BRIEF COMMUNICATIONS

Possible role of hypothyroidism in the prognosis of COVID-19

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Abstract
In patients with COVID-19, certain medical conditions could result in poorer clinical outcomes. However, the prognostic role of hypothyroidism in COVID-19 is still unknown. In the present retrospective study, we estimated the prevalence of hypothyroidism in COVID-19 admitted patients in Tehran, Iran. Among 390 COVID-19 admitted patients, 21 hypothyroid cases (5.4%) were found, in which nearly 90% were aged 50 years and older. Regarding the effect of hypothyroidism on COVID-19 mortality, 60 (15.3%) of total patients and 4 (19%) of hypothyroid patients died, and no significant difference was found between the two groups.

In late December 2019, China reported a cluster of cases with atypical pneumonia which ultimately was diagnosed to be a novel coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Owing to rapid spread, on 11 March 2020 the World Health Organization declared it a pandemic disease. While preparing this paper, over 5.7 million definite cases were identified worldwide and over 350 000 patients died.1,2

COVID-19 patients with certain comorbid medical conditions, such as diabetes mellitus, hypertension and cardiovascular diseases are prone to develop severe infection with poorer clinical outcomes and the ones with more comorbidities have a worse prognosis.3,4 However, the possible role of autoimmune diseases such as hypothyroidism in COVID-19 remains unknown.

Thyroid hormones modulate the immune system, especially cellular immunity. The immune system dysregulation seen in hypothyroidism may increase the risk of infection. However, after proper hormone replacement therapy, the immune system restores its normal function.5–8

In this retrospective observational study, we evaluate the prevalence of hypothyroidism in patients with COVID-19 and its possible effect on clinical outcomes.

We reviewed medical records of patients admitted to Amir-Alam hospital, one of the COVID-19 referral centres in Tehran, Iran, from 25 February to 7 March 2020. We included all the definite (confirmed by polymerase chain reaction) and probable (compatible clinical, laboratory and imaging findings) COVID-19 cases in the study. The demographic and clinical characteristics as well as all the underlying comorbidities of the patients were analysed. The continuous data were expressed by the mean and standard deviation. SPSS software (SPSS v22; SPSS, Armonk, NY, USA) was used for data analysis.

A total number of 390 patients, including 264 (67.7%) males and 126 (32.3%) females, was included in the study. Among the COVID-19 cases, 21 (5.4%) patients (5 (23.8%) men and 16 (76.2%) women) had a history of hypothyroidism who received oral levothyroxine (Table 1). The mean age of patients with hypothyroidism was 58.1 ± 14.9 years (range 23–86 years).

Out of 390 patients, 76 (19.4%) cases were admitted to the intensive care unit (ICU) and 60 (15.3%) patients died. Among patients with hypothyroidism, four (19%) cases died; one of them had a history of metastatic breast cancer and another had rheumatoid arthritis receiving immunosuppressive medication (methotrexate). There was no significant difference (P = 0.5) between the two groups regarding mortality. The most common presenting symptoms and signs of COVID-19 in patients with hypothyroidism were fever, dyspnoea and...
decreased arterial oxygen saturation. The demographic and clinical characteristics of hypothyroid cases are shown in Table 1.

**Table 1** Demographic and clinical characteristics of hypothyroid patients infected by novel coronavirus (Amir-Alam hospital, 25 February to 7 March 2020)

| Characteristic                  | n (%)   |
|---------------------------------|---------|
| Total number of cases           | 21      |
| Age (years)                     |         |
| <50                             | 3 (14.3) |
| 50–<70                          | 14 (66.6) |
| ≥70                             | 4 (19.0)  |
| Gender                          |         |
| Male                            | 5 (23.8) |
| Female                          | 16 (76.2) |
| Smoking status                  |         |
| Smoker                          | 0 (0.0)  |
| Non-smoker                      | 21 (100) |
| Admission site                  |         |
| Ward                            | 15 (71.4) |
| Intensive care unit             | 6 (28.6)  |
| Outcome                         |         |
| Cured                           | 17 (81.0) |
| Death                           | 4 (19.0)  |
| Comorbidities                   |         |
| Hypertension                    | 7 (33.3) |
| Diabetes mellitus               | 5 (23.8) |
| Ischaemic heart disease         | 3 (14.3) |
| Chronic renal failure           | 3 (14.3) |
| Malignancy                      | 2 (9.5)  |
| Rheumatoid arthritis            | 1 (4.8)  |
| Symptoms                        |         |
| Fever                           | 14 (66.7) |
| Shortness of breath             | 13 (61.9) |
| Cough                           | 12 (51.7) |
| Chill                           | 6 (28.6)  |
| Fatigue                         | 5 (23.8) |
| Nausea/vomiting                 | 5 (23.8) |
| Headache                        | 3 (14.3) |
| Myalgia                         | 3 (14.3) |
| Vital signs on admission        |         |
| Decreased O2 saturation         | 15 (71.4) |
| Fever                           | 11 (52.4) |
| Tachycardia                     | 2 (9.5)  |
| Hypotension                     | 1 (4.8)  |

Discussion

We found 5.4% of COVID-19 inpatients were hypothyroid in our hospital. Approximately 90% of patients were aged 50 years and older, and over two-thirds were female. The prevalence of overt hypothyroidism in the Iranian general population is estimated to be 2%. However, in line with our study, the prevalence of hypothyroidism rises to 4.6% with increasing age, particularly in women. Surveys from other countries also showed a higher prevalence (6%) of overt hypothyroidism in older ages.

Although few reports indicated a higher risk of infections in hypothyroid patients, the British Thyroid Association/Society for Endocrinology (BTA/SFE) states that controlled hypothyroidism does not significantly increase the risk or severity of viral infections. In 2017, Journy et al. stated although hypothyroid patients have a higher mortality rate due to malignancy, cardiovascular and diabetes mellitus; other causes – including infectious disease – did not contribute. Based on Horisberger et al.’s review, limited evidence suggests autoimmunity per se does not increase the complications of COVID-19.

In a cohort by Guan et al., the data of 1590 COVID-19 patients were reviewed. They showed the mortality rate of COVID-19 in patients with chronic obstructive pulmonary disease, diabetes, hypertension, cardiovascular and cerebrovascular diseases was higher than the general population (25, 10, 10.4, 13.6 and 20% respectively). In the present study, although the mortality rate in patients with hypothyroidism was approximately 20%, 14 (66.6%) patients had at least one other comorbid condition. However, the mortality rate among hypothyroid patients did not significantly differ from non-hypothyroid patients. To the best of our knowledge, this is the first report to assess the prevalence of hypothyroidism in COVID-19 patients. The limitations of our study were the single-centre design and relatively few studied populations.

The prevalence of hypothyroidism appears similar in COVID-19 patients compared to the general population. While there was no significant difference in COVID-19 mortality in hypothyroid versus other patients on univariable testing, because of the small numbers we were unable to assess this using multivariable analysis. Therefore, multicentre prospective cohort studies on a larger scale should be considered.

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