ORIGINAL ARTICLE

Correlation between IL-17, TGF-β and PTPN-22 Levels and Covid-19 Severity in Patients with and without Autoimmune Diseases

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ABSTRACT

Background: *The Coronavirus pandemic is the most significant global health crisis of our era. Since it first appeared in late 2019, the virus has spread to every continent. Furthermore, systemic inflammation is a common feature in many autoimmune diseases, increasing the risk of cardiovascular and thromboembolic diseases, which have also been linked to COVID-19.* ***Objectives:*** *This study aimed to identify the expression of IL-17 and TGF-β as predictors of COVID-19 severity in patients with and without autoimmune disease. Additionally, the study sought to investigate the role of protein tyrosine phosphatase non-receptor type 22 (PTPN-22) in the progression of COVID-19 in patients with autoimmune disease.* ***Methodology:*** *The study involved 52 COVID-19 patients, 26 having autoimmune disease and 26 not having any known autoimmune disease, along with 26 healthy controls. The expression levels of Il-17, TGF-β, and PTPN-22 were determined using the qRT-PCR technique. Data was collected and analyzed using SPSS.* ***Results:*** *Levels of IL-17 and PTPN-22 were significantly elevated in non-autoimmune COVID-19 patients, while TGF-β levels were significantly higher in the autoimmune group. Furthermore, all markers showed significant correlations with various laboratory biomarkers in both groups.* ***Conclusion:*** *The study found that IL-17 and PTPN-22 were significantly upregulated in patients without autoimmune inflammatory diseases (AID), with IL-17 showing strong correlations with inflammation and coagulation markers. Pro-inflammatory cytokines, including IL17A, were found to have the strongest association with COVID, and their levels may serve as potential risk factors for the severe progression of COVID to acute respiratory distress syndrome (ARDS).*

INTRODUCTION

In December 2019 the WHO notified that, Chinese health authorities had considered the outbreak of the COVID-19 disease to be a serious threat to public health. Meanwhile, the WHO again notified and advised the health authorities of Hong Kong, Macau and Taiwan to rapidly setup of border surveillance regarding this issue [1]

Covid-19 virus is a positive sense, non-segmented, single-stranded RNA virus without a DNA stage. The coronavirus has both linear and helical capsids on its surface, but the nucleocapsid is found inside the virion's envelope[2]. The virus carries pleomorphic RNA, also known as spike (S) proteins, which are peplomers with a size of 80–160 nM and a positive polarity of 27–32 kb. [3]

SARS-CoV-2 is transmitted between humans mainly via respiratory droplets. It can happen in 1-4 meters. Fomite transmission from contact with contaminated surfaces, is possible with high rates of contamination of floors and the soles of healthcare staff as well as computer mouse, doorknobs, and trash cans[4]. Cell surface molecules like CEACAMs, ACE2, DPP4, and APN play a role in coronavirus entry. Coronaviruses engage their receptors through the surface glycoprotein (spike or S), a class I fusion protein, which is activated through two sequential cleavage event[5]. The first cleavage 'priming' occurs at the boundary of the S1 and S2 domains (S1/S2) that typically occurs during S protein biogenesis and virus assembly. The second cleavage (S2') is the critical 'activating' event for membrane fusion, as it liberates what is formally an internal fusion peptide within the S2 domain[5]. The virus causes different clinical pictures in infected people. In 80% of the cases, it is asymptomatic, or it causes mild upper respiratory tract symptoms. However, pneumonia along with fever,

cough, dyspnea, and fatigue occurs in 20% of the patients, which progresses in some cases, leading to respiratory failure as well as multiple organ failure [6].

Due to its great transmissibility and capacity to elude the immunological response, the Omicron variation, specifically BA.1, quickly replaced the Delta variant [7]. The Omicron variety has mostly superseded all other variants to date. It has expanded and evolved into multiple sublineages, some of which have taken on global dominance. The S protein is a primary target for selection, and changes in its amino acid composition are typically linked to changes in biological characteristics[7]. COVID-19's immunopathology includes lymphopenia, lymphocyte dysfunction, granulocyte and monocyte abnormalities, elevated cytokine production, and elevated antibody levels.[8]. Numerous autoimmune disorders involve systemic inflammation, which raises the risk of cardiovascular [9] and thromboembolic disease[10], both of which have been linked to COVID-19 lately.

Autoimmune patients on immunosuppressive drugs had lower hospitalization and ICU admission odds, but the risk of COVID-19 illness remained consistent [11]. Among the many cytokines involved in the storm, IL-17 is a notable and predominant mediator of pulmonary inflammation. The pro-inflammatory properties of IL-17 also make it crucial to mediators of inflammation and immunopathology[12]. IL-17 cooperatively encourages the survival of viruses by preventing virus-infected cells from dying [13]. Targeting IL-17 can be an effective alternative treatment to decrease viral infections and minimize tissue damage in a variety of human disorders. IL-17 functions are critical in several viral infection situations [14]. Zumla et al[15]. hypothesize that blocking IL-17 could improve COVID-19's immune response and reduces mortality rates in critical-care patients compared to controls and non-intensive care. Also Interleukin-17 induces pro-inflammatory cytokines like TNF-a, IL-1b, and IL-6 in bone cells, cartilage, synoviocytes, and macrophages, leading to autoimmune diseases like rheumatoid arthritis flare-ups.[16]. In addition, SARS-CoV-2 virus infection induces massive increases of neutrophil infiltration into the lungs where, the neutrophils can release stored transforming growth factor-beta (TGF-β) that can be activated by elastase in neutrophils. TGF-β itself can be a potent chemokine-like molecule that recruits more neutrophils into lungs to form a positive feedback loop, which can contribute to local increases in total TGF-β release and TGF-β activation [17]. The TGF family members play a role in pathophysiological processes leading to various illnesses, with lungs having latent reserves of TGF-β that can be released into active form upon inflammatory stimuli[18]. In this case, the release of TGF-β is a crucial factor that triggers the post-inflammatory tissue repair stage of the disease [19]. Tissue fibrosis could therefore result from continuous TGF-β stimulation[20]. Strong data suggested that TGF-β 1 has a major role in the pathogenesis of acute respiratory distress syndrome (ARDS) prior to the COVID-19 pandemic[21]. Furthermore, increased blood TGF-β levels were characteristically correlated with increased disease severity[22]. Corona virus Antigen recognition triggers T cell activation via T cell receptors. PTPN22, a negative regulator, is a key protein involved in T cell activation, with the PTPN22R620W variant frequently found in Alzheimer's disease.[23]. Such a variant may also contribute to the T cell depletion and immunoparalysis seen in severe COVID-19 cases[24]. A single nucleotide polymorphism in PTPN22 has been reported as an autoimmune susceptibility locus that associates with type 1 diabetes, rheumatoid arthritis, systemic lupus erythematosus, Hashimotos thyroiditis, Graves' disease, Addisons disease, Myasthenia Gravis, vitiligo, systemic sclerosis, and juvenile idiopathic arthritis [25]. The study aims to correlate the expression of IL-17 and TGF-β as severity predictors of COVID-19 disease in autoimmune patients using real-time PCR, studying the role of PTPN22 in progression of covid-19 disease in patient with autoimmune disease, compare levels of IL-17, TGF-β and PTPN22 in patients with and without autoimmune diseases and to assess the correlations of gene expression levels with the laboratory indices of lung injury in the different groups of autoimmune patients.

METHODOLOGY

This study is a case-control study. It was presented to and approved by the ethics committee of the Faculty of Medicine at Assiut University (IRB NO: 04-2023-200157). Informed consent was obtained from each patient and control before their participation in the study.

This study included hospitalized patients who have been diagnosed with COVID-19 disease, with or without prevalent autoimmune diseases such as type 1 diabetes mellitus, rheumatoid arthritis (RA), ulcerative colitis, or Crohn's disease.

Exclusion criteria:

Patients under the age of 18 years, pregnant patients, those with mixed autoimmune diseases (more than one type), viral induced hepatitis and patients with HIV or malignancy have been excluded from this study.

Sample Collection and Preparation:

Patients enrolled in the study were divided into 2 groups:

1. Group 1 consisted of 52 COVID-19 patients.

This group was further divided into two subgroups based on the presence of autoimmune diseases:

- Group 1A: 26 COVID-19 patients with autoimmune disease
- Group 1B: 26 COVID-19 patients without autoimmune disease

2. Group 2 included 26 completely healthy volunteer controls matched for age and sex.

All participants underwent a thorough medical history assessment, focusing on age, gender, comorbid conditions, and clinical symptoms at the time of hospital admission. Additionally, patients underwent CT examinations. Baseline laboratory investigations, including complete blood count, C-reactive protein, ferritin, and D-dimer, were performed at The Central Laboratories of Assiut University Hospitals.

All demographic and clinical data of the patients were recorded from patient files, severity also sub classified according to patients' records. Laboratory investigations were performed at central laboratories of Assiut university hospitals.

5 ml of whole blood samples were collected in EDTA tubes from patients at the time of hospitalization. Each tube was labeled with the subject's name and the date of collection.

RNA Extraction:

Total RNA extraction was performed on all included samples using the Thermo Scientific Gene JET RNA purification Kit (catalog No. #K0731) according to manufacture instruction. RNA isolation took place in the RNase-free environment of the Medical Research Center at Assiut University, with all steps performed at room temperature.

Complementary DNA (cDNA) synthesis:

Total RNA (500 ng) from each sample was transcribed into cDNA using the Thermo Scientific Revert Aid First strand cDNA synthesis Kit (catalog No, #k1622) according to manufacture instruction.

Quantitative real-time polymerase chain reaction (qRT-PCR):

qRT-PCR was used to determine the expression of IL-17, TGF-β, and PTPN-22 using the Thermo Scientific Maxima SYBR Green qPCR Master Mix, Catalog no. #K0251. The qRT-PCR reaction was performed at the Medical Research Center, Assiut University. The primer sequences for the forward and reverse primers are shown in table 1.

Table 1: The sequences of the PCR primers

Gene	*5'-3' primer sequence*	*Annealing Temp (°c)*
IL-17	Forward:3′-CAAGACTGAACACCGACTAAG-5′ Reverse: 3′-TCTCCAAAGGAAGCCTGA-5′ [26]	60 °C
TGF-β	Forward: AACCCACAACGAAATCTATGACAAG Reverse: AGAGCAACACGGGTTCAGGTAC [27]	56 °C
PTPN-22	Forward: 5'-AGGCAGACAAAACCTATCCTACA-3' Reverse:5'-TGGGTGGCAATATAAGCCTTG-3'[28]	56 °C
GABDH	Forward: GAAGGTGAAGGTCGGAGTC Reverse: GAAGATGGTGATGGGATTTC [29]	60 °C

****GAPDH primer used as endogenous control*.

Calculation of the results:

The gene expression levels were assessed using the comparative cycle threshold (CT) method (ΔΔCT method) (Livak and Schmittgen, 2001). ΔCT was calculated using the formula: ΔCT = CT (target gene) − CT (endogenous reference gene, GADPH). The relative fold-change in expression was calculated by 2−ΔΔCT where ΔΔCt = (CT Target – CT GAPDH) disease − (CT Target – CT GAPDH) control.

Statistical analysis of data:

Data was collected and analyzed using SPSS (Statistical Package for the Social Science, version 20, IBM, Armonk, New York). Continuous data was expressed as mean ± standard deviation (SD), median and range, while nominal data was expressed as frequency (percentage). Chi²-test was used to compare the nominal data of both studied groups, while Mann Whitney-U test and independent sample t-test were used to compare the mean of continuous variables between both study and control groups. Spearman's correlation coefficient and Fischer exact test were used to measure the statistical association between the continuous variables. A probability (P-value) of < 0.05 was considered statistically significant.

RESULTS

The study included 52 patients, with 27 males and 25 females, and a mean age of 58.87 ± 18.41. As shown in table 2, there was a significant difference in the p-value for the fold change of IL-17 and PTPN-22 between the study and control groups, but TGF-β expression did not significantly change.

Table 2: Differences in fold change gene expression of IL-17, TGF and PTPN-22 in COVID-19 patients and controls

Folds	Patients (n= 52)	Controls (n= 26)	P-value
Fold IL-17: Mean ± SD Median (Range)	 3.28 ± 5.96 0.24 (0.01-17.68)	 1.00 ± 0.00 1.00 (1.00-1.00)	0.005*
Fold TGF: Mean ± SD Median (Range)	 2.45 ± 4.17 0.80 (0.01-18.87)	 1.00 ± 0.00 1.00 (1.00-1.00)	0.400
Fold PTPN-22: Mean ± SD Median (Range)	 8.62 ± 11.21 2.32 (0.01-36.81)	 1.00 ± 0.00 1.00 (1.00-1.00)	0.002*

Table 3: Differences in fold change gene expression of IL-17, TGF and PTPN-22 in Auto-immune COVID-19 patients and non auto-immune COVID-19.

	Auto-immune (n= 26)	Non auto-immune (n= 26)	P-value
Fold IL-17 Mean ± SD Median (Range)	 2.64 ± 5.21 0.24 (0.01-17.24)	 3.92 ± 6.68 0.36 (0.01-17.68)	0.884
Fold TGF: Mean ± SD Median (Range)	 3.10 ± 3.95 1.80 (0.01-14.80)	 1.79 ± 4.36 0.30 (0.06-18.87)	0.003*
Fold PTPN-22: Mean ± SD Median (Range)	 5.16 ± 9.00 1.69 (0.02-33.16)	 12.08 ± 12.27 8.58 (0.01-36.81)	0.176

According to TGF-β expression, it was highly significant in the non-autoimmune group compared to the autoimmune group, as shown in table 3. The difference in fold change in the tested markers between the autoimmune and non-autoimmune groups is presented in figure 1.

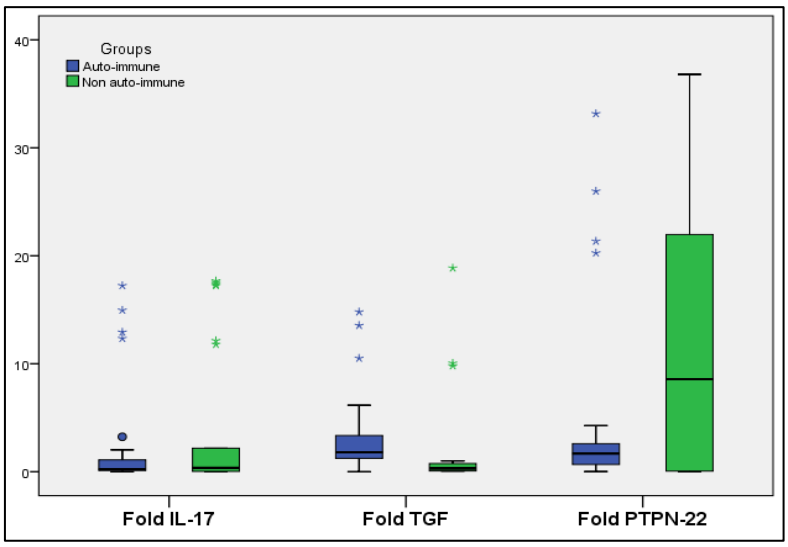

Fig. 1: Comparison between the fold change in indicated gene expression levels between autoimmune and non autoimmune covid-19 groups

Regarding the severity and outcome data of the groups involved in our study, as shown in table 4, there was insignificant decrease in severity and mortality among AID with Covid-19 group compared with non-AID Covid-19 group.

Table 4: Covid-19 severity and outcome

	Auto-immune (n= 26)		Non auto-immune (n= 26)		P-value
	No.	%	No.	%	
Severity:					
Moderate	16	61.5%	10	38.5%	0.096
Severe	10	38.5%	16	61.5%	
Outcome:					
Recovery	15	57.7%	12	46.2%	0.405
Death	11	42.3%	14	53.8%	

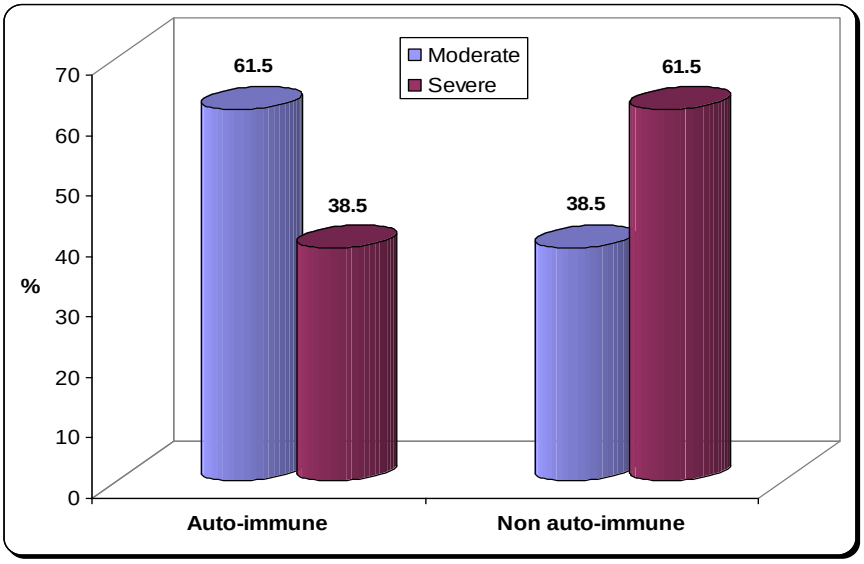

Fig.2: Correlation between severity and presence of AID with Covid-19

Table 5 shows correlations between gene expression levels with age and laboratory data in AID and non-AID groups:

In the autoimmune group, there were significant positive correlations between levels of IL-17 with age, and red cell distribution width RDW. There were also significant negative correlations between IL-17 levels with alanine transaminase ALT, albumin, hematocrit HCT, and hemoglobin Hb. Additionally, there was a significant positive correlation between TGF-β and d-dimer.

In the non-autoimmune group, there were significant positive correlations between levels of IL-17 with absolute basophils, absolute monocytes, absolute lymphocytes, and platelets. There were also significant negative correlations between IL-17 levels with c-reactive protein blood urea nitrogen BUN, creatinine, neutrophils, absolute neutrophils, mean corpuscular hemoglobin MCH, mean corpuscular volume MCV (r=-0.460, p=0.018), and white blood cells WBCs. Additionally, there were significant positive correlations between TGF-β with both age and d-dimer.

On the other side, there were significant negative correlations between TGF-β with neutrophils, absolute neutrophils, mean corpuscular hemoglobin concentration MCHC, hematocrit HCT, hemoglobin Hb, red blood cells RBCs, and white blood cells WBCs.

Another significant positive correlation was found between PTPN-22 with both absolute eosinophils and absolute lymphocytes. But there were significant negative correlations between PTPN-22 with c-reactive protein, ferritin, prothrombin time PT, blood urea nitrogen, alkaline phosphatase ALP and mean platelet volume MPV.

Table 5: Correlations between gene expression levels and laboratory parameters of patients with and without AID with their covid-19

	Auto-immune						Non-auto-immune					
	Fold IL-17		Fold TGF		Fold PTPN-22		Fold IL-17		Fold TGF		Fold PTPN-22	
	r-value	P-value	r-value	P-value	r-value	P-value	r-value	P-value	r-value	P-value	r-value	P-value
Age (years)	**0.500**	**0.009***	0.035	0.866	-0.002	0.992	0.311	0.122	**0.454**	**0.020***	-0.116	0.571
CRP	0.138	0.502	0.045	0.828	0.018	0.930	**-0.502**	**0.009***	-0.206	0.313	**-0.644**	**0.000***
Ferritin	-0.028	0.891	-0.225	0.268	-0.074	0.721	-0.164	0.422	0.059	0.774	**-0.547**	**0.004***
D-dimer	0.215	0.291	**0.408**	**0.039***	0.268	0.185	0.151	0.462	**0.409**	**0.038***	0.010	0.960
INR	0.302	0.134	0.093	0.652	0.050	0.808	0.330	0.100	0.377	0.058	-0.229	0.261
PT	0.330	0.099	0.096	0.639	0.014	0.947	0.111	0.588	0.193	0.346	**-0.430**	**0.028***
BUN	0.133	0.516	0.003	0.988	-0.076	0.711	**-0.472**	**0.015***	-0.040	0.847	**-0.622**	**0.001***
Creatinine	0.185	0.365	-0.036	0.862	-0.081	0.695	**-0.408**	**0.039***	0.216	0.290	-0.240	0.237
ALP	-0.076	0.711	0.156	0.446	-0.189	0.356	-0.242	0.234	-0.091	0.658	**-0.405**	**0.040***
ALT	**-0.475**	**0.014***	0.031	0.879	-0.123	0.550	-0.215	0.291	0.015	0.942	-0.031	0.881
AST	-0.335	0.094	0.235	0.248	0.060	0.770	-0.096	0.642	0.166	0.417	-0.352	0.078
Direct bilirubin	0.048	0.814	0.083	0.688	0.058	0.777	-0.207	0.309	-0.138	0.501	-0.194	0.342
Total bilirubin	-0.009	0.967	-0.024	0.909	0.170	0.407	-0.182	0.373	-0.179	0.381	-0.222	0.275
Albumin	**-0.436**	**0.026***	0.113	0.583	0.211	0.300	-0.267	0.188	-0.083	0.687	0.002	0.993
Total protein	-0.334	0.096	0.016	0.939	0.082	0.690	-0.242	0.233	0.251	0.216	-0.111	0.590
BASO	0.208	0.308	0.072	0.726	-0.028	0.892	0.174	0.394	0.002	0.991	-0.154	0.453
BASO%	-0.017	0.933	0.003	0.988	-0.172	0.400	**0.511**	**0.008***	0.172	0.401	0.156	0.447
EOSINO	0.005	0.979	0.040	0.847	-0.053	0.797	0.163	0.426	-0.069	0.736	0.260	0.199
EOSINO%	-0.315	0.117	-0.151	0.462	-0.327	0.103	0.383	0.054	0.344	0.085	**0.451**	**0.021***
MONO	0.107	0.602	-0.255	0.209	-0.044	0.831	0.034	0.868	-0.384	0.053	-0.309	0.124
MONO%	-0.156	0.447	-0.150	0.465	-0.202	0.322	**0.425**	**0.030***	0.262	0.197	0.041	0.844
LYMPH	-0.137	0.506	-0.045	0.828	0.048	0.816	0.308	0.125	-0.206	0.313	0.376	0.058
LYMPH%	-0.233	0.253	0.068	0.741	-0.123	0.551	**0.667**	**0.000***	0.177	0.388	**0.419**	**0.033***
NEUTRO	0.169	0.410	-0.201	0.325	0.043	0.834	**-0.613**	**0.001***	**-0.558**	**0.003***	-0.191	0.350
NEUTRO%	0.316	0.116	0.073	0.722	0.312	0.121	**-0.776**	**0.000***	**-0.435**	**0.026***	-0.280	0.166
PLT	0.180	0.379	-0.326	0.105	-0.086	0.676	**0.505**	**0.009***	0.183	0.370	0.113	0.584
MPV	-0.182	0.374	0.280	0.166	-0.031	0.881	-0.288	0.154	-0.039	0.849	**-0.568**	**0.002***
RDW	**0.530**	**0.005***	-0.100	0.628	0.011	0.959	0.377	0.058	0.172	0.402	0.034	0.868
MCHC	-0.163	0.425	0.168	0.413	0.157	0.444	-0.329	0.100	-0.401	0.043*	-0.019	0.928
MCH	-0.298	0.139	0.005	0.981	-0.117	0.569	**-0.454**	**0.020***	-0.181	0.375	-0.215	0.292
MCV	-0.202	0.322	-0.178	0.383	-0.370	0.063	**-0.460**	**0.018***	-0.098	0.632	-0.131	0.523
HCT	**-0.432**	**0.028***	-0.077	0.708	-0.025	0.905	-0.380	0.056	**-0.537**	**0.005***	0.031	0.882
Hb	**-0.423**	**0.032***	-0.016	0.936	0.048	0.815	-0.323	0.108	**-0.475**	**0.014***	0.059	0.773
RBCs	-0.323	0.108	-0.080	0.699	0.049	0.814	-0.250	0.217	**-0.472**	**0.015***	0.108	0.598
WBCs	0.129	0.530	-0.205	0.315	0.066	0.747	**-0.666**	**0.000***	**-0.641**	**0.000***	-0.212	0.299

Abbreviations: CRP, c reactive protein; INR, international normalized ratio; PT, prothrombin time; BUN, blood urea nitrogen; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transferase; BASO, basophils; BASO%, absolute basophils; EOSINO, eosinophils; EOSINO%, absolute eosinophils; MONO, monocytes; MONO%, absolute monocytes; LYMPHO, lymphocytes; LYMPHO%, absolute lymphocytes; NEUTRO, neutrophils; NEUTRO%, absolute neutrophils; PLT, platelets; MPV, mean platelet volume; RDW, red cell distribution width; MCHC, mean corpuscular hemoglobin concentration; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; HCT, hematocrit; HB, hemoglobin; RBCs, red blood cells; WBCs, white blood cells.

DISCUSSION

There is concern that patients with autoimmune diseases are at an increased risk of infection and complications, exacerbated by the nature of their disease and/or the use of immunosuppressive therapies[30]. Furthermore, a number of autoimmune illnesses have systemic inflammation, which raises the risk of cardiovascular[9] and thromboembolic disease[31], which have also been recently reported to be associated with COVID-19. The IL-17 family of cytokines plays a central part in the induction of inflammation to limit numerous pathogenic insults[32]. The study aimed to compare the expression profiles of pro-inflammatory

cytokine IL-17, down-regulating cytokine TGF-β, and gene included in AID PTPN-22 in COVID-19 patients with and without AID, to understand the mechanistic role of these markers in chronic inflammation and COVID-19 severity.

Generally, the analysis of patients' demographic characteristics, in the current study, revealed that COVID-19 is more common in older ages. In agreement with the present study, others reported that SARS-CoV-2 can infect people with the median age of the patients being 47 years; 41.9% of the patients were female. but it is much less common in people under 14 years old and it is often asymptomatic in young people[33]. The study revealed that males are more susceptible to COVID-19 and autoimmune COVID-19, with higher expression levels of IL17A, TGF-β, and PTPN-22 genes, which may impact disease severity and prognosis. Clinical reports showed that both the mild and the severe forms of COVID-19 result in up-regulation of the cytokine secretion, particularly IL-1β, IL-6, IL-10 and IL-17 [34]. But still, the elevation in the expression of TGF-β in the present study is not significant (p-value 0<.05). In accordance with the current study, others found a non-significant increase in TGF-β and FGF-2 levels. Colarusso et al[35] demonstrated significantly increased serum TGF-β values of patients who developed pulmonary fibrosis after the COVID-19 compared to healthy subjects.

The meta analysis showed that autoimmune disease was associated with a 1.21-fold increased risk of severe COVID-19 disease and found that autoimmune disease was associated with a 1.31-fold increased risk of mortality in patients with COVID-19[36]. This was against the current study which showed that there was an insignificant decrease in severity and mortality among AID with Covid-19 group compared with the non-AID Covid-19 group this may be due to using of immunosuppressant therapy; but in agreement of our study others reported that patients with autoimmune and auto-inflammatory conditions could exhibit mild COVID-19[37]. Another study reported that; no significant association between autoimmune disease and risk of mortality in patients with COVID-19[38].

In the present study, we found that circulating IL-17 was the most significantly regulated in relation to laboratory results in both autoimmune and non-autoimmune groups. In accordance with others, it will result in an increase in red cell distribution width RDW and this may be instead a clinically useful parameter for predicting the future development and the prognosis of many CV diseases, such as stroke, AF, and HF [39]. Although this will cause a decrease in alanine transaminase ALT, albumin, hematocrit HCT, and hemoglobin Hb and this agrees with the results of Ogura et al., who reported that higher serum levels of IL-17 could be also responsible for the induction of anemia in SLE[40].

The current study showed non-significant differences in IL-17 and PTPN-22 levels between autoimmune and non-autoimmune groups. However, a higher expression of PTPN-22 was found in the study group, suggesting it may trigger autoimmune diseases after COVID-19 or worsen current masked autoimmune diseases. The study found significant negative correlations between CRP levels and elevated IL-17 and PTPN-22 in non-autoimmune group, suggesting a less severe COVID, also found positive correlation between elevated levels of IL-17 with absoluand this agrees with Elsheshtawy et al [41].

Although others found negative correlation between TGF-β and d-dimer in Covid-19 patients[42], but our study reported a significant positive correlation between d-dimer levels and elevated TGF-β levels in both autoimmune and non-autoimmune groups, potentially predicting thromboembolism risk in both groups with p value slightly elevated in autoimmune group than non-autoimmune group, but others reported that; patients with autoimmunity had higher D-dimer plasma levels[43]. Also our study found negative correlations between PT, ferritin, CRP, BUN, ALP and PLT with elevated levels of PTPN-22 in the non-autoimmune group and this agrees with others study which reported that PTPN22 plays a negative role in platelet function and thrombosis[44].

CONCLUSION

Covid-19 patients exhibit a distinct gene expression profile (IL-17, TGF-β and PTPN22) compared to healthy individuals. Pro-inflammatory cytokines like IL17A are strongly linked to the disease and could be risk factors for severe disease progression. TGF-β, a down-regulating cytokine; was elevated in all autoimmune patients. Patients without autoimmune disease (AID) showed significantly higher expression levels of IL-17 and PTPN-22 genes, with IL-17 significantly correlated with inflammation and coagulation biomarkers. In patients without AID, TGF-β gene expression was up-regulated; with a significant correlation with thromboembolism d-dimer.

Declarations:

Consent for publication: Not applicable

Availability of data and material: Data are available upon request.

Competing interests: The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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