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Diabetes or endocrinopathy admitted in the COVID-19 ward

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Abstract

The Covid-19 pandemic confronted us with unknown clinical pictures, also in diabetology and endocrinology. Sharing clinical experiences is therefore of enormous importance. Actually, information about the care given in the Covid-19 ward (in contrast to that provided in the Emergency Room/ICU) is still sparse. The last weeks we built experience and gathered knowledge while giving hospital care to patients who had a pre-existent endocrine disease (and diabetes; most patients suffered from a type two diabetes). In our contribution we presented our insights obtained from this intensive period obtained in the Covid-19 ward.

KEYWORDS

COVID-19, diabetes, endocrinology

1 | INTRODUCTION

The COVID-19 pandemic is emerging around the world with a devastating force.[1] Majority of all people, especially when they are young, are suffering from a subclinical course of COVID-19 and 20% among them need to be hospitalized. It should be seriously noted that most of our patients in the COVID-19 ward did not only suffer from (type-2) diabetes; the largest amount of them had an age of more than 65 years old, with various other diseases as well (obesity, priory treated tumours, hypertension, heart failure, kidney function impairment).

Our community hospitals, situated in the Northern Antwerp region (Belgium), were restructured in COVID-19 hospitals in just a few days permitting a lot of patients to be admitted, and pushing aside regular inside hospital care (with exception of critical care medicine). Triage and making the COVID-19 diagnosis were performed in the emergency room. Patients with a respiratory failure, expected being artificially ventilated in some hours, were directed towards the intensive care unit (ICU). All other patients screening positive for COVID-19, with either coronavirus PCR or CT, went to the COVID-19 ward for close observation, single, in an isolated room. Our hospitals contained three COVID-19 wards, and each ward was homing forty-five patients most of the time. In the current epidemic (March-April 2020), we recognized two phases for patients who were admitted in the COVID-19 ward; a first one from patients coming out of the general population, and a second one from patients out of other institutions, like nursing homes and rehabilitation centres. The mortality rate appeared to be apparently higher in the second phase (own observation; our data are currently collected).

2 | OUR RECENT EXPERIENCE IN DIABETES CARE IN THE COVID-19 WARD

As found repeatedly in prior studies from China and Italy, patients with diabetes have a similar risk of being infected with the coronavirus as subjects from the general population (Figure 1).[2,3] However, the moment COVID-19-positive patients, with pre-existent diabetes, are hospitalized, their clinical course is often more complicated with a subsequently higher morbidity and mortality rate.[4] This is theoretically explained by more expression of ACE2 receptors in the lungs during hyperglycaemic states (diabetes animal models).[5]

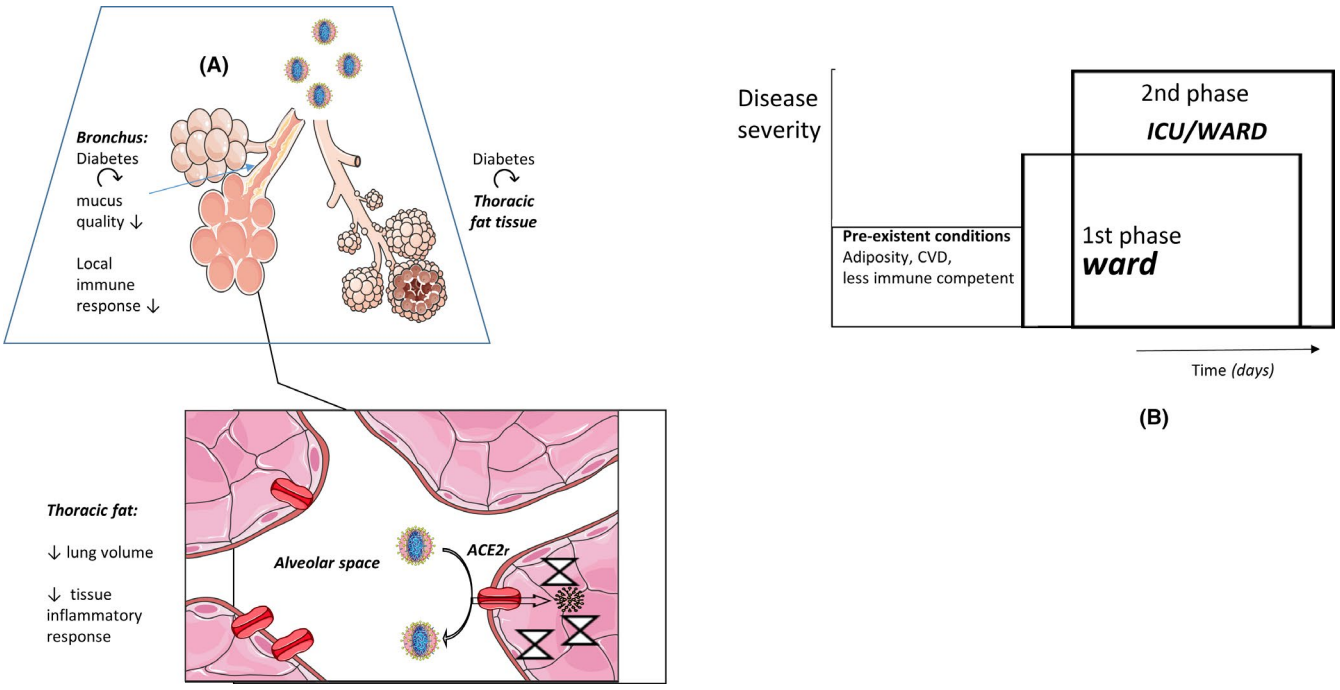

FIGURE 1 Covid presentation in patients with diabetes/endocrine disease. A, Corona virus entering the alveolar space and interacts with ACE2 receptors (ACE2r). Hyperglycemia gives a higher expression of ACE2r at the alveolar endothelium, making more entrance possible. Local damage, virus replication and initiation of cytokine storm afterwards. The immune response is impaired in less-controlled diabetic conditions. And the amount of thoracic fat in functionally hindering respiratory function. All these combined factors make a patient with diabetes more vulnerable in the clinical Covid-course. B, The course of disease in Covid-19. A first stable clinicl phase could be followed by a rapidly progressive, clinically unstable 2nd phase

And in vitro models showed a higher facilitated entrance of coronavirus through these ACE2 receptors. In rodent diabetes models, the level of expression of ACE2 receptors is regulated differently among distinctive organs (eg more expression in kidney cortex, compared to the heart), with an upregulated expression in a state of glycaemia.[6] However, administration of insulin to lower the high glycaemic states did not decrease tissue ACE2 receptor expression in the lung (only the circulating ACE2 protein decreased).[7] Translating these rodent-derived results towards human conditions is not easy to make and is still ongoing in actual research. However, these first rodent-derived results motivated us to prevent hyperglycaemia in patients admitted in our COVID-19 ward, preventing them from respiratory failure.

In our COVID-19 wards, all patients start recording capillary daytime glucose levels, the first 24 hours of admission. HbA1c measurement was performed in all COVID-19 patients with a disturbed glycaemic level (>140 mg/dL or 7.7 mmol/L) in order to diagnose pre-existent type-2 diabetes or to define their glucose control. All patients with COVID-19 had their glucose levels strictly titrated with subcutaneous basal-bolus insulin therapy in line with the ADA/AACE and Endocrine Society guidelines[8,9] dealing with in hospital glucose control seriously ill patients (with avoidance of glycaemia less than), stopping all oral antidiabetic drugs for several considerations. Due to significant (acute or chronic) decrease in kidney function (clearance <35 mL/min) in many of our hospitalized patients, biguanides and other glucose-lowering drugs were all to be discontinued. In elderly, sulfonylurea is better avoided, especially during acute disease and malnutrition. A possible increased risk for pneumonia while using DDP-IVs is part of discussion.[10] In patients with COVID-19, the therapeutic use of steroids is very restricted and therefore steroid-associated glycaemia was a rare phenomenon in our COVID-19 ward. Patients using a glucose sensor (such as that of Medtronic) should stop measuring glycaemia with this modality (as paracetamol, even in a low dose as 1 g could hinder accurate measurements) and always start to measure capillary glucose levels with use of a finger prick. Paracetamol is often used in the COVID-19 ward.

Not only known patients with diabetes exert a disturbed daytime glucose profile. As expected from prior literature, almost a third of in-hospital patients with a disturbed daytime glucose level have been diagnosed as a de novo diabetes (HbA1c at admission >6.5%). Using Hba1c as a diagnostic cool was not always possible in the active phase of COVID-19 infection. A large amount of patients displayed a significant anaemia due to systemic pro-inflammation. In one case report, the anaemia was successfully corrected with erythropoietin infusion.[11]

Another large group of patients in the ward displayed a stress-associated hyperglycaemia. In our COVID-19

population, this last group was frequently overrepresented. It is not known whether an acute rise in glucose levels could affect ACE2 receptor expression at the alveolar endothelium, or whether chronic hyperglycaemic conditions should be needed. Due to this lack of knowledge, we treated both similar with insulin therapy during their stay in the ward.

In case of respiratory failure at the ward, transition to the ICU was performed, and subcutaneous insulin is changed into intravenously administered insulin. Most patients remained, however, in our COVID-19 ward during a week and when they went home insulin could be stopped in almost all patients. From our (still limited) experience, COVID-19 patients with a pre-existent diabetes and a well-controlled glycaemia (HbA1c) before admission did not transfer more to ICU.

A moderate improvement in insulin sensitivity (and lipid profile) is observed after starting the antimalarial drug hydroxychloroquine.[12] Therefore, closely monitoring daytime glucose levels is recommended, especially for them under insulin therapy. In line with this fact, one case report described a patient with a type-1 diabetes and a severe hypoglycaemia.[13] In our COVID-19 ward, we did not observe any accidents due to hypoglycaemia after hydroxychloroquine was started in the course of disease.

Another challenge will be in reopening Society with presence of viral clusters and a low continuous viraemia amid its general population. A lot of patients have been limited in their visits to caregivers in hospital during the active period of the COVID-19 pandemic. Some of them neglected alarming symptoms or high glucose levels because of fear being infected not daring to contact hospitals.[14] For instance, we experienced a higher rate of patients presenting with complicated sepsis by a diabetic foot or not mentioning active coronary signs with a serious delay. Telemedicine or telephone consultations did not always prevent these late presentations with complicated disease, making us to reconsider the real effectiveness of such applications in daily clinic, especially in patients with a low health literacy or not native speaking (despite that we were encouraged to do so, by government-related bodies and commercial companies). The first period after reopening Society, most patients with diabetes (and not hospitalized with COVID-19) should be treated more intensively in order to achieve their distinctive metabolic targets (HbA1c, blood pressure, LDL-cholesterol, et cetera). Not only to prevent cardiovascular risk (how we were used to do today), but also to prevent them for a complicated course in next coming COVID-19 outbreaks. Both immunization for influenza and the immune host response during respiratory viral infections showed different patterns in multi-omics associations between insulin-sensitive persons, and insulin-resistant persons (prediabetes), suggesting an impaired immune capacity in tackling viral respiratory infections.[15] As long as no efficient vaccine with subsequent group protection will be obtained, COVID-19 outbreaks could be foreseen. A Cochrane analysis, however, showed that vaccines preventing influenza in the elderly with diabetes (living in long-term care facilities, and not in community) could not significantly being effective, and only reduces its mortal complications (total mortality reduction; such as bacterial pneumonia and hospitalizations).[16] With COVID-19, the viral pneumonia was rarely complicated with a bacterial infection, making the comparison with prior incoherent literature concerning vaccines and COVID-19 in the elderly with diabetes even more a challenge with a certain doubt it may not be its simple panacea. From recent observations, the current antibody levels against the coronavirus in the general Dutch population, and a preselected Belgium population are not passing 10% (after the first corona peak, March-April 2020). So this underlines the need for original and fundamental research at COVID-19, and not just the trust to replicate prior concepts that may lead towards fast therapeutic achievements.

Patients with a low health literacy are more found among those with worse clinical outcomes.[17] In the Netherland, we found that about 20% of patients with a type-2 diabetes express a less health literacy.[18] In prior studies (not dealing with COVID-19 pandemic), patients' presentation in the emergency room is delayed compared to them with a higher health literacy. Public information is later translated and applied in this group of patients, giving a more serious patients' delay. Most patients with a lower health literacy are supported by others in their daily life activities and in their daily diabetes management. In COVID-19 pandemic, the availability of the other supporting person is much less present due to all kind of local measures restricting social contact (such as quarantine or closure of schools with children at home hindering visiting mum or dad suffering diabetes).[19] These necessitate social restrictions during the COVID-19 pandemic will certainly affect negatively patients with a low health literacy with more risk to run into complications.

3 | OUR RECENT EXPERIENCE IN ENDOCRINOLOGY CARE IN THE COVID-19 WARD

Patients with an adrenal insufficiency are rare among patients entering the COVID-19 ward. However, one should not underestimate the hidden part of patients with a (partial) adrenal insufficiency. For instance, patients who used a high cumulative dose of steroids (in rheumatoid disease or chronic obstructive pulmonary disease), could present with a disturbed stress response symptoms due to an impaired adrenal function, especially under severe infectious stress (as could be in the initial course of COVID-19).[20] Against this specific background, other special groups of patients should not be forgotten. For

instance, patients with a high need for morphine-like drugs (secondary adrenal insufficiency) or those who are recently treated with the new anticancer drugs, the immune-modulators (with hypophysitis as secondary side effect; secondary adrenal insufficiency).[21] These patients could be safely tested with a Synacthen test in the COVID-19 ward. In case of urgency, such as a fast hemodynamic deterioration, intravenous Solucortef (50 mg three times a day) could be started immediately (without a Synacthen test).

Patients with a primary or secondary adrenal insufficiency who already take hydrocortisone substitution before admission should be switched to intravenously administered hydrocortisone (50 mg three times a day).[22] Diarrhoea and vomiting (without fever) may be symptoms related to COVID-19 infection.

In case of a diabetes insipidus (disease of the neuro-pituitary), salt water balance should have full attention. In COVID-19 patients, one wants to avoid a hypervolemic condition and therefore the 24 hours volume and composition of applied intravenous solutions are strictly motivated, aiming to achieve a cumulative 24 hours nil balance. So, the dose of desmopressin should be adjusted accordingly.

As a disturbed thyroid function could negatively affect heart function, and in the COVID-19 cytokine storm troponins are often elevated suggesting significant cardiac stress, controlling the thyroid function is mandatory. In the acute phase, most deterioration in thyroid function is due to nonthyroid illness with no need for thyroxin substitution. Some of them use amiodarone. Mostly, this gives not a significant orientation during their stay in the COVID-19 ward. Hyperthyroidism, mostly due to a toxic adenoma, is dealt with according to current guidelines.

Patients with COVID-19 who are admitted in the ward are a serious challenge for both junior and senior doctors. Numerous pathologies should be mastered in order to improve their outcomes and this demand a multidisciplinary approach. Metabolic disorders are often present. They should be diagnosed and treated against the background of the COVID-19-related cytokine storm that is characterizing the initial phase of disease.

CONFLICT OF INTERESTS

Both authors have no conflict of interest.

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