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(RESEARCH ARTICLE)

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The comparison study to Triiodothyronine (T3) levels in severe and non-severe covid-19 infections in Babylon province

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Abstract

In addition to evaluating thyroid hormone levels as a possible predictor of illness severity, this reading sought to regulate the reminder among disease severity and demographic characteristics (age, gender, blood group, vaccination status, and geographic distribution) in recovered COVID-19 patients. 76 COVID-19 patients who received treatment at Babylon Province's Merjan Teaching Hospital between November and December 2021 were examined. Age was significantly correlated with severity ($p \leq 0.0001$), with non-severe cases being more common in those under 30 and severe cases being more common in those over 40. Gender differences were not statistically significant, despite the fact that males outnumbered females ($p > 0.0001$). Although there were variations between rural and urban cases ($p \leq 0.0357$), geographic location had no discernible effect. While ABO blood type affected severity While ABO blood type had no effect on severity, vaccination status did ($p > 0.0001$). Significant differences in T3 levels between severe and non-severe patients point to a possible function in predicting the severity of the disease. These results shed light on the biological and demographic variables affecting COVID-19 outcomes.

Keywords: T3; Covid; Thyroid; Severity and Cytokine

1. Introduction

A severe breathing tract infection of unidentified source, coronavirus disease 2019 (COVID-19) began in Wuhan, China in January 2020 and quickly feast throughout the nation and the rest of the world. In mainland China, 14% of cases were severe and 5% were critical, depend on several researches from the Chinese Center for Disease Control and Prevention. The COVID-19 mortality proportion was 2.3%. the infections may be improved by classifying them based on their clinical severity. Critically ill individuals often have euthyroidal sickness (NTIS), which is characterized by a decreased blood triiodothyronine (T3) content. In patients with acute myocardial infarction and chronic renal failure (CRF), lower T3 concentration has been linked to death (1).

Triiodothyronine T3, a thyroid hormone, binds to high-affinity nuclear receptors to control gene expression. In response to hormones, thyroid hormone receptors (TRs) either activate or repress transcription by identifying particular shape of response, The TR proteins, bind to are reviewed in this study, along with the interacting proteins involved in these complexes. One The hypothesis that T3 may also operate quickly through non-genomic activities on membranes is then briefly discussed, along with the cross-talk with other signaling pathways (2).

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2. Material and methods

2.1. Study Populatin

The 76 COVID-19 patients that were enrolled in the trial from the province of Al-Hillah/Babylon between November and December 2021 made up the study subjects. Under the guidance of a specialist physician, blood samples from severe cases with an average age range of 18 to 90 years were chosen from Merjan Teaching Hospital.

2.2. Blood Samples

Each trial participant had roughly five milliliters of venous blood drawn. To determine the blood type, the blood was separated into two portions, one of which (about two milliliters) was collected into tubes containing EDTA. Centrifugation was used for 15 minutes at 3000 rpm to separate the second portion of the blood. Until immunological parameters are measured, the leftover sera are kept frozen at -20 °C.

2.3. Estimation of ABO blood group system

2.3.1. Principle

Agglutination response is the foundation for the ABO and Rh blood classification systems. Red blood cells containing one or both antigens interrelate with one another to produce apparent clumping or agglutination when they are exposed to the appropriate antibodies. The terminal sugar residues that are visible at the red blood cell surface of the O-linked glycoproteins that make up the ABO blood group antigens identify them as either A or B. People with blood group A have anti-B antibodies in their serum and A antigens on their red blood cells. Similarly, people with blood type B have anti-A antibodies in their serum and B antigens on their red blood cells. RBCs from people with blood group AB contain both A and B antigens, and their serum contains neither anti-A nor anti-B antibodies.

Blood group O persons, on the other hand, have both anti-A and anti-B antibodies in their serum but neither A nor B antigens. The Rh antigens are transmembrane proteins that interact with the matching antibodies through exposed loops on the surface of red blood cells. (Himedia business).

- Step 1: To improve blood flow in the fingers, hang the hand downward.
- Use spirit or 70% alcohol to clean the fingertip (typically the middle or ring finger) that will be pierced.
- Insert one drop of blood into each of the cavities after puncturing the fingertip with the sterile lancet.
- As indicated below, put one drop of antiserum into each cavity.
- Using a new mixing stick, combine each drop of blood with the antiserum.
- Within 30 seconds, see agglutination in the form of tiny crimson granules. In figure (1), Anti Rh D agglutinates a little more slowly than Anti A and Anti B.AS.

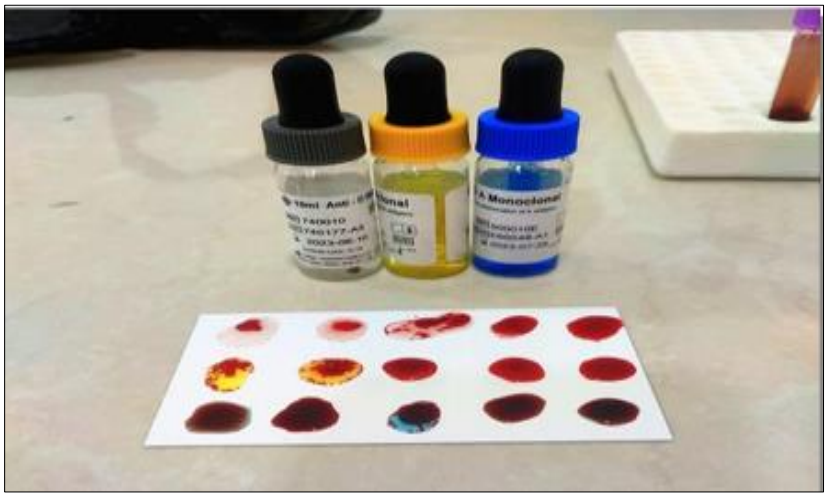

Figure 1 Detection of ABO blood grouping

Figure 2 ELISA device used to read the concentration of T3

2.4. Estimation of T3

2.4.1. Principle

Native antigen, enzyme-antigen conjugate, and immobilized antibody are the necessary components for a solid phase enzyme immunoassay. A competition response between the native antigen and the enzyme-antigen conjugate for a restricted number of insolubilized binding sites occurs when immobilized antibody, enzyme-antigen conjugate, and serum carrying the native antigen are combined. The following equation provides an illustration of the interaction:

$$^{Enz}Ag + Ag + Ab_{C.W.} \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} AgAb_{C.W.} + {}^{Enz}AgAb_{C.W.}$$

$Ab_{C.W.}$ = Monospecific Immobilized Antibody (Constant Quantity)
Ag = Native Antigen (Variable Quantity)

Ab C.W. = Monospecific Immobilized Antibody (Constant Quantity)

Ag = Native Antigen (Variable Quantity)

- EnzAg = Enzyme-antigen Conjugate (Constant Quantity)
- AgAbC.W. = Antigen-Antibody Complex
- EnzAgAbC.W. = Enzyme-antigen Conjugate -Antibody Complex
- ka = Rate Constant of Association
- k-a = Rate Constant of Disassociation
- K = ka / k-a = Equilibrium Constant

Decantation or aspiration are used to separate the antibody-bound fraction from the unbound antigen once equilibrium has been reached. The concentration of native antigen is negatively correlated with the enzyme activity in the antibody-bound fraction. It is possible to determine the antigen concentration of an unknown by creating a dose response curve using multiple serum reference calibrators with known antigen concentrations.

2.5. Assay procedure

All of the controls, reference calibrators, and reagents were brought to room temperature (20–27°C).

- The microplates' designated wells for each patient specimen, control, and serum reference calibrator to be tested twice. Any unused microwell strips should be put back into the aluminum bag, sealed, and kept between 2 and 8 °C.
- 0.050 milliliters (50 microliters) the proper serum reference calibrator, control, or specimen was pipetted into the designated well.
- 0.100 milliliters (100 µl) T3 Enzyme Reagent and Working Reagent A were added to each well (according to the Reagent Preparation Section).
- To combine and cover, gently swirl the microplate for 20 to 30 seconds.

- Let it sit at room temperature for half an hour.
- Use aspiration or decantation to discard the microplate's contents. Use absorbent paper to blot the plate dry if decanting.
- Add aspirate, decant (tap and blot), or 0.350 ml (350 µl) of wash buffer (see to the Reagent Preparation Section). To complete three (3) washes, repeat two (2) more times. You can use a manual or automatic plate washer. For correct usage, adhere to the manufacturer's instructions. If using a squeeze bottle, fill each well by pressing down on the bottle to release the wash, being careful not to create air bubbles. Repeat two (2) more times after decanting the wash.
- Fill each well with 0.100 ml (100 µl) of substrate solution. To reduce reaction time variations between wells, always add reagents in the same order.
- Incubate for fifteen (15) minutes at room temperature.
- Fill each well with 0.050 ml (50 µl) of stop solution, and stir gently for 15 to 20 seconds. To reduce reaction time variations between wells, always add reagents in the same order.
- Read the absorbance in each well at 450nm (using a reference wavelength of 620-630nm to minimize well defects) on a microplate reader. After adding the stop solution, the results should be read within thirty minutes

2.6. Statistical Analysis

The study data was analyzed by using mean ±standard deviation in XLXs program from office, 2016. The significance tested at probability less than 0.05 by using online tool: https://www.medcalcc.org/calc/comparison_of_means.phpp

3. Results and discussion

3.1. Distribution of age in COVID-19 case for both severe and non-severe

Seventy-six (100%) of the patients in this study were treated at the Merjan Teaching Hospital in Babylon Province. The majority of the severe cases were over forty years old, whereas the majority of the non-severe cases were under thirty. There were 38 (50%) severe instances and 38 (50%) non-severe cases. Table (1) displays the results of the current investigation, which indicate highly important changes among severe and non-severe cases with p values less than 0.0001. The COVID-19 incidence was highest among those aged 18–25 years (31.6%) for the non-sever group and 17.1% for the sever group, followed by those aged 25–40 years (14.4%) for the non-sever group and 10.6% for the sever group, (3.9%) for the non-sever and 10.6% for the 40–60 years, and 0 percent for the non-sever group and 11.9 percent for the sever. These four age-based categories are significant (p≤0.0001).

Table 1 Age distribution of Covid-19 severity cases

Cases of Covid -19	Mean ± SD	95%CI	t/statistic	P value
Sever n=38	42.15 ± 19.69	23.1917 to -9.8041	-4.911	< 0.0001
Non-sever n=38	25.66 ± 6.39			

Table 2 Distribution of patients according to age

Severity Age	Non sever	sever	p-value
	No. (%)		
18-25	24(31.6%)	13(17.1%)	0.0902*
25-40	11(14.4%)	8(10.6%)	0.6895
40-60	3.(3.9%)	8(10.6%)	0.8683
60-96	0(0%)	9(11.9%)	0.011*

This study is the first to look at the connection between age group and the severity of COVID-19 disease. Age and infections may be impacted by changes in testing across age groups. Case and research laboratory investigation are predicated on the reliable obtainability of analytic difficult to all sections of the community. It is doubtful that the

observed age shift was caused exclusively by variations in testing obtainability, even if testing availability has changed by location, time, and test provider.

According to this study, the age group of 18 to 25 years old was the most impacted by the corona virus when compared to either younger or older groups. Despite this, research indicates that older adults are more likely than younger persons to contract COVID-19 (3). Furthermore, children's systems have developed immunity that may help them fight infection more effectively than older adults because of their comprehensive immunization schedule and frequent exposure to respiratory diseases (4).

Additionally, the respiratory system's inherent pathophysiological changes may be responsible for the worst aging outcomes, as may the increased prevalence of chronic comorbidities with aging (5). In order to diagnose and assess the current outbreak in clinical decision-making, a meta-analysis study, examined the effect of age on COVID-19 severity. The study found that while comorbidities and clinical manifestations could have a significant impact on the prognosis and severity of COVID-19, elderly or older patients (age ≥50 years) are at higher risk of developing severity (6). Over 3.54 million cases of SARS-CoV-2 infection have been reported in the pediatric population, although illness is less common in this age group than in adults. Children and adolescents have been hospitalized, admitted to intensive care units (7).

3.2. Distribution of gender in COVID-19 case for both severe and non-severe

Male patients outnumbered female patients by a wide margin. The results indicated non-significant differences ($p>0.0001$) by gender, with males having a non-sever rate of 31.6% and a sever rate of 23 (30.3%). In contrast, there were 18.4% of non-severe cases and 19.8% of severe cases in the female group.

Table 3 Gender distribution in severity of COVID-19 cases

Severity gender	**Non sever**	**sever**	**P value**
	No. (%)		
Male	24 (31.6%)	23 (30.3%)	0.47775
Female	14 (18.4%)	15(19.8%)	0.3815

Our findings imply that epidemiologic disparities by sex might be influenced by gender inequity. It's unclear, though, if this indicates real disparities in the risks of contracting COVID-19 for men and women or only variations in who is getting or seeking testing. According to this review, men are more susceptible to coronavirus than women. New research also showed that women are less likely than men to get the condition. Males are more likely than females to die with COVID-19 and will generally have worse clinical outcomes (8). Gender differences in the likelihood of obsession with contacts in the workplace that are necessary for the spread of infectious diseases spread by respiratory or close contact courses, such as COVID-19, are among the social factors contributing to this gender gap. For instance, 95.4% of male patients were not active, whereas only 89.3% of female patients were not. Sex and sex-related factors have been observed to have a significant impact during the ongoing pandemic. notable disparities between the sexes, with males at greater risk than women (9). This might be related to the existence of other risk factors and sex hormones like estrogen and testosterone, which seem to be crucial in shaping the body's immunological response, For instance, men are more likely than women to suffer from diabetes, high blood pressure, and cardiovascular disease.

3.3. Detection T3 in severe and non-severe patient with COVID-19

Out of 76 COVID-19 instances, both severe and non-severe, that were submitted to detection T3 parameters, the results showed that there were no significant differences between male and female in non-severe cases or between non-severe and sever cases when comparing the mean±SD of these parameters.

Table 4 T3 concentration for COVID-19 severity cases

Covid-19 cases	**Male T3 level mean ± sd N=22**	**Female T3 level Mean ± sd N=16**	**P value**	**Total T3 level Mean ± sd n=38**
Sever N=38	2.769±0.875	3.343±0.898	0.2020	3.162±1.053
Covid-19 Cases N=38	Male T3 level mean ± sd N=23	Female T3 level Mean ± sd N=15	P value	Total T3 level Mean ± sd n=38
Non sever N=38	2.748±0.721	3.068±1.131	0.146	2.756±0.769
P value Cases N=76	0.9304	0.4568		0.0587

According to the study's findings, T3 rose in COVID-19 patients as the virus's clinical severity worsened. in patients who are very or very sick. Another study found that in individuals with acute myocardial infarction, and all contribute to the death of individuals suffering from chronic renal failure (10). Reduced TSH, not low T3 or low T4, was sovereign analyst of death in individuals with acute-on-chronic liver failure (11).

Lower TSH was linked to a higher risk of death in a population of older individuals who were monitored for nine years (12). According to studies, the primary cause of the drop in T3 concentration was the peripheral tissues' conversion of T4 to T3. Short-term elevations in TSH and T4 were also noted during the acute period. Central suppression of the thyroid axis may be a significant factor throughout the extended period of critical illness, likely leading to a decrease in T3, T4, and TSH concentrations (13).

The median period between the onset of symptoms and ICU admission for COVID-19 critically sick patients, according to a prior study on the subject (14). However, T3 had already dropped in a study of patients having abdominal surgery even if IL-6 had not yet increased (15). Our study's single-center design is one of its shortcomings. Higher severity COVID-19 patients were assigned to the ward that our medical team took over. The findings of this study are therefore more indicative of the features,

About two weeks passed on average between the patient's manifestation of infection symptoms and their ward. It was challenging to ascertain if function was connected to the advancement of the disease because many individuals only received athyroid function measurements at the time of admission. Additionally, 12 patients were not released at the conclusion of the follow-up. A tiny percentage of the participants in our study had previously used glucocorticoids. The sensitivity analysis results following the removal of these patients, however, did not differ from the primary research findings, suggesting that the usage of glucocorticoids in these patients had no appreciable impact on the study's findings.

In summary, patients with severe COVID-19 had a considerably lower FT3 concentration than patients who were not as sick. Patients with severe COVID-19 had their all-cause mortality independently predicted by their lower FT3.

4. Conclusion

According to the study's findings, those over 40 are more likely to have severe COVID-19 cases, whereas people under 30 years, Furthermore, there is a greater prevalence of severe instances in rural areas as opposed to urban ones, and in males as opposed to females. Patients who are not vaccinated have more severe sickness, while those who are vaccinated had fewer severe instances. Additionally, higher levels of triiodothyronine (T3) are linked to more severe results, and blood types O and A are linked to increased severity of COVID-19. These results emphasize the complex relationship between demographic characteristics, immunization status, genetic predispositions, and hormone levels, underscoring the diverse nature of COVID-19 severity. Comprehending these correlations is essential for formulating focused interventions and therapeutic approaches to mitigate the impact of the disease.

Recommendations

The study suggests that immunization is lower the risk of contracting of infection in light of these findings. Maintaining personal cleanliness and social separation are crucial preventative strategies. To clarify the distinctions made by novel coronavirus strains, more investigation is required to create sophisticated diagnostic assays. To identify the best pharmacological interventions for every COVID-19 instance, more research is needed. It is essential to look at the connection between chronic illnesses and the severity.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Ethical approval was obtained.

Statement of informed consent

All subjects participating in this study were given a written consent contains the information about participant and the aim of the study and by filling the consent they approved their enrollment and the procedure that involve drawn blood samples.

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