Alteration of lipid profile, kidney functions, D-dimer and some anti-inflammatory parameters in samples of Iraqi patients with Covid-19

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ABSTRACT

Objective: The Aim of our research was to look into the association between various biochemical indicators and COVID-19 infection in Baghdad, Iraq.

Methods: From the 15th of March to the August 2022, a cohort of 45 people with positively COVID-19 and 45 healthy controls visited Al-Yarmouk Teaching Hospital in Baghdad, Iraq. All of the patients have been diagnosed with COVID-19 and are experiencing symptoms and indicators. Each of the patients and healthy controls had their whole blood samples taken to be analyzed for; Lipid profile (triglycerides, Total cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein (HDL) values) Kidney function test (Urea and Creatinine), by using an enzymatic method, Anti-inflammation parameters (INF-, TGF, Interleukin—12, and Interleukin 18), The (Biosours) ELISA kit was used to assess the results., and D-dimer was quantified using mini vidas kits donated by Bio Meriux-France.

Results: The results showed that The majority of COVID-19 patients showed elevated lipid profiles and kidney function tests, as well as the anti-inflammatory parameters with increase the levels of D-dimer compared to healthy controls.

Conclusion: The present study concludes that Covid-19 cause alteration in lipid profile, kidney functions, D-dimer and some anti-inflammatory parameters.

Keywords: Five Minute Preceptor, critical thinking, nursing profession students

INTRODUCTION

The virus that causes COVID-19 is an enveloped, single-stranded, positive-sense RNA virus belonging to the Coronaviridae family. It belongs to the Nidovirales family of viruses. It can cause a variety of respiratory and gastrointestinal illnesses, ranging in severity from a simple cold to MERS and SAR (1). Structures, energy sources, signaling mediators, and functions in infections, particularly viral infections, are all played by lipids (2) Lipids are involved in a number of macrophage regulatory and immune-modulation mechanisms.(3) It has also been discovered that lipid metabolism has a role in lung infections and inflammatory conditions. (4)
Prior to the current epidemic, coronaviruses were found to alter lipid metabolism and serum lipid profile items. Several investigations have found significant alterations in the lipid profile of COVID-19 infected patients (5).

Changes in innate and adaptive immunity are linked to chronic kidney disease (CKD) (6). In patients with CKD, both the risk of pneumonia and the incidence of pneumonia-related death are higher than in the general population (7). According to the European Renal Association—European Dialysis and Transplant Association (ERA-EDTA), COVID-19 infection and related death are more common in CKD patients (8). According to recent studies, acute kidney damage (AKI) has also been connected to mortality in coronavirus infections, specifically COVID-19., (9). Formal research on the impact of admission renal function on COVID-19 mortality are, however, scarce.

The fibrinolytic system degrades the fibrin mesh after the clot has formed. The D-dimer, which is composed of two D fragments of fibrin, is created by the plasmin enzyme being activated. This implies that there is degraded fibrin in the bloodstream. The D-dimer represents the activity of the coagulation and fibrinolysis systems (10). Technically, the amount of D-dimer in the body is measured using a monoclonal antibody and a variety of commercial tests. To rule out deep vein thrombosis (DVT), pulmonary embolism (PE), and to establish the diagnosis of disseminated intravascular coagulation (DIC), the D-dimer test proved crucial in clinical examinations (11). Nearly all patients with severe venous thromboembolism experience the D-dimer levels was increased (VTE). High D-dimer levels can be found in pathological conditions including cancer, inflammation, and surgery as well as physiological conditions like pregnancy (12). D-dimer kit sensitivity ranges from one manufacturer to the next, with findings between 93% and 95%. (13). Additionally, numerous studies have demonstrated that COVID-19 puts people at risk for thrombosis in both veins and arteries (14). Because of this, people with COVID-19 had a 25% greater risk of DVT, VTE, and perhaps PE (15). In COVID-19, severe inflammation (cytokine, endothelial, and macrophage activations), diffuse intravascular coagulation, immobility, and hypoxia because of considerable lung injury can all lead to VTE episodes (16). The D-dimer, lactate dehydrogenase was increased, the changing in ptt and pt were minor to nonexistent, and higher levels of antiphospholipid antibodies were all linked to corona infection (17).

The evidence for many specific immunity system cytokines affecting COVID-19 susceptibility is limited. (18). Although interleukin 6 modulation may be a successful therapeutic. However, a genetic variation that affects the immune response to interferon gamma (IFN) causes extremely severe disease when specific pathogens, such as tuberculosis-causing mycobacteria, are encountered (19). COVID-19 has also been determined to be important (20). In 2003, IFN was related with the raised risk of severe acute respiratory syndrome (SARS) (21). Functional study of SARS-CoV-2 proteins, on the other hand, reveals that the virus is susceptible to IFN (22). These findings show that IFN or its antecedents, such as interleukin-18, may play a role in inflammation (23), COVID-19 may be influenced by interleukin-12 or interleukin-23. IL-18 has been proposed as a possible intervention target in COVID-19 (24). Interleukin-18’s importance in immune function is further supported by its role in various autoimmune illnesses (including inflammatory bowel disease and eczema-dermatitis) (25).

MATERIALS AND METHODS

Subjects and blood sample collection
From March 15th to August 2022, this study was conducted at Al-Yarmouk Teaching Hospital. This research was done on the Covid-19 group, This includes 45 patients, aged between (40-65)of both sexes , The control group apparently consists of 45 healthy individuals. After collecting the serum, we divided it into several parts to perform tests on lipid profiles (TC, TG, HDL, and LDL), kidney function parameters (urea and creatinine), D-dimer levels, NF-, TGF, IL-12, and IL-18, and other measurements.

Body mass index (BMI) was computed by dividing the subjects' weight in kilograms by
their height in meters (m2). BMI is computed as follows (26):

\[
\text{BMI} = \frac{\text{weight (kg)}}{(\text{height (m)})^2}
\]

Biochemical analysis for Lipid profile tests by using an enzymatic method as specialized kits for each test for them. Friedewald's equation, an indirect simplified mathematical approach to estimating low-density lipoproteins, was used to calculate serum low-density lipoprotein-cholesterol (LDL-C). It only apply to TG levels of less than 400 mg/dL.

\[
\text{LDL-C} = \text{TC} - [\text{HDL-C} + \text{TG}/5].
\]

The concentration of D-Dimer was measured quantitatively according to miniVIDAS auto analyzer, (bioMérieux Company) France. The INF-α, TGF and IL-18 concentrations were measured by the (Biosours) ELISA kit. The information analyzed utilizing Factual bundle to social Sciences (SPSS) adaptation. 25. the information introduced Similarly as mean , standard deviation What's more ranges. Level for p – esteem under 0. 01and 0.05 was acknowledged significant.

RESULT AND DISCUSSION

Table 1 displays the distribution of study groups by age, gender, and BMI. Study participants ranged in age from 20 to 55 years, with a mean age of 44.68 years and a standard deviation (SD) of 11.54 years, respectively. Participants were split evenly between men and women, with a gender ratio of 44.4% male and 55.5% female. Age and gender comparisons between research groups revealed no appreciable differences (P 0.05).

Gao et al., 2021, showed a strong interaction between BMI, age, and ethnicity, with younger persons having greater HR per kg/m2 over BMI 23 kg/m2 than older people. Age is the most significant factor for raising a person’s COVID-19 mortality risk. (109 [95% confidence interval 108–110] in the 20-39 age group versus 80-100 years 1 07 [1 06–1 08] versus 1 04 [1 04-1 05]) and Black individuals (107 [1 06–1 08] vs 1 04 [1 04–1 05]). In those with type 2 diabetes, hypertension, and cardiovascular disease, COVID-19 related to a unit increase in BMI revealed a marginally lower risk of hospitalization and ICU admission than those without these morbidities (27). These results were mainly unaffected by other health issues, such as type 2 diabetes. COVID-19 related death risk per BMI unit is higher in the younger age groups and diminishes with age. Despite the fact that severe COVID-19 effects in young people are uncommon, the attributable risk was highest in people in their middle years (40–59 years). The huge sample size also, allowed for the evaluation of additional possible interactions. Despite the fact that the risks associated with a BMI were larger for those of Black ethnicity than for people of White ethnicity, they found no indication of a link between BMI and sex or Asian or Chinese ethnicity (27).

In a community-based cohort analysis, Williamson et al. (2020) found that those with high blood pressure or a diagnose of hypertensions had reduced chances of COVID-19 related death association with obesity than the general population (28).

In younger age groups, fattness and presistent disease are important risk factors for in-hospitaldead people, with the conecting of presistent disease and obesity being mainly significant in those less than 50. The public health depeding on this inference., vaccine schedules, and hospital clinical decision-making (29).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients No(45)</th>
<th>Control No(45)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>(20/25) (44.44/55.55)%</td>
<td>(23/22) (51.11/48.88)%</td>
<td>/</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>44.68±11.54</td>
<td>40.2±8.61</td>
<td>0.126</td>
</tr>
</tbody>
</table>
Table 3 shows the comparison in Biochemical, The means of TC, TG, and LDL were all substantially higher in the sick group than in the control group of healthy individuals for all values of, TC, TG, LDL were (184.33±19.77 versus 146±14.26 mg/dl, P= 0.01; 130.42±18.77 versus 92.53±26.59 , P= 0.01; 119.36±19.80 versus 75.12±17.23 mg/dl, P= 0.0 the lipid profile 1; respectively). the lipid profile are linked to severity with mortality in patient of COVID-19. As a result, the lipid profile can be utilized to determine the severity of COVID-19 and its prognosis.

### Patients' and control groups' lipid profiles were compared.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patients No(45)</th>
<th>Control No(45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC(mg/dl)</td>
<td>184.33±19.77</td>
<td>146±14.26</td>
<td>0.05*</td>
</tr>
<tr>
<td>TG(mg/dl)</td>
<td>130.42±18.77</td>
<td>92.53±26.59</td>
<td>0.05*</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>40.88±2.41</td>
<td>55.36±3.35</td>
<td>0.05*</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>119.36±19.80</td>
<td>75.12±17.23</td>
<td>0.05*</td>
</tr>
</tbody>
</table>

p0.05 indicates significance, whereas p0.01 indicates high significance.
expression. (39), It increases the pro-inflammatory serum amyloid protein A (SAA) binding, which lowers and displaces ApoA-I levels in HDL (40). It was discovered that SAA-loaded HDL particles cleared the bloodstream more quickly than regular HDL particles. The decreased of lecithin cholesterol acyltransferase (LCAT) in an inflammatory situation can reduce badly inflammatory response with HDL use. (41). Third, because of the virus's inflammatory response, vascular permeability may be affected, allowing cholesterol molecules to enter tissues like alveolar gaps and create exudates. Exudates include large amounts of protein and cholesterol (42). SARS patients' lungs and those of cynomolgus macaques that have the SARS-CoV infection can both exhibit exudates (43), as do the premature phases of the lung disease of COVID-19 (44). Fourth, viral infection induces host cells to produce more free radicals (45). In COVID-19 individuals, this could hasten lipid breakdown. Fifth, decreased LDL-C levels may higher LDL absorption when IL-6 generated by immunocytes activated LDL receptor expression in hepatocytes, resulting in greater LDL absorption (46). Finally, because cholesterol is produced primarily through the diet, COVID-19's hypcholesterolemia could be linked to starvation. (47). A recent study found that COVID-19 patients' nutritional status has deteriorated, as seen by consistently lower albumin levels in the extreme Patients with COVID-19 (48). The concentrations of HDL-C and LDL-C gradually increased after recovery from COVID-19. (49). This could be owing to the fact that the patient's condition has improved. In addition, TC, HDL-C, and LDL-C values were lower in individuals who did not survive upon hospital admission and persisted until death (50).

On admission, COVID-19 patients had a significant rate of early kidney function impairment. Clinicians may be able to identify patients with a bad prognosis if they have early kidney injury.

In the study of Xia et al. (2021), In COVID-19 individuals, a substantial relationship was shown between early renal function damage and poor outcomes (51).

As a result of the SARS-CoV-2 virus propagated primarily with signs of viral pneumonia, across the respiratory airway being the most common and initial symptom, Clinicians have concentrated on a lot of awareness on pneumonia treatment.

But the quantity of ACE2 expression in the kidney, namely in the renal tubules comparable to that in the lung, indicating that the kidney may some other significant organ for SARS-CoV-2 to infect (52). Proof from the Middle East respiratory syndrome coronavirus (MERS-CoV) suggests that SARS-CoV-2 may directly strike renal tubular epithelial cells (53). SARS-CoV-2 granules have been found in the urine of patients. Autopsy electron micrographs of kidneys revealed viral particles, confirming theory of a direct viral attack in kidneys. (54). Despite the

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### TABLE 3: Kidney Function Test measured between Patients and control groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patients No(45)</th>
<th>Control No(45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>68.15±4.31</td>
<td>30.9±1.90</td>
<td>0.01*</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.11±0.10</td>
<td>0.71±0.07</td>
<td>0.05**</td>
</tr>
</tbody>
</table>

p0.05 indicates significance, whereas p0.01 indicates high significance.
fact that the mechanism of SARS-CoV-2 kidney injury is still unknown. In order to fully investigate these issues, more research is required.

In the present study showed that D-dimer in (ng/ml) for covid-19 patients was (581.82±78.21)ng/ml, while for control group was (194.63±18.11)ng/ml, a highly significant differences (p<0.0001) was found between patients and control groups as showed in table 4.

**TABLE 4:** D-Dimer Test measured between Patients and control groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patients No(45)</th>
<th>Control No(45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>D-Dimer (ng/ml)</td>
<td>581.82±78.21</td>
<td>194.63±18.11</td>
<td>0.0001***</td>
</tr>
</tbody>
</table>

p<0.05 indicates significance, whereas p<0.01 indicates high significance.

The relationship between increased D-dimer levels and COVID-19 disease severity was investigated in this study in patients was analyzed and comparison with control. COVID-19 patients had higher D-dimer levels, according to the study, and this agree with (55) which showed that very high D-dimer levels are common in COVID-19 pneumonia and correlate with a worse prognosis. In the lungs, the inflammatory response results in small vessel endothelialitis, which set off the clotting cascade and produces microvascular and macrovascular thrombosis (56). In COVID-19 patients, scientists discovered anomalies in the vascular endothelium, changed blood flow, and platelet dysfunction, all of which led to repeated thromboses. The clinical development of COVID-19 has been linked to aberrant coagulation function, particularly high D-dimer levels. These findings are helpful in the early detection and treatment of serious disease (57).

Table 5 showed the comparison between patients and control group according some anti-inflammation parameters such as (INF-Ɣ, TGF, IL-12 and IL-18) the results found that mean of them as (7.30±1.21 versus 36.66±5.44; p<0.001; 56.91±9.17 versus 14.76±4.12; P= 0.001; 385.44±29.05 versus 126.93±14.32, P= 0.001; 35.18±8.80 versus 100.13±16.73, P= 0.001; respectively).

The present study found that the control group was higher levels in INF-Ɣ and TGF than the patients group with highly significant decreased (P= 0.001), while the levels of other parameters (IL-12 and IL-18) were higher significant increased in patients group than in control group with (P= 0.001).

One of the most common side effects of SARS-CoV-2 infection is pulmonary fibrosis (58). SARS-CoV-2 is an RNA virus with an envelope that causes severe pneumonia symptoms and is closely linked to SARS-CoV and MERS-CoV (59). The virus is transferred through respiratory droplets, close contact, and other means, and asymptomatic people may unintentionally infect others (60). According to current evidence, SARS-CoV-2 has a lesser pathophysiology than SARS but a more strong transmission competence. Both the ACE2 receptor and the S protein priming serine protease TMPRSS2 are abundantly expressed in respiratory epithelial cells and are essential for its entrance into target cells (61).
TABLE 5: Anti-Inflammation parameters measured between Patients and control groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patients No(45)</th>
<th>Control No(45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>INF-α (ng/ml)</td>
<td>7.30±1.21</td>
<td>36.66±5.44</td>
<td>0.001 **</td>
</tr>
<tr>
<td>TGF (ng/ml)</td>
<td>35.18±8.80</td>
<td>100.13±16.73</td>
<td>0.001 **</td>
</tr>
<tr>
<td>IL-12 (ng/ml)</td>
<td>56.91±9.17</td>
<td>14.76±4.12</td>
<td>0.001 **</td>
</tr>
<tr>
<td>IL-18(ng/ml)</td>
<td>385.44±29.05</td>
<td>126.93±14.32</td>
<td>0.001 **</td>
</tr>
</tbody>
</table>

p0.05 indicates significance, whereas p0.01 indicates high significance.

Following infection, infected cells secrete a large amount of chemokines and cytokines, resulting in cytokine storm. ARDS, severe pneumonia, and inflammatory-induced lung injury can all be brought on by a cytokine storm that harms microvascular endothelial cells, ischemia, and hypoxia in addition to lung epithelial cells (62). If the cytokine storm is not cleared promptly, the lung tissue will be damaged, which will result in pulmonary fibrosis. TGF is a cytokine with anti-inflammatory properties that is important in acute lung injury. One of the most crucial areas for anti-fibrotic treatment is its route (63). The goal of Hu et al (2020)’s study was to see if there was a link between pulmonary fibrosis and pro-inflammatory cytokines in COVID-19 patients. They have not found a link between TGF-beta and lung fibrosis because TGF-beta is an anti-inflammatory cytokine. In COVID-19 patients, they discovered an inverse link between basal IFN-α level and lung fibrosis at discharge. Lymphocytes, particularly T cells and NK cells, create IFN-α when they are stimulated by specific antigens or mitogens. IFN-α signaling is involved in a variety of cellular processed, including macrophage activation and host defense against pathogen infection. The increase in fibrosis volume in COVID-19 at discharge was inversely linked with baseline levels of IFN-α. These findings imply that early antiviral infection utilizing IFN-α may have a significant impact on fibrosis inhibition and functional recovery (64).

The major purpose of IL-12 is to promote cytolysic activity and IFN production by NK cells and T cells (65). IL-12-independent T-cell activation and IFN-α release have been observed after a number of viral infections, including infection with the systemic lymphocytic choriomeningitis virus (66) and a respiratory tract infection brought on by the influenza virus (67). This may be the case because type I IFN stimulates the release of IFN by cells (68).

Interleukin-18 is thought to perform a wide range of roles in infection defense (69). Interleukin-18’s role in lowering the incidence of COVID-19 is only supported by observational studies (70).

Interleukin-18 is difficult to interpret in observational studies of patients since it may represent a protective response, a symptom, or the root of problems. As far as we are aware, there is no experimental proof of interleukin-18’s involvement with COVID-19. Experimental data, however, suggest that interleukin-18 also works with other viruses. It has been shown that interleukin-18, in particular, prevents mice from dying from herpes simplex 1 (71), possibly through the action of natural killer cells (70) or IFN (72). Interferon (IFN)-mediated inhibition of viral replication by IL-18 has also been shown to protect mice against the murine coronavirus mouse hepatitis virus strain A59, although IL-1 was not (73). Rats have also been shown to be protected from the rotavirus by IL-18, possibly through caspase-inducing apoptosis (74). As a result, it’s been recommended as a possible way to deal with new and stubborn viruses (75). Interleukin-18’s ability to guard against infection is consistent with it raising the likelihood of autoimmunity and atopic diseases (76), IL-18 also reduced the number of children, confirming the duplication and continuity are mutually exclusive. COVID-19 may be protected by interleukin-18. COVID-19 could be a result of the immune system’s initial failure. It’s possible that recombinant interleukin-18 could prevent some of these failures (77).
CONCLUSION
The present study concludes that Covid-19 cause alteration in lipid profile, kidney functions, D-dimer and some anti-inflammatory parameters.

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