TITLE: Coronavirus Disease 2019

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Hello, my name is Giuseppe Lippi. I am Director of the Laboratory of Clinical Chemistry and Hematology at the University Hospital of Verona, Italy, and Full Professor of Clinical Biochemistry and Clinical Molecular Biology. Welcome to this Pearl of Laboratory Medicine on "Coronavirus Disease 2019"

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A new viral outbreak has recently emerged in Wuhan, China, and is now spreading all around the world. As of March 8, 2020, more than 105,000 people have been affected, from over 90 countries, causing nearly thirty three hundred deaths, though numbers are still exponentially growing. This new viral epidemic has been recently defined Coronavirus Disease 2019, (COVID-19), and is sustained by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Molecular analysis has revealed that SARS-CoV-2 has most probably originated from recombination of a bat coronavirus, which has been then been transmitted to humans.

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COVID-19 outbreak is the third documented spillover of animal coronaviruses to humans during the past two decades, after Severe Acute Respiratory Syndrome (SARS) in 2002 and the Middle East Respiratory Syndrome (MERS) in 2012.

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A recent study has shown that the virus SARS-CoV-2 mainly targets the alveolar epithelial type II cells, which hence function as a reservoir for viral invasion in lung tissue.

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Information on the more representative clinical features of this syndrome are obviously still accumulating, and it cannot be excluded that the virus may interplay differently with human genetics and epigenetics. The largest data have been published in the Asian population, where the outbreak has begun, but it cannot be excluded that the clinical features may be partially different in other populations around the world.

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Although the risk of being infected by a patient with COVID-19 is the highest after the onset of symptoms, high viral loads in nose can be detected before the patient will become symptomatic. Moreover, the viral loads of non-symptomatic patients subjects tend to be similar to those of symptomatic patients, thus contributing to the risk of human-to-human transmission of the virus even during the non-symptomatic phase of disease. There are also anecdotal reports of possible transmission of the virus after remission of the symptoms. Information on the incubation period of COVID-19 is rather heterogeneous, thought the vast majority of patients develops the first symptoms between 2-14 days after being infected.

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As regards the clinic, the most frequently reported symptoms of COVID-19 encompass fever, cough, shortness of breath, myalgia and fatigue. A number of patients also report unusually frequent episodes of headache. Nasal congestion and diarrhea are apparently not so frequent.

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According to the World Health Organization, 80% of patients with COVID-19 only experience mild symptoms, very similar to those of a common influenza, but nearly 10-15% may progress towards a more severe form of disease, for example needing mechanical ventilation, while 2-5% of patients may then become critically ill and, for example, may need to be admitted to the intensive care unit.

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According to the World Health Organization, the risk of developing a severe form of COVID-2019 seems to be higher in elderly patients and in those with important co-morbidities, such as diabetes, cancer, cardiovascular and chronic respiratory diseases. No definitive data are available on the severity in patients with previous respiratory diseases, such as asthma.

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The recent statistics of the World Health Organization attests that despite the number of people that can be infected by a positive patient is higher for COVID-19 than for the previous two coronavirus syndromes SARS and MERS, the pathogenicity of COVID-19 appears globally lower. Current mortality data are the highest for MERS, around 34%, intermediate for SARS, around 10% and apparently the lowest so far for COVID-19, around 2-4%.

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As regards the distribution of the number of deaths across different ages, it is the highest between 30 and 79 years, then followed by the age range comprised between 20 and 29 years. Data garnered so far attests that COVID-19 may only produce a mild disease in children, which is then reflected by the low mortality rate. On the other hand, the presence of mild symptoms or even the non-symptomatic course of disease would make children important reservoirs and carriers of the virus.

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The etiological diagnosis of SARS-CoV-2 infection is currently based on collection of an upper respiratory specimen (typically nasopharyngeal AND oropharyngeal swabs) and further analysis of the sample using (real-time) reverse transcription polymerase chain reaction (rRT-PCR).

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A validated diagnostic workflow for detecting SARS-CoV-2 in Europe is based on three sequential real-time reverse-transcription polymerase chain reaction (rRT-PCR) assays, which encompass analysis of E gene as first line screening assay, analysis of RdRp gene as confirmatory assay and analysis of N gene as an additional confirmatory assay.

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According to a recent literature review, the most frequent laboratory abnormalities found in patients with COVID-19 encompass lymphopenia (in 35-75% of cases), increased values of C reactive protein (in 75-93% of cases), increased values of lactate dehydrogenase (in 27-92% of cases), increased values of erythrocyte sedimentation rate (in up to 85% of cases), increased values of D-dimer (in 36-43% of cases), along with low concentration of serum albumin (in 50-98% of cases) and low hemoglobin values (in 41-50% of cases).

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According to a recent literature review, the most frequent laboratory tests predicting progression toward severe forms of COVID-19 include decreased value of hemoglobin and albumin, as well as increased values of neutrophils, lactate dehydrogenase, aminotransferases, cardiac biomarkers (especially cardiac troponins), D-dimer , procalcitonin and C reactive protein.

Slide 16: References

Slide 17: Disclosures

Slide 18: Thank You from www.TraineeCouncil.org

Thank you for joining me on this Pearl of Laboratory Medicine on "**COVID-2019**"