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# C-Reactive Protein versus Chest Computerized Tomography in Follow up The Severity of Corona Virus Disease Patients in Suez Canal University Hospital

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## ABSTRACT

**Background:** Coronavirus disease 2019 (COVID-19), which happens due to SARS-CoV-2, rapidly evolved into a global health emergency with high morbidity and mortality. Identifying reliable, accessible markers to monitor disease severity remains a clinical challenge. Both C-reactive protein (CRP), which is an acute-phase reactant, and chest computed tomography (CT) have been investigated as tools for assessing progression and guiding management.

**Objective:** This review article aimed to compare the value of serum CRP levels with chest CT findings in evaluating and following the severity of COVID-19 among hospitalized patients at Suez Canal University Hospital.

**Methods:** We used Google Scholar, Science Direct, PubMed, and other internet databases for relevant literature with emphasis on studies addressing the pathophysiology of SARS-CoV-2 infection, the inflammatory role of CRP, and radiological manifestations on chest CT. Data were synthesized to highlight diagnostic accuracy, prognostic value, and the complementary role of these two modalities in patient monitoring. Due of lack of translation-related sources, documents in languages other than English were excluded. Also, works in progress, unpublished publications, abstracts from conferences, and dissertations that did not form part of broader scientific investigations were excluded.

**Conclusion:** CRP was consistently elevated in patients with severe disease and correlated with adverse outcomes such as respiratory failure, cardiovascular complications, and sepsis. Serial CRP measurements often preceded radiological worsening, making it a sensitive early marker of progression. Chest CT demonstrated characteristic ground-glass opacities, consolidations, and vascular changes that reflected the extent of pulmonary involvement and disease stage. CT severity scores paralleled CRP levels and clinical status, although routine CT use was limited by resource constraints and infection-control considerations. CRP is a cost-effective, practical biomarker for early risk stratification and follow-up in COVID-19, while chest CT remains valuable in selected scenarios, particularly for unexplained clinical deterioration and complication assessment. A combined approach enhances patient monitoring.

**Keywords:** COVID-19, SARS-CoV-2, CRP, Chest CT, Inflammatory markers.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) evolved in December 2019 in Wuhan, China, with early clusters linked to a seafood market; the precise zoonotic source, however, remains unresolved. From December 31, 2019 to early January 2020, 44 cases were reported, and within weeks, infections were detected in Thailand, Japan, and South Korea, highlighting rapid cross-border spread. Soon after, the causative agent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified and the outbreak accelerated worldwide [(1)]. By March 30, 2021, the WHO recorded 127,349,248 confirmed cases and 2,787,593 deaths. In Egypt, between January 3, 2020 and September 24, 2021, 298,988 confirmed cases and 17,043 deaths were reported, with 12,964,351 vaccine doses administered by September 16, 2021[(2)].

The swift global dissemination of SARS-CoV-2, evolving clinical presentations and increasing mortality created an urgent need for early prognostic markers. CRP, a hepatic acute-phase reactant measurable within hours of inflammatory stimulation, rises with infection, burns, trauma, inflammatory disorders, and malignancy, and is used clinically to help distinguish bacterial from viral etiologies and to monitor response to therapy [(3)]. Emerging observations indicated that higher CRP values accompany more severe pneumonia [(4)]. Accordingly, this review evaluates the association of C-reactive protein and chest CT as an indicator of the severity of COVID-19 patients.

## CORONAVIRUS DISEASE 2019 (COVID-19)

The Latin word for "crown" (corona) is the origin of the acronym "CoV" for coronavirus. Coronaviruses in humans can cause anything from a mild cold to a life-threatening respiratory collapse. The current SARS-CoV-2 epidemic has emerged as a significant obstacle to public health on a worldwide scale [(5)].

### Etiology

To the subfamily Coronavirinae of the family Coronaviridae, order Nidovirales, belong the positive-sense, single-stranded RNA viruses that are coronaviruses. Large RNA genomes, conserved genome organization that allows for rapid replication, specialized enzymes, and planned ribosomal frameshifting to express many non-structural genes are significant features of nidovirales. Based on genomic and phylogenetic characteristics, the four genera that make up Coronavirinae are alpha, beta, gamma, and delta [(6)].

### Viral structure

Enveloped positive-sense RNA viruses with some of the biggest genomes in the RNA virus family are coronaviruses. They have a functionally split genome



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that encodes replication-related non-structural proteins at the 5′ end and key structural components at the 3′ end. Proteins such as spike (S), membrane (M), nucleocapsid (N), and envelope (E) are present in these viruses. Additionally, some betacoronaviruses express hemagglutinin-esterase (HE). The primary target of antibodies designed to neutralize certain proteins is the S protein, which plays a crucial role in receptor binding and membrane fusion. An essential function of the N protein is to aid in the packaging of RNA and to facilitate transcription and assembly. The M protein, the viral envelope's most abundant structural constituent, dictates its overall architecture. Viruses express the little E protein, which aids in assembly and pathogenicity, as they replicate. Viral tropism and host interaction are both improved in HE-expressing strains [(7)].

**Transmission and pathogenesis**

**Zoonosis:** CoVs circulate widely in animals, bats in particular act as a reservoir and a key source of coronavirus diversity. In livestock and companion animals, CoVs cause diverse illnesses. In humans, alpha- and betacoronaviruses range from mild upper-respiratory infections (HCoV-229E, HCoV-NL63, HCoV-OC43, HCoV-HKU1) to life-threatening ARDS. Early Wuhan cases were probably associated with zoonotic exposure at the Huanan seafood market [(8)]. Comparative genomic analyses suggested recombination between a bat coronavirus and another coronavirus of uncertain origin, codon-usage analyses also point to bats as a likely reservoir. Homologous recombination is well-documented in other viruses, including classical swine fever virus, hepatitis C virus, HBV, HIV, and dengue [(9)].

**Modes of spread (Figure 1):** Droplets, aerosol-generating techniques, contaminated surfaces, and direct touch are the main vectors for person-to-person transmission. Typical routes include close contact with mucosa (oral, nasal, and ocular), coughing, and sneezing. Saliva, feces, urine, and respiratory secretions have all shown SARS-CoV-2. In severe cases, the viral loads are often larger and remain for longer. There have been reports of transmission to healthcare personnel and other close contacts [(10)].

**Virus–host interaction (Figure 2):** Detailed structural investigations have demonstrated that the receptor-binding domain of the viral spike (S) protein specifically interacts with the angiotensin-converting enzyme 2 (ACE2) receptor, a mechanism that facilitates both interspecies transmission and efficient human-to-human spread. ACE2 is abundantly expressed in type II alveolar epithelial cells and is also present in extrapulmonary tissues including the esophagus, small and large intestines, renal proximal tubules, myocardium, bladder urothelium, and oral mucosa, thereby providing multiple sites for viral attachment and replication. The pathogenic cascade begins with S1 subunit attachment and priming by the host serine protease TMPRSS2, followed by ACE2 engagement. Subsequent downregulation of ACE2 activity disrupts normal homeostatic pathways, promoting pro-inflammatory signaling, vasoconstriction, and tissue injury across affected organs [(11-12)].

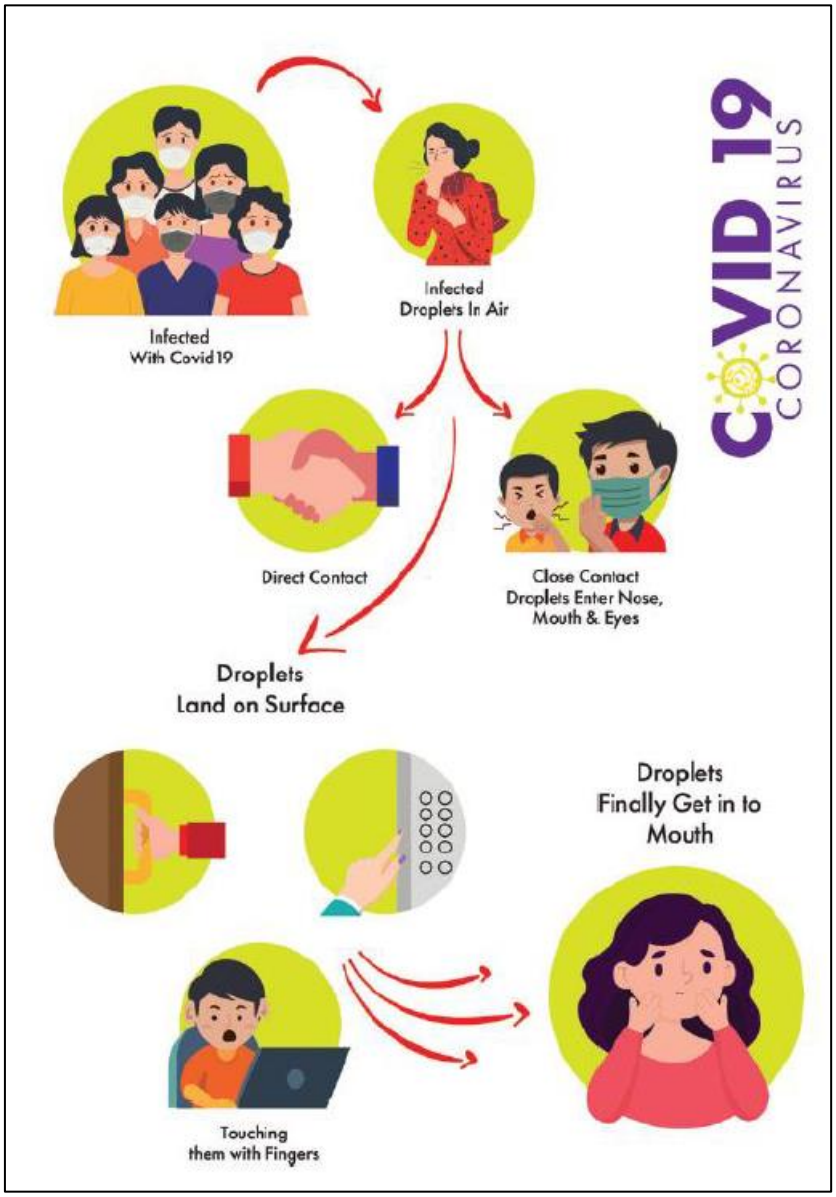


**Figure (1):** Modes of transmission [(11)].

## CLINICAL PRESENTATION AND DIAGNOSIS

**Demographics:** Across early series, the median age clustered around the mid-50s, with a male predominance sometimes attributed to differential ACE2 expression. Time to illness onset was typically about a week. Risk factors resembled those for SARS/MERS—smoking, hypertension, diabetes, cardiovascular disease, and other chronic conditions. Mortality increased with age. Children appeared less affected, potentially because of immunologic differences [(13)].

**Signs and symptoms:** Disease severity spans from mild to critical. Fever, cough, and myalgia are common; sore throat, headache, chills, gastrointestinal symptoms, anosmia/ageusia, and conjunctival congestion are less frequent. Clinical categories include mild–moderate (non-pneumonia/pneumonia), severe (dyspnea, RR >30/min, $SpO_2$ <93%, $PaO_2/FiO_2$ <300, or >50% radiographic progression in 24–48 h), and critical (respiratory failure, shock & multiorgan dysfunction). Severe illness in older adults often coincides with comorbidities [(14)].

**Laboratory evaluation and confirmation:** Typical laboratory abnormalities include lymphopenia, elevated CRP, and increased ESR. Lymphopenia likely reflects lymphocyte depletion and correlates with severity. Procalcitonin may be elevated with bacterial coinfection, especially in children. Diagnosis rests on RT-PCR from nasopharyngeal/oropharyngeal swabs, sputum, or feces, supported by imaging and inflammatory markers. Fecal nucleic acid detection can be comparable to pharyngeal swabs. Elevated cytokines include IL-7, IL-8, IL-9, IL-10, G-CSF, GM-CSF, TNF-α, and VEGFA [(15)].

**Radiological findings:** Common CT findings are ground-glass opacities, ill-defined margins, interlobular septal thickening, air bronchograms, crazy-paving, and adjacent pleural thickening. CT is a sensitive imaging tool in COVID-19 but must be interpreted in clinical context [(15)].

## MANAGEMENT

Initial management of clusters combined antivirals, antibiotics, and glucocorticoids. Observation is

appropriate for mild disease and hospitalization is advised for moderate disease with significant comorbidity and immunosuppression or pregnancy. Hydroxychloroquine/chloroquine showed early in-vitro activity; an early multinational registry analysis reported increased mortality and arrhythmias [16].

**Treatment of systemic complications in COVID-19:** While intubation and high-flow oxygen are commonplace in patients with ARDS who have respiratory failure, extracorporeal membrane oxygenation is an option to consider. Some patients with refractory hypoxemia may benefit from neuromuscular blockade, prone positioning, inhaled nitric oxide (5-20 ppm), and PEEP modification. Dialysis can help maintain a negative fluid balance, which is crucial in shock patients with acute renal injury. It is important to manage fluids to alleviate pulmonary edema and to administer antibiotics for prevention and to decrease subsequent infections. The risks associated with glucocorticoids make them a poor choice for treating viral pneumonia and acute respiratory distress syndrome. One possible strategy for reducing systemic inflammation and vascular injury in sepsis/ARDS is to administer intravenous vitamin C [17].

**Role of vaccines:** Vaccine development constraints include the need for trials in areas with ongoing transmission, platform partnerships, and rigorous safety evaluation—timelines often extend over a year. mRNA and other platforms, leveraging SARS/MERS immunology, target B- and T-cell epitopes within S and N proteins. Effective vaccination should limit spread and support viral clearance [18].

## C-REACTIVE PROTEIN AND ITS ROLE IN PREDICTING THE SEVERITY OF COVID-19

CRP is a sensitive but nonspecific marker of inflammation, infection, and tissue injury. While not diagnostic alone, paired with clinical and laboratory data it substantially informs management. First identified by reactivity with pneumococcal C-polysaccharide, CRP's key ligand is phosphocholine within bacterial teichoic acids [19].

CRP demonstrates broad ligand-binding capacity, enabling activation of the classical complement pathway, enhancement of phagocytosis, and interaction with Fcγ receptors. Following acute inflammatory stimuli, hepatic synthesis of CRP can increase dramatically, with plasma concentrations rising up to a thousand-fold within hours. This surge reflects the liver's wider shift in protein production characteristic of the acute-phase response. CRP circulates primarily in two structural forms: The native pentameric isoform (nCRP) and a monomeric or modified form (mCRP), each exerting distinct biological effects on inflammation. At the functional level, CRP serves as a pattern recognition molecule by identifying and binding to altered self-antigens and microbial structures. These include phosphatidylcholine residues on damaged cell membranes, exposed or denatured chromatin, and small nuclear ribonucleoproteins (snRNPs). Through these interactions, CRP promotes immune clearance by engaging complement components and Fc receptors, thereby linking innate recognition to effective immune elimination of targets [20].

**Regulation of CRP expression:** The CRP gene is located on chromosome 1 and is characterized by a simple structure, containing only a single intron that separates the sequences encoding the signal peptide from those of the mature protein. Its hepatic expression is primarily induced by interleukin-6 (IL-6), with interleukin-1 (IL-1) serving as an important co-activator. This process is mediated through the coordinated action of transcription factors including STAT3, members of the C/EBP family, and NF-κB–related proteins. In particular, the β and δ isoforms of C/EBP play a pivotal role, while STAT3 and Rel-binding elements within the proximal promoter enhance the stability of C/EBP attachment and transcriptional activation. Although CRP expression has also been detected in extrahepatic tissues, the regulatory mechanisms governing this peripheral production and its actual impact on circulating CRP concentrations remain uncertain [21].

**The acute-phase response:** C-reactive protein (CRP), historically recognized as the first acute-phase protein, demonstrates a rapid and marked elevation during systemic inflammation and tissue injury. This rise is part of the broader acute-phase response, a coordinated set of physiological and biochemical changes largely mediated by pro-inflammatory cytokines, with interleukin-6 playing a central role in stimulating hepatocyte protein synthesis. Among the various acute-phase reactants, serum amyloid A (SAA) displays a dynamic pattern of elevation comparable in scale to that of CRP, underscoring their combined diagnostic value in monitoring inflammatory activity [22].

**Circulating CRP concentration:** The median C-reactive protein level in relatively healthy young individuals is approximately 0.8 mg/L, with a range of 3.0 mg/L in the 90th centile and 10 mg/L in the 99th centile. Following an abrupt shock, levels can increase from less than 0.05 mg/L to more than 500 mg/L. Synthesis usually starts within a few hours and reaches its peak at about 48 hours, when it usually surpasses 5 mg/L. Circulating levels represent the rate of synthesis and, consequently, the severity of the inciting process, as the plasma half-life is approximately 19 hours and remains constant. Drops in value occur at the clearance rate as stimulus wears off. Baseline levels are heritable and generally steady, with occasional spikes from minor concurrent illnesses; median C-reactive protein increases with age in general populations, perhaps indicating subclinical disease. When it comes to real-

time inflammation indicators, CRP typically beats ESR and plasma viscosity. Few medications reduce CRP unless they inhibit the underlying process; severe hepatic dysfunction decreases production [23].

**CRP protein structure:** CRP is a pentraxin comprising five identical ~23-kDa subunits arranged symmetrically around a central pore. Each subunit forms two antiparallel β-sheets in a flattened jelly-roll; the recognition face contains a phosphocholine-binding site coordinated by two $Ca^{2+}$ ions adjacent to a hydrophobic pocket, while the effector face binds C1q and likely Fcγ receptors [24].

**Phylogeny of CRP:** All members of the pentraxin family, including CRP and SAP, are related. The five non-glycosylated protomers that make up Human CRP (Mr ~115 kDa) are bound together as a cyclic pentamer, with each protomer containing 206 residues. Though all vertebrates and Limulus species possess pentraxins, the specificity of their ligands, glycosylation, starting concentration, acute-phase behavior, and complement activation can vary among species. Because no other CRP reliably activates complement in autologous serum but human CRP, extrapolation across species is limited [25].

**Ligand binding and biological role of CRP:** CRP binds phosphocholine with high affinity and recognizes numerous autologous and microbial ligands (native/modified lipoproteins, damaged membranes, snRNPs, glycans and phospholipids from bacteria, fungi, parasites, and plants), leading to aggregation or precipitation of ligand-bearing structures. Ligand-bound CRP activates classical complement (C1q→C3→C5–C9) and recruits factor H to modulate the alternative pathway, thereby supporting opsonization and clearance. These functions resemble antibody activity and contribute to innate defense. Evolutionary conservation and links to autoimmunity suggest roles in maintaining self-tolerance [26].

**CRP in COVID-19:** Hyperinflammation drives critical illness and mortality in COVID-19. CRP, induced largely by IL-6 and TNF-α, tracks tissue injury and correlates with disease progression where it may rise before characteristic CT changes. Retrospective analyses have demonstrated that non-survivors of COVID-19 frequently exhibit rising levels of CRP, procalcitonin (PCT), and interleukin-6, whereas survivors tend to show stable or declining trends. Elevated CRP, in particular, has been strongly linked to worse outcomes, including an increased risk of thrombotic complications. The presence of metabolic comorbidities such as obesity, metabolic syndrome, hypertension, and atherosclerosis further amplifies this risk, often accompanying higher CRP concentrations. In elderly populations, a combination of elevated body mass index, lymphopenia, hypomagnesemia, and raised CRP and/or creatinine on admission has been associated with greater mortality. Collectively, these findings underscore CRP as not only a sensitive marker of systemic inflammation but also a prognostic correlate of adverse outcomes in patients with COVID-19 [27-28].

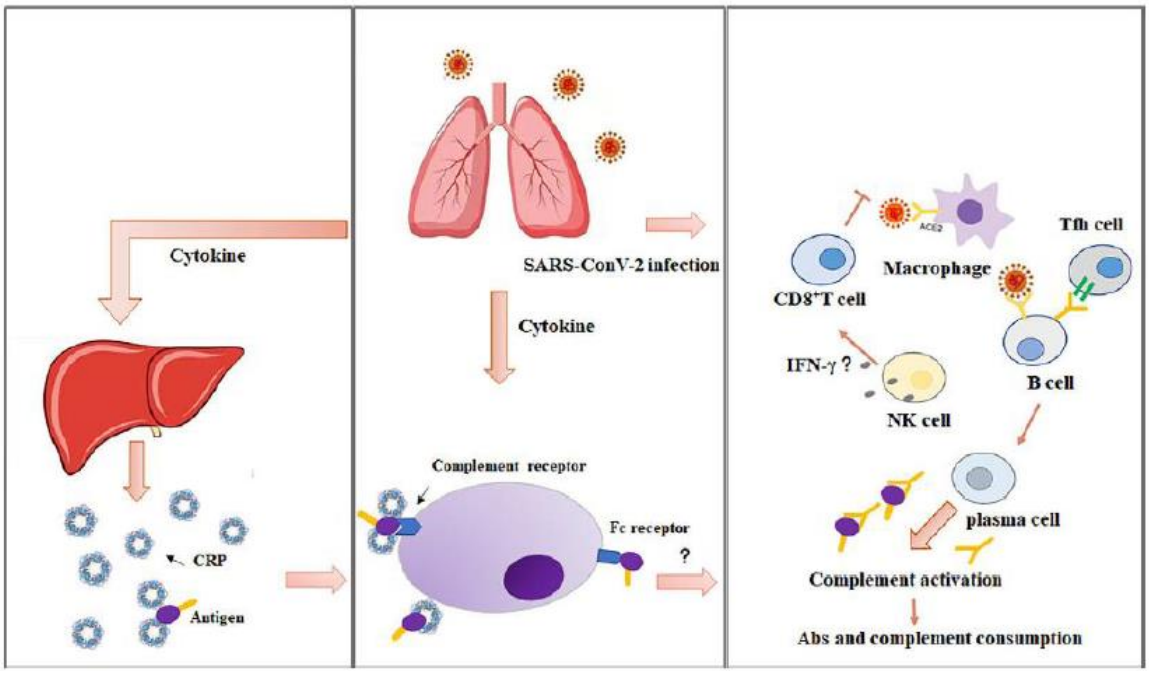


**Figure (2):** Outlines of immune-regulatory pathways [29].

**CRP and cardiovascular disease (CVD) in COVID-19:** SARS-CoV-2 affects the vascular system through ACE2-expressing tissues. Arterial/venous thrombosis is characteristic in severe cases. Patients with CVD display worse clinical trajectories and higher CRP. Older patients with CVD and elevated TnI, CRP, and creatinine were more likely to progress to severe/critical disease. Large European cohorts found

strong associations between cardiovascular comorbidity, myocardial injury (troponin), and CRP. Inflammation underlies atherosclerosis and plaque instability; CRP may participate in endothelial activation, macrophage function, and complement activation [30].

**CRP and stroke in COVID-19:** Severe COVID-19 increases stroke risk through hypoxia, coagulopathy, neuroinvasion, and immune-mediated injury; acute ischemic stroke in this context carries high mortality. CRP rises after stroke and correlates with vascular complications. In COVID-19-related strokes, elevated D-dimer, fibrinogen, and CRP reflect hyperinflammation and hypercoagulability [31].

**CRP and type 2 diabetes mellitus (T2DM) in COVID-19:** Diabetes increases COVID-19 mortality risk, especially in older adults, and COVID-19 may precipitate new-onset diabetes. In T2DM, chronic inflammation impairs immunity and increases infection susceptibility. CRP correlates positively with HbA1c and mortality in COVID-19 cohorts and may amplify inflammatory signaling [32].

**CRP and COVID-19-induced sepsis (Figure 3):** Severe COVID-19 shares features with viral sepsis; many ICU deaths are septic. Early hypercytokinemia may give way to immunosuppression. With severe disease, epithelial/endothelial barrier failure leads to leakage of serous components, robust cytokine/chemokine release, macrophage infiltration, acute lung injury, multiorgan involvement, systemic inflammation, and microcirculatory dysfunction. CRP correlates with APACHE II and SOFA scores and reflects sepsis severity/prognosis. Functionally, CRP binds pneumococcal C-polysaccharide and membrane phosphocholine ($Ca^{2+}$-dependent), engages chromatin, activates complement, enhances leukocyte phagocytosis, and acts as an opsonin [29].

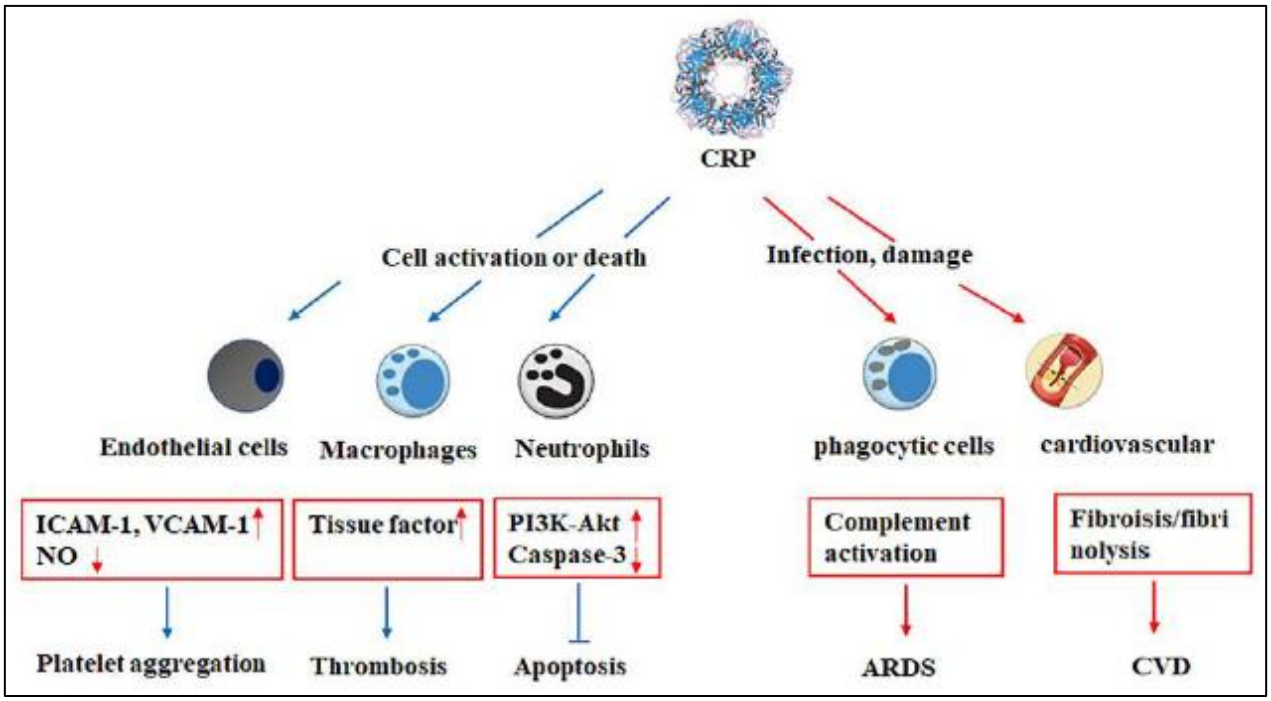


**Figure (3):** The critical role of CRP in acute or chronic inflammatory diseases [29].

**CRP and COVID-19 severity:** IL-6 is a principal inducer of CRP in COVID-19. Higher IL-6 corresponds to higher CRP, making CRP a practical surrogate for inflammatory activity and a severity marker [20]. CRP predicts severe disease and adverse outcomes. Admission CRP distinguishes severe from non-severe cases and survivors from non-survivors and associates with ICU admission and mortality [33].

Combining CRP with other biomarkers (e.g., NLR, leukocytosis, SAA, ferritin) enhances predictive

performance; elevations across multiple markers identify patients at higher risk [34]. CRP correlates with CT severity. Higher initial CRP predicts more extensive pulmonary involvement and ARDS risk; CRP may increase before radiographic worsening, making serial measurement useful when imaging capacity is limited [35].

Dynamic trends are informative. Longitudinal increases in CRP outperform single measurements for anticipating respiratory deterioration. Sex differences. After adjusting for confounders, CRP tends to be higher in men with COVID-19, paralleling greater severity in men [20]. Mechanical ventilation. Markedly elevated CRP (driven by IL-6) predicts need for mechanical ventilation [35].

## COMPUTED TOMOGRAPHY CHEST IN COVID-19

Because COVID-19 primarily affects the lungs, chest CT plays a valuable but context-specific role. Laboratory tests may lack sensitivity in early stages, so imaging can assist in diagnosis and monitoring when clinically indicated. International consensus statements, including those from the Fleischner Society, emphasize selective use rather than routine application [12, 15].

**Routine screening and suspects:** Routine CT for screening is not recommended because many early COVID-19 cases present with normal scans, and findings often overlap with other viral pneumonias. Additional concerns include infection-control challenges during repeated scanning. However, CT may be justified in RT-PCR–negative patients with moderate-to-severe symptoms and high suspicion despite normal or indeterminate chest X-ray. In such scenarios, typical CT findings—ground-glass opacities, patchy consolidation, interlobular septal thickening, crazy-paving, or the reverse-halo sign—support diagnosis. Effusions and lymphadenopathy are uncommon [12, 24]. Accuracy improves when CT results are interpreted together with laboratory markers such as lymphopenia, CRP, D-dimer, ferritin, and IL-6[15, 27].

**RT-PCR–positive patients:** In confirmed COVID-19, CT adds value when deterioration is unexplained or when coexisting disease (such as pulmonary embolism & tuberculosis, or malignancy) is suspected. In older patients or those with comorbidities like diabetes & CVD or obesity, CT can assist in triage, especially if hypoxemia is disproportionate to symptoms [12, 15].

**Role of CT in pneumonia:** Although RT-PCR remains the diagnostic gold standard, non-contrast CT has been widely studied for assessing pneumonia severity in COVID-19. Professional bodies no longer recommend CT as a frontline diagnostic tool but reserve it for patients at risk of progression, those with worsening symptoms, or cases where test access is limited [12, 15].

**CT features and disease severity:** Characteristic CT findings reflect diffuse alveolar damage and cytokine-driven lung injury. Bilateral, multilobar, and peripheral ground-glass opacities are common, with consolidations increasing in advanced stages. Severe disease is marked by extensive lung involvement, dense consolidations, and "crazy-paving" patterns. Vascular enlargement adjacent to lesions is frequently observed, potentially reflecting localized inflammation [24].

**Evolution of CT findings:** Radiologic changes follow a predictable course: Early ground-glass opacities (days 0–4), progressive multilobar involvement (days 5–8), peak consolidation (days 9–13), and gradual absorption with residual fibrotic streaks during recovery. Semi-quantitative CT scoring has shown strong correlation with severity indices and outcomes [24, 27].

Further studies are required to improve the predictive use of CRP in COVID-19, particularly for risk stratification and monitoring treatment response. Integrating CRP with other biomarkers such as IL-6, ferritin, and D-dimer may enhance prognostic accuracy and should be validated in larger cohorts [20, 27]. Similarly, CT scoring systems need refinement and correlation with clinically meaningful outcomes. Prospective research focusing on serial CRP measurements alongside standardized CT protocols could help determine optimal cutoffs and timing for interventions [24, 27].

## CONCLUSION

CRP is a practical, inexpensive marker that reflects inflammatory burden in COVID-19 and correlates with clinical severity, adverse outcomes, and imaging progression. When interpreted alongside clinical context and other biomarkers, CRP supports early risk stratification and monitoring. Chest CT adds value in specific scenarios—especially for unexplained deterioration and complications—while routine screening is not recommended. Standardized units, consistent terminology (SARS-CoV-2; COVID-19), and careful citation practices strengthen the scientific clarity of this review.

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