

REVIEW

Impact of diabetes on COVID-19 and other infection: Report from the 22nd Hong Kong Diabetes and Cardiovascular Risk Factors—East Meets West Symposium

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has posed enormous challenges to healthcare systems worldwide. The negative impact of COVID-19 is widespread and includes not only people who contracted the disease but also those with chronic morbidities such as diabetes whose care is compromised due to diversion of medical resources. People with diabetes are generally more susceptible to infection as a result of altered immunity. People with diabetes have a worse prognosis from COVID-19 and there is evidence to suggest that severe acute respiratory syndrome coronavirus 2 may directly affect pancreatic function precipitating hyperglycaemic crises. In the United Kingdom, one of the most heavily affected countries, guidelines are in place to unify the management of people with diabetes hospitalized for COVID-19. Diabetes services are re-organized to ensure that medical care of people with diabetes is maintained despite resource and other practical constraints. Public health measures including social distancing, hand hygiene and the use of face masks are crucial in containing community transmission of the virus. Hong Kong, one of the most densely populated city in the world, is particularly vulnerable and has in place a stringent containment policy and aggressive contact tracing to ensure public safety during this pandemic.

KEYWORDS

COVID-19, diabetes, infection

1 | INTRODUCTION

Until recently, infection has been an under-recognized and under-studied complication of diabetes. The coronavirus disease 2019 (COVID-19) pandemic has brought into spotlight the vulnerability of people with diabetes during this medical catastrophe. At the time of writing, severe acute respiratory syndrome (SARS) coronavirus (CoV)-2 has infected over 90 million people causing 2.0 million deaths worldwide.¹ Although it is unclear whether diabetes increases the risk of contracting the virus, people with diabetes are more likely to progress to severe disease and die than those without diabetes.^{2–4} Furthermore, COVID-19 predisposes to acute

hyperglycaemic emergencies including diabetic ketoacidosis (DKA) and hyperosmolar, hyperglycaemic state (HHS) in people with or without pre-existing diabetes.⁵ The rampant spread of COVID-19 poses an unprecedented burden to our healthcare systems. As healthcare workers are being recruited to attend to people with COVID-19, they are no longer able to support care of those others with less pressing medical conditions. Delivery of many routine services is being disrupted or compromised and this has critically affected the care of people with diabetes (S1). The impact of this pandemic on the diabetes community is widespread, and healthcare workers need support and resources to allow them to continue to provide care to people in need and minimize adverse outcome.

In recognition of the importance and urgency to find solutions to maintain diabetes care during the pandemic, the 22nd Diabetes and Cardiovascular Risk Factors—East Meets West Symposium in Hong Kong co-hosted at a session with Diabetic Medicine on 4 October 2020, on the theme of diabetes, infection and COVID-19. The symposium began with a discussion of the association between diabetes and infection based on epidemiological studies and summarized the possible mechanisms for the increased risk of infection in diabetes. The next talk described the effect of COVID-19 on people with diabetes and highlighted the challenges faced by healthcare workers during this crisis and the impacts on people with diabetes. As the United Kingdom (UK) is among one of the most heavily affected countries, the work of the UK National In-patient Diabetes COVID-19 Response Group including guidelines on in-patient management of infected individuals and re-organization of diabetes services was discussed. The final talk addressed public health measures to combat COVID-19 including physical distancing, hand hygiene and the use of medical masks. The similarities and differences between the previous severe acute respiratory syndrome (SARS) epidemic and the present COVID-19 outbreak in Hong Kong were discussed.

2 | DIABETES AND INFECTION: TRENDS AND UPDATES

The relationship between diabetes and infection has been recognized for over a century.⁶ Among small case series of death in people with diabetes, up to one third were directly related to acute infections.⁶ Furthermore, diabetes was often first detected when a person presented with an infective illness, and this holds true even in the present day especially in places with under-developed healthcare systems and without effective diabetes screening measures.

2.1 | Epidemiology of diabetes and infection

The Emerging Risk Factors Collaboration analysed individual-level data of 0.8 million participants for the association between blood glucose and death.⁷ For an average middle-aged person with diabetes compared with their counterpart without diabetes, 30% of excess deaths were attributable to non-vascular non-cancer causes including infection.⁷ Several large-scale epidemiological studies have also reported an increased risk of common infections with diabetes.^{8–12} Despite differences in methodologies used to define infections with some studies using hospital admission records and others relying on clinic records or prescription of antibiotics, the magnitudes of the excess risks are similar

across studies. Compared with the general population, the rates of pneumonia were increased 1.4- to 2.6-fold,^{8–11} kidney infections 3.0- to 4.9-fold,^{8,9,11} skin infection 1.4- to 2.4-fold^{9,10,12} and general sepsis 2.0- to 3.2-fold^{8,10–12} in people with diabetes. When stratified by diabetes types, the risks for infections were increased in both type 1 diabetes and type 2 diabetes with a larger disparity observed with type 1 diabetes.¹⁰ It should be noted that the greater tendency of people with diabetes to seek medical attention for infection and the lower threshold to initiate treatment may inflate the risk difference when compared against people without diabetes. Additionally, the presence of co-morbidities such as cardiovascular disease, chronic kidney disease and obesity, which are themselves independent risk factors for infection, may confound the association between diabetes and infection, although among studies that have adjusted for underlying medical conditions, the risk relationships were held significant.^{9,10} Death from infection is also increased in people with diabetes. In a study of over 1 million Australians with diabetes, standardized mortality ratios for death attributable to infections and parasitic diseases, pneumonia, osteomyelitis and sepsis ranged between 1.2 and 3.3 for type 2 diabetes, and between 4.4 and 29.6 for type 1 diabetes.¹³

Two recent population-based studies examined the temporal trends for infection rates. In a national survey conducted in the United States, the annualized rates of infection-related hospitalization were increased or stagnant in people with diabetes but decreased in the general population.¹¹ Similarly, using the Hong Kong Diabetes Surveillance Database of over 0.7 million individuals with diabetes, rates of hospitalization for most infection types were unchanged with the exceptions of tuberculosis and influenza which showed a decreasing and an increasing trend respectively.⁸ These observations are disturbing when they are contrasted against large declines in rates of other major diabetes-related complications including cardiovascular disease, kidney disease, lower-extremity amputation and hyperglycaemia crises in these regions.¹⁴ In Hong Kong, pneumonia has surpassed cardiovascular disease as the most common cause of death in people with diabetes and accounted for close to one third of death in this population in 2016.¹⁵ Hence, improvements in diabetes management including developments in pharmacotherapeutics and other technological advances have not translated into reduction in infection risks. The reasons for the unchanging rates are unclear but may relate to an ongoing lack of awareness about infection risks leading to delays in presentation, changing pathogenicity of invading organisms, inappropriate use of antibiotics and other environmental factors such as overcrowding and climate change. Of note, sodium-glucose cotransporter-2 (SGLT-2) inhibitors increase the risk of genital tract infection. However, given the low uptake of this drug class during the surveillance period, it is unlikely that the use of SGLT-2 inhibitors has contributed to the observed trends.

2.2 | Mechanisms for increased risk of infection in people with diabetes

Several mechanisms explain the increase in infection risk in diabetes Figure 1. First, a high glucose milieu has suppressive effects on the immune function, especially innate immunity, and lowers host defence against invading pathogens.^{16,17} Mechanistic studies have demonstrated impairments across a range of neutrophilic function. Adaptive immunity is deemed less disturbed although delayed or ineffective antigen presentation may alter T-helper cell response. Second, diabetes affects the micro- and macro-vasculatures leading to reduced tissue perfusion which in turn may impede the delivery of immune cells to the site of infection. Third, co-morbidities and complications of diabetes are themselves independent risk factors for infection.¹⁸ For instance, smoking and obesity increase the risks of severe presentation from pneumonia due to their harmful effects on pulmonary function, while people with previous stroke are more susceptible to aspiration causing both chemical pneumonitis and bacterial pneumonia. Among people with COVID-19, chronic kidney disease, in particular end-stage kidney disease, chronic dialysis or previous kidney transplant, predicts a worse outcome.

Glycaemic control has been shown to be a significant determinant of infection. In a large longitudinal cohort of

Chinese with type 2 diabetes, up to 20% required hospitalization for major infection over a follow-up period of 5 years.¹⁸ During this time, a U-shape relationship between glycated haemoglobin (HbA_{1c}) and incident infection including infection of the respiratory tract, genitourinary tract and skin/subcutaneous tissue was detected, adjusted for other clinical covariates including age, sex, smoking, obesity and comorbidities. In another study conducted in the UK, HbA_{1c} levels were also correlated with infection-related hospitalization and death from infection.¹⁹ Compared with the reference group with HbA_{1c} ≥ 42 to 53 mmol/mol (≥ 6 to $< 7\%$), the hazard ratio for infection-related hospitalisation was 1.1 in the group with HbA_{1c} ≥ 53 to < 64 mmol/mol (≥ 7 to $< 8\%$) and increased to 3.0 in those with HbA_{1c} ≥ 97 mmol/mol ($\geq 11\%$). Again, a modest elevation in risk was observed in individuals with very low HbA_{1c} (hazard ratio 1.2 in the group with HbA_{1c} < 42 mmol/mol [$< 6\%$]), who were also older and had a lower body mass index.¹⁹ Notably, the hazards conferred by elevated blood glucose were greater among the younger age group aged 40–64 years than those at or above 65 years. Indeed, an age-differential in the risk for infection in people with diabetes was observed in other studies.^{8,11} Among Chinese men with diabetes, the group aged 20–44 years had 3.6-fold increase in risk for pneumonia and 11.2-fold increase in risk for general sepsis compared with their age-matched

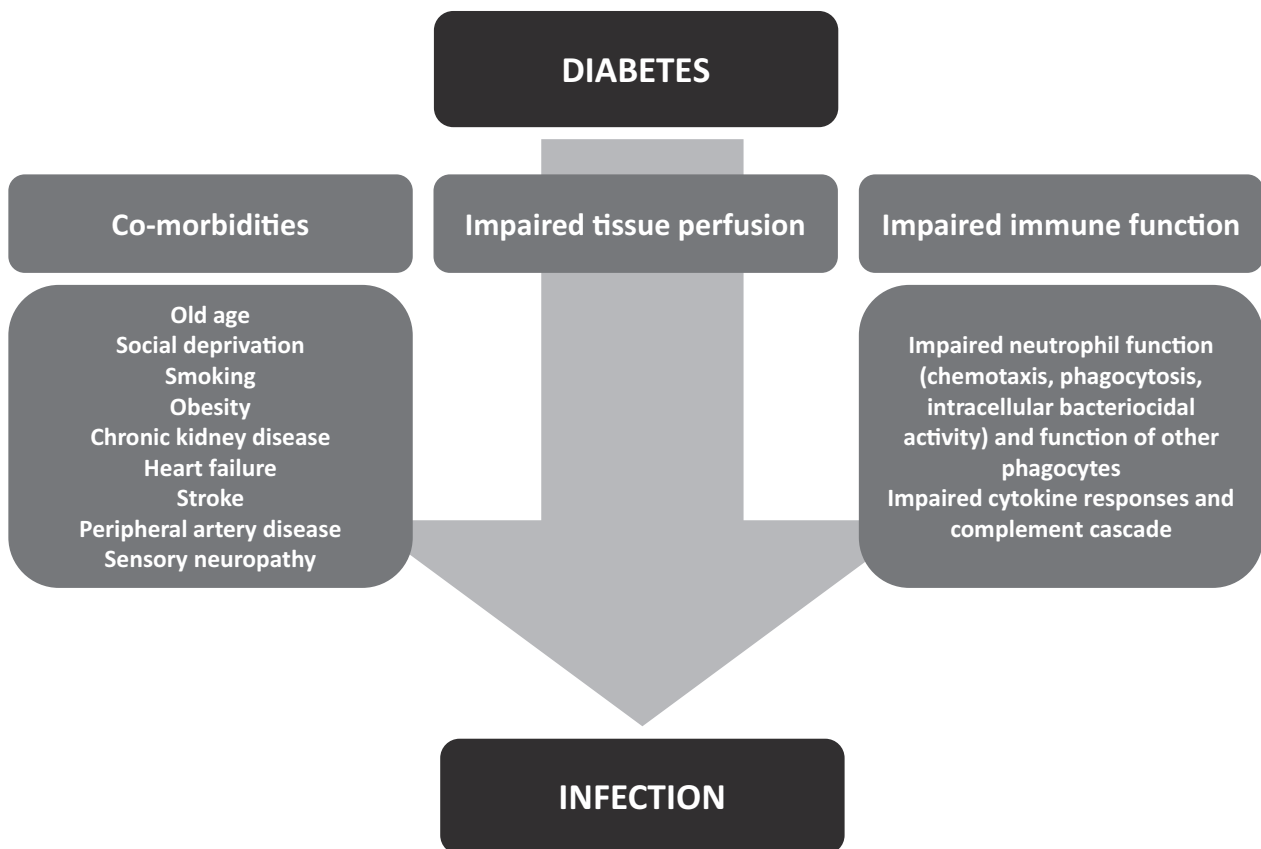


FIGURE 1 Mechanisms for increased risk of infection in people with diabetes

counterparts without diabetes, while the corresponding rate ratios were 1.2 and 1.7 for the oldest age group aged over 75 years.⁸

2.3 | Influenza and diabetes

Seasonal influenza infects more than a billion people worldwide each year. People with diabetes are more vulnerable to serious presentation and are more likely to die from influenza.²⁰ Recent studies indicate that the incidence of hospitalization due to influenza is 1.3- to 2.6-fold higher in those with diabetes.^{7,10} Besides the respiratory tract, influenza may precipitate acute cardiovascular events probably related to activation of inflammatory cells in atherosclerotic plaques, prothrombotic state and increase in metabolic demand during acute infection.²¹ Importantly, the increase in risk persists for weeks to months depending on the intensity of the infective event and inherent cardio-metabolic risks.²¹

In regions with available data on trends, the rates of severe influenza are rising in both diabetes and the general population. In Hong Kong, an annual increase of 15% was recorded for the incidence of hospitalization for influenza between 2001 and 2016.⁸ Influenza is listed as one of the vaccine-preventable diseases by the World Health Organisation (WHO) (S2) and many health guidelines advocate yearly influenza vaccination in people with diabetes irrespective of age (S3 and S4). Despite suppressed immunity associated with diabetes, there is no evidence that the level of antibody response from influenza vaccination is reduced (S5). In an analysis of a diabetes registry in Denmark, influenza vaccine was shown to lower all-cause death by 17% and cardiovascular death by 16% (S6). However, immunization uptake varies markedly across countries depending on local health policies. In countries in Europe, between 50 and 85% of individuals with diabetes have received influenza vaccination, whereas the rates were only 37% in South Korea and below 1% in China (S7–S10).

3 | DIABETES AND COVID-19

The association between diabetes and infection has been brought into stark relief by the emergence of the COVID-19 pandemic. The responsible virus, SARS-CoV-2 belongs to the family *Coronaviridae* and order *Nidovirales*, which encompasses positive-sense, single-stranded RNA viruses. Most of the human coronaviruses are betacoronaviruses; by contrast, all bat coronavirus are alpha- or betacoronaviruses.²² While human coronavirus (HCoV) HKU1, HCoV-NL63, HCoV-OC43 and HCoV-229E are associated with mild symptoms, SARS-CoV-1, Middle-East respiratory syndrome (MERS)-CoV and SARS-CoV-2 can all cause severe

disease.²³ Many European countries are currently experiencing a third wave of infection with a substantial rise in the incidence of new cases in recent weeks, that exceeds the initial wave in the Spring of 2020.

Clinical presentation of COVID-19 varies, ranging from no symptoms, to mild symptoms of the upper respiratory and gastrointestinal tract, to severe illness with fever, shortness of breath and respiratory failure.²³ Most people achieve a smooth recovery although some will progress to multi-organ complications and even death. Among survivors who have recovered from mild to severe pneumonia, impairment of diffusion capacity may persist suggesting lung function disruption due to the virus.²⁴ Some individuals experience long-term symptoms following recovery from the acute infection, now termed long COVID. These symptoms include fatigue, shortness of breath, chest pain or tightness, memory problems, insomnia, palpitation, dizziness, palpitation, arthralgia, depression, tinnitus, gastrointestinal upset and temperature.

3.1 | Risk factors for adverse outcome from COVID-19 infection

As the pandemic progresses, the epidemiology has become clearer and risk factors for severe COVID-19 have emerged.²⁵ The most important is age, with the case fatality rates rising from 0.07 deaths per 1000 adults aged 20 years to 60 deaths per 1000 adults aged 85 years.²⁶ Men are twice more likely to die than women.² People from Black, Asian and Minority ethnicities compared with people of White European ancestry and those from lower socio-economic backgrounds are also more vulnerable.² Several physical co-morbidities increase the risk of severe infection including cardiovascular disease, hypertension, malignancy, chronic respiratory disease, immunosuppressive conditions, including organ transplantation and chronic kidney disease. Among this list are both diabetes and obesity. The relative risk appears higher for type 1 diabetes than type 2 diabetes and for those with higher HbA_{1c}, emphasising the importance of achieving excellent glycaemic management during the pandemic.² Nonetheless, the absolute risk of severe disease remains low among people with type 1 diabetes as they are generally younger. A meta-analysis of 18 studies with 14,558 people with COVID-19 infection showed that 11.5% had diabetes, compared with 22.9% with hypertension and 9.7% with cardiovascular disease.²⁷ By contrast, fewer than 4% had pre-existing respiratory system disease, cancer or chronic kidney disease.²⁷ Early reports from China indicated that between 7.4% and 20% of in-patients with COVID-19 had diabetes.²⁸ Within hospital, diabetes is associated with more severe infection, respiratory distress requiring intensive ventilatory support, cardiac injury and death.²⁸ Fasting hyperglycaemia per se is also associated with a higher risk of death.²⁸

3.2 | Why does diabetes increase the risk of severe COVID-19 infection?

The precise mechanisms by which diabetes increases the risk of severe COVID-19 infections are not fully understood and likely to be multifactorial (S11). In addition to a compromised innate immune system as discussed above, diabetes is characterized by an inappropriately exaggerated pro-inflammatory state, as shown by higher serum concentrations of interleukin-6 (IL-6), C-reactive protein and ferritin in people with diabetes than those without (S12). The pro-inflammatory state associated with diabetes may render the individual more vulnerable to the cytokine storm associated with more severe COVID-19 infection. The higher burden of obesity in people with type 2 diabetes further contributes to the increased risk. Obesity alters the mechanical properties of the lungs including reduction in lung compliance, lung volume and respiratory muscle strength (S13) which in turn increases the need for invasive mechanical ventilation (S14).

Angiotensin-converting enzyme 2 (ACE2) and dipeptidyl peptidase-4 (DPP-4), which are coronavirus receptor proteins, are critically involved in metabolic signals and pathways regulating inflammation, renal and cardiovascular physiology, and glucose homeostasis.²⁹ Observational studies on the association between pre-admission use of DPP-4 inhibitors and outcome from COVID-19 reported conflicting results (S15–S17). However, in an Italian case–control study of people with diabetes admitted with COVID-19, reduced rates of adverse outcome including deaths were observed in the group initiated sitagliptin during the in-patient period (S18).

3.3 | Effect of COVID-19 on glycaemic management

In addition to the effect of diabetes on the risk of severe infection, COVID-19 appears to increase the risk of acute metabolic decompensation by inducing insulin resistance and impairing insulin secretion, beyond the stress of critical illness. The insulin resistance is driven in part by the pro-inflammatory state and may be compounded by an effect of obesity, that further aggravates the cytokine response.³⁰ Earlier studies have identified SARS-CoV, the related virus responsible for SARS, in the pancreas of people who died implying that the virus may be able to directly damage β -cell function resulting in acute insulinopaenia.³¹

Several studies have observed higher than expected rates of glycaemic decompensation with DKA or HHS in people admitted with COVID-19 and increases in insulin requirement that were disproportionate to the severity of the pneumonia.^{5,32} In one UK teaching, although the rate of admissions with DKA during the COVID-19 outbreak was

similar to previous years, a higher proportion of those admitted had type 2 diabetes, who were less likely to be treated with insulin prior to admission (S19). It seems likely in these cases, that the DKA was specifically associated with the viral infection. In another London teaching hospital, 17 of the 21 people admitted with a hyperglycaemic diabetes emergency between March and April 2020 tested positive for COVID-19 (S20). Seven were admitted DKA and 10 with HHS. Those with COVID-19 infection were older, more likely to have type 2 diabetes and have co-morbidities. Their admissions were longer and more frequently needed critical care. With the emergence of dexamethasone as a potential treatment for severe COVID-19 infection, the likelihood of acute hyperglycaemic emergencies is further increased. Follow-up studies are needed to investigate if the risk of developing diabetes is increased after recovery from COVID-19.

3.4 | Guidance from the UK National In-patient diabetes COVID-19 response group

The challenges of meeting the increased demand for in-patient diabetes care brought about by the pandemic have stretched diabetes teams, not least because of redeployment of in-patient diabetes team members to other parts of the hospital. Furthermore, the increased need for pumps to deliver inotropes led to early concerns that certain items of basic equipment, such as syringe drivers, may run into short supply. In order to help address the unique difficulties posed by COVID-19 for people in hospital, the UK National In-patient diabetes COVID-19 response group, supported by Diabetes UK and the Association for British Clinical Diabetologists, created a series of guidelines for healthcare professionals, both specialists and non-specialists, managing people with COVID-19 infection.^{33–36} These documents cover the management from the point of admission to discharge and discuss how services should be organized to optimize diabetes care.

It is recognized that many healthcare professionals seeing people with diabetes and COVID-19 on admission will not be diabetes specialists; nevertheless, this is a key time point to identify diabetes and acute metabolic decompensation.³³ Blood glucose should be checked for all individuals and ketones in those with known diabetes or hyperglycaemia. Metformin and SGLT-2 inhibitors should be stopped and replaced with alternative treatments, likely insulin. Where DKA or HHS is identified, care is needed with the normal regimens of fluid replacement because of the risk of ‘lung leak’ or myocarditis in people with COVID-19 infection.³⁶ Importantly, clinical judgement, frequent senior review and regular monitoring of fluid balance and oxygen saturations are needed. Insulin regimens may also require adjustment from the norm because of the marked insulin resistance seen in some people with COVID-19 infection. Infusion

rates of up to 20 units of insulin per hour are not unusual. By contrast, these high doses of insulin may be associated with a paradoxical risk of hypoglycaemia. People with severe COVID-19 are often nursed prone and so feeding may be accidentally interrupted if a nasogastric tube is dislodged. Alternative subcutaneous insulin regimens may be required for those with hyperglycaemia or mild DKA if syringe drivers are unavailable to administer intravenous insulin safely. The UK National In-patient diabetes COVID-19 response group provides specific guidance on the management of diabetes during dexamethasone treatment, highlighting the need for regular glucose monitoring and insulin treatment if required.³⁵

Diabetes teams have a key role in preventing admissions to hospital and part of this involves close liaison with community services at the time of discharge. During the admission, diabetes treatments may have changed and new support, particularly for vulnerable people with specific care needs, may be required after discharge to prevent hypoglycaemia, recurrence of hyperglycaemia and DKA. It is essential that there is a clear follow-up plan in the community. Despite the increased demands to support other aspects of care within the hospital, in-patient diabetes teams have a critical role in ensuring that people with diabetes receive the care they need to maintain patient safety and prevent destabilization of glycaemic management during admission.³⁴

4 | PUBLIC HEALTH MEASURES TO COMBAT COVID-19 IN HONG KONG

Since the beginning of 2020, we have faced four waves of COVID-19 outbreak in Hong Kong. The first wave occurred at the end of January from imported cases from mainland China and the scale of the outbreak was limited. By the end of February and March, there was an influx of returnees from Europe and North America. The third wave which swept through the territory in July mainly came from people who have been exempted from testing including aircrews and sailors, who have spread the infection via taxi drivers to local restaurants. This third and fourth wave was exacerbated by general public fatigue with social distancing measures and cases were transmitted silently in the community including in nursing homes and more being untraceable as of 22 January 2021, there were more than 9000 infected cases and 170 deaths in Hong Kong.³⁷ Globally, the confirmed cases and mortality are still on the rising trend.¹ The pandemic not only poses extra burden on healthcare systems across the world, it also causes economic disruption. According to the WHO, preventing and slowing the transmission of the virus is one of the key areas of public health measures for COVID-19 in which physical distancing, hand hygiene and use of medical

masks in healthcare workers, sick people and their caregivers are emphasized.³⁸

Coronaviruses are respiratory pathogens and are transmitted through droplets from person-to-person through breathing, coughing, or sneezing, and aerosols generated by medical procedures, including positive pressure ventilation, tracheal intubation and airway suctioning. During the outbreak of SARS in Hong Kong in 2003, transmission through fomites or small aerosols was suggested among medical students exposed to the first SARS patient in a hospital as the risk of contracting the virus was sevenfold greater among those who were in close proximity to the patient.³⁹ Apart from this, there was a report of a high SARS-CoV-2 infection rate following exposure at a choir practice as transmission was likely facilitated by close proximity (within 6 feet) during practice and augmented by the act of singing.⁴⁰ A recent systematic review of 172 studies on COVID-19, SARS and MERS found that greater than 1 metre of physical distancing was associated with a reduced rate of infection compared with a distance of less than 1 metre (adjusted odds ratio 0.18), and distances of 2 metres might be even more effective (change in relative risk 2.02 per metre).⁴¹ Multiple variants of SARS-CoV-2 are circulating globally with several new variants emerged in the fall of 2020, from the United Kingdom (known as 201/501Y.V1, VOC 202012/01, or B.1.1.7), South Africa (known as 20H/501Y.V2 or B.1.351) and Brazil (known as P.1) with particular concern about an increased risk of transmission and death from B.1.1.7 when compared with other variants (S21). There were few sporadic cases with variant viruses detected from imported cases in late December. Since then, the quarantine period has been extended from 14 days to 21 days for travellers coming back from the United Kingdom to reduce the spread of the new virus strain into the community (S22).

Apart from the quarantine measures for inbound travellers, the WHO has recommended non-contact greetings and maintaining physical distance from other people, including minimizing social and religious gatherings. Other possible actions include establishing one-way system for pedestrian, ground markings, setting up physical barriers in communal facilities and scheduling different times for different groups to leave and return home so as to support physical distancing.³⁸

4.1 | Promote hand hygiene and respiratory etiquette

A recent study reported that the SARS-CoV-2 can survive on items such as banknotes and phones for up to 28 days in cool, dark conditions.⁴² Hand disinfection therefore becomes highly crucial. Handwashing with soaps or alcohol-based sanitizers is an effective measure in preventing microbial disease transmission, especially after coughing

or sneezing or taking care of a sick person. Since the outbreak of COVID-19, there has been a massive demand for hand sanitizers in the market leading to unconventional production from chemical industries or perfumeries. Hand hygiene includes: (1) handwashing using soap and water, (2) antiseptic handwashing using antiseptic detergent and water; and (3) antiseptic hand sanitization using hand rubs, or alcohol-based hand rub, which is less irritating and easy to use.⁴³ Together with appropriate cleaning and disinfection of surfaces, these strategies might prevent indirect transmission through touching surfaces contaminated with virus.⁴⁴

4.2 | Provide medical masks to health care workers, sick people and their caregivers

Unlike SARS, a substantial proportion of infected people (40%–45%) with SARS-CoV-2 remain asymptomatic indicating that the virus can spread silently and rapidly through human populations.⁴⁵ From a statistical model analysing the time of infection among the COVID-19 cases on board the Diamond Princess Cruise ship in Japan, the asymptomatic proportion was estimated at 18%.⁴⁶ In contrast, another report from a different cruise ship outbreak in Argentina where all passengers were given surgical masks and all staff provided N95 respirators after the index case of COVID-19 described a high proportion of asymptomatic infection (81%).⁴⁷ Stringent precaution is needed to prevent silent spread.

Minimizing respiratory infection at source using a face mask is a well-established strategy similar to the prevention of pulmonary tuberculosis and influenza. A recent meta-analysis examined the effectiveness of N95, surgical and cloth masks in community and healthcare settings for preventing respiratory virus infections.⁴⁸ In community settings, use of surgical masks was associated with a lower risk for SARS-CoV-1 infection in observational studies. Unfortunately, direct evidence on the comparative effectiveness of masks for preventing SARS-CoV-2 infection is limited. In healthcare settings, using N95 respirators versus surgical masks might lower the risk of SARS-CoV-1 infection. Although data for SARS-CoV-2 are not available, it is reasonable to assume that N95 respirators compared with surgical masks may offer better protection for healthcare workers in close contact with people with COVID-19. The WHO has suggested that surgical masks should be reserved for healthcare workers, sick people, their carers and other workers who may be exposed to COVID-19 cases. However, the use of masks in community setting is not discouraged even though scientific evidence is still lacking. The correct use and compliance of face mask are equally important and thus the Centers for Disease Control and Prevention suggested that everyone should wear a mask in public settings.⁴⁹

Since the outbreak of COVID-19 worldwide and the implementation of the public health measures, influenza activity has decreased in United States, Australia, Chile and South Africa.⁵⁰ Nevertheless, public health measures should be balanced against the adverse effects on socio-economic function and psychological health of residents. Territory wide education on personal hygiene, social responsibility in creating a safe and healthy place, and vaccination will become the cornerstones of our victory in this battle. Given that people with diabetes are more susceptible to serious infection, both people with diabetes and those living in the same household should be aware of this increased risk and exercise appropriate precautionary measures including maintenance of personal hygiene, avoidance of crowds and vaccination. For healthcare professionals, a lower threshold for hospital admission and close clinical observation should be considered in people with diabetes contracting COVID-19.

5 | CONCLUSION

Diabetes is a risk factor for many severe infections including COVID-19. People with diabetes also have other comorbidities such as obesity and cardiovascular diseases that independently predispose to infection. In this review, we have summarized the current evidence related to diabetes and infection, including an update on trends in infection rates among people with diabetes. The relationship between diabetes and COVID-19 is reviewed, and the collateral consequences of this pandemic on people with diabetes are discussed. Lastly, we described the various public health measures that have shown to be effective in controlling the spread of COVID-19 in the community. Until effective vaccines against COVID-19 and their implementation become widely available, the world must maintain a high level of vigilance and agility to maximize health and safety especially for those at risk for serious complications, which includes people with diabetes.

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CONFLICT OF INTEREST

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REFERENCES

- World Health Organization. <https://covid19.who.int>. Accessed January 22, 2021.
- Barron E, Bakhai C, Kar P, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a while-population study. *Lancet Diabetes Endocrinol.* 2020;8:813-822.
- Wu J, Zhang J, Sun X, et al. Influence of diabetes mellitus on the severity and fatality of SARS-CoV-2 (COVID-19) infection. *Diabetes Obes Metab.* 2020;22:1907-1914.
- Grasselli G, Greco M, Zanella A, et al; COVID-19 Lombardy ICU Network. Risk factors associated with mortality among patients with COVID-19 in Intensive Care Units in Lombardy, Italy. *JAMA Intern Med.* 2020;180:1345-1355.
- Li J, Wang X, Chen J, Zuo X, Zhang H, Deng A. COVID-19 infection may cause ketosis and ketoacidosis. *Diabetes Obes Metab.* 2020;10:1935-1941.
- Lichty JA. The acute infections in diabetes mellitus. *Trans Am Clin Climatol Assoc.* 2015;31:83-89.
- Seshasai SRK, Kaptoge S, Thompson A, et al; The Emerging Risk Factors Collaboration. Diabetes, mellitus, fasting glucose, and risk of cause-specific death. *N Engl J Med.* 2011;364:829-841.
- Luk AOY, Wu H, Lau ESH, et al. Temporal trends in rates of infection-related hospitalisations in Hong Kong people with and without diabetes, 2001–2016: a retrospective study. *Diabetologia.* 2021;64:109-118.
- Benfield T, Jensen JS, Nordestgaard BG. Influence of diabetes and hyperglycaemia on infectious disease hospitalisation and outcome. *Diabetologia.* 2007;50:549-554.
- Carey IM, Critchley JA, DeWilde S, Harris T, Hosking FJ, Cook DG. Risk of infection in type 1 and type 2 diabetes compared with the general population: a matched cohort study. *Diabetes Care.* 2018;41:513-521.
- Harding JL, Benoit SR, Gregg EW, Pavkov ME, Perreault L. Trends in rates of infections requiring hospitalization among adults with versus without diabetes in the U.S., 2000-2015. *Diabetes Care.* 2020;43(1):106-116.
- Shah BR, Hux JE. Quantifying the risk of infectious diseases for people with diabetes. *Diabetes Care.* 2003;26:510-513.
- Magliano DJ, Harding JL, Cohen K, Huxley RR, Davis WA, Shaw JE. Excess risk of dying from infectious causes in those with type 1 and type 2 diabetes. *Diabetes Care.* 2015;38:1274-1280.
- Wu H, Lau ESH, Yang A, et al. Trends in diabetes-related complications in Hong Kong, 2001–2016: a retrospective cohort study. *Cardiovasc Diabetol.* 2020;19:60.
- Wu H, Lau ESH, Ma RCW, et al. Secular trends in all-cause and cause-specific mortality rates in people with diabetes in Hong Kong, 2001–2016: a retrospective cohort study. *Diabetologia.* 2020;63:757-766.
- Stegenga ME, van der Crabben SN, Blümer RME, et al. Hyperglycaemia enhances coagulation and reduces neutrophil degranulation, whereas hyperinsulinemia inhibits fibrinolysis during human endotoxemia. *Blood.* 2008;112:82-89.
- Delamaire M, Maugendre D, Moreno M, Le Goff MC, Allanic H, Genettet B. Impaired leucocyte functions in diabetic patients. *Diabet Med.* 1997;14:29-34.
- Luk AOY, Lau ESH, Cheung KKT, et al. Glycaemia control and the risk of hospitalisation for infection in patients with type 2 diabetes: Hong Kong Diabetes Registry. *Diabetes Metab Res Rev.* 2017;33(8):e2923.
- Critchley JA, Carey IM, Harris T, DeWilde S, Hosking FJ, Cook DG. Glycemic control and risk of infections among people with type 1 or type 2 diabetes in a large primary care cohort study. *Diabetes Care.* 2018;41:2127-2135.
- Lina B, Georges A, Burtseva E, et al. 2017–2018 study collaborators. Complicated hospitalization due to influenza: results from the Global Hospital Influenza Network for the 2017–2018 season. *BMC Infect Dis.* 2020;20:465.
- Musher DM, Abers MS, Corrales-Medina VF. Acute infection and myocardial infarction. *N Engl J Med.* 2019;380:171-176.
- V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. *Nat Rev Microbiol* 2020;19(3):155–170.
- Guan WJ, Ni ZY, Hu Y, et al.; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2019;2020(382):1708-1720.
- Mo X, Jian W, Su Z, et al. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J.* 2020;55:2001217.
- ALAMA Covid-19 Medical Risk Assessment. <https://alama.org.uk/covid-19-medical-risk-assessment/>. Accessed January 22, 2021.
- Coggon D, Croft P, Cullinan P, Williams A. Assessment of workers' personal vulnerability to covid-19 using "covid-age". *Occup Med.* 2020;70:461-464.
- Singh AK, Gillies CL, Singh R, et al. Prevalence of co-morbidities and their association with mortality in patients with COVID-19: a systematic review and meta-analysis. *Diabetes Obes Metab.* 2020;22:1915-1924.
- Zhang Y, Cui Y, Shen M, et al. Association of diabetes mellitus with disease severity and prognosis in COVID-19: a retrospective cohort study. *Diabetes Res Clin Pract.* 2020;165:108227.
- Drucker DJ. Coronavirus infections and type 2 diabetes – shared pathways with therapeutic implications. *Endocr Rev.* 2020;41(3):bnaa011.
- Kassir R. Risk of COVID-19 for patients with obesity. *Obes Rev.* 2020;21:e13034.
- Ding Y, He L, Zhang Q, et al. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. *J Pathol.* 2004;203:622-630.
- Wu L, Girgis CM, Cheung NW. COVID-19 and diabetes: Insulin requirements parallel illness severity in critically unwell patients. *Clin Endocrinol (Oxf).* 2020;93:390-393.
- Rayman G, Lumb A, Kennon B, et al. New guidance on managing inpatient hyperglycaemia during the COVID-19 pandemic. *Diabet Med.* 2020;37:1210-1213.
- Rayman G, Lumb A, Kennon B, et al. London Inpatient Diabetes Network-COVID-19. Guidelines for the management of diabetes

- services and patients during the COVID-19 pandemic. *Diabet Med.* 2020;37:1087-1089.
35. Rayman G, Lumb AN, Kennon B, et al. Dexamethasone therapy in COVID-19 patients: implications and guidance for the management of blood glucose in people with and without diabetes. *Diabet Med.* 2021;38:e14378. [Online ahead of print].
 36. Rayman G, Lumb A, Kennon B, et al. Guidance on the management of Diabetic Ketoacidosis in the exceptional circumstances of the COVID-19 pandemic. *Diabet Med.* 2020;37:1214-1216.
 37. The Government of the Hong Kong Special Administrative Region. Coronavirus Disease (COVID-19) in HK. <https://www.coronavirus.gov.hk/eng/index.html>. Accessed January 22, 2021.
 38. World Health Organization. Public health and social measures for COVID-19 preparedness and response in low capacity and humanitarian settings. <https://www.who.int/publications/m/item/public-health-and-social-measures-for-covid-19-preparedness-and-response-in-low-capacity-and-humanitarian-settings>. Accessed Jan 22, 2021.
 39. Wong TW, Lee CK, Tam W, et al. Cluster of SARS among medical students exposed to single patient, Hong Kong. *Emerg Infect Dis.* 2004;10:269-276.
 40. Hamner L, Dubbel P, Capron I, et al. High SARS-CoV-2 attack rate following exposure at a choir practice - Skagit County, Washington, March 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:606-610.
 41. Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schunemann HJ. COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet.* 2020;395:1973-1987.
 42. Riddell S, Goldie S, Hill A, Eagles D, Drew TW. The effect of temperature on persistence of SARS-CoV-2 on common surfaces. *Virol J.* 2020;17(1):145.
 43. Edmonds SL, Macinga DR, Mays-Suko P, et al. Comparative efficacy of commercially available alcohol-based hand rubs and World Health Organization-recommended hand rubs: formulation matters. *Am J Infect Control.* 2012;40:521-525.
 44. Honein MA, Christie A, Rose DA, et al. Summary of guidance for public health strategies to address high levels of community transmission of SARS-CoV-2 and related deaths, December 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:1860-1867.
 45. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. *Ann Intern Med.* 2020;173:362-367.
 46. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro Surveill.* 2020;25(10):2000180.
 47. Ing AJ, Cocks C, Green JP. COVID-19: in the footsteps of Ernest Shackleton. *Thorax.* 2020;75:693-694.
 48. Chou R, Dana T, Jungbauer R, Weeks C, McDonagh MS. Masks for prevention of respiratory virus infections, including SARS-CoV-2, in health care and community settings: a living rapid review. *Ann Intern Med.* 2020;173:542-555.
 49. Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>. Accessed date January 22, 2021.
 50. Olsen SJ, Azziz-Baumgartner E, Budd AP, et al. Decreased influenza activity during the COVID-19 pandemic - United States, Australia, Chile, and South Africa, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:1305-1309.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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