Laboratory Diagnostics in COVID-19

Role of Biochemistry Lab in COVID-19

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Abstract:
Laboratory medicine plays an essential role in timely detection, diagnosis and management of diseases. During this pandemic, clinical biochemistry laboratory has played a pivotal role in management of COVID-19 disease. Biochemical analytes play a key role in assessing the severity of disease, prediction of complications and monitoring of treatment responses.

Keywords:
COVID-19, Inflammatory markers, C-reactive protein, Interleukin-6.

Introduction:
COVID-19 pandemic is causing devastating death worldwide. Biochemical investigations encompass one third of all laboratory investigations in the hospital. COVID-19 patients with comorbidities such as diabetes, chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD), malignancies, hypertension, HIV are predisposed to life-threatening complications [1]. Apart from Real-time reverse transcriptase polymerase chain reaction (RT-PCR), a gold standard test for diagnosis of SARS-CoV-2 many supportive laboratory tests and imaging techniques give clear picture about patient’s condition [2]. From asymptomatic individuals to severe cases, a wide range of clinical outcomes was seen due to heterogeneity in patient population [3]. Clinical chemistry assays give information about diagnosing, prognosticating and monitoring individuals affected by COVID-19 disease. Anti-COVID-19 IgG, IgM antibodies detection in serum samples of COVID-19 patients by fully-automated
immunoassay systems provides crucial information on prevalence and epidemiologic surveillance which pave the way for planning vaccination strategies [4].

Role of Clinical biochemistry laboratory in analysis of COVID-19 samples:

i) Specimen collection and processing: At the Clinical Biochemistry laboratory it is imperative to follow the biosafety measures to control infections. The Phlebotomist should wear Personal Protective Equipment (PPE) and collect samples carefully. Sample handling and aerosol generating procedures such as centrifugation and opening of vacutainers should be done using Class II Biosafety Cabinets [5]. After centrifugation there should be a waiting time of 10 mins before the lid of the centrifuge is opened so aerosols generated during centrifugation settle down. Vacutainers should be opened with gauze piece dipped in 1% hypochlorite with face away from the vacutainer. Based on World Health Organization (WHO) guidelines the collected specimens should be carefully transported and stored for analysis with minimal risk of infections [6]. Pre-analytical variables such as improper collection, inappropriate handling, transport, storage, manual errors and presence of interfering substances should be avoided to minimize risk of errors [7]. Following steps should be followed for sample collection & transport.

- Specimens must be collected in appropriate vacutainers with correct labelling.
- Vacutainers placed in air tight zip lock cover and the surface cleaned with 1% sodium hypochlorite solution.
- Zip lock pouch should be placed in sample transport box dedicated for COVID-19 samples.
- Outer and inner surface of transport box should be cleaned with 1% sodium hypochlorite solution before transportation.
- Serum samples should be analyse within 2 hours or stored at 2-8°C if sample will be processed within 24 hours.

ii) Preanalytical Variables in estimation of inflammatory markers: Sample should be transported and centrifuged within 02 hours for IL-6 estimation. If IL-6 cannot be estimated immediately them the serum should be stored at 2-8°C. IL6 is stable at 2-8°C for 24 hours. IL-6 levels increase during pregnancy and sleep. 25% IL-6 secreted comes from adipocytes. CRP increases with BMI. Obese individuals have a higher baseline CRP level compared to individuals with normal BMI. CRP levels are linked to in-vivo release of IL-6 from adipocytes [8].

Like all other biochemical analytes icteric, haemolytic & lipemic samples effect reports.

iii) Biochemical analytes in COVID-19: Patients are diagnosed as COVID-19 positive based on RT-PCR tests, they undergo biochemical tests to assess various organ involvement, disease severity, predict mortality and morbidity risk [9]. The most frequently assessed biochemical parameters of COVID-19 positive/ suspected patients shown in Table 1.
<table>
<thead>
<tr>
<th>S.No</th>
<th>Analytes</th>
<th>Abnormalities</th>
<th>Diagnostic diseases/ Potential clinical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Alanine transaminase (ALT)</td>
<td>Increased</td>
<td>Hepatic injury and other organ damage</td>
</tr>
<tr>
<td>2.</td>
<td>Albumin</td>
<td>Decreased</td>
<td>Response to severe inflammation, Impairment of liver function</td>
</tr>
<tr>
<td>3.</td>
<td>Aspartate transaminase (AST)</td>
<td>Increased</td>
<td>Hepatic injury and other organ damage</td>
</tr>
<tr>
<td>4.</td>
<td>C-reactive protein (CRP)</td>
<td>Increased</td>
<td>Inflammation, Severe viral infection/ viremia/ viral sepsis</td>
</tr>
<tr>
<td>5.</td>
<td>Cardiac troponin (cTnI)</td>
<td>Increased</td>
<td>Cardiac injury</td>
</tr>
<tr>
<td>6.</td>
<td>Creatine Kinase (CK-MB)</td>
<td>Increased</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>7.</td>
<td>Creatinine</td>
<td>Increased</td>
<td>Kidney damage</td>
</tr>
<tr>
<td>8.</td>
<td>Interleukin-6 (IL-6)*</td>
<td>Increased</td>
<td>Cytokine storm syndrome/ Hyperinflammatory syndrome, Predicts respiratory failure</td>
</tr>
<tr>
<td>9.</td>
<td>D-dimer</td>
<td>Increased</td>
<td>Venous thromboembolism, Disseminated intravascular coagulation</td>
</tr>
<tr>
<td>10.</td>
<td>Ferritin*</td>
<td>Increased</td>
<td>Severe inflammation</td>
</tr>
<tr>
<td>11.</td>
<td>Gamma-glutamyl transferase (GGT)</td>
<td>Increased</td>
<td>Damage in the biliary pole of hepatocytes and cholangiocytes</td>
</tr>
<tr>
<td>12.</td>
<td>High-sensitivity C-reactive protein (hsCRP)</td>
<td>Increased</td>
<td>Cardiac risk stratification, Neonatal sepsis</td>
</tr>
<tr>
<td>13.</td>
<td>Lactate dehydrogenase (LDH)</td>
<td>Increased</td>
<td>Pulmonary injury and/or widespread organ damage</td>
</tr>
<tr>
<td>14.</td>
<td>Myoglobin</td>
<td>Increased</td>
<td>Myocardial injury</td>
</tr>
<tr>
<td>15.</td>
<td>NT-proBNP*</td>
<td>Increased</td>
<td>Heart failure and systemic inflammation</td>
</tr>
<tr>
<td>16.</td>
<td>Procalcitonin* (PCT)</td>
<td>Increased</td>
<td>Sepsis, Bacterial(superscript) infection</td>
</tr>
<tr>
<td>17.</td>
<td>Total bilirubin</td>
<td>Increased</td>
<td>Liver damage</td>
</tr>
<tr>
<td>18.</td>
<td>Urea</td>
<td>Increased</td>
<td>Renal impairment</td>
</tr>
</tbody>
</table>

* indicates esoteric tests.
All India Institute of Medical Sciences, Delhi / Indian Council of Medical Research – COVID-19 National Task Force/ Joint Monitoring Group published clinical guidelines for supporting the monitoring and management of moderately and severely affected SARS-CoV-2 patients. Table-2 describes the time sequence of performing biochemical tests for monitoring and management of adult COVID-19 patients with moderate and severe infections [10].

*Table-2: Guidance of biochemical tests for management of adult COVID-19 patients – ICMR:*

<table>
<thead>
<tr>
<th>S.No</th>
<th>Parameters</th>
<th>Moderate disease</th>
<th>Severe disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>CRP &amp; D-dimer</td>
<td>48 – 72 hourly</td>
<td>24 – 48 hourly</td>
</tr>
<tr>
<td>2.</td>
<td>KFT &amp; LFT</td>
<td>24 – 48 hourly</td>
<td>Daily</td>
</tr>
<tr>
<td>3.</td>
<td>IL-6</td>
<td>To be done if deteriorating and if available</td>
<td>To be done if deteriorating and if available</td>
</tr>
</tbody>
</table>

*iv) Role of inflammatory markers in COVID-19 patients:* Inflammatory and immune biomarkers are critical parameters during SARS-CoV-2 viral infections. Elevated levels of CRP, IL-6 and ferritin are associated with disease development and are early predictors of disease severity [11]. Positive acute phase reactants such as C-reactive protein and ferritin were increased, but in contrast albumin (negative acute phase reactant) was decreased during COVID-19 infection [12]. During initial phase of infection, CRP level is found to be significantly elevated. The serum levels of CRP and IL-6 can efficiently evaluate the kinetics of disease severity, immune-inflammatory features and outcome of the patients.

CRP is a better marker for monitoring response to therapy in COVID-19 patients as compared to IL-6 due to its stability for prolonged time periods and half-life of 19-20 hours [13]. IL-6 has a short half-life and peaks within 02 hours whereas CRP levels begin to rise rapidly within 6-8 hours from disease onset [14], [15] and peaks at 1-2 days. In contrast to IL-6 and CRP, PCT levels are positively associated with severity of disease along with bacterial co-infections [15]. PCT peaks by 06 hrs. Unlike CRP (widely available), PCT and IL-6 tests are not available in all hospitals, but many laboratories use IL-6 exclusively for research purposes. Inflammatory biomarkers need to be performed for monitoring disease course and evaluating response to therapy. Other inflammatory markers such as ferritin, albumin were also considered for better outcomes and clinical management.
Conclusion:
COVID-19 patients demonstrate different degrees of biochemical abnormalities. This can be identified by quantifying various analytes which include routine biochemical parameters and immune-inflammatory biomarkers. Better laboratory management can avoid various pre-analytical, analytical and post-analytical errors. Advanced equipped clinical biochemistry laboratories with COVID preparedness, co-operation with administration, risk-based management system provides reliable, truthful results culminating in rapid turnaround time. In vitro diagnostic tests are critical for assessing extent of disease severity, multiple organ dysfunctions, and progression as well as monitoring therapeutic interventions.

Reference


