



ORIGINAL ARTICLE

DIAGNOSTIC PERFORMANCE OF SERUM C-REACTIVE PROTEIN, ASPARTATE AMINOTRANSFERASE, ALANINE AMINOTRANSFERASE, AND LACTATE DEHYDROGENASE AS ADJUNCTS TO RT-PCR IN DETECTION OF COVID-19

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Background: COVID-19 is a highly transmissible viral infection caused by SARS-CoV-2, with clinical manifestations ranging from asymptomatic disease to severe pneumonia and multi-organ involvement, necessitating timely and accurate diagnosis. Aim was to determine the diagnostic accuracy of serum C-reactive protein (CRP), Aspartate Aminotransferase (AST), Alanine aminotransferase (ALT), and Lactate dehydrogenase (LDH) levels as detecting COVID-19, using RT-PCR as gold standard. **Methods:** This Cross-sectional study was conducted in Department of Pathology, Bahawal Victoria Hospital/Civil Hospital Bahawalpur, from 10th Jan to 9th Jul 2023. After informed consent nasopharyngeal swab for RT-PCR and blood samples for CRP, AST, ALT, and LDH were collected from 165 symptomatic patients suspected of COVID-19. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated. **Results:** Sensitivity, specificity, PPV, NPV, and diagnostic accuracy of serum CRP in Detecting COVID-19 taking RT-PCR as a gold standard were 83.87, 69.44, 78.0, 76.92 and 77.58% respectively. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of serum AST levels were 80.65, 68.06, 76.53, 73.13 and 75.15% respectively. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of the serum ALT were 81.72, 68.06, 76.77, 74.24 and 75.76% respectively. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of the serum LDH were 86.02, 72.22, 80.0, 80.0 and 80.0% respectively. **Conclusion:** CRP and LDH demonstrated relatively higher diagnostic performance than AST and ALT, therefore these serum markers may be used as an adjunct diagnostic tool in detecting COVID-19 in settings where RT-PCR is not available.

Keywords: COVID-19, CRP, LDH, RT-PCR, Sensitivity, Specificity

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) is caused by the transmission of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). This virus was first detected in Wuhan China in 2019. It spread rapidly across the world leading to a global outbreak in 2020.¹ As of mid-2025 confirmed cases of COVID-19 have exceeded 767 million and the number of reported deaths due to COVID-19 ranging between 6.9–7.1 million.² COVID-19 spreads when people are in close proximity. The main mode of transmission is air bone transmission. The clinical presentation of this infection varies from asymptomatic infection to severe pneumonia and multiorgan failure.³

There is a variety of diagnostic tests used for the detection of COVID-19 including Polymerase Chain Reaction (PCR) and isothermal nucleic acid amplification assays. Serological tests, including ELISA and lateral flow immunoassay are also used to test patients who develop antibodies against the virus.⁴

The US Centers for Disease Control and Prevention (CDC) has declared Reverse Transcriptase Polymerase chain reaction (RT-PCR) test as a gold standard for the detection of COVID-19. RT-PCR detects viral genetic material from a sample taken from nose or throat swab. However, PCR is associated with several limitations including high false negatives, high turnaround time, requirement of trained staff and specialized equipment. The sensitivity of RT-PCR as reported by Woloshin S, and colleagues is only 70%.⁵

To address these limitations, researchers developed a machine learning (ML) model based upon routine blood tests which revealed that inflammatory markers such as C-reactive protein (CRP) and enzymes like lactate dehydrogenase (LDH), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) are significantly altered in COVID-19.⁶ COVID-19 triggers the release of inflammatory cytokines, particularly IL-6, resulting in increased hepatic production of CRP, while immune-mediated injury,

hypoxia, and direct viral effects contribute to elevated AST and ALT levels. Widespread cellular damage also increases LDH release, reflecting tissue injury and disease severity.⁶ Therefore, these biochemical markers, can be utilized as one of the diagnostic tools for the detection of COVID-19.⁷ A study published in Clinica Chemica Acta showed that raised serum CRP, serum LDH and lymphocytopenia are commonly observed abnormalities in COVID-19 infection. Levels of AST, ALT and Creatinine kinase are also elevated.⁸ As serum level of ALT and LDH are highly sensitive to presence of COVID-19, therefore can be utilized as surveillance indicator for detection of COVID-19.⁹ Many published articles have reported the epidemiological and clinical characteristics of COVID-19 disease, but data regarding the laboratory findings of infected individuals are limited.^{10,11}

The rationale of this study was to evaluate the diagnostic potential of routine biochemical tests like CRP, ALT, AST and LDH for early detection of COVID-19. As biochemical tests are cost effective, less time consuming and more feasible in resource constrained setups. These tests require less skill and expertise to be performed. If these commonly available tests demonstrate high diagnostic value in detecting COVID-19, they could serve as alternatives/adjuncts in resource limited settings, particularly where RT-PCR is not available. These tests can be used to complement RT-PCR by increasing combined sensitivity or can also serve as initial screening tool to identify individual who should undergo RT-PCR especially when the capacity of testing is limited. Early detection via routine biochemical investigation can facilitate timely detection, isolation and management of cases by improving the patient outcome and reducing disease transmission.

METHODOLOGY

This cross-sectional study was conducted at the Department of Pathology, Bahawal Victoria Hospital/ Civil Hospital Bahawalpur from 10th January to 9th July 2023, after obtaining ethical clearance from Institutional Review Board. A sample size of 165 was estimated using Buderer's formula through a Sensitivity and Specificity calculator, using 75% sensitivity, 70% specificity,⁸ and 26.3% prevalence.¹² Ninety-five percent confidence level and 13% margin of error was used. After informed consent 165 patients with signs and symptoms consistent with COVID-19 were included.

Patients who had recovered from COVID-19, declined consent, or were diagnosed with other respiratory illnesses like asthma, chronic bronchitis, emphysema, lung cancer, cystic fibrosis, bronchiectasis, pneumonia, pleural effusion, liver disease, metabolic syndrome, or on medication were excluded.

Nasopharyngeal swab samples (for RT-PCR) and venous blood samples for CRP, AST, ALT, LDH

were collected at the time of initial presentation, before initiation of treatment and analysed on respective automated analyzers. Demographic data and results of tests were recorded on a predesigned proforma. The predefined cut-off values for the index tests were CRP >5 mg/dL, AST >35 U/L, ALT >45 U/L, and LDH >360 U/L; values above these thresholds were considered positive (abnormal) for COVID-19.¹³

Data were analysed using SPSS-23. Numerical Data (Age, AST, ALT, LDH, CRP levels) were expressed as Mean±SD. Categorical variables like gender, RT-PCR result, CRP, LDH, AST, ALT (positive/negative) were reported as frequencies and percentages. A 2×2 table was constructed and diagnostic indices (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy) were calculated for CRP, AST, ALT and LDH by taking RT-PCR as gold standard.

Effect modifiers like age and gender were controlled through stratification. Post-stratification diagnostic accuracy was also calculated.

RESULTS

Out of 165 patients, 111 (67.27%) were male and 54 (32.73%) were female. Age of the participants was between 10–90 years with majority of the patients 125 (75.76%), within the 10–50 years age group Table-1. Mean age of the patients was 43.90±8.14 years.

Table-1: Age-wise distribution of patients

Age (years)	No. of Patients	Percentage
10–50	125	75.76
51–90	40	24.24
Total	165	100.0

Mean ALT levels were 93.85±14.28 U/L. Mean AST levels were 42.33±12.39 U/L. Mean CRP levels was 8.45±4.33 mg/dL. Mean LDH levels were 423.12±22.73 U/L. Among the patient with positive serum CRP, 78 were True Positive and 22 were False Positive. Among 65 CRP negative patients, 15 (False Negative) had SAR-CoV-2 infection on PT-PCR whereas 50 (True Negative) had no SAR-CoV-2 infection on PT-PCR ($p=0.0001$). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of the serum CRP levels in detecting Covid-19 taking RT-PCR as a gold standard was 83.87, 69.44, 78.0, 76.92 and 77.58% respectively. The diagnostic accuracy of the serum LDH, serum ALT and serum AST in detecting COVID-19 taking RT-PCR as a gold standard was 80.0, 75.76, and 75.15% respectively. Comparison of diagnostic accuracy of various serum biomarkers with RT-PCR is given in Table-2.

Stratification of diagnostic accuracy with respect to age groups and gender is shown in Tables-3 and 4. Stratified analysis revealed higher sensitivity for CRP and LDH in the 51–90 years age group and among females.

Table-2: Comparison of diagnostic accuracy of serum biomarkers (CRP, AST, ALT, LDH)

Parameter	TP	FP	FN	TN	Sensitivity	Specificity	PPV	NPV	Accuracy	p
					Percentages					
CRP	78	22	15	50	83.87	69.44	78.00	76.92	77.58	0.0001
LDH	80	20	13	52	86.02	72.22	80.00	80.0	80.0	0.0001
AST	75	23	18	48	80.65	68.06	76.53	73.13	75.15	0.0001
ALT	76	23	17	49	81.72	68.06	76.77	74.24	75.76	0.0001

TP=True positive, FP=False positive, FN=False negative, TN=True negative, PPV=Positive Predictive value, NPV=Negative Predictive value

Table-3: Stratified diagnostic accuracy of serum biomarkers (CRP, AST, ALT and LDH) with respect to age

Parameter	TP	FP	FN	TN	Sensitivity	Specificity	Accuracy	p
Percentage								
Age: 10-50 Years (n=125)								
CRP	56	14	15	40	78.87	74.07	76.80	0.001
AST	53	15	18	39	74.65	72.22	73.60	0.001
ALT	55	15	16	39	77.46	72.22	75.20	0.001
LDH	58	12	13	42	81.69	77.78	80.0	0.001
Age: 51-90 Years (n=40)								
CRP	22	8	0	10	100	55.56	80.0	0.001
AST	22	8	0	10	100	55.56	80.0	0.001
ALT	21	8	1	10	95.45	55.56	77.50	0.001
LDH	21	8	1	10	95.45	55.56	77.50	0.001

TP=True positive, FP=False positive, FN=False negative, TN=True negative

Table-4: Stratified diagnostic accuracy of serum biomarkers (CRP, AST, ALT and LDH) with respect to gender

Parameter	TP	FP	FN	TN	Sensitivity	Specificity	Accuracy	p
Percentage								
Male (n=111)								
CRP	55	14	12	30	82.09	68.18	76.58	0.001
AST	55	15	12	29	82.09	65.91	75.68	0.001
ALT	53	15	14	29	79.10	65.90	73.87	0.001
LDH	57	13	10	31	85.07	70.45	79.28	0.001
Female (n=54)								
CRP	23	8	3	20	88.46	71.43	79.63	0.001
AST	20	8	6	20	76.92	71.43	74.07	0.001
ALT	23	8	3	20	88.46	71.43	79.63	0.001
LDH	23	7	3	21	88.46	75.0	81.48	0.001

TP=True positive, FP=False positive, FN=False negative, TN=True negative

DISCUSSION

This study determined diagnostic accuracy of serum biomarkers in detecting COVID-19 using RT-PCR as gold Standard. The results revealed that the highest diagnostic accuracy was shown by LDH (80.0%), followed by CRP (77.58%), ALT (75.76%), and AST (75.15%). LDH also showed the highest sensitivity (86.02%) and specificity (72.22%), whereas CRP exhibited slightly lower sensitivity (83.87%) and specificity (69.44%). All findings were statistically significant ($p=0.0001$). These findings are consistent with international literature. A study by Poggiali *et al*⁸, found that raised levels of LDH and CRP are strongly associated with respiratory failure in patients of COVID-19. It showed CRP at a cutoff of 11 mg/L had sensitivity and specificity of 72% and 71%, while LDH at cutoff of 450 U/L had sensitivity of 75% and specificity of 70%. These findings are comparable to our study.

Observation by Chen *et al*¹⁴, revealed significantly elevated LDH in most COVID-19 patients, while elevated ALT and AST levels was more observed

in severe cases. Similarly, a Pakistani study by Asghar *et al*, reported that elevated CRP and LDH were associated with disease severity, with CRP predicting ICU admission (AUC= 0.806) and LDH predicting mortality (AUC= 0.877), highlighting the prognostic value of these biomarkers in hospitalized COVID-19 patients.¹⁵

In another study Fan *et al*, compared the hematological indices of COVID-19 patients between the intensive care unit (ICU) and non-ICU patients. They showed lymphopenia and raised LDH levels were associated with higher rate of ICU admissions.¹⁶

Many patients with MERS-CoV had liver function abnormalities with increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), and LDH.¹⁷

In a study, CRP was elevated in 60.7% of patients and lactate dehydrogenase (LDH) in 41% of COVID-19 patients.¹⁸ A study by Wang *et al*, showed that a CRP level of 26 mg/L could serve as a cut-off to predict progression to severe disease.¹⁹

A systematic review by Fu *et al*, showed that increased CRP, increased LDH and reduced lymphocyte count were among the most consistent laboratory abnormalities in COVID-19.²⁰

In the multicenter study by Gao *et al*, early-stage COVID-19 patients were examined, serum CRP and ALT levels as well as the presence of comorbidities were found to be predictors of disease progression.²¹

Similarly, Tan *et al*, reported a positive correlation between serum CRP levels and chest CT severity scores, suggesting that CRP reflects disease severity.²² In another study, a significant correlation was found between chest CT scores, serum CRP and D-dimer levels, further supporting the role of inflammatory biomarkers in accessing COVID-19 severity.²³

Mardani *et al*, reported that patients with RT-PCR-confirmed COVID-19 had significantly higher serum levels of CRP, LDH, AST, ALT, urea, and neutrophil counts than RT-PCR-negative patients. Furthermore, patients with positive RT-PCR had significantly higher neutrophil (NEU) count ($p=0.0001$), and C-reactive protein (CRP) ($p=0.04$), lactate dehydrogenase (LDH) ($p=0.0001$), aspartate aminotransferase (AST) ($p=0.001$), alanine aminotransferase (ALT) ($p=0.0001$), and Urea ($p=0.001$) levels in serum. ALT (AUC= 0.879), CRP (AUC= 0.870), NEU (AUC= 0.858), LDH (AUC= 0.835), and Urea (AUC= 0.835) had very good accuracy in predicting cases with positive RT-PCR for COVID-19, respectively.²⁴

Our study is limited by its single center design and moderate sample size. Lack of disease severity classification, vaccination status, serial biomarker measurements may have affected the interpretation of the results. Future research should focus on multicenter studies with larger cohorts. Integration of these markers with clinical findings and imaging may further enhance diagnostic precision. It is recommended that serum CRP and LDH levels should be used routinely as an adjunctive biomarker to support early detection of COVID-19 infection, particularly in resource-limited settings where RT-PCR availability is limited.

CONCLUSION

Diagnostic accuracy of serum CRP and LDH levels is superior to Serum AST and ALT levels in detecting COVID-19. These serum markers may be used as an adjunct diagnostic tool in detecting COVID-19 in settings where RT-PCR is not available.

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MZ: Study design, Data acquisition and analysis, Manuscript drafting

RS: Critical review and final approval

AF: Data collection and formatting of manuscript

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