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Serum Total and Free Prostate Specific Antigen Levels as Novel Biomarker in Patients with COVID-19

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Abstract
Objectives: This study aimed to evaluate the diagnostic value of TPSA and FPSA for early detection of COVID-19 and compare it with a control group.
Methods: This is a retrospective study of 146 patients from the Respiratory Clinic in Sebha city, 73 of whom have COVID-19 PCR-confirmed and 73 who do not have COVID-19 (group control).
Results: The mean and standard division age in the PCR-confirmed COVID-19 group was 61.51 ± 16.40. In the PCR-confirmed COVID-19 group, the mean and standard division serum biomarker level for TPSA was 0.51 ± .26 ng/ml, and 0.57 ± 0.32 for FPSA.
Conclusion: For the biomarkers TPSA and FPSA, there were no significant differences between the control and PCR-confirmed COVID-19 groups. These findings suggest that the tumor biomarker may be ineffective in detecting COVID-19.
Keywords: COVID-19, pneumonia, pandemic biomarker, prostate-specific antigen

Introduction

The spread of emerging infectious diseases, such as the ongoing new Coronavirus pneumonia (Corona Virus Disease 2019, COVID-19) outbreak, is one of the 21st century's major challenges. COVID-19, the most recent infectious disease, has triggered a global pandemic.[1-3] The name derives from the virions' typical appearance under electron microscopy, in which they all have a glycoprotein spike on the surface that resembles the shape of a crown. Coronaviruses are common in nature and can infect birds, mammals, and humans.[4,5] Coronavirus disease 2019 (COVID-19) was discovered in December 2019 in Hubei Province, China.[6] This novel single-stranded enveloped RNA virus is the seventh human coronavirus discovered. SARS-CoV-2 is not related to the coronaviruses known to cause the common cold (229E, OC43, NL63, and HKU1), but it is related to the zoonotic severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV) from 2002. 2 and the Middle East respiratory syndrome (MERS) coronavirus from 2012. 3 SARS-CoV-2, like many other coronaviruses, is thought to have originated in bats because it shares 89 to 96 percent nucleotide identity with bat coronaviruses.[7]

SARS-CoV-2 can be passed from person to person. The current theory holds that the first transmission occurred between bats and an as-yet-unidentified intermediate host animal. A SARS-CoV-2-infected person is expected to infect three new people (the reproductive number is estimated to be 3.28).[8]

Cancer patients are more vulnerable to infections than non-cancer patients due to systemic immunosuppression caused by cancer or anticancer treatments such as chemoradiation.[9-12] As a result, cancer patients may be at a higher risk of COVID-19 infection. Furthermore, unplanned interruptions in regular anti-tumor therapies as a result of overburdened healthcare systems in the pandemic battle expose cancer patients to the adverse clinical risks of uncontrolled primary disease.[13]

From the start of the pandemic, the link between cancer and COVID-19 has gotten a lot of attention. An early study by Liang et al reported a cancer prevalence of 1.13% (95% CI, 0.61% to 1.65%) among 1,590 cases of COVID-19 in China (only 18 patients with cancer), which was higher than the Chinese population's overall cancer incidence of 0.29%.[14] Serum tumor markers can be used to assess cancer's response to treatment, detect cancer relapse early, and, in some cases, diagnose cancer.[15] Increasing evidence suggests that, in addition to the lung, this novel disease can affect multiple organs, including the heart, liver, and gastrointestinal tract, and results in abnormalities in several biomarkers.[16,17]

Since the early 1990s, prostate-specific antigen (PSA) has been widely used as a biomarker to screen for prostate cancer, and there is strong evidence that PSA testing reduces prostate cancer mortality.[18–20] However, the test is not specific to prostate cancer, but its value may increase when cancer is present, and the PSA-test is used for cancer detection.[21] PSA is a glycoprotein whose glycan changes significantly with PCa progression,[22,23] because glycosylation is a driver of cancer development/progression,[24,25] glycoprofiling PSA may outperform currently used PCa tests.[26] PSA value is often used during the prostate cancer trajectory as a marker of progression or response to treatment.[27] PSA is not an exclusive marker of cancer because it is produced by cancerous prostate cells and by healthy prostate cells.[28] However, to our knowledge, there is no study has comprehensively evaluated the value of Total Prostate Specific Antigen (TPSA) and Free Prostate Specific Antigen (FPSA) for the diagnosis of COVID-19 in the Libyan population. Therefore, this study aimed to explore the value of these markers for the diagnosis of COVID-19 in Libya, where the population includes patients in the respiratory clinic, sebha branch, Libya.

Materials and Methods

Patients and Samples

This is a retrospective study conducted at the Department of Biotechnology, Faculty of Science, Sebha University and Respiratory Clinic, Sebha Branch from August 15 to

March 3, 2021, with a 146 total of patients, 73 of COVID-19 PCR-confirmed patients admitted to the Respiratory Clinic as COVID-19 group and 73 of COVID-19 non-PCR-confirmed patients selected as control group included in this study. The informed consent form was taken from all participants.

Serum Biomarkers Test

5 mL whole blood samples were collected and subjected from the peripheral vein, after diagnosis of the disease. The blood was kept into the plain tube for separation by centrifugation at 4500 rpm for 5 minutes to get serum specimen from whole blood and stored at –20°C until analysis. The serum biomarker level of TPSA and FPSA were analyzed by an immunoassay analyzer (Roche Diagnostics, IN, USA), with a normal upper limit of 4 ng/mL.

Data Statistical Analysis

All statistical analyses were conducted by using PSPP version 1.2.0-g0fb4db software (PSPP, Inc., 51 Franklin Street, USA). The data are expressed as means ± SD was used to compare the values between the patients with COVID-19 and controls. *P*-value < 0.05 was considered as a significant difference. Receiver Operating Characteristic (ROC) analysis of biomarker proteins were determined and calculated the cut-off values, Areas Under the Curve (AUCs) with 95% Confidence Intervals (CIs), and Standard Errors (SEs) each marker's ability to detected covid-19.

Results

The pandemic of COVID-19 has had a significant impact on clinical microbiology laboratories. The initial challenge was to improve the ability of reverse transcriptase-polymerase chain reaction (RT-PCR) to diagnose acute COVID-19.[29] Plasma proteomic analysis identified biomarkers of COVID-19 disease progression in a cohort of patients with varying severity of COVID-19 disease, including non-survivors.[30] The COVID-19 pandemic affects people of all ages, but it appears to affect the elderly the most.

Table 1. **Serum tumor biomarkers TPSA and FPSA levels in PCR confirmed COVID-19 group and healthy control group**

Parameters	PCR-confirmed COVID-19 cases Mean (± SD) or *N* (%)	Healthy cases (Control Group) Mean (± SD) or *N* (%)	*P*- value
Age	61.51 (± 16.40)	41.95 (± 17.11)	0.520
Gender			
Male	54 (73.97%)	42 (57.53%)	0.202
Female	19 (26.03%)	31 (42.46%)	
Serum TPSA ng/ml	0.51 (± .26)	0.38 (± 0.20)	0.043
Serum FPSA ng/ml	0.57 (± 0.32)	0.39 (± 0.21)	0.205

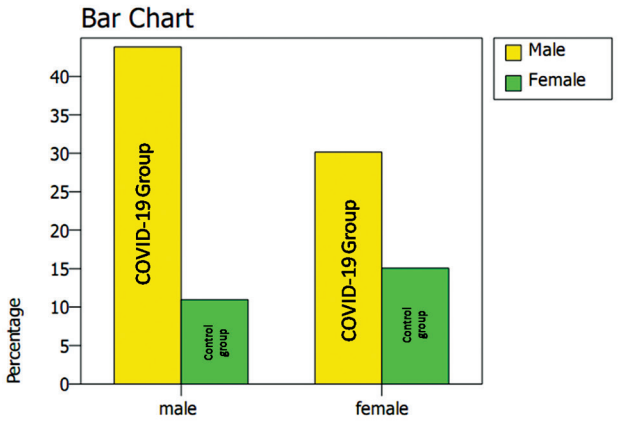

Fig. 1 **Prevalence of covid-19 according to gender in this study.**

Table 2. **AUC for covid-19 estimating serum biomarker TPSA and FPSA**

Serum biomarkers	Cutoff	St error	*P*- value	95% Confidence interval
TPSA	0.53	0.08	0. 674	0.41–0.66
FPSA	0.53	0.08	0. 664	0.40–0.67

Discussion

This current study is the first of its kind to examine some biomarkers of early detection of COVID-19, it was focused on the levels of biomarker consisted of TPSA, and FPSA were statistically significant among groups, among all patients with COVID-19, 73 patients affected to COVID-19 and with an average age of 61.51 ± 16.40 years compared to an average age of 41.95 ± 17.11 years were studied. Our findings were supported by others, such as Du et al, who discovered that people over the age of 60 had a 3.7-fold increased risk of COVID-19 infection.[31] inflammatory markers.[32] Another study found that 6% were 85 years old, 25% were 65 to 84 years old, 18% were 55 to 64 years old, 45 to 54 years old, and 29% were 20 to 44 years old.[33] A similar study by Lingaiah et al found that 44.3 percent of COVID-19 infected patients and inflammatory markers were in the elderly age group.[32]

In this study, we discovered gender data in Table 1 and Figure 1, which showed 54 (73.97%) of males and 19 (26.03%) of females in the PCR-confirmed COVID-19 group and 42 (57.53%) of males and 32 (42.46%) of females in the control group, similar to Lingaiah et al who discovered men were 83 (72.3%).[32] In Table 1, the PCR-confirmed COVID-19 group, the mean and standard division serum biomarker level for TPSA was 0.51 ± .26 ng/ml, and 0.57 ± 0.32 ng/ml for FPSA, compared to the control group, where the mean and standard division serum biomarker level for TPSA was 0.38 ± 0.20 ng/mL and 0.39 ± 0.21 ng/mL for FPSA. The respective *P*-values were 0.043 and 0.205.

There were no statistically significant differences between the control and COVID-19 PCR-confirmed groups. These findings agreed very well with the findings of previous studies, such as Yu et al, who discovered no difference in AFP levels.[34] On the other hand, He et al found that all five tumor biomarkers were significantly higher in the plasma of COVID19 patients than in healthy controls.[35]

In the ROC curve analysis of biomarker proteins, the AUC of covid-19 for estimating TPSA was 0.53 (95% CI, 0.41–0.66; *P* = 0. 674), and the AUC of covid-19 for estimating FPSA was 0.53 (95% CI, 0.40–0.67; *P* = 0. 664), respectively in Table 2.

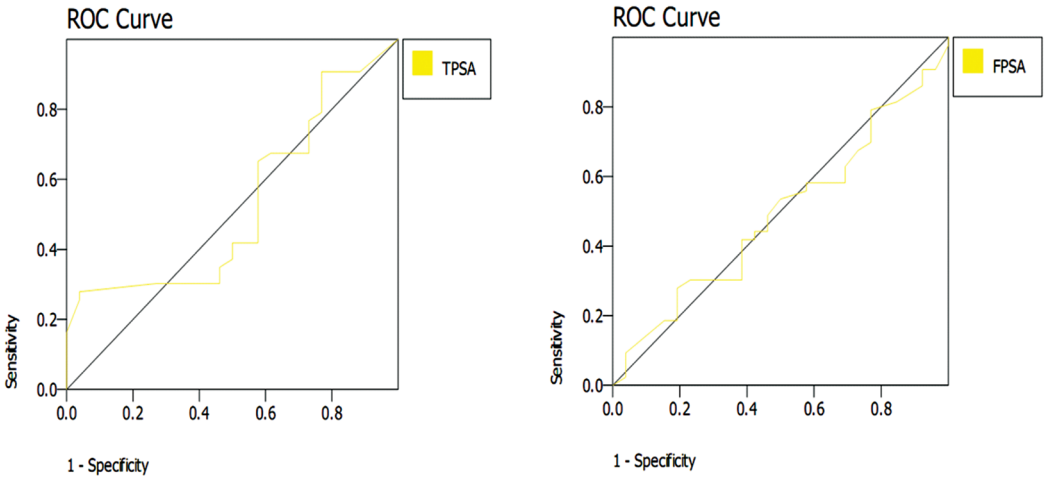

Fig. 2 **The ROC curve analysis of covid-19 estimating serum biomarker CEA, CA19.9, CA15.3, and AFP.**

The ROC curves are depicted in Figure 2. According to our findings, COVID-19 did not affect tumor markers TPSA and FPSA, as reported by Purut et al.[36]

Conclusion

To the best of our knowledge, this is the first study in Libya that focuses on potential biomarkers to investigate the utility of these markers in the diagnosis of COVID-19. Our findings suggest that evaluating tumor biomarkers TPSA and FPSA may be ineffective in determining COVID-19. COVID-19 research is still in its early stages, and more research is needed around the world to better combat this pandemic. A protein biomarker must be able to distinguish between normal and disease condition levels to be useful.

Limitation

The number of patients in our study can be increased in the future to confirm these findings.

Conflicts of Interest Disclosure

No conflicts of interest.

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