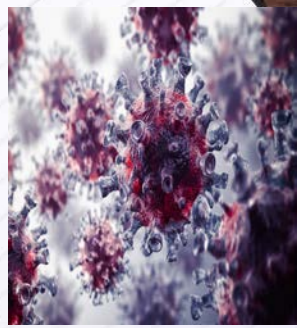
THE RELATIONSHIP BETWEEN THYROID HORMONE ALTERATIONS IN ACUTE PHASE OF COVID-19 AND POST-COVID SYNDROME AMONG SEVERE AND CRITICAL COVID-19 PATIENTS

DR SARA PEZESHKI
ASSISTANT PROFESSOR OF KMU



A G E N D A :

- About the article
- Back ground
- Question of the study
- Material and method
- Results
- Discussion
- Conclusion

About the article:

- Authors:

Sara Pezeshki, Mojgan Sanjari, Mohammad Hossein Gozashti, Mohammad Hasannejad, Fatemeh Doostmohammadi, Reza Sinaei

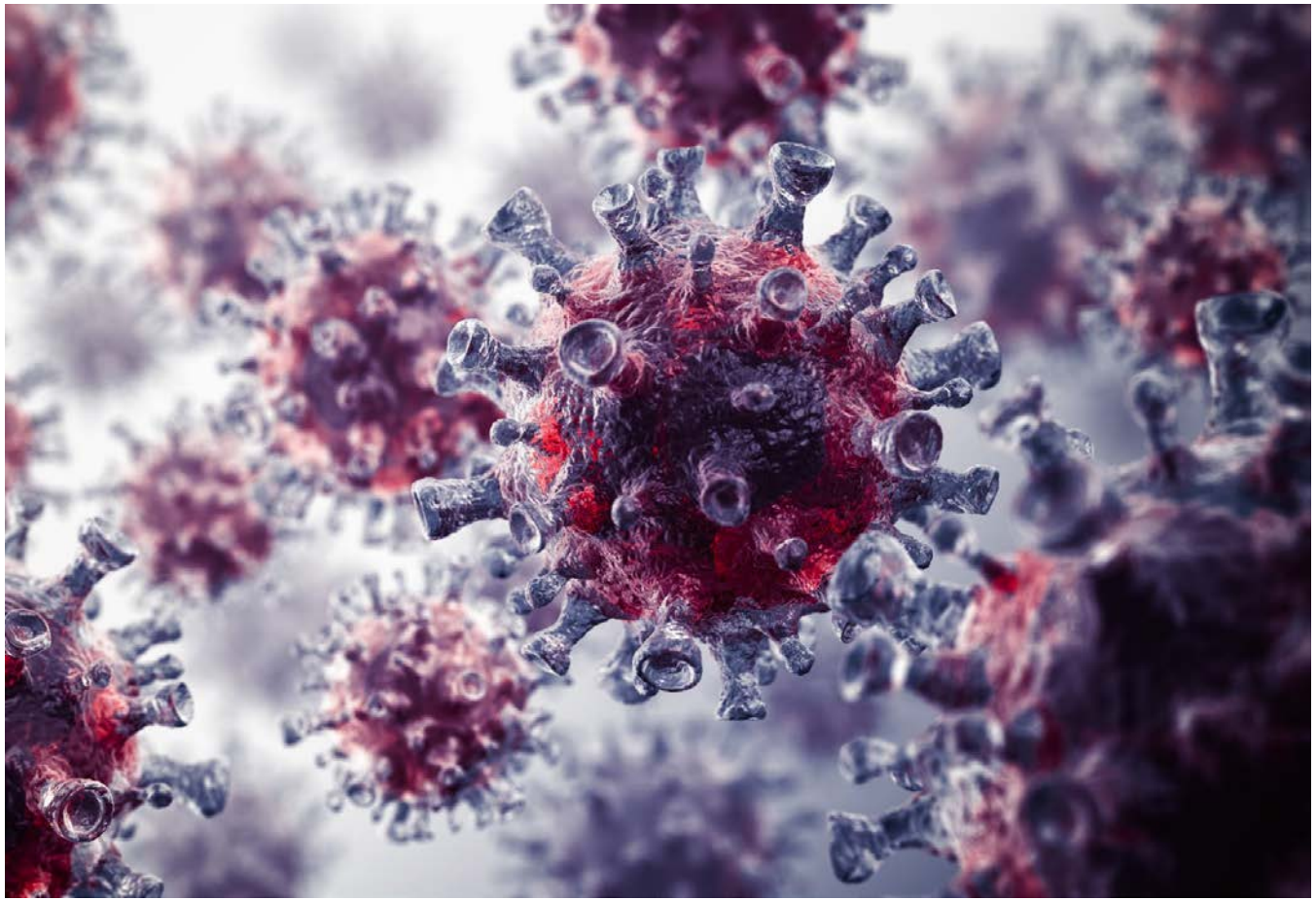
- Place of study:

Afzalipour Hospital of Kerman Medical University

- Study design:

Bidirectional cohort study

Background:



- The SARS-CoV-2 which first appeared in China had become a **global health threat** with several impacts on human physical and mental health .

Thyroid hormones alterations:

- Several **extra-pulmonary organ manifestations** including the endocrine organ, especially thyroid gland have been recently emerged.
- **Alteration of thyroid hormones** can occur in the setting of COVID-19 infection:

✓ Non thyroidal illness

✓ Hyperthyroidism

✓ Hypothyroidism

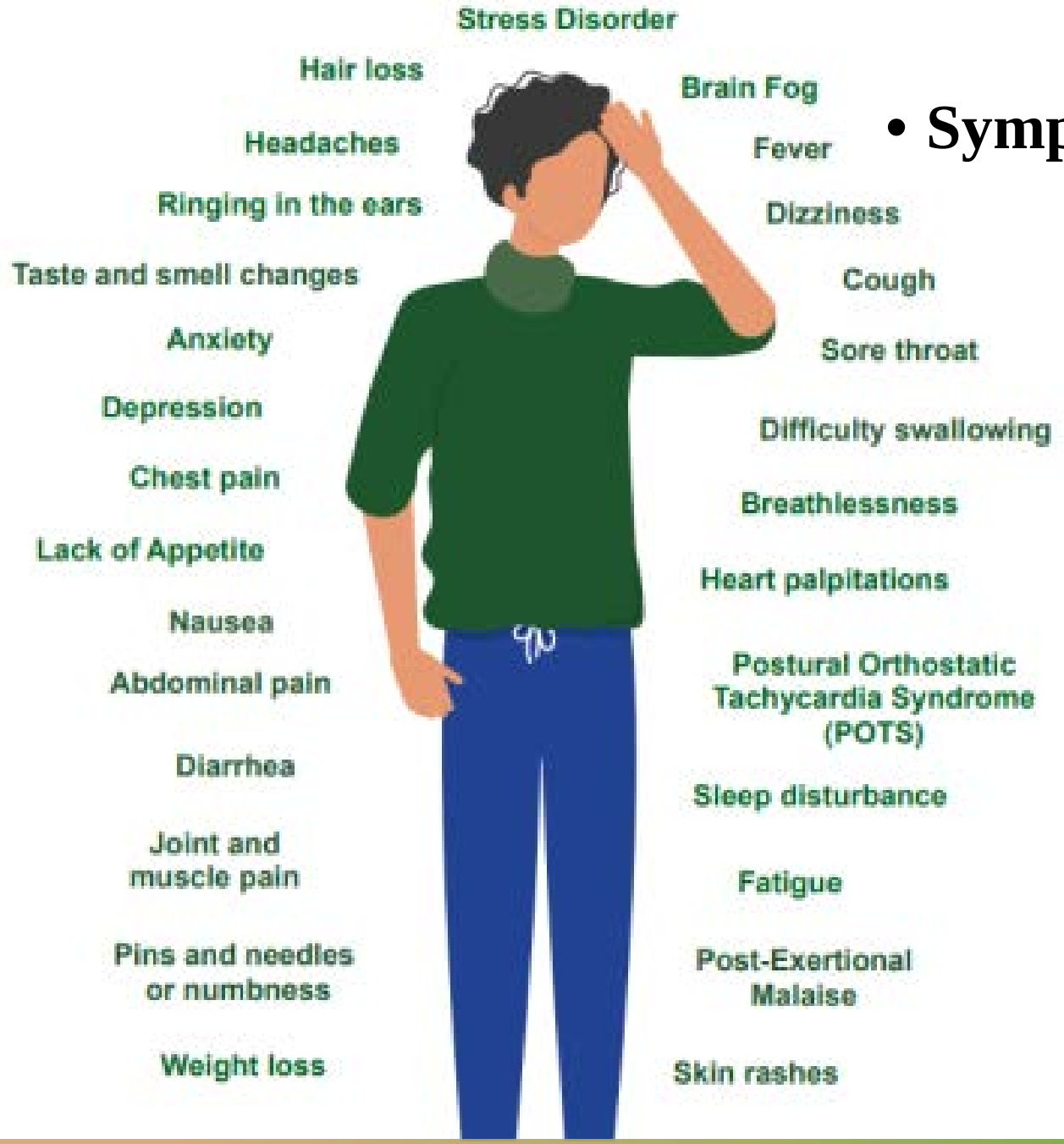
✓ Sub acute thyroiditis

Post-COVID Syndrome:

- Some people, especially those who present with severe COVID-19, experience multiorgan impacts or autoimmune conditions with symptoms lasting for weeks, months, or even years after COVID-19 illness.
- Several organ-systems including the heart, lung, kidneys, and endocrine systems may involve.
- This condition is called **Post-COVID Syndrome**.

Post-COVID Syndrome:

- The UK′s National Institute for Health and Care Excellence (**NICE**) published their **guidance** regarding the long-term consequences of COVID-19 .
- According to this, ongoing COVID-19 last from 4 to 12 weeks and post-COVID-19 syndrome develop during or after the active phase and continue for **more than 12 weeks,** while cannot be explained by an alternative diagnosis.



- **Symptoms of post COVID syndrome**

Post-COVID Syndrome:

- Witch people are more likely to have long-COVID?
- The etiology and risk factors of this condition are not clear yet.

Questions of the study?

- Since alterations in thyroid hormones have an effects on acute phase of COVID-19 severity and short term outcomes, the question is :
- Is there the relationship between thyroid hormone alterations in acute phase of COVID-19 and post-COVID syndrome among severe and critical COVID-19 patients?

Material and Method:

Study design	Bidirectional cohort study
Source of data	Kerman University of Medical Science, Afzalipour Hospital, ICU unit
Study subjects	adult participants (aged>18 years) with severe and critical course needed to ICU admission
Time of study	From January 2021 to January 2022

Inclusion and Exclusion criteria:

Inclusion criteria
All adult patients aged more than 18-years with definitive severe or critical COVID-19 who admitted in ICUs during 2021, transferring to ICU during the early five days of admission

Exclusion criteria
A history of previous thyroid, hypothalamic, or pituitary disorders
The use of medications that may impact on thyroid function
The use of thyroid hormone replacement or anti-thyroid agents
End stage organ disease
Chronic Kidney Disease (CKD)
Hematologic disease such as Leukemia, Lymphoma, Multiple Myeloma, etc
Psychologic disorders such as major depression and psychosis
Pregnant and lactating women
COVID-19 suspected patients without a positive RT-PCR testing
Mild to moderate admitted patients or severe and critical patients who admitted in the wards except ICUs

Laboratory tests	
TFT	Total T3, Total T4, Free T4, TSH
severity related factors	ESR, CRP, LDH, CPK, absolute lymphocyte count
method of measuring thyroid hormones	ElectroChemiLuminescence (ECL), which was performed with the kits of ROCH belongs to Germany

Data collection:

- Demographic information
- Major comorbidities
- laboratory tests related to the severity of the disease
- Respiratory rate, baseline oxygen saturation by pulse oximetry and
- oxygen requirement and oxygenation type on admission and in the time of ICU entry
- The underlying non-excluded disease
- Post covid syndrome symptoms after 3 and 6 month after discharg

Outcomes:

- **Short term outcomes:**

✓Primary end point of intra-hospital death

✓ Need to ventilator and BiPAP or face mask

✓The duration of ICU stay

- **Long term outcomes:**

✓remaining or new-onset symptoms according to post covid syndrome were included after 90 and 180 days follow up in survivors

Statistical Analysis:

After collecting the data, we utilized descriptive statistical methods and the SPSS software (version 20) for analysis.

Two-sided P. Values of less than 0.05 were considered statistically significant.

Data were presented as median, number or percentage, as appropriate.

Comparison between groups were done by t-test or Mann-Whitney U-test for continues variables, as appropriate, and X^2-test or Fisher exact test for categorical variables, as appropriate.

Multivariable logistic regression analysis was performed to identify variables independently associated with both short-term outcomes and long-term symptoms under the post-acute syndrome umbrella.

Results:

- Participant:

✓**150 hospitalized patients** with severe and critical COVID-19

✓Including 83 **men (55.3%)** and 67 **women (44.7%)**

✓ Average age of **62±16 years** (18-89 years)

✓ The average length of ICU admission was **11.86±8.1** days

✓Mortality: 77 patient (**51.3%**) were died

✓Vaccination history: 51 % had no history of vaccination against SARS-CoV-2

Determining the mean of initial tests of the study

Laboratory test	Minimum	Maximum	Mean
TSH	0.50	6.80	2.69± 1.02
TT4	4.70	20.00	10.67±3.4
TT3	0.30	3.70	1.17±0.42
FT4	0.50	3.80	1.32±0.42

- Thyroid function test disorders

Thyroid function test disorders	Prevalence
Total	48%
Low TT3	18
High TT4	14.6
High FT4	12
Low FT4	10
High TSH	6
High TT3	0.7

- There was a significant inverse association between the level of TT3 and FT4 with the mortality rate.
- so that the average of T3 was significantly higher in survivors than non-survivors (1.22±0.35 vs 1.13±0.56; P=0.015)
- Similarly, the average of FT4 was higher in survivors than non-survivors (1.43±0.46 vs 1.22±0.35; P=0.001).
- There was a significant relationship between lower FT4 and the need for more advanced oxygen delivery methods of BIPAP and Ventilator

L O N G - C O V I D S Y M P T O M S :

3 month later

the most common symptom were:

✓fatigue (45.2%)

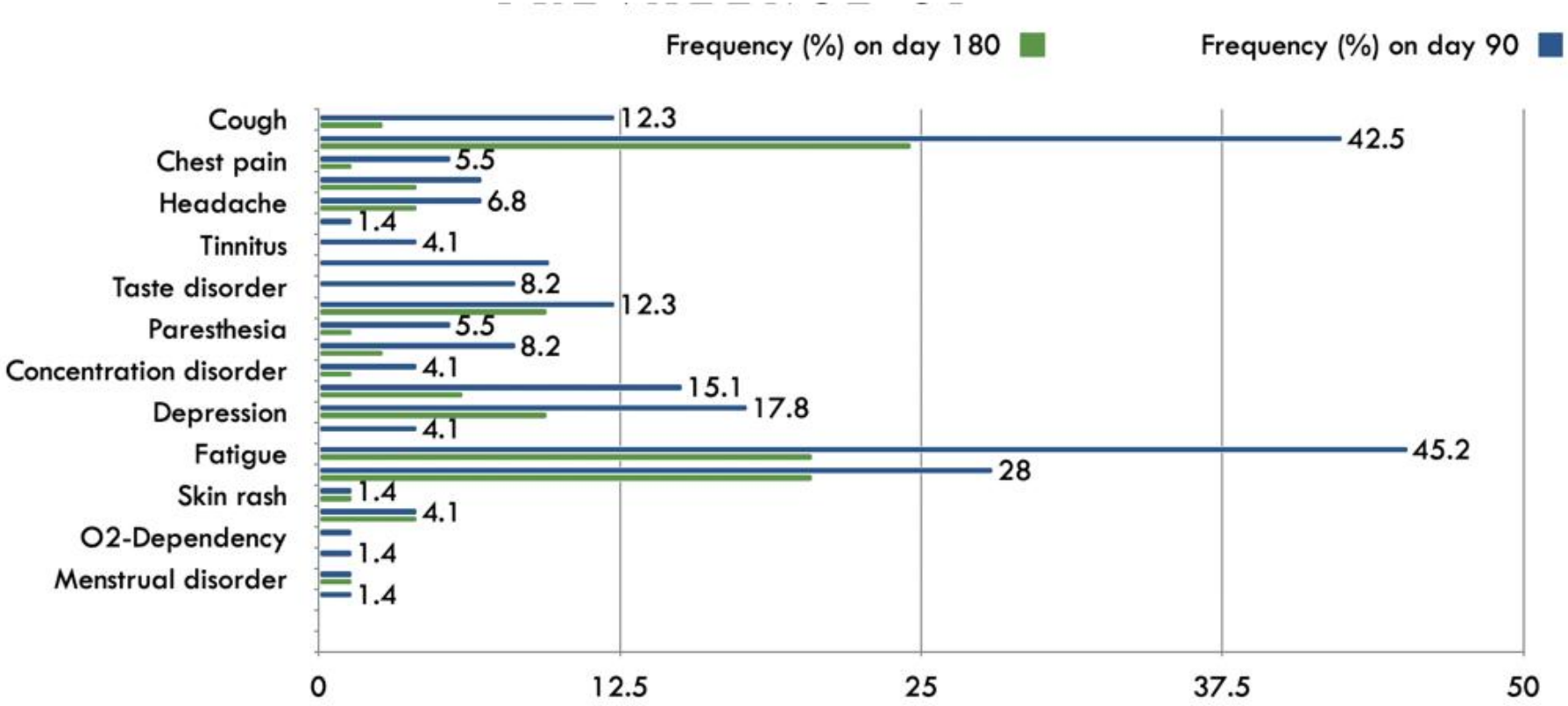
✓ shortness of breath (42.5%)

6 month later

the most common symptoms were

✓the shortness of breath (24.6%)

✓ fatigue/muscle pain (20.5%)


Frequency (%) on day 180
Frequency (%) on day 90
Cough
Chest pain
Headache
Tinnitus
Taste disorder
Paresthesia
Concentration disorder
Depression
Fatigue
Skin rash
O2-Dependency
Menstrual disorder
12.3
42.5
5.5
6.8
1.4
4.1
8.2
12.3
5.5
8.2
4.1
15.1
17.8
4.1
45.2
28
1.4
4.1
1.4
1.4
0
12.5
25
37.5
50

- After an average of 90 days, high TSH levels had a significant relationship with:

✓ persistent chest pain (P=0.002)

✓ palpitations (P=0.00), tinnitus (P=0.00)

✓paresthesia (P=0.00)

✓ muscle pain (P=0.001)

✓ depression (P=0.004)

✓ Concentration disorder (P=0.00)

✓hair loss (P=0.00)

- Furthermore, high levels of TT4 were associated with:

✓ palpitation (P=0.001)

✓tinnitus (P=0.00)

✓paresthesia (P=0.024)

✓concentration disorder (P=0.02)

✓depression (P=0.004)

✓ anxiety (P=0.00)

- There was also a correlation between high fT4 and :

✓palpitations (P=0.00)

✓ headache (P=0.003)

✓paresthesia (P=0.00)

✓concentration disorder (P=0.00)

✓and hair loss (P=0.02)

- After an average of 180 days, high levels of TSH were significantly associated with :

✓sleep disorder

✓ headache

✓anxiety

✓ depression

✓ hair loss

- Also high TT4 levels were associated with depression and anxiety.
- There was significant relationship between high levels of fT4 with headaches and palpitations.
- Additionally, low levels of fT4 were associated with hair loss.

Discussion:

- A number of reports have described the relationship between SARS-CoV-2 infection and TFT alterations.
- Furthermore ,there are many study about causes and risk factors of the post-COVID syndrome.
- But there is little regarding the relation between TFT alterations in acute phase of disease and the post-acute or prolonged symptoms related to COVID-19

- we evaluated the association of these **hormonal alterations with both short- and long-term outcomes** in the context of COVID-19.

- Throughout the COVID-19 pandemic, TFT alterations have been abundantly reported all over the world.

Country	Study	Sample size	TFT Abnormalities (%)	TFT Alterations
India	Cross-sectional	60	35% had one or more TFT abnormalities	thyroiditis and NTIS
China	Cross-sectional	50 hospitalized patients	64%	reduction in TSH, T3, both TSH and T3, both T3 and T3, and the combination of TSH, T3 and T4 in 34%, 6%, 18%, 2%, and 4%, respectively
England	Case-Control	334 admitted patients with COVID-19 and 122 non-COVID hospitalized patients	86.6% of participants were euthyroid	low TSH and T3 levels favored the diagnosis of NTIS

- In our study, changes in thyroid hormones, in the acute phase of the disease,had a statistically significant relationship with the occurrence of some symptoms of post COVID syndrome.
- These changes include: high TSH, low TT3,low TT4,high TT4, high TT3

- According to these findings, COVID induced hypothyroidism or thyrotoxicosis maybe one of the causes of post-COVID syndrome.

- One of the most common TFT abnormalities reported is low TSH levels along with normal or abnormal T3 and T4 levels, which is reported in 15-56% of COVID-19 patients in several studies.
- To date, studies in patients with COVID-19 have shown that TFT abnormalities are seen related to the severity of illness .

Conclusion:

- Although there have been numerous reports of thyroid hormonal abnormalities in the context of COVID-19, researchers have paid less attention regarding the association between these alterations and long-term outcomes of COVID-19.
- To our knowledge, this is the first cohort to evaluate the possible role of thyroid function among COVID19 survivors who have had post-COVID syndrome. Considering the significant relationship between the thyroid hormones alterations and the occurrence of long COVID in this study, further studies with larger sample sizes are recommended.

THANKS FOR YOUR ATTENTION