Research Paper

Prevalence of Hypothyroidism Among Patients With COVID-19 in Tehran City, Iran

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ABSTRACT

Background and Purpose: Numerous comorbidities are involved in the severity of the new coronavirus disease 2019 (COVID-19). Hypothyroidism's impact on COVID-19 is yet to be adequately understood. Thyroid disorders are thought to play a role in the development and progress of COVID-19. This study aimed to determine the frequency of hypothyroidism among COVID-19 patients in hospitalized patients.

Materials and Methods: This retrospective cross-sectional study was conducted at a tertiary hospital in Tehran City, Iran. Demographic information and other specified data related to our research, mainly comorbidities, were collected using a structured questionnaire from electronic patient health records. A total of 493 medical records of COVID-19 patients were used for this study according to the inclusion criteria. Subsequently, the data were analyzed with SPSS, version 25, using descriptive and analytic statistics.

Results: The prevalence of hypothyroidism was 13.2% (n=65) in hospitalized COVID-19 patients. This was higher (13.4% vs 2.3%) compared with the prevalence of hypothyroidism in the general Iranian population. Overall, in patients with hypothyroidism, about 21 patients (32.3%) expired, of whom 14 patients (66.7%) were female, and 7 (33.3%) were male. In these patients, no statistically significant difference was observed between the expired and discharged groups (Adjusted Odds Ratio: 1.04; 95% CI 0.59-1.83; P=0.87). As a result, hypothyroidism was not linked to an increased risk of death.

Conclusion: Hypothyroidism in hospitalized COVID-19 patients appears to be low. However, it seems more prevalent in the female gender but without significant adverse effects on the risk of mortality from this disease.

Keywords: COVID-19, Prevalence, Hypothyroidism, Comorbidities

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1. Introduction

The name "COVID-19" was first created by the WHO on February 11th, 2020, regarding the disease with similarity to SARS or "severe acute respiratory syndrome", which was later recognized as SARS-CoV-2, a novel and incredibly contagious virus that resulted in a pandemic [1, 2]. Unfortunately, both the severe and fatal rates of COVID-19 infection continue to rise rapidly [3]. As a result, determining the predictors of severe COVID-19 infection is critical for early intervention therapy. Recent reports show that the novel coronavirus can be identified through various nonspecific symptoms, including fever, cough, dyspnea, loss of sense of smell, shortness of breath, and fatigue [4]. Decreased appetite, nausea, vomiting, diarrhea, and chest discomfort are common symptoms of COVID-19 that are not directly related to the respiratory system [5, 6].

Endocrine and metabolic problems may increase the likelihood of SARS-CoV-2 infection [7-9], and thyroid hormone may contribute to coronavirus infection by altering the interaction between coronaviruses and integrin αvβ3 in airway epithelial cells [10]. Hypothyroidism is a common endocrine disorder when the thyroid gland does not produce enough thyroid hormone [11]. While there is limited data on the relationship between COVID-19 and hypothyroidism, some studies have suggested that COVID-19 infection can exacerbate pre-existing thyroid dysfunction. Patients with hypothyroidism may be at a higher risk of severe COVID-19 infection due to their compromised immune systems [12]. Furthermore, some COVID-19 treatments, such as dexamethasone, can also affect thyroid function.

Although the harmful effect of many underlying diseases, such as diabetes mellitus, hypertension, obesity, age >70 years, coronary artery disease, and heart failure on the severity and mortality of COVID-19 patients has been established in many studies [13], the definitive role of hypothyroidism on the prognosis of COVID-19 positive patients is still unknown [14]. It is important for healthcare providers to closely monitor thyroid function in COVID-19 patients with pre-existing hypothyroidism and consider thyroid function testing in patients with new onset hypothyroidism during COVID-19 infection. Hence, this study aimed to estimate the prevalence of hypothyroidism in confirmed COVID-19 cases in the hospital within a specified period and its possible influence on the clinical outcomes.

2. Materials and Methods

Study design and subjects

This retrospective cross-sectional study was performed on patients infected with COVID-19 admitted at Imam Khomeini Hospital Complex, a referral center in Tehran City, Iran, from February 20th to April 19th, 2020.

Eligibility criteria

All patients had PCR-confirmed COVID-19 or compatible clinical, laboratory, and imaging findings for COVID-19. Regarding the time frame and inclusion criteria, the medical records of 493 patients were reviewed, while the only relevant and useful data from them were collected for our study. COVID-19 patients were identified as having hypothyroidism as a comorbidity when the reliable medical history in the medical record mentioned "hypothyroidism".

Study measurements

All information in this study was obtained using a structured questionnaire from electronic patient health records. Table 1 presents the variables in the questionnaire in collecting the data.

Statistical analysis

Our data extraction and analysis were done with IBM SPSS, version 25. We evaluated the proportion of COVID-19 patients, along with 95% CI, and stratified by demographics, and comorbidities, especially hypothyroidism. $P<0.05$ were considered statistically significant.

3. Results

Characteristics of study subjects

Characteristics of included participants are provided in Table 1. Out of 493 patients with COVID-19, 67% (n=332) were males, and 33% (n=161) were females. The male-to-female ratio was 2:1. The total discharge rate was higher than the expired rate (68.6% vs 31.4%). Generally, the male gender recorded most cases of death (57.4%). The 50–59 age group represented the age group with the highest discharge rate, accounting for 27.2% (n=92) of the total discharged group. On the other hand, patients above the age of 70 made up the largest percentage of patients who perished (32.9%) out of the total case mortality rate. Fortunately, most patients (73.1%) were discharged from the hospital in less than 5 days.

Prevalence of hypothyroidism

Among COVID-19 cases, 65 patients (13.2%), including 39 (60%) females and 26 (40%) males, had pre-existing hypothyroidism and were on replacement therapy. The prevalence of hypothyroidism among patients with COVID-19 was statistically significantly higher in women (P<0.001). Among the 65 COVID-19 patients with hypothyroidism, 21 patients (32.3%) expired, of whom 14 patients (66.7%) were females, and 7 (33.3%) were males. There was no statistically significant difference between the mortality of male and female patients with hypothyroidism (P=0.44). Furthermore, out of the 65 hypothyroidism cases hospitalized, 44 patients (67.7%) were discharged from the hospital, while 21 patients (32.3%) died. As a result, hypothyroidism was not linked to an increased risk of death (Adjusted Odds Ratio: 1.04; 95% CI: 0.59-1.83; P=0.87).

Comorbidities

The most common underlying diseases in our patients were hypertension (36.7%), diabetes mellitus (27%), and coronary artery disease (26.9%). The total case fatality rate reported from our study was 155 (31.4%). Of this case fatality rate, 21 patients (13.5%) had both hypothyroidism and COVID-19, while 134 (86.5%) had COVID-19 without hypothyroidism. Furthermore, hypertensive patients had the highest comorbid case fatality (41.9%). Significantly, cancer patients with COVID-19 had an increased chance of death (P<0.001). Case fatality rates for the stratified age groups and other comorbidities assessed in this study can be seen in Table 2.

4. Discussion

In COVID-19 patients, hypothyroidism can cause complications as the virus already weakens the immune system. COVID-19 patients with pre-existing hypothyroidism need proper care and monitoring to prevent further health complications. The principal findings from this retrospective study indicate that the commonness of hypothyroidism among COVID-19 patients was low. Additionally, comorbidities such as hypertension and cancer may play a critical role in the poor outcome of COVID-19 patients.

With a prevalence of 13.2%, of which 60% of the patients were females, and 40% were males, this may seem low; however, compared with the prevalence of hypothyroidism in the general Iranian population, this was higher (13.4% vs 2.3%) [15]. Therefore, our study supports the available research data that hypothyroidism is more common in Iranian women than men. Additionally, we found that the general case mortality rate was higher in males than in females (57.4% vs 42.6%). This also confirms the hypothesis that COVID-19 mortality is higher in the male gender [16]. Fortunately, among the study subjects, most were discharged, out of which 87.0% did not have a history of hypothyroidism, and 13.0% had a history of hypothyroidism. Approximately 32.3% of patients with pre-existing hypothyroidism expired. As shown in Table 2, there was no statistically significant difference between expired and discharged groups in patients with hypothyroidism (32.3% vs 67.7%) (P=0.87). Our findings and hypothesis align with van Gerwen et al. retrospective cohort study on 3703 patients with COVID-19 in the United States. They reported that 6.8% had hypothyroidism, and 68.1% of the patients with hypothyroidism needed hospitalization. Nonetheless, hypothyroidism was not linked with an increased risk of COVID-19 hospitalization or other worse possibilities, such as death, compared to non-hypothyroid cases [17].

Table1. List of the variables included in the data analysis

Demographics	Comorbidities
Gender	Coronary artery disease (CAD)
Age	Hypertension
Marital status	Diabetes mellitus (DM)
Duration of admission	Chronic pulmonary disease
	Cancer
	Chronic renal failure (CRF)
	Chronic liver disease
	Hypothyroidism

Table 2. Demographic and comorbid findings of patients with COVID-19 based on two groups, a Referral Hospital, Tehran, 2020

Variables		No. (%)		Odds Ratio (95% CI)	P
		Expired Group	Discharged Group		
Gender	Male	89(57.4)	243(71.9)	0.52 (0.35-0.78)	0.002
	Female	66(42.6)	95(28.1)	Referent	Referent
Age (years)	<39	17(11.0)	50(14.8)	Referent	Referent
	39-49	16(10.3)	61(18.0)	0.52 (0.29-0.94)	0.51
	50-59	27(17.4)	92(27.2)	0.56 (0.35-0.91)	0.67
	60-69	44(28.4)	80(23.7)	1.28 (0.83-1.97)	0.15
	≥70	51(32.9)	55(16.3)	2.52 (1.62-3.93)	0.003
Coronary artery disease (CAD)	Yes	49(31.6)	84(24.9)	1.39 (0.91-2.11)	0.12
	No	106(68.4)	254(75.1)	Referent	Referent
Hypertension	Yes	65(41.9)	116(34.3)	1.38 (0.93-2.04)	0.10
	No	90(58.1)	222(65.7)	Referent	Referent
Diabetes mellitus (DM)	Yes	44(28.4)	91(26.9)	1.05 (0.68-1.61)	0.82
	No	111(71.6)	247(73.1)	Referent	Referent
Chronic pulmonary disease	Yes	13(8.4)	27(8.0)	1.05 (0.52-2.10)	0.88
	No	142(91.6)	311(92.0)	Referent	Referent
Chronic liver disease	Yes	4(2.6)	8(2.4)	1.09 (0.32-3.68)	0.89
	No	151(97.4)	330(97.6)	Referent	Referent
Chronic renal failure (CRF)	Yes	11(7.1)	14(4.1)	1.76 (0.78-3.98)	0.17
	No	144(92.9)	324(95.9)	Referent	Referent
Cancer	Yes	24(15.5)	16(4.7)	3.68 (1.89-7.16)	<0.001
	No	131(84.5)	322(95.3)	Referent	Referent
Hypothyroidism	Yes	21(13.5)	44(13.0)	1.04 (0.59-1.83)	0.87
	No	134(86.5)	294(87.0)	Referent	Referent
Total (N=493)		155(31.4%)	338(68.6)		

In pathogenic COVID-19 infections, various factors determine illness severity, including initial viral titers in the airways and the infected person's age and concomitant diseases [18]. Current evidence suggests that people with comorbidities such as diabetes, obesity, heart failure, and kidney failure experience more severe illnesses than others. Still, there is insufficient evidence for the effects of hypothyroidism on COVID-19 prognosis [19]. According to the pathophysiology, some may hypothesize that the prognosis of COVID-19 patients with a history of hypothyroidism, especially Hashimoto's thyroiditis, will worsen than the normal population. Our findings do not support this hypothesis, and in addition, this hypothesis seems to be in contrast with the results of Chen et al., which

stipulates that individuals with COVID-19 had considerably lower thyroid stimulating hormone (TSH) and serum total triiodothyronine (TT3) levels than healthy controls and non-COVID-19 pneumonia cases. A comparable study conducted in Iran on 390 COVID-19-admitted patients reported 5.4% hypothyroid instances, with approximately 90% of participants above 50. Regarding hypothyroidism's impact on COVID-19 death rates, about 19% of hypothyroid patients died [14]. Thyroid disease (TD) is not known to be related to an increased risk of viral infections in general, nor is there an increased chance of developing more severe COVID-19 disease, according to the British Thyroid Association and the Society for Endocrinology in their joint paper. Interestingly, there are notable reports that are in contrast to our findings. A study discovered that COVID-19 patients with hypothyroidism had a greater in-hospital death rate than COVID-19 patients with euthyroidism [12].

Hypothyroidism, like thyrotoxicosis, but to a lesser level, may harm COVID-19 results. They added that the degree of COVID-19 appears to be the most important factor in thyroid injury. As a result, there is a chance that primary hypothyroidism might develop during or after COVID-19 [12]. Wang et al. also performed a study on 84 hospitalized COVID-19 patients, reporting common thyroid function abnormalities in patients with COVID-19, especially in severe cases. During the disease, thyroid dysfunction appeared to vary continuously and recovered steadily and spontaneously. Thyroid malfunction was also linked to viral nucleic acid cleanup time, implying that virus infection and replication seem to be implicated in aberrant thyroid hormones [20]. Hariyanto Ti et al. also confirmed that the severity of the COVID-19 infection is increased among patients with thyroid disease. Their hypotheses highlighted the critical role of thyroid hormones in controlling innate immune responses. Consequently, dysregulation of the innate immune response, as demonstrated by greater neutrophil counts, increased CD14+ monocyte and macrophage count, reduced NK cell counts, and elevated complement levels, were found to be substantially related to severe COVID-19 infections. In addition, individuals with thyroid dysfunction had higher levels of pro-inflammatory cytokines, notably tumor necrosis factor and interleukin-6 [21].

5. Conclusions

The current study found that the prevalence of hypothyroidism in hospitalized COVID-19 patients was not high. However, it seems more prevalent in females though the general case mortality rate in males is higher than the females. Consequently, women with hypothyroidism and COVID-19 seem to have a higher mortality rate than men, but there was no statistically significant difference. Hence, hypothyroidism alone does not seem to affect patients' outcomes, but comorbidities such as hypertension and cancer in COVID-19 patients could warrant poor prognoses.

Limitations and recommendations

A limitation of our study is that we lacked access to the patient's thyroid tests since this was a retrospective study, and we used data gathered from electronic medical records. Hence, the results could be strongly influenced by differences in the definition of thyroid malfunction, the timing of the dysfunction, and whether or not the problem was treated. Furthermore, thyroid hormone levels could be normal when thyroid hormone or anti-thyroid medicines are administered in patients with thyroid dysfunction. Nonetheless, due to a lack of reliable data on thyroid hormone levels, there is no direct evidence to indicate a link between COVID-19 severity and thyroid hormone levels. Further studies should address the influence of thyroid dysfunction treatment on the prognosis of COVID-19.

Ethical Considerations

Compliance with ethical guidelines

Written informed consent was obtained from the patients to publish this report per the journal's patient consent policy.

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Authors contributions

The conception and design of the study: Fatemeh Esfahanian; Analysis, interpretation of data, and revising: Seyedahmad Seyedalinaghi; Drafting the article and final approval of the version to be submitted: Nazanin Janfaza; Rewriting and editing of text for submission: Marcarious Moorkereh Tantuoyir.

Conflict of interest

The authors declared no conflict of interest.

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