Update: 2 - 4 September, 2020

UPDATE ON GLOBAL DEVELOPMENTS ON COVID-19

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Summary

- A systematic review of 77 cohort studies comparing pregnant and non-pregnant women reported slightly different symptom profile (less fever and myalgia in pregnant women); more complicated course with increased hospitalization and ICU admission; increased preterm birth; with neonates at increased risk of admission. Gestational diabetes and other comorbid conditions were associated with the diagnosis of COVID-19.
- Randomized controlled phase 1 trial of a vaccine called NVX-CoV2373, evaluated primary safety and immunogenicity analyses and found at day 35 it had acceptable safety findings with high immune responses. Phase II and phase III trials are underway.
- Recommendations for post-COVID health service recovery with focus on mental health has been published.

Recommendations

Pregnant women need to be considered among at the risk group.

Not premature to consider for post-covid health service recovery plan.

Update on pathogenesis

- A systematic review was done on clinical manifestations, risk factors, and maternal and perinatal outcomes of COVID-19 in pregnancy. A total of 77 cohort studies (55 comparative, 22 non-comparative) were included in the final analysis of studied published between Dec 2019 and June 2020. Forty cohort studies reported on clinical manifestations (13,018 pregnant, 85 084 non-pregnant women), 45 studies reported on COVID-19 related maternal outcomes (14,094 pregnant, 85,169 non-pregnant women), and 35 studies reported on pregnancy related maternal (6,279 women) and perinatal outcomes (2,557 neonates). The study revealed that;

➢ The overall rate of COVID-19 diagnosis in pregnant and recently pregnant women attending or admitted to hospital was 10% (95% CI 7% to 14%).

➢ A diagnosis of COVID-19 in pregnancy was associated with maternal obesity, pre-existing comorbidities, asthma and gestational diabetes.

➢ Compared with non-pregnant women of reproductive age, pregnant and recently pregnant women with COVID-19 were less likely to report symptoms of fever (OR= 0.43, 95% CI 0.22 - 0.85) and myalgia (OR = 0.48, 95% CI 0.45- 0.51).

➢ Pregnant women with COVID-19 were more likely to be admitted to ICU (OR= 1.62, 95% CI 1.33 -1.96) and required invasive ventilation (OR= 1.88, 95% CI 1.36 - 2.6). Pre-existing maternal condition was a risk factor for both ICU admission and invasive ventilation.

- 73 pregnant women with confirmed COVID-19 (0.1%, 26 studies, 11 580 women) died from any cause.
- Preterm birth was higher in pregnant women with COVID-19 compared with those without the disease (OR = 3.01, 95% CI 1.16 - 7.85).
- Neonates born to mothers with COVID-19 were at increased risk of admission to the neonatal unit (OR = 3.13, 95% CI 2.05 - 4.78). [Allotey et al, 2020].

Update on vaccine

- One of the studies funded by the Coalition for Epidemic Preparedness Innovations, conducted a randomized, placebo-controlled phase 1 trial to evaluate the safety and immunogenicity of recombinant SARS-CoV-2 vaccine or NVX-CoV2373. NVX-CoV2373 is a recombinant severe acute respiratory syndrome coronavirus 2 (rSARS-CoV-2) nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins and Matrix-M1 adjuvant. The vaccine was administered in two doses (in 5-µg and 25-µg) 21 days apart with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments in 131 healthy adults. After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. The primary safety and immunogenicity analyses at day 35 indicate, in healthy adult participants 18 to 59 years of age, two-dose regimens of rSARS-CoV-2 plus the Matrix-M1 adjuvant had acceptable safety findings. Moreover, reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. Additionally, the vaccine induced high immune responses, with levels of neutralizing antibodies that closely correlated with anti-spike IgG. Neutralizing antibody responses after the second vaccination with rSARS-CoV-2 plus Matrix-M1 exceeded values seen in symptomatic COVID-19 outpatients and were of the magnitude seen in convalescent serum from hospitalized patients with COVID-19. The benefit of the Matrix-M1 adjuvant was clear in the magnitude of the antibody and the T-cell response, the induction of functional antibodies, and antigen dose sparing. Major limitation of this trial includes the small size of the trial, and the populations at greatest risk for serious COVID-19 which is the older population were not included in the trial. The researchers revealed that based on this results Phase 2 trial is already under way and they are in the preparatory stages of starting phase 3(Keech, Albert et al. 2020).

Update on treatment

- A multicenter randomized double-blind sequential trial that aimed to determine the effect of hydrocortisone on treatment failure on day 21 in critically ill patients with SARS-CoV-2 infection and acute respiratory failure was discontinued by the DSMB following evidence of effectiveness of dexamethasone. The study was conducted in France, with 149 patients. Patients were randomized to receive low-dose hydrocortisone (n = 76) or placebo (n = 73) and interim analyses planned every 50 patients. The trial was terminated prematurely after the press release of the dexamethasone trial. According to those findings, dexamethasone may reduce mortality on day 28 in mechanically ventilated patients and, to a lesser extent, in oxygen-dependent patients. The DSMB therefore recommended stopping the trial after 149 patients of the planned maximum of 290 had been enrolled considering that it would be unethical to resume a corticosteroid vs placebo trial in light of the changes in treatment recommendations based on the result from the dexamethasone trial. One hundred forty-eight patients (99.3%) completed the study, and there were 69 treatment failure events, including 11 deaths in the hydrocortisone group and 20 deaths in the placebo group. The primary outcome, treatment failure on day 21, occurred in 32 of 76 patients (42.1%) in the hydrocortisone group compared with 37 of 73 (50.7%) in the placebo group (difference of proportions, –8.6% [95.48% CI, –24.9% to 7.7%]; P = .29). Of the 4 prespecified secondary outcomes, none showed a significant difference. No serious adverse events were related to the study treatment. Therefore, hydrocortisone, compared with placebo, did not significantly reduce the rate of treatment failure, defined as death or persistent dependency on mechanical ventilation or high-flow oxygen therapy, on day 21 among critically ill patients with COVID-19. In addition, hydrocortisone, compared with placebo, did not significantly reduce the proportion of patients receiving mechanical ventilation on day 21. However, the study was stopped early and likely was underpowered to find a statistically and clinically important difference in the primary outcome (Dequin, Heming et al. 2020).

Psychosocial wellbeing updates

The Lancet Psychiatry (Lamp et al, 2020) has published a commentary with recommendations for recovery planning applicable to the UK National Health Service. Four recommendations are presented below (cited word for word).

- First, giving thanks, both written and verbally, which acknowledges the challenging work undertaken, can foster individual resilience. This communication should include accurate up-to-date information about potential psychological difficulties and supports.
- Second, return-to-normal work interviews by supervisors who feel confident speaking about mental health. These interviews allow for a better understanding of a staff member's experiences, while identifying secondary stressors in order to collaboratively design individualised recovery plans. Such discussions reduce sickness absence in other trauma-exposed occupations.
- Third, active monitoring for anyone exposed to potentially traumatic events, particularly individuals considered to be at higher risk of developing mental health problems. An anonymous online self-check tool might encourage honest and meaningful responses while providing automated tailored feedback.
- Fourth, group discussions to help staff to develop a meaningful narrative that reduces risks of harm. Schwartz rounds, a structured forum for clinical and non-clinical staff to discuss emotional and social aspects of work, are one such evidence-based model.

Reference list

- Dequin, P.-F., N. Heming, F. Meziani, G. Plantefève, G. Voiriot, J. Badié, B. François, C. Aubron, J.-D. Ricard, S. Ehrmann, Y. Jouan, A. Guillon, M. Leclerc, C. Coffre, H. Bourgoin, C. Lengellé, C. Caille-Fénérol, E. Tavernier, S. Zohar, B. Giraudeau, D. Annane, A. Le Gouge, f. t. C. C. T. Group and t. C.-T. Network (2020). "Effect of Hydrocortisone on 21-Day Mortality or Respiratory Support Among Critically Ill Patients With COVID-19: A Randomized Clinical Trial." JAMA.
- Keech, C., G. Albert, I. Cho, A. Robertson, P. Reed, S. Neal, J. S. Plested, M. Zhu, S. Cloney-Clark, H. Zhou, G. Smith, N. Patel, M. B. Frieman, R. E. Haupt, J. Logue, M. McGrath, S. Weston, P. A. Piedra, C. Desai, K. Callahan, M. Lewis, P. Price-Abbott, N. Formica, V. Shinde, L. Fries, J. D. Lickliter, P. Griffin, B. Wilkinson and G. M. Glenn (2020). "Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine." New England Journal of Medicine.
- Kisely S, Warren N, McMahon L, Dalais C, Henry I, Siskind D. Occurrence, prevention, and management of the psychological effects of emerging virus outbreaks on healthcare workers: rapid review and meta-analysis. bmj. 2020;369.

- Lamp D, Greenberg N, Stevelink A MS, Wessely S. Mixed signals about the mental health of NHS workforce. Lancet psychiatry. Published:September 03, 2020DOI: https://doi.org/10.1016/S2215-0366(20)30379-5
- Allotey, J., Stallings, E., Bonet, M., Yap, M., Chatterjee, S., Kew, T., . . . Thangaratinam, S. (2020). Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. [Research Support, Non-U.S. Gov't]. BMJ, 370, m3320. doi: 10.1136/bmj.m3320