

COMMENTARY

The “Investigating and translating genomic evidence for public health response to SARS-CoV-2 (INSIDE SARS-CoV-2)” project – Network of excellence

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Abstract

The “Investigating and translating genomic evidence for public health response to SARS-CoV-2 (INSIDE SARS-CoV-2)” project is part of the initiative “Joint science and technology cooperation call for joint project proposals for the years 2021-2023” promoted by the Italian Ministry of Foreign Affairs and International Cooperation (MAECI) and the Republic of India.

To start the project activities, the pandemic response and the epidemiological situation in Italy and in India, together with the genomic surveillance strategies for SARS-CoV-2 virus in the two countries, are here described.

Key words

- SARS-CoV-2
- genomic analysis
- pandemic
- surveillance

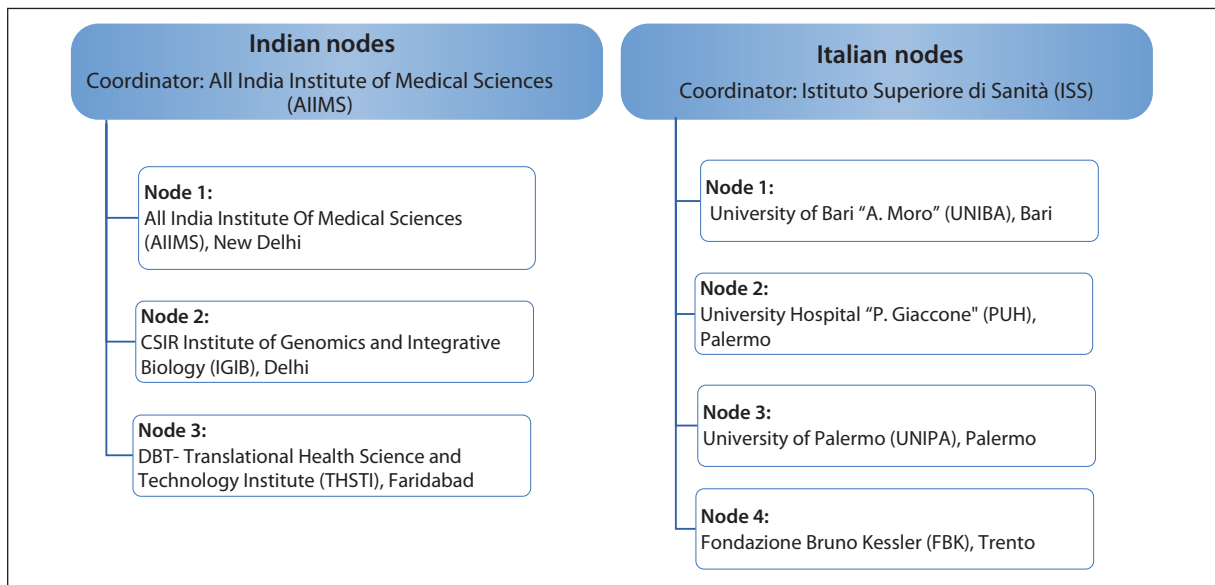
INTRODUCTION

The INSIDE SARS-CoV-2 project is establishing a scientific network of excellence composed by Indian and Italian academia, research institutions and laboratories with already existing infrastructure and funding to create a solid framework for collaboration for the investigation of SARS-CoV-2 virus variants in Italy and India. The participating nodes and the main objectives

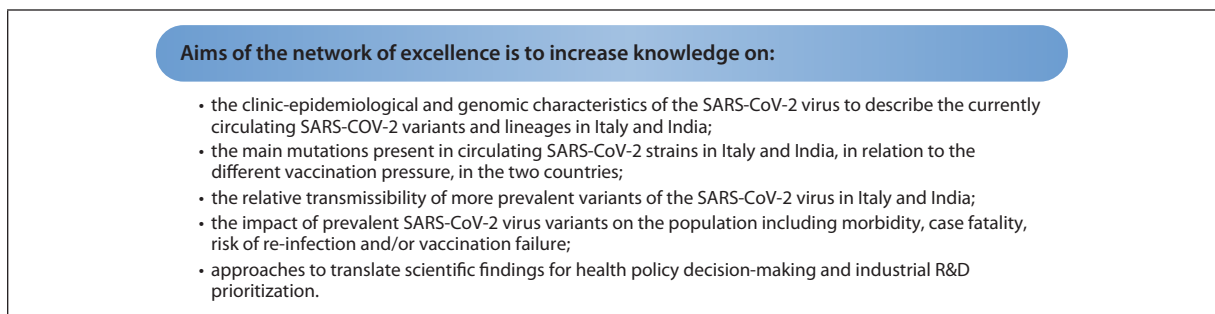
of the INSIDE SARS-CoV-2 project are shown in *Figure 1* and *Figure 2*.

THE PANDEMIC RESPONSE AND THE EPIDEMIOLOGICAL SITUATION Italy

Italy was the first western country to detect local SARS-CoV-2 transmission in February 2020 [1]. Since

**Figure 1**

The “Investigating and translating genomic evidence for public health response to SARS-CoV-2 (INSIDE SARS-CoV-2)” project – Network of excellence participating nodes.

**Figure 2**

Aims of “Investigating and translating genomic evidence for public health response to SARS-CoV-2 (INSIDE SARS-CoV-2)” project – Network of excellence.

then, as of the 20th of December 2023, almost 27 million cases of confirmed SARS-CoV-2 infection were reported in Italy, including over 190,000 COVID-19 related deaths with a crude case fatality rate that progressively decreased from over 11% in 2020 to 0.7% in 2023.

The Italian pandemic response was structured in three different phases modelled on the epidemiological evolution. The first phase was aimed at controlling the spread of infection and was enacted through a nationwide lockdown that effectively reduced the transmission of SARS-CoV-2 below epidemic levels [2]. Following a gradual reopening in late 2020, the fall-winter recrudescence of SARS-CoV-2 circulation was successfully contrasted through the establishment of a tier-based response [3] applied within the 21 regions and autonomous provinces of Italy according to epidemiological data and weekly subnational rapid risk assessments [4]. This phase of response (Phase 2A) was aimed at suppressing the excessive spread of infection. The availability of effective vaccines and the rapid increase in vaccination coverage in 2021, gradually changed the epidemiology of COVID-19 in Italy.

Notwithstanding an increase in the number of cases of infection due to the emergence of more transmissible variants of SARS-CoV-2, the proportion of severe and lethal SARS-CoV-2 infections decreased [5]. This led to a change in the parameters used to trigger the tier system from indicators of viral transmission to indicators of hospital burden. This shift (Phase 2B) characterized a change in the response strategy from suppression of viral circulation to mitigation of disease impact. Phase 3, with the suspension of non-pharmaceutical control measures, was reached with the end of the emergency in March 2022. The Italian pandemic response strategy was found to be evidence based [6] and in line with the response strategy described by the Lancet Commission on lessons for the future from the COVID-19 pandemic [7].

India

The COVID-19 pandemic in India started in the southern state of Kerala when a group of Indian students studying in China returned home in January, 2020 [8]. Initial reports suggested that the elderly (>65

years of age) and people with co-morbidities (hypertension and diabetes) were especially vulnerable to the severe symptoms. The spread of a respiratory pathogen is aided by high population density, a figure which stands at an average of about 464 per square kilometer in India. However, a demography with almost 40% of the population in the age group of <18 years, who did not show symptomatic infection, probably worked as a retardant to an early spread. In addition, on the 24th of March, 2020, the Government of India (GoI) imposed a country-wide lockdown, restricting population movement. Consequently, till the 12th of April, 2020 India reported lesser than 9000 cases of COVID-19. The lockdown was imposed till 17th of May, after which it was lifted in phases, a pre-unlock from 18th-31st of May, unlock 1.0 from 1st-30th of June and unlock 2.0 from 1st-31st of July, 2020.

During the lockdown, as part of the India COVID-19 Emergency Response and Health system Preparedness 2020, various steps were taken to support, train and protect the healthcare workforce, expand diagnostic facilities countrywide, deploy referral transport and enhance surveillance. For this, five objective measures to curb the growth in COVID-19 cases were taken, namely, imposition of COVID-appropriate behaviour (CAB), “Test, Track, Treat and Vaccinate”. For the purpose of testing, the number of laboratories capable of performing real time polymerase chain reaction (RT-PCR) based diagnosis for SARS-CoV-2 RNA from nasopharyngeal and oropharyngeal (NP/OP) sample was augmented substantially, from a very few in the month of January, to 669 in May, 1,614 in September and 2,172 by December 2020. Tracking positive cases was done through the Unique-Identification-Authority of India (UIDAI) database wherein each NP/OP sample was necessarily tagged with the corresponding UIDAI-ID which contained the address and phone number of the patient. For contact tracing and help to create infection hotspot maps, a mobile application termed Arogya Setu (literally meaning “bridge to health”) was created. Geographical areas with a cluster of cases were marked as “containment zone”, which was surrounded by a “buffer zone” outside of which free movement was allowed once the lockdown was withdrawn. Diagnostic techniques and kits were rapidly developed by various institutes of national eminence.

The National Institute of Virology, Pune, India developed a whole-virus inactivated vaccine against COVID-19, which was manufactured as “Covaxin” by the Indian vaccine manufacturing company Bharat Biotech Pvt. Ltd. Apart from this, the ChAdOx1 nCoV-19 vaccine, developed in a collaboration between the Oxford University and AstraZeneca, was produced as “Covishield” by an Indian company, the Serum Institute of India Pvt. Ltd., globally the biggest manufacturer of vaccine products. The Drug Controller General of India (DCGI) gave approval for human trials of Covaxin in June, 2020 and for Covishield in August, 2020. Approval for human trials for an indigenous DNA-vaccine (Zycov-D) developed by the Indian pharma Cadilla healthcare, a sub-unit vaccine (Corvevax) and for an indigenous mRNA vaccine being developed by Genno-

va Biopharmaceutical Ltd. (India) were also provided within December 2020. In January 2021, the emergency use authorization (EUA) for both Covishield and Covaxin was given for mass immunization in India. A total budget of US\$ 4.4 billion was allocated by the GoI for all these efforts.

Once the EUA for Covaxin and Covishield were issued, immunization of the population in India was initiated in a structured manner. The healthcare workers received the vaccines first, closely followed by the front-line workers involved in different essential services. This was followed by vaccination for persons at high risk for severe infection, and subsequently the people in the age group of 44-59 and 18-44 were allowed to get vaccinated. In the year 2022, precautionary vaccine for the age group of <18 years and booster doses for the vulnerable population was also permitted.

GENOMIC SURVEILLANCE

Italy

Genomic surveillance of SARS-CoV-2 has played a significant role in the early identification of new emerging variants and in monitoring their circulation during the COVID-19 pandemic.

Following the international recommendations from WHO and ECDC (<https://iris.who.int/bitstream/handle/10665/338480/9789240018440-eng.pdf?sequence=1>, <https://www.ecdc.europa.eu/sites/default/files/documents/Guidance-for-representative-and-targeted-genomic-SARS-CoV-2-monitoring-updated-with%20erratum-20-May-2021.pdf>) Italy has implemented, in accordance with the Italian Ministry of Health, the sequencing strategy continuously updated according to the epidemiological situation (<https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2022&codLeg=86233&parte=1%20&serie=null>, <https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2023&codLeg=93585&parte=1%20&serie=null>), based on two distinct sequencing flows with specific objectives and different sampling criteria. A periodic flow based on monthly flash surveys, is carried out in collaboration with the Bruno Kessler Foundation, to estimate the variants prevalence. Samples are collected on an agreed week of the month from subjects with suspected SARS-CoV-2 infection and based mainly on samples collected by general practitioners and paediatricians of free choice in the framework of the RespiV-irNet network activities. In addition, all samples from swab points or drive-in organised by ASLs and samples from outpatient services are collected.

Moreover, to early identify the emergence of new or already known SARS-CoV-2 variants of public health interest in hospitalised COVID-19 patients a continuous sequencing flow has been implemented. Sampling is focused on hospitalised patients with severe COVID-19 disease and/or persistent SARS-CoV-2 infection in order to identify the most significant genomic features associated with COVID-19 outcome.

Data from both flows are regularly published on the Istituto Superiore di Sanità, ISS website (<https://www.epicentro.iss.it/coronavirus/sars-cov-2-monitoraggio-varianti>) and all SARS-CoV-2 sequences are uploaded

in the Italian COVID-19 genomic (I-Co-Gen) platform, accessible to all peripheral laboratories, and then shared in GISAID (<https://gisaid.org/>).

I-Co-Gen was developed by ISS for the collection of national sequencing data, their analysis (using specific international tools such as Pangolin and PUSHER for the lineage assignment), the early warning and for the international sharing in GISAID.

The network involves around 70 laboratories across the country and more than 200,000 sequences have been collected at the time of writing (October 2023).

India

Large scale sequencing of SARS-CoV-2 samples was initiated worldwide; in India, a conglomerate of institutes constituted the Indian SARS-CoV-2 Genomics Consortium (INSACOG) and led these efforts. An update in real-time showed different variants to emerge at varying frequency (frequency of detection) which reflected their predominance among the genomes sequenced from patients' samples. Based on this frequency and the meta data about patient clinical history variants were marked into different categories like variant being monitored (VBM) or variant of interest (VOI), variant of concern (VOC) or variant of high consequence (VOHC).

CONCLUSIONS

The COVID-19 pandemic has highlighted the need to enhance national and subnational preparedness specifically directed to fighting future epidemic/pandemic threats. This includes strengthening surveillance and diagnostic capacity not restricted to healthcare facilities but at a community level. Increased simulation exercises and communication efforts on pandemic response could increase the health workforce's capacity to implement national pandemic plans, increase coordination between health agencies at the state and national level as well as enhancing awareness and know-how in the general population on how individual behaviour can support control efforts during epidemics and pandemics. This should be integrated with umbrella organizations like the WHO to facilitate international collaborations in fighting an epidemic/pandemic.

This project represents a unique opportunity for an exchange of past experience for preparing the future.

Conflict of interest statement

No potential conflict of interest was reported by the Authors.

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