- Maintenance of key non-pharmaceutical interventions (i.e. mask wearing, social distancing and avoiding crowds, good ventilation, working from home) is also crucial to contain the spread of the Omicron variant as much as possible

Public Health implications

- Countries with higher vaccine uptake will now also likely see a period of substantial strain on healthcare systems and on functioning of the society as a whole (i.e. absence from work, particularly in the healthcare sector, & education)
- Moving forward, there is **still a need for multi-layered surveillance, preparedness, and readiness of response strategies** for addressing potential pandemic scenarios
- Increasing overall vaccination uptake, especially boosters for the older and at-risk population will help to protect against the high hospitalisation burden
- The development of variant-independent vaccines and that confer a longer lasting immunity should be prioritised

1 See p.11 of this report: these data may be misleading, however, and care needs to be taken so as to not underestimate the severity of disease caused by Omicron

3. SARS-CoV-2 Omicron variant replication in human bronchus and lung ex vivo

Hui, Ho, Cheung, Ng et al.
In Press 27 January 2022
Journal of Orthopaedic & Sports Physical Therapy
Editorial article; University of Sherbrooke, Canada

Article Significance

The emergence of variants of concern (VOC), including the Omicron COVID-19 variant with significantly faster community transmission is recognized as a threat to global public health. The Omicron variant has been shown to evade immunity from natural infection or currently used vaccines, and is therefore of serious concern. This study compared replication competence of a variety of variants including Delta and Omicron in ex vivo cultures of human bronchus and lung.

Key findings

- Omicron replicated faster than all other SARS-CoV-2 variants in the bronchus, but less efficiently in the lung parenchyma
- The higher replication competence of Omicron in the human bronchus was substantial (over 70-fold increase)

Implications of findings

- The lower replication competence of Omicron in human lung may explain the reduced severity of Omicron now being reported by epidemiological research, however, disease severity is determined by multiple factors
- The authors propose that the higher infectious virus load in conducting airways might result in increased amounts of infectious virus released while breathing or speaking, thus enhancing airborne transmission
- Even if disease severity is modestly reduced, the very efficient transmissibility of Omicron poses a major public health threat and risk of potential burden on healthcare systems
- Further research on preventing Omicron via vaccination booster and other therapeutic options is urgently needed