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# SARS CoV-2 patients at hospital admission and plasma level of KL-6 for predicting lung damage

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## PURPOSE / OBJECTIVES

Coronavirus disease 2019, abbreviated to COVID-19, is an emerging global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As the number of individuals infected with COVID-19 continues to rise globally and healthcare systems become increasingly stressed, it is clear that the clinical laboratory will play an essential role in this crisis, contributing to patient screening, diagnosis, monitoring/treatment, as well as epidemiologic recovery/surveillance. Coronavirus disease 2019 (COVID-19) is currently spreading worldwide. Patients at hospital admission are assessed by several blood laboratory tests and chest CT. This study examined whether serum Krebs von den Lungen-6 (KL-6) level is a useful biomarker for evaluating the severity of COVID-19 patients. KL-6 is a mucin-like high molecular weight glycoprotein produced and secreted in the serum by pulmonary type II pneumocytes.

## MATERIALS & METHODS

We examined patients diagnosed with COVID-19 at St. Ekaterina Hospital between February 1, 2021, and May 1, 2021. All patients were tested for KL-6 one week after diagnosis of Covid-19. The results were compared with the clinical assessment of the severity of the disease, lung CT and other laboratory markers of inflammation. Laboratory method is Chemiluminescent Enzyme Immunoassay (CLEIA). Lumipulse G KL-6 is an assay system including a set of immunoassay reagents, for the quantitative measurement of KL-6 in specimens based on CLEIA technology, by a two-step sandwich immunoassay method on the LUMIPULSE G System (FUJIREBIO). The Assay is fully automated. The measurement range of method is from 50 to 10000 U/mL.

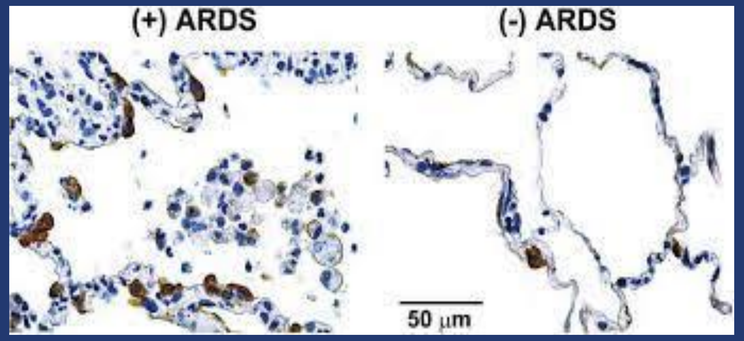
| Patients admitted to the hospital | Number (n) | Age range (years) | Average age in group |
|---|---|---|---|
| Total patient | 68 | 70.9 | 51-89 |
| Non - severe group | 43 | 63.4 | 52-73 |
| Severe group | 25 | 79.9 | 68-89 |

A total of 68 patients were tested, including 43 in the non-severe group and 25 in the severe group, of which four died. Compared with those in the non-severe group, more patients in the severe group were significantly older and had comorbidities.

## RESULTS

Serum KL-6 value at peak levels within one week after diagnosis of Covid-19 and hospital admission were significantly higher in the severe group (average value 797 U/mL) than in the non-severe group (average value 347 U/mL) and both $p < 0.001$.

| Severity of the disease | Number of patients | Average value and range KL-6 (U/mL) | p |
|---|---|---|---|
| non severe | 43 | 347 (128-577) | 0.001 |
| severe | 25 | 797 (617-1012) | 0.001 |




Immunohistochemical staining for KL-6 in lung post mortem

**Serum KL-6 reflects alveolar damage and regeneration of type II pneumocytes, indicating disease activity in various interstitial lung diseases.**
**The histomorphological changes of lung damage in severe Covid-19 have not yet been adequately characterized.**
**KL-6 analyses may be useful to predict severity of Covid-19 disease in elder patients.**

## RESULTS

LUMIPULSE G600II (FujiRebio) is an assay system, including a set of immunoassay reagents, for the quantitative measurement of KL-6 in specimens. This is a CLEIA technology by a two-step sandwich immunoassay method. Calibration of Lumipulse KL-6 is traceable to in-house reference calibrators, whose values have been assigned to correlate to EIDAs KL-6 ECLIA. No international standard exists for KL-6. The LOD for KL-6 in this assay was 13.47 U/mL. The LOQ was 13.47 U/mL. Lumipulse KL-6 demonstrated precision about 3.3% (CV). An average interference is less 20%. The linearity is up to 500 U/mL and diluted linearity is found in the range 674-10000u/mL.

Serum spesimens obtained from apparently healty donors are tested. The observed range is 118-627 U/mL.

Serum KL-6 value at level > 369 U/mL was used as the optimal cut-off to evaluate disease severity (sensitivity, 85.7%; specificity, 96.6%).

## SUMMARY/CONCLUSION

Covid-19 is a new disease with new viros. The autopsy findings document a sequence of processes that damage the lungs in patients with lethal Covid-19 disease. Pulmonary microvascular thromboses playing a central role. They have implications to therapeutic approaches that may help to lessen the percentage of patients with Covid-19 who experience a severe clinical course. They also provide a basis for further studies of the pathophysiologic mechanisms that underline this disease.

Serum KL-6 levels were significantly elevated in severe COVID-19 and it is a useful laboratory marker for evaluating its severity. KL-6 values more then 369 U/mL a few days after beginning of disease is a predictor for future complication of the disease and more severe lung damage.