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UPDATE ON GLOBAL, REGIONAL AND NATIONAL DEVELOPMENTS ON COVID-19

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Summary

- A whole population study in England indicated the association between Diabetes and COVID-19 related mortality. Another study showed higher risk of COVID-19 related mortality in this group.
- Being underweight (BMI <20) increase risk of mortality as is the case with BMI >40.
- Scientists globally have condemned the development of vaccines as dangerously rushed.
- Yet, recommendation is being made that the safety of vaccines for pregnant and lactating women should also be studied.

Recommendations

- Consider inclusion of the potential risk of increased mortality from COVID-19 among underweight individuals in awareness raising packages.
- There is risk from the current rush for vaccine development. Strategies for any rollout and decisions for adaptation of vaccines or safety standards need to be determined at this point. Any major problem in implementation of vaccines in the era of 'infodemics' can have major health and political repercussions. It can also have consequences in the control of future epidemics.

Update on pathogenesis

Diabetes Mellitus and COVID-19

- A whole population study was conducted in England with the aim of assessing the association between type 1 and type 2 diabetes with COVID-19 related mortality. The study compared in- hospital COVID-19-related death among a total of 61,414,470 people; 263,830 (0.4%) with type 1 diabetes, 2,864,670 (4·7%) type 2 diabetes, 41,750 (0·1%) other types of diabetes, and 58,244,220 (94·8%) had no diabetes). Another study was also done on the same cohort and the researchers identified some risk factors for COVID-19-related mortality among this population. Weekly number of deaths during the first 19 weeks of 2020 was compared with the mean number of deaths for the corresponding weeks in 2017, 2018, and 2019. The main findings of the two studies are summarized as follow:
  - After adjusting for age, sex, deprivation, ethnicity, and geographical region, the odds ratio for in-hospital were 3·51 (95% CI 3·16–3·90) in people with type 1 diabetes and 2·03 (1·97–2·09) in people with type 2 diabetes compared with people without diabetes.
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- When it's further adjusted for previous hospital admissions with coronary heart disease, cerebrovascular disease, or heart failure, the OR became 2·86 (2·58–3·18) for type 1 diabetes and 1·80 (1·75–1·86) for type 2 diabetes [Barron, 2020].
- Male sex, older age, renal impairment, non-white ethnicity, socioeconomic deprivation, and previous stroke and heart failure were associated with increased COVID-19-related mortality in both type 1 and type 2 diabetes [Holman, N., 2020].
- People with HbA1c of 86 mmol/mol (10·0%) or higher had increased COVID-19-related mortality (hazard ratio 2·23 [95% CI 1·50–3·30] in type 1 diabetes and 1·61 [1·47–1·77] in type 2 diabetes) compared with those people with HbA1c of 48–53 mmol/mol (6·5–7·0%).
- BMI and COVID-19-related mortality has a u-shaped association both in type 1 and type 2 diabetes. Compared to people with BMI of 25-30 kg/m², those with less than 20 kg/m² and >40 kg/m² had hazard ratio of 2·45 (95% CI 1·60–3·75) and 2·33 (1·53–3·56) respectively among type 1 diabetes. Similarly, for type 2 diabetes, the hazard ratio is 2·33 (2·11–2·56) and 1·60 (1·47–1·75) in these BMI categories [Holman, N, 2020].

Update on Epidemiology (Incidence, mortality, recovery & epidemiologic parameters)

- The number of new cases and deaths continue to increase globally, especially in the USA, Brazil, Russia, India and south Africa. There is concern among experts of influenza pandemic in the context of uncontrolled COVID-19, especially in the USA.

Update on Diagnosis

- In one study, the analytical sensitivity (lower limit of detection, LOD) of seven commonly used qualitative SARS-CoV-2 molecular assays: the Abbott Molecular RealTime SARS-CoV-2 assay, the NeuMoDx™ SARS-CoV-2 assay, the Roche Cobas®SARS-CoV-2 assay, the BD SARS-CoV-2 reagents for BD MAX™ system, the Hologic Aptima® SARS-CoV-2 assay, the Xpert Xpress SARS-CoV-2 test, and the GenMark ePlex SARS-CoV-2 test were compared. The comparison was performed utilizing a single positive clinical specimen that was serially diluted in viral transport media and quantified by the EUA approved SARS-CoV-2 droplet digital PCR assay. Replicate samples were prepared and evaluated for reproducibility across different molecular assays with multiple replicates per assay. It was demonstrated that the seven assays could detect 100 % of replicates at a nucleocapsid gene concentration of (N1 = 1,267 and N2 = 1,392) copies/mL. Roche and Abbott were found to be the most sensitive platforms (Mostafa et al., 2020).

Update on treatment

- A perspective piece in the journal of Lancet infectious disease that discusses the need for inclusion of pregnant women in COVID-19 vaccine development. According to the article there are a number of questions that have yet to be answered in regards to COVID-19 and pregnancy such as the effect of COVID-19 on miscarriage, intrauterine fetal growth restriction, congenital anomalies, long-term growth, and neurodevelopmental outcomes. However, there are no studies thus far that indicate pregnant women to be at increased risk of complications due to COVID-19 compared with non-pregnant women. An additional consideration for pregnant women with COVID-19, especially among those with severe infection, is that access to effective drugs might be restricted, considering the scarcity of data on most drugs in pregnancy. The need for intensive care support among patients with COVID-19 is of particular concern for pregnant women who reside in low-income and middle-income countries. As a result, pregnant women should be considered as candidates for preventative measures, of which vaccination is the gold standard. Heath, Le Doare et al point out that since the immune responses to vaccination in pregnant women cannot be assumed from that of non-pregnant women and because the assessment of safety of vaccination in pregnancy is unique, pregnant women should be included in appropriately designed vaccine trials. However it is important to note that to enable the inclusion of pregnant and lactating women in the development of COVID-19 vaccines, key questions need to be answered: what is the short-term and long-term burden of COVID-19 in pregnant women, the fetus, and infants (in all populations and ethnic groups) and if the risk of complication of having COVID 19 outweigh the risk of taking the vaccine. A number of specific strategies were suggested to ensure that pregnant women and lactating women are included in vaccine research. These strategies include ensuring that at least some of the candidates prioritised for development should use platforms and adjuvants that would be suitable for use in pregnancy; the need to include developmental toxicology studies early in the clinical development programme; and the need to plan systematic collection of data on immunogenicity and pregnancy-specific indicators of safety from participants (and their infants) who are not aware of their pregnancy at the time of exposure in vaccine trials (Heath, Le Doare et al. 2020).
- Russian President Vladimir Putin announced on 11 August that the country's health regulator had become the first in the world to approve a coronavirus vaccine for widespread use. So far what we know about the Gamaleya vaccine is that it has been given to 76 volunteers as part of two early-stage trials listed on ClinicalTrials.gov, but no results from those trials or

other preclinical studies have been published, and little else is known about the experimental vaccine. According to the ClinicalTrials.gov listings, the vaccine, which is given in two doses, is made of two adenoviruses that express the coronavirus's spike protein. The first dose contains an Ad26 virus and the second, 'booster' dose is made of an Ad5 virus. According to the vaccine's Russian-language registration certificate, 38 participants who received one or two doses of the vaccine had produced antibodies against SARS-CoV-2's spike protein, including potent neutralizing antibodies that inactivate viral particles. These findings are similar to the results of early-stage trials of other candidate vaccines. Side effects were also similar, such as fever, headache and skin irritation at the site of injection. Scientists globally have condemned the vaccine as dangerously rushed. The fact that Russia hasn't completed Phase III trials to test the vaccine's safety and efficacy, and rolling out an inadequately vetted vaccine could endanger people who receive it. It could also impede global efforts to develop quality COVID-19 immunizations. There is fear that any problem with the Russian vaccination campaign would be disastrous both through its negative effects on health, but also because it would further set back the acceptance of vaccines in the population (Callaway 2020).

Update on personal protective equipment

Face mask use

- One study, from the United States, assessed the fitted filtration efficiencies (FFEs) for face mask alternatives used during the COVID-19 pandemic. They used the Occupational Safety and Health Administration's Quantitative Fit Testing Protocol for Filtering Facepiece Respirators in a laboratory atmosphere supplemented with sodium chloride particles to assess the FFEs of a variety of respirators. A total of 29 different fitted face mask alternatives were tested on 1 man and 1 woman. Out of the 29 masks tested, six of them are not approved by the US National Institute for Occupational Safety and Health which included KN95 (NIOSH) and two of them were only CDC-approved (non-NIOSH-approved_. The results showed expired N95 respirators with intact elastic straps and respirators subjected to ethylene oxide and hydrogen peroxide sterilization had unchanged FFE (>95%). The performance of N95 respirators in the wrong size had slightly decreased performance (90%-95%FFE). All of the respirators not listed as approved by NIOSH failed to achieve 95% FFE. Neither of the 2 imported respirators authorized for use by the CDC achieved 95% FFE, and the more effective of the 2 functioned at approximately 80% FFE. Surgical masks (with ties)

and procedural face masks (with ear loops) had filtering performance that was lower relative to that of N95 respirators (98.5% overall FFE), with procedural face masks secured with elastic ear loops showing the lowest efficiency (38.1% overall FFE). The authors concluded that expired N95 respirators and sterilized, used N95 respirators can be used by clinicians interacting with patients during the COVID-19 pandemic when new N95 respirators are not available and that other alternatives may provide less effective filtration (Sickbert-Bennett et al., 2020).

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