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Urine metabolomics links dysregulation of the tryptophan-kynurenine pathway to inflammation and severity of COVID-19
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Abstract
SARS-CoV-2 causes major disturbances in serum metabolite levels, associated with severity of the immune response. Despite the numerous advantages of urine for biomarker discovery, the potential association between urine metabolites and disease severity has not been investigated in coronavirus disease 2019 (COVID-19). In a proof-of-concept study, we performed quantitative urine metabolomics in patients hospitalized with COVID-19 and controls using LC–MS/MS. We assessed whether metabolites alterations were associated with COVID-19, disease severity, and inflammation. The study included 56 patients hospitalized with COVID-19 (26 non-critical and 30 critical disease); 16 healthy controls; and 3 controls with proximal tubule dysfunction unrelated to SARS-CoV-2. Metabolomic profiling revealed a major urinary increase of tryptophan metabolites kynurenine ($P < 0.001$), 3-hydroxykynurenine ($P < 0.001$) and 3-hydroxyanthranilate ($P < 0.001$) in SARS-CoV-2 infected patients. Urine levels of kynurenines were associated with disease severity and systemic inflammation (kynurenine, r 0.43, $P = 0.001$; 3-hydroxykynurenine, r 0.44, $P < 0.001$). Increased urinary levels of neutral amino acids and imino acid proline were also common in COVID-19, suggesting specific transport defects. Urine metabolomics identified major alterations in the tryptophan-kynurenine pathway, consistent with changes in host metabolism during SARS-CoV-2 infection. The association between increased urinary levels of kynurenines, inflammation and COVID-19 severity supports further evaluation of these easily available biomarkers. © 2022, The Author(s).

Index Keywords
biological marker, kynurenine, tryptophan; human, inflammation, liquid chromatography, metabolism, metabolomics, tandem mass spectrometry; Biomarkers, Chromatography, Liquid, COVID-19, Humans, Inflammation, Kynurenine, Metabolomics, SARS-CoV-2, Tandem Mass Spectrometry, Tryptophan

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