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SYSTEMATIC REVIEW OF COVID-19 MORTALITY IN DIABETIC PATIENTS AND THYROID DISEASE PATIENTS

Hanin Abdulkhaliq Almehmadi[1], Hanan abdulkhailq almehmadi[2]

Hera General Hospital[1], King Faisal Hospital[2]

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Abstract:

Introduction: *A pneumonia outbreak of unknown etiology occurred in Wuhan, China, in December 2019. The cases were associated with a local seafood market selling live animals, suggesting that the pathogens were transmitted from animals to humans, which soon escalated to human-to-human transmission. This pathogen was identified and named as 2019 novel coronavirus (2019- nCoV) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing diseases named coronavirus disease 2019 (COVID-19). The clinical manifestations of SARS-CoV-2 are very similar to that of SARS, and infected patients may develop acute respiratory distress syndrome (ARDS) and, in the unlikely event, admission to the intensive care unit (ICU) and subsequent mortality. These severe cases are often associated with comorbidities, especially diabetes and others like thyroid disorders.*

Aim of the Study: *To undertake a systematic review to understand the mortality rate in diabetic and thyroid disease patients suffering from COVID-19 and the possible implication.*

Methodology: *The systematic review is a comprehensive research of PUBMED from the November 2019 till May 2021. All hospital and community settings were included in study*

Conclusion: *COVID-19 in patients with already present underlying diseases can have an increased mortality rate if remained unchecked. Various comorbidities increasing the risk of severe illness of COVID-19 are diabetes mellitus, hypertension, cardiovascular diseases, asthma, thyroid disorder. Diabetes mellitus, in association with poor glycemic control, obesity, and complications of diabetes, including renal, cardiac, and peripheral vascular diseases, can be additive risk factors and can be a call for specific attention. Thyroid disorder itself is not associated with increased mortality among COVID-19 patients, but suppression of the immune system may pose a risk.*

Corresponding author:

Hanin Abdulkhaliq Almehmadi,

Haninalmehmadi@hotmail.com - 0500200567

QR code

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BACKGROUND:

Diabetes Mellitus and COVID-19

Signs and symptoms of SARS-CoV-2 infections vary from mild and asymptomatic infections (seen in 20-86%) of all infections to a very severe respiratory distress characterized by the spread of infection-causing inflammation and pneumonia. These manifestations are more accentuated in patients with comorbidities such as asthma, diabetes, hypertension, and cardiovascular disease, and chronic obstructive pulmonary disease (COPD). COVID-19 victims with diabetes mellitus (DM), severe obesity, CVD, and hypertension are at a higher risk of poor outcome from the disease leading to increased mortality. [1,2]

METHODOLOGY:

We undertook a systematic review of other review articles and case series regarding risk factors that increase mortality rate with COVID-19 infection.

Review question

Our question: Does COVID-19 infection increase mortality rate in patients who have diabetes and thyroid diseases?

Search Strategy

We researched the following databases: PubMed, medRixv, European PMC, COVID-19 Living Evidence databases. We used the search terms: COVID-19, COVID-19 in diabetics, SARS-CoV-2 in diabetics, mortality in type 2 diabetes from COVID-19, mortality in type 1 diabetes from COVID-19 infection, immunity in diabetes, mortality rate in thyroid patients from COVID-19 infection. We included data from 17 studies in our article.

RESULT AND DISCUSSION:

Among 44,672 confirmed COVID-19 cases in China with infection confirmed by mid-February, 87% were between 30 and 79 years old. The mortality rate was 7.3% in people with diabetes mellitus, which was more than three times that of the overall population.[3]

A report by Guan WJ, Ni ZY, Hu Y, et al. included clinical data of 1099 patients collected up to the end of January, hospitalized with laboratory-confirmed infection in China showed the most common symptoms such as fever and cough, and radiologic evidence of pulmonary disease. Among these patients hospitalized, 6.1% met the primary endpoint (a necessity for ICU or mechanical ventilation, or death. In the whole population, diabetes was prevalent among 7.4 %, but 27% of those meeting the primary endpoint had diabetes with an overall death rate of 1.4%.[4]

The mortality among confirmed COVID-19 cases with diabetes was compared with those without diabetes by Chen et al. He investigated whether the type of prior glucose-lowering therapy was associated with outcomes among people with diabetes in 904 patients hospitalized with either a laboratory or clinical diagnosis of infection, of whom 15% had diabetes and concluded that death rates in diabetics were two to three times higher than non-diabetic individuals. Within subgroups of diabetics, multivariable analyses identified two risk factors for a predictor of death which was older age and higher C-reactive protein among these individuals. [5]

Rao et al. (2019) assessed possible associations of various medical comorbidities and traits with the expression of angiotensin-converting enzyme 2 (ACE2 using Mendelian randomization). ACE2 molecule may be a site of attachment of the virus to cells in the lung and elsewhere. The study also concluded that "diabetes and related traits may increase ACE2 expression, which may influence susceptibility to more severe infection and may become fatal." However, these observations are not definitive and pose the possibility that increased ACE2 in diabetes could mediate increased vulnerability and mortality among these patients. Drugs that affect the renin-angiotensin-aldosterone system may either be detrimental or favorable on COVID-19 infections, but no definitive evidence on the study. [6,7]

Chinese Centre for Disease Control and Prevention reported increased death in individuals with diabetes after analyzing a case-cohort of 70,000 COVID-19 infected individuals, showed mortality increased from 2.3% in the general population to 7.3% in diabetics. The increased vulnerability for COVID-19 in diabetic patients is possible because of improved binding affinity and easy virus entry, diminished viral clearance, weakened T-cell role, greater susceptibility to cytokine storm disorder, and the presence of the cardio vascular disorder. [7]

The earlier studies done demonstrated that individuals with diabetes have a similarly high risk for SARS and MERS. Among the infected patients, it has been shown that history of diabetes and hyperglycemia are independent predictors of mortality and morbidity. In these cases, metabolic control might improve their prognosis and become less fatal. Hyperglycemia is known to be a strong prognostic predictor of outcome in hospitalized patients with COVID-19. Hyperglycemic patients with COVID-19 displayed a higher incidence of severe disease than normoglycemic controls.[8]

The probable reason for increased mortality is hyperglycemia-induced changes in the immune system and increases in inflammatory cytokines. 26.8% of elderly individuals who were at higher risk of death from COVID-19 were diabetic. Obese people, too, are at higher risk of developing complications from SARS-CoV-2.[8]

Thyroid disorder and COVID-19

SARS-CoV can cause multiple organ failures, but its damage to the thyroid gland showed inconsistent evidence. T3, T4, and TSH levels in the serum of patients suffering from SARS-CoV are significantly lower during in both the development and recovery phases than those in the controls. In a study, 61 survivors showed 7% of patients having hypothyroidism. All these findings support central hypothyroidism induced by hypothalamic damage or hypophysitis. Hypocortisolism and hypothyroidism together justify the common occurrence of the wide range of non-specific symptoms present in SARS patients and is known as post-SARS sickness syndrome. [9,10]

The direct molecular analysis of surgical samples of thyroid tissues indicated that thyroid follicular cells express ACE2, which makes the gland susceptible to SARS-CoV-2 injury.[11]

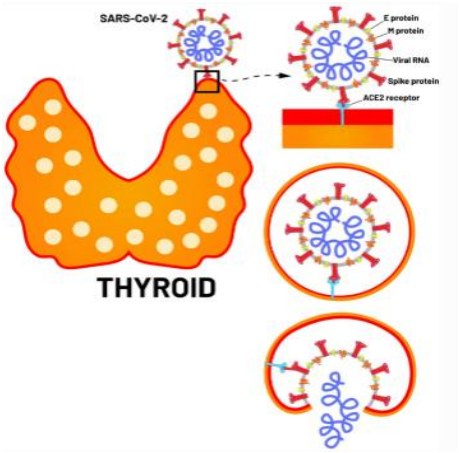


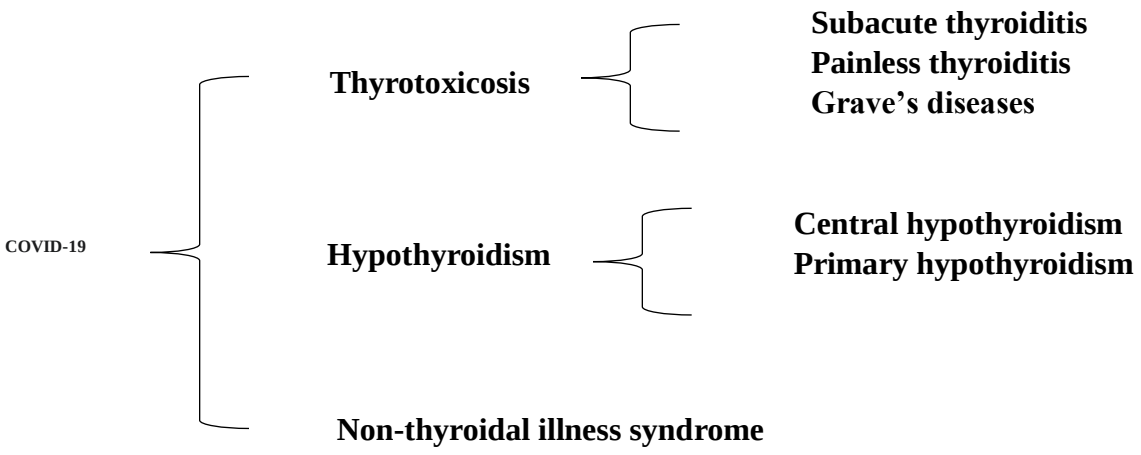
Figure showing ACE-2 receptors in thyroid follicular cells and SARS-CoV-2 entry.[12]

Subacute thyroiditis, autoimmune thyroiditis, and an atypical form of thyroiditis are complications of COVID-19. Thyroid hormone dysfunction affects the outcome by increasing mortality in critical illnesses like acute respiratory distress syndrome, which is a leading complication in COVID-19.[13]

A study by Lania et al. demonstrated a high number of patients (20.2%) hospitalized for COVID-19 in non-intensive care units was found to be affected by thyrotoxicosis with the absence of symptoms like neck pain; these patients are identified as COVID-19-related painless or silent thyroiditis. Overt thyrotoxicosis is defined as a condition in which low TSH values with FT3 and/or FT4 above the reference ranges are present. Overt thyrotoxicosis was diagnosed in 31 of 58 patients with thyrotoxicosis (53.4%).[14]

Atrial fibrillation and thromboembolism were seen in 32% and 16% of overt thyrotoxic patients with COVID-19. The mortality and longer duration of hospitalization were higher in thyrotoxic patients as compared to COVID-19 patients with normal thyroid function. Therefore, thyrotoxicosis holds to be clinically relevant in COVID-19 patients, impacting poor prognosis and mortality. The presence of thyroid disease conferred a more severe degree of infection to COVID-19. [14,15]

In a retrospective observational study done on 390 COVID-19 patients admitted to a hospital, there were 21 hypothyroid cases (5.4%), most of whom were 50 years and older. As for the effect of hypothyroidism on COVID-19 mortality, 60 (15.3%) of total patients and 4 (19%) of hypothyroid patients died. Only a few reports suggested a higher risk of infection in hypothyroid patients. According to the British Thyroid Association/Society for Endocrinology (BTA/SFE), controlled hypothyroidism does not pose an increased risk or severity of the viral infection, and hence the mortality is more of a contribution of already present other underlying diseases such as malignancy, cardiovascular and diabetes mellitus.[16]



Covid-19-related thyroid disorder.[17]

Very few COVID-19 patients with thyrotoxicosis and low TSH concentrations require a high intensity of care, present in line with SARS-CoV-2-induced subacute thyroiditis and in a setting of non-thyroidal illness syndrome.[18]

It is to be noted that anti-thyroid drugs inhibit thyroid activity in the case of hyperthyroidism while not increasing the risk of COVID-19 infection or the probability of developing a more serious disease process. This can lead to neutropenia in those individuals who are susceptible and experience symptoms such as sore throat, mouth ulceration, fever, and flu-like illness, mimicking the symptoms of COVID-19 and therefore, making it difficult for physicians to distinguish between these two diagnoses. The neutropenia induced by anti-thyroid drugs is associated with an increased risk of infections; this adverse effect may be rare but favors the progression of COVID-19 by impairing immunity, reduction of the innate immune response, or a generalized suppression of the immune system.[19]

CONCLUSION:

COVID-19 is known to be confined to the respiratory system, but the complications are often associated with all the vital organs, especially more severe and fatal in people with comorbidities such as diabetes, hypertension, cardiovascular diseases, and thyroid disorders. It makes the patients more vulnerable to complications associated with them. A major risk factor for diabetes is diabetes and appears to be an independent risk factor for severe illness in COVID-19. This, in association with hyperglycemia, leads to more severe pulmonary and systemic illness. COVID-19 survivors had thyroid abnormalities, but most data do not state that thyroid diseases represent a risk factor for the development of COVID-19, and a higher prevalence of thyroid disease in patients with COVID-19 has not been detected frequently. But anyhow, thyroid evaluation subsequent follow-up could be useful for the prevention of COVID-19 progressing to severe diseases form.

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