

In order of importance, list of ten best papers of the candidate, highlighting the important discoveries/contributions described in them briefly (not to exceed 3000 words)

1. Murhekar MV et al. Prevalence of IgG Antibodies Against SARS-CoV-2 Among the General Population and Healthcare Workers in India, June–July 2021. (Preprint) <https://papers.ssrn.com/sol3/results.cfm>
2. Murhekar MV, et al. SARS-CoV-2 seroprevalence among the general population and healthcare workers in India, December 2020-January 2021. *Int J Infect Dis.* 2021 Jul;108:145-155. doi: 10.1016/j.ijid.2021.05.040.
3. Murhekar MV et al. SARS-CoV-2 antibody seroprevalence in India, August–September, 2020: findings from the second nationwide household serosurvey. *Lancet Glob Health.* 2021 Mar;9(3):e257-e266. doi: 10.1016/S2214-109X(20)30544-1.

Population-based serosurveys for SARS-CoV-2 are considered as a valuable tool in measuring the extent of spread of infection, and help understand the future course of pandemic. During the COVID-19 pandemic, the Indian Council of Medical Research conducted four nationally representative serosurveys at different time-points in the pandemic to estimate the age-specific seroprevalence of IgG antibodies against SARS-CoV-2. These surveys were conducted in the same 700 clusters (villages in rural and wards in urban areas) from 70 districts in 21 Indian states covering a sample size of more than 28,000 during each survey. The first survey was conducted among adults, second and third among individuals aged ≥ 10 years and fourth among individuals aged ≥ 6 years.

During May-June 2020, at the beginning of the pandemic, less than 1% (0.73%, 95% CI: 0.34%-1.13%) of India's adult population was exposed to SARS-CoV-2 (1). The prevalence among adults increased from 7.1% (95% CI: 6.2-8.2) by August – September 2020 (2) to 24.1% (95% CI: 23.0-25.3%) during December 2020 – January 2021. The fourth serosurvey conducted during June- July 2021 indicated that 67.6% (66.4 - 68.7) of the surveyed population had antibodies against SARS-CoV-2.

Besides the rising trend of seroprevalence, these serosurveys also provided insights about the spread of infection by age group, sex and areas of residence. The serosurveys during the first wave of pandemic showed that the seroprevalence was highest among individuals residing in urban slums followed by urban non-slum areas and lowest in rural areas. After the second wave of COVID-19, this gradient in the seroprevalence seems to have faded, indicating that the infection was widespread in rural areas.

These serosurveys also provided information about the adequacy of COVID-19 testing by estimating the infection to case ratio (ICR, defined as number of SARS-CoV-2 infection per laboratory confirmed COVID-19 case) at different time-points in the pandemic. During May-June 2020, there were an estimated 81.6 (95% CI: 48.3-141.4) infections per reported COVID-19 case in India, indicating the need for increasing the testing capacity and expanding testing strategy. The ICR improved subsequently, from 26–32 during August – September 2020, to 26 – 27 during December 2020 – January 2021 to 22-27 during June – July 2021.

The findings of the recent serosurvey could help in understanding the future course of the pandemic and guide the response activities. With one third of the general population not having detectable antibodies against SARS-CoV-2 by June 2021, it is

therefore possible that more COVID-19 cases are likely to occur in coming months, especially in areas where the proportion of people without detectable antibodies is higher. It is also reasonable to expect that the future surge of cases in India would be lower than the second wave. Based on these findings, ICMR recommended acceleration of coverage of COVID-19 vaccination and ensuring adherence to non-pharmaceutical interventions, continuing surveillance for early detection of cluster of cases and monitor emergence of VOC for prevention of the transmission in the country and preparedness for the possible third wave.

4. Murhekar MV et al. Burden of dengue infection in India, 2017: a cross-sectional population based serosurvey. Lancet Glob Health. 2019 Aug;7(8):e1065-e1073. doi: 10.1016/S2214-109X(19)30250-5.

The dengue disease burden in India is poorly quantified. Existing public health surveillance systems are not sensitive; mild febrile illnesses are less likely to be diagnosed and reported. The data from the private sector, where most patients seek care, largely remains untapped. Moreover, surveillance systems are not designed to capture subclinical infections, which account for about 75% of dengue infections. Dengue endemicity data was required for a policy decision for introduction of a dengue vaccine in India. To address the data gap, a national level serosurvey was conducted during 2017-18, in 60 randomly selected districts of 15 Indian states covering 5 geographic regions of India. The survey covered three age groups: 5-8, 9-17 and 18-45 years. The overall seroprevalence of dengue infection was 48.7% (95% CI: 48.7% (95% CI 43.5–54.0), increasing from 28.3% among children aged 5–8 years to 41.0% among children aged 9–17 years and 56.2% among individuals aged between 18–45 years. The seroprevalence was high in the southern (76.9%), western (62.3%), and northern (60.3%) regions.

A catalytic model constructed based on the age specific seroprevalence indicated that in 2017, there were about 9 million (based on age dependant force of infection)– 13 million (based on constant force of infection) primary dengue infections in 2017 among individuals aged 5–45 years from 30 Indian states.

This study also generated data about the profile of dengue serotype-specific neutralising antibodies. In eastern and northeastern regions, where dengue seroprevalence was low, most infections were monotypic in nature; while in northern, western, and southern regions most dengue infections were multitypic in nature.

Besides understanding the disease burden, the findings of our survey will be useful in making informed decisions about the introduction of newer dengue vaccines in the country.

5. Murhekar MV et al. Immunity against diphtheria among children aged 5-17 years in India, 2017-18: a cross-sectional, population-based serosurvey. Lancet Infect Dis. 2021 Jun;21(6):868-875. doi: 10.1016/S1473-3099(20)30595-8

Diphtheria is re-emerging as a public health problem in several Indian states, with most cases occurring among children older than 5 years. In this study, the residual serum samples from the national serosurvey for dengue infection were tested to estimate the age group-specific seroprevalence of antibodies to diphtheria in children aged 5–17 years in India.

The findings of this study indicated that less than one-third (29.7%, 95% CI 26.3–33.4) of children aged 5–17 years were immune to diphtheria, 10.5% (8.6–12.8) were non-immune, and 59.8% (56.3–63.1) were partially immune. The proportion of children non-immune to diphtheria was higher in northeast region and urban areas.

This was the first study documenting the population level immunity against diphtheria at the national level. The study findings have important programmatic implications. With a substantial proportion of children non-immune or partially immune to diphtheria, transmission is likely to continue in India until the immunity gap is bridged through adequate coverage of primary vaccination and booster doses administered as a part of universal immunisation and school health programmes. Being a nationally representative survey, the study findings could serve as a baseline of population immunity for assessing the effect of introduction of tetanus-diphtheria vaccine in India.

6. **Santhosh Kumar M, Kamaraj P, Khan SA, Allam R, Barde PV, Dwibedi B, Kanungo S, Mohan U, Mohanty SS, Roy S, Sagar V, Savargaonkar D, Tandale BV, Topno RK, Girish Kumar CP, Sabarinathan R, Saravana Kumar V, Bitragunta S, Grover GS, Lakshmi PVM, Mishra CM, Sadhukhan P, Sahoo PK, Singh SK, Yadav CP, Ramya Dinesh E, Karunakaran T, Govindhasamy C, Daniel Rajasekar T, Jeyakumar A, Suresh A, Augustine D, Ashok Kumar P, Kumar R, Dutta S, Toteja GS, Gupta N, Clapham HE, Mehendale SM, Murhekar MV. Seroprevalence of chikungunya virus infection in India, 2017: a cross-sectional population-based serosurvey. *Lancet Microbe*. 2021, 2: e41-e47**

Following the re-emergence of Chikungunya virus (CHIKV) in 2005, transmission has been documented in most Indian states. Information is scarce regarding the seroprevalence of CHIKV in India. In this study, we estimated the age-specific seroprevalence, force of infection (FOI), and proportion of the population susceptible to CHIKV infection, using the residual sera from the national serosurvey for dengue virus infection.

The overall prevalence of IgG antibodies against CHIKV was 18.1%. The seroprevalence was lowest in the northeast region (0.3%) and highest in the southern region (43.1%), with a significant difference in seroprevalence between rural (11.5%) and urban (40.2%) areas. The FOI was lowest in the eastern and northeastern regions. The estimated proportion of the population susceptible to CHIKV in 2017 was lowest in the southern region (56.3%) and highest in the northeastern region (98.0%).

Higher proportion of the population susceptible to CHIKV in the eastern and northeastern regions suggests a susceptibility of these regions to outbreaks in the future. With several CHIKV vaccine candidates in different phases of development, this serosurvey findings would be useful in identifying appropriate target age groups and sites for setting up surveillance and for future CHIKV vaccine trials in India.

7. Murhekar MV et al. Hepatitis-B virus infection in India: Findings from a nationally representative serosurvey, 2017-18. *Int J Infect Dis.* 2020 Nov;100:455-460. doi: 10.1016/j.ijid.2020.08.084.

Hepatitis-B (HB) vaccine was introduced in the Universal Immunization Program in India during 2002–2003 on a pilot basis, expanded to ten states in 2007–2008 (phase-1), and the entire country in 2011–2012 (phase-2). Except for a few small scale studies, there are no data regarding the impact of the hepatitis B vaccine introduction at the national level in India.

This study assessed the impact of HB vaccination by comparing the prevalence of different markers of HB infection among children born before and after introduction of HB vaccine in India, using the sera from the nationally representative serosurvey. The study findings indicated that compared to children born before introduction of HB vaccination (age: 11-17 years), children born after the HB vaccine introduction (age: 5-10 years) had a lower prevalence of past HBV infection (4.9% vs. 7.6%, $p < 0.001$) and a higher prevalence of anti-HBs (37.7% vs. 14.7%, $p < 0.001$). However, HBsAg positivity, was not different in the two age groups.

The findings of this study could be considered an interim assessment of the impact of the hepatitis B vaccine introduction, which indicates that India is on track for achieving the South East Asia Regional goal of 1% HBsAg prevalence among 5- year-old children.

8. Shanmugasundaram D, Awasthi S, Dwibedi B, Geetha S, Jain M, Malik S, Patel B, Singh H, Tripathi S, Viswanathan R, Agarwal A, Bonu R, Jain S, Jena SK, Priyasree J, Pushpalatha K, Ali S, Biswas D, Jain A, Narang R, Madhuri S, George S, Kaduskar O, Kiruthika G, Sabarinathan R, Sapakal G, Gupta N, Murhekar MV. Burden of congenital rubella syndrome (CRS) in India based on data from cross-sectional serosurveys, 2017 and 2019-20. *PLoS Negl Trop Dis.* 2021 Jul 23;15(7):e0009608. doi: 10.1371/journal.pntd.0009608.

India is committed to eliminate measles and rubella/Congenital Rubella Syndrome (CRS) by 2023. Towards this goal, India conducted nationwide supplementary immunization activity (SIA) with measles-rubella containing vaccine (MRCV) targeting children aged between 9 months to <15 years and established a hospital-based sentinel surveillance for CRS. Reliable data about incidence of CRS is necessary to monitor progress towards the elimination goal.

As an adjunct activity to CRS surveillance, serosurveys were conducted among pregnant women attending the antenatal clinics of the 12 sentinel hospitals where CRS surveillance is ongoing. This study estimated the burden and incidence of CRS using catalytic models constructed based on the age-specific seroprevalence data of IgG antibodies against rubella. Based on the constant and age-dependent force of infection models, the annual incidence of CRS in India was 225.58 per 100,000 live births (95% CI: 217.49–232.41) and 65.47 per 100,000 live births (95% CI: 41.60–104.16) respectively. This translated to an estimated 14,520 (95% CI: 9,225–23,100) and 50,028 (95% CI: 48,234–51,543) infants with CRS every year based on age-dependent and constant force of infection models respectively.

The estimates of CRS incidence will serve as a baseline to monitor the impact of MRCV SIAs, as well progress towards the elimination goal of rubella/CRS.

9. Kumar CPG, Sugunan AP, Yadav P, Kurup KK, Aarathee R, Manickam P, Bhatnagar T, Radhakrishnan C, Thomas B, Kumar A, Jayasree J, Philomina B, Kumar KGS, Thulaseedharan NK, Gupta N, Rajendran R, Saritha RL, Mourya DT, Gangakhedkar RR, Murhekar MV. Infections among Contacts of Patients with Nipah Virus, India. *Emerg Infect Dis.* 2019 May;25(5):1007-1010. doi: 10.3201/eid2505.181352.

Nipah virus (NiV) infection is an emerging zoonotic disease which can cause severe disease in both animals and humans. Although NiV is known to cause subclinical infections, the extent of these infections among close contacts showed wide variations between outbreaks in Bangladesh (no subclinical infection) to about 5-15% subclinical infections during outbreaks in Malaysia and Singapore.

This study documents the extent of subclinical infections among close (hospital and household/community) contacts during the 2018 NiV outbreak in Kozhikode and Malappuram districts, Kerala. The overall seroprevalence of subclinical infections among 279 contacts was 1.08% (95% CI 0.37–3.11). Two of the three contacts were family members of a laboratory-confirmed patient, and the third was a HCW in the emergency medicine department. All 3 had a history of exposure to body fluids of >1 NiV patient. None of the NiV seropositive contacts had history of febrile illness. These findings have important implications for contact tracing among the close contacts of laboratory confirmed NiV cases in future outbreaks.

10. Vivian Thangaraj JW, Mittal M, Verghese VP, Kumar CPG, Rose W, Sabarinathan R, Pandey AK, Gupta N, Murhekar M. Scrub Typhus as an Etiology of Acute Febrile Illness in Gorakhpur, Uttar Pradesh, India, 2016. *Am J Trop Med Hyg.* 2017 Nov;97(5):1313-1315. doi: 10.4269/ajtmh.17-0135.

Gorakhpur and the adjoining districts of Indian state of Uttar Pradesh have been witnessing seasonal outbreaks of acute encephalitis syndrome (AES), causing high morbidity and mortality especially among children. Investigations conducted during the 2014 and 2015 outbreaks revealed presence of immunoglobulin M (IgM) antibodies against *O. tsutsugamushi*, a causative agent of scrub typhus, in more than 60% of AES cases, suggesting a role for scrub typhus among the etiological agents of AES. Studies also indicated that AES cases were hospitalized late. This study was conducted to estimate the proportion of fever cases attending peripheral health facilities because of scrub typhus.

A facility based surveillance among children attending peripheral health facilities in Gorakhpur indicated that scrub typhus was one of the commonest aetiology of acute febrile illness in monsoon and post-monsoon season, accounting for about one-fifth (18%, 95% CI: 13.3–23.3) of all patients. Children with scrub typhus were more likely to have hepatomegaly (adjusted odds ratio, AOR = 3.2, 95% CI: 1.3–7.8), or lymphadenopathy (AOR: 2.9, 95% CI: 1.3–7.3) and did not have cough (AOR: 2.5, 95% CI: 1.1–6.9).

The evidence generated by this study, as well as other investigations (including studies among AES patients and entomological investigations) conducted in the region, was the basis of ICMR recommendations for early treatment of suspected scrub typhus cases with doxycycline or azithromycin in order to prevent their progression to AES.