The case of predicting and monitoring the impact of COVID-19 pandemic in Rwanda

Dr. Esperance Munganyinka[1], Thierry Habyarimana[2], and Gabriele Costantino[3]

[1]Head of Department of National Research and Innovation Fund at Rwanda National Council for Science and Technology, [2] Lecturer and Head of Department of Biomedical Laboratory Sciences, INES-Ruhengeri, Rwanda, [3]Professor of Medicinal Chemistry and Director, Department of Food and Drugs, University of Parma, Italy

Background: Rwanda has an ambition to leverage the transformative potential of Science, Technology, and Innovation (STI) to position herself as a globally-competitive knowledge based economy. This strategic orientation is founded on the premise that knowledge is essential to addressing social-economic challenges, and is a key driver of growth, competitiveness, and is indispensable in achieving high quality of living. The Government of Rwanda through the National Strategy for Transformation (NST-1) and Vision 2050 envisions the need for Rwanda to promote Research, Development and Innovation, as a key enabler for national economic and social transformation especially in the area of technology for industrial development. Rwanda has specifically established R&D funding instrument through the National Research and Innovation Fund (NRIF) to facilitate researchers who are expected to play a critical role in finding solutions to address social, economic and environmental challenges, as well as increasing research performance and productivity, and stimulate competitiveness.

COVID-19 Pandemic in Rwanda and interventions: On 14 March 2020, *Rwanda* confirmed its first *COVID-19* case which ranked *Rwanda* the *19*th African country to report the existence of the disease on its land. The interventions started across the country to fight against this virus including lockdowns, control and surveillance systems, and measures to limit the spread of the disease. Moreover, research activities on this pandemic were also taken into consideration where researchers, Institutions (RBC, IPAR-Rwanda), Universities (UR, INES-Ruhengeri); development partners (World Bank, UNDP), public institution (NCST) intervene as research implementers or/and funders of research activities on COVID-19.

Research on COVID-19 in Rwanda: Various research activities on COVID-19 Pandemic are implemented under various support. For instance, through the National Research and Innovation Fund at NCST, seventeen (17) research projects were supported with a total amount of around 1 billion Rwandan Francs to address COVID-19 pandemic into four main areas based on priorities that would address national interest: a) improving diagnostics; b) society resilience; c) innovative protective equipment; and d) monitoring and predicting the impact of COVID-19 pandemic.

Research projects are being implemented for instance to provide longitudinal datasets hub for predicting and monitoring COVID-19 evolution in the community and mitigation measures outcomes in Rwanda; to develop a mathematical modeling framework for predicting and monitoring the COVID-19 pandemic in Rwanda. Developed models will help in understanding the disease transmission dynamics, as well as give insights into the effectiveness of control strategies. In addition, a research project is being implemented to predict the risk of SARS-Cov2 infection and co-morbidity and reducing socioeconomic Impacts by identifying the high-risk population.

Predicting and Monitoring the Impact of COVID-19 pandemic: Clinical presentations of COVID-19 range from no symptoms (asymptomatic) to severe pneumonia. In European countries, 30% of diagnosed COVID-19 cases were hospitalized and 4% had severe illness, and this changes from time to time depending on availability and use of vaccines and measures to prevent ad curtail COVID-19. The trend is similarly high in the America countries, and higher in some countries. In most African countries, morbidity and mortality rates are lower than in European and American countries. The existing research studies will use existing data to generate a model to predict COVID-19 infection and morbidity rates to inform policy and practice on measures for containment and slowing the virus spread to prompt 'flattening of the curve' of COVID-19 infection, as well as continuation of social economic activities. Besides, from a public healthcare perspective, the goal is to assess and characterize public health preparedness levels in terms of setting up quarantine facilities to prevent risks of widespread infectious and assess uncertainties associated with the virus regarding infectivity during the incubation period and recovery.

Predicting the risk of SARS-Cov2 infection and co-morbidity and reducing socioeconomic impacts: identification of high-risk population: The goal of the project to validate the use of the plasma oxidative status as an early biomarker for stratifying sub-populations which are at higher risk to develop severe COVID-19. Early identification of individuals at risk is expected to provide a better use of the public health resources, to prioritize the delivery of vaccines, and to reduce the mitigation measures – including schools and economic activity closure or limitations- for those who are predicted to be at low risk of severe outcome. The rational for achieving this important goal is that severe COVID-19 is mostly due to an exacerbated inflammatory response, of autoimmune nature, which affects vascular endothelium and lung epithelium. Individuals with an unbalanced oxidative status are less likely to compensate this inflammatory state and can thus develop serious outcomes.

Objectives: Objective of the project is to carry out a community-wide analysis of the oxidative status of healthy population by using the Free Radical Analytical System (FRAS) technology to measure the derivative-Reactive Oxygen Metabolites (d-ROMs) and plasma antioxidant test (PAT), based on the evaluation of the redox potential of capillary blood (collected through simple and noninvasive finger prick). This analysis is expected to define a background signal of the oxidative status in the studied community and to identify those individuals who are statistically unbalanced in terms of oxidative level and/or antioxidant potentials. These individuals will be evaluated for underlying clinical conditions and, where the case, flagged for potentially high risk of inflammatory outcome. A secondary -but still very important- objective is to train the researchers and technical operators to the use of novel medical devices at high technological content through strengthening the collaboration with external partners i.e. University of Parma, Italy.

Preliminary Findings / achievements: A consultative meeting with different stakeholders (including clinical staff and local leaders) was organized for the presentation of the project, active inclusiveness/engagement, and identification of hotspots and development of protocols. In addition, a throughout training session was organized on sample collection and analysis using the new equipment's of FRAS technology for the measurements of the level of oxidative stress and antioxidant capacity.

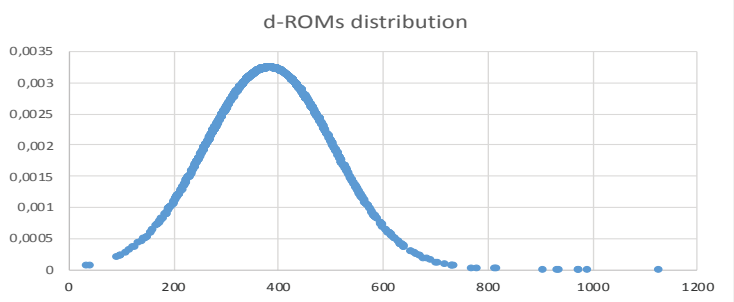
Training staff: sample collection and analysis (University of Parma and INES- Ruhengeri)

Data & Sample collection process at different public places (e.g. University and markets)

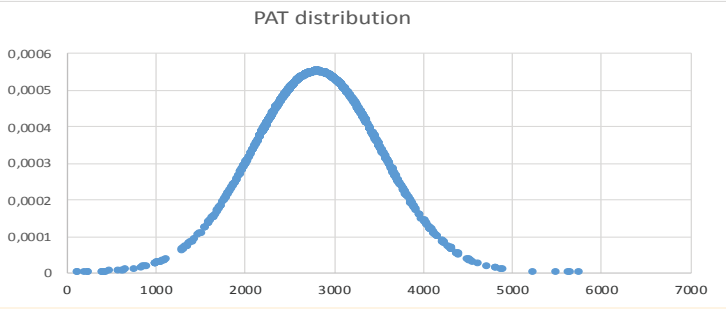
A population-wide screening was carried out in Musanze district, between March-June 2021. Blood samples collected from more than 1300 volunteers were screened and their demographic data were recorded. The overall oxidative status of individuals was assessed by measuring spectrophotometrically d-ROMs and PAT.

The preliminary findings are very interesting. First, a sharp normal distribution of values was obtained, indicating the technical robustness of the analyses. Then, a marked difference was noted in the value of the oxidative status, but not on the antioxidant potential, of the Musanze population with respect to the published data on European (Caucasian) population[5]. The collected data indicated a statistically significant higher average of dROMs. The reason for this is being investigated and can be attributed to several causes, including nutrition, exposition to high UV radiation and genetic background variability. Another very interesting preliminary findings is that the value distribution allowed to identify people with extreme values in both high and low directions.

Individuals with high d-ROMs values (coupled with low PAT values) are those tentatively classified as a higher risk of developing a severe form of COVID-19 and consequently need to be followed up. Individuals with very low values of d-ROMs, a condition which is rather infrequent in the Caucasian population, can be at risk of developing infections-possibly as a consequence of underlying and non-diagnosed comorbidities or an unbalanced nutritional state-since the production of physiological level of plasma reactive oxygen species is one of the main defense mechanisms against infective pathogens including SARS-CoV2[6].



The average d-ROM is 384.4, with a SD of 123.1. The value is significantly higher than expected, as this value corresponds to a medium-high oxidative stress according to the averaged values for a health -Caucasian- population.



The average value of 2853.6, with a standard deviation of 635.7. The value is at the upper limit of what is considered normal according to the published data for healthy Caucasian populations.

Expected outputs and outcomes: While the implementation of project has been partly delayed due to the continuous SARS-Cov2 waves and the consequent contentment measures, we expect all the major expected outcome to be achieved. The results can stratify the population on the basis of their plasma competence in clearing oxidative stress and/or the use of oxygen radicals to cope with infection. This would constitute an ideal approach to identify and isolate only individuals who are at risk to develop hyperimmune response and sustained inflammatory states[7]. This is particularly important in the context of the SARS-Cov2 pandemics, but it is also of great significance for non-communicable conditions such as nutritional unbalance, cancer, inflammation. Furthermore, it will contribute at implementing an efficient system of measure and analysis of biomarkers for oxidative stress as surrogate points for the risk of hyperimmune response[8], in the perspective of an efficient and optimized use of clinical resources as well as preservation of socioeconomic activities[9].

In addition, this study will report the first –to the best of our knowledge- a community-wide analysis on the oxidative status of the population in Sub-Saharan Africa, and can become a best practice also for other countries. Last but not least, the project has allowed to increase the exposition of Rwandan scientists i.e. INES-Ruhengeri staff, to new technology and scientific approaches and to strengthen the scientific collaboration with University of Parma, Italy.

Finally, these preliminary results give a more systematic analysis and provide an operational basis for the use of the d-ROMs and PAT tests for screening/follow-up purposes and may help public decision makers to take the right measure in the interest of both the public health and the public wealth. This is particularly relevant in the context of public health preservation and of optimal allocation of public health systems resources for preservation of socioeconomic activities. In the second phase of the project, individuals with COVID-19 infection, those who are recovered, and those who have been double dose vaccinated against SARS-Cov2 will be screened. This will allow to project the oxidative status of people exposed to the virus on the curve of the general population, thus indicating windows of values which are more likely to be associated with poor outcomes.

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