Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Journal Pre-proof

Community seroprevalence and risk factors for SARS CoV-2 infection in different subpopulations in Vellore, India and its implications for future prevention

Divya Dayanand , Indhuja Irudhayanathan , Debasree Kundu , Abi Manesh , Vinod Abraham , Kundavaram PP Abhilash , Binila Chacko , Mahesh Moorthy , Prasanna Samuel , Pimnara Peerawaranun , Mavuto Mukaka , Jayaraj Joseph , Mohanasankar Sivaprakasam , George M Varghese

PII: S1201-9712(21)01255-8
DOI: https://doi.org/10.1016/j.ijid.2021.12.356
Reference: IJID 5913

To appear in: *International Journal of Infectious Diseases*

Received date: 10 November 2021
Revised date: 22 December 2021
Accepted date: 22 December 2021

Please cite this article as: Divya Dayanand , Indhuja Irudhayanathan , Debasree Kundu , Abi Manesh , Vinod Abraham , Kundavaram PP Abhilash , Binila Chacko , Mahesh Moorthy , Prasanna Samuel , Pimnara Peerawaranun , Mavuto Mukaka , Jayaraj Joseph , Mohanasankar Sivaprakasam , George M Varghese , Community seroprevalence and risk factors for SARS CoV-2 infection in different subpopulations in Vellore, India and its implications for future prevention, *International Journal of Infectious Diseases* (2021), doi: https://doi.org/10.1016/j.ijid.2021.12.356

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2021 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.
This is an open access article under the CC BY-NC-ND license
(http://creativecommons.org/licenses/by-nc-nd/4.0/)

Highlights

- The seroprevalence of SARS CoV 2 in Vellore, India reached above 70% by July 2021
- Seroprevalence varied by subpopulations, with highest among urban slums
- The vast majority of the infections (75%) were asymptomatic
- Vaccine uptake among urban slums and rural population was poor
- A targeted vaccination for high-risk individuals is suggested

Journal Pre-proof

Journal Pre-proof

Community seroprevalence and risk factors for SARS CoV-2 infection in different subpopulations in Vellore, India and its implications for future prevention

Authors:

Divya Dayanand[1], Indhuja Irudhayanathan[1], Debasree Kundu[1],Abi Manesh[1],Vinod Abraham[2], Kundavaram PP Abhilash[3], Binila Chacko[4], Mahesh Moorthy[5], Prasanna Samuel[6], Pimnara Peerawaranun[7], Mavuto Mukaka[7,8],JayarajJoseph[9,10],MohanasankarSivaprakasam[9,10], George M Varghese[1*]

[1]Department of Infectious Diseases, Christian Medical College, Vellore, Tamil Nadu, India

[2]Department of Community Health, Christian Medical College, Vellore, Tamil Nadu, India

[3]Department of Emergency Medicine, Christian Medical College, Vellore, Tamil Nadu, India

[4]Department of Critical Care Medicine, Christian Medical College, Vellore, Tamil Nadu, India

[5]Department of Clinical Virology, Christian Medical College, Vellore, Tamil Nadu, India

[6]Department of Biostatistics, Christian Medical College, Vellore, Tamil Nadu, India

[7]Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

[8]Centre for Tropical Medicine and Global Health, University of Oxford, UK

[9]Department of Electrical Engineering, Indian Institute of TechnologyMadras, Tamil Nadu, India

[10]Healthcare Technology Innovation Centre (HTIC), Indian Institute of Technology Madras, Tamil Nadu, India

***Corresponding author:**

Dr. George M Varghese MD, DNB, DTMH, FRCP, FIDSA

Professor & Head, Department of Infectious Diseases

Christian Medical College, Vellore 632004

Phone: +91-9487393015, Email address: georgemvarghese@hotmail.com

Abstract:

Objectives

To inform public health policy decisions through assessment of IgG antibody seroprevalence in the population and the risk factors for SARS-CoV-2 infection.

Methods

We estimated the seroprevalence of IgG antibodies among different subpopulations at the end of the first and second waves of the pandemic. We also assessed various risk factors associated with the seropositivity including socio demography, IgG antibodies against endemic human coronavirus and vaccination status.

Results

Of the 2433 consented participants, the overall estimated seroprevalence at the end of first and second waves were 28.5% (95% CI:22.3%-33.7%) and 71.5% (95% CI:62.8%-80.5%), respectively. The accrual of IgG positivity was heterogeneous, with highest seroprevalence among the urban slum population(75.1%). Vaccine uptake was varied among the subpopulations, with low rates (<10%) among the rural and urban slums. The majority of seropositive individuals (75%) were asymptomatic. Residence in urban slums (OR 2.02; 95% CI:1.57-2.6; p<0.001), middle socioeconomic status (OR 1.77; 95% CI:1.17-2.67; p=0.007), presence of diabetes (OR 1.721; 95% CI:1.148-2.581; p=0.009), and hypertension (OR 1.75; 95% CI:1.16-2.64; p=0.008) were associated with seropositivity on multivariable analyses.

Conclusion

Although considerable population immunity has been reached with more than two-thirds seropositivity, improved vaccination strategies among unreached subpopulations and high-risk individuals are suggested for better preparedness in future.

Key words

Seroprevalence, SARS CoV 2, COVID, India

Journal Pre-proof

Introduction

The coronavirus disease (COVID-19)pandemic has caused an unprecedented public health challenge in India with over 32 million confirmed cases and over 400 thousand deaths as of the end of August 2021(JHU CSSE 2021).India had a universal, strict lockdown which started in March 2020 as the pandemic started, and lasted for several months.This provided a window of opportunity to prepare the healthcare system and helped in flattening the epidemic curve and reducing mortality.Afterthe first wave, by the end of January 2021, a low case fatality rate (CFR) of 1.4%was reported with154,428deaths among the 10.76 million cases (Purkayastha et al.,2021). However, the second wave which was largely caused by the delta variant caught the nation uninformed with its rapidity and magnitude.A much greater number of cases were reported during the second wave when compared with the first; andIndia's most recent serosurvey which is yet to be published shows that two-thirds of the Indian population carries antibodies against COVID-19 either because of prior exposure to the virus or a vaccine (Anand et al.,2021).

A serosurvey from 70 districts across India conducted between December 2020 and January 2021 reported a population-weighted seroprevalence of 24.1%(Murhekar et al.,2021). However, a cross-sectional study conducted among people living in urban slums during a close timeperiod reported a much higher seroprevalence of 57.9%(George et al., 2021). The extent of the spread of infection into the general population is underestimated, as themajority of the infections are pre-symptomatic or asymptomatic(Wuet al.,2020). Indeed, there is heterogeneity in the transmission dynamics and a resultant seroprevalence among the population. A vast majority(90-99%) of transmission in the community is reported to be asymptomatic(George et al., 2021, Kshatriet al.,2021).Such asymptomatic cases complicate and prevent reliable estimation of transmission and tracking strategies for containing the spread of infection.Nevertheless,

asymptomatic infections contribute substantially to community transmissionand population immunity(Oran et al., 2020).Based on the seroprevalence and proportion of asymptomatic transmission in the community, the estimated infection fatality rate (IFR) in Indiais reported to be 0.04% which is lower when compared to the reported IFR of 0.31% from high-income countries like the USA during the same period (Laxminarayan et al., 2021, Pei et al.,2020).This could be due to due to a much younger median age of the population.Whether factors such as pre-existing seasonal coronavirus antibodies offer any partial cross-protection leading to milder or asymptomatic disease is unclear(Anderson et al.,2021, Song et al.,2021).As the number of cases has come down significantly and subsequent return to near normalcy is seen in most states, studying the current seroprevalence and vaccination rates in the community could inform future response and prevention strategies.

This cross-sectional studyassesses the seroprevalence of IgG antibodies to SARS-CoV-2 infection in Vellore district of Tamil Nadu and compares the same among participants across four different subpopulations:urban slum, urban affluent,rural areas, and healthcare workers (HCW). We investigated the IgG seropositivity at two time periods, at the end of wave 1(January 2021) and wave 2(July 2021) in the four subgroups. We also evaluated various risk factors associated with SARS CoV-2 infection:IgG antibodies against two other endemic strains (NL63 and OC43) of human coronaviruses (HCoV)to evaluate possible cross-protection to the SARS-CoV-2 and vaccination status at the end of wave 2.The seropositivity rates at the end of wave 1 and wave 2 combined with the vaccination status at the end of wave 2 in the four subgroups will provide valuable insights on the proportion of populationimmunity developed against SARS-CoV-2 infection. Based on this information subgroups that warrant attention can be targeted for futureprevention strategies.

Methods

Journal Pre-proof

Study design and participants:

This cross-sectional serosurvey was performed among the permanent residents of Vellore district, Tamil Nadu in South India at two time periods: January 2021, at the end of wave 1 and July 2021, at the end of wave 2 (Figure 1). Vellore district with six taluks (Vellore, Katpadi, Gudiyattam, Anaicut, Pernambet, and KV Kuppam) had 57% of the population living in rural areas and 43% in urban areas according to the 2011 census. Villages in each of the taluks were randomly selected for the survey. Additionally, two different subpopulations in theurban area of Vellore, namely urban slums and urban affluent areas, were also surveyed separately. The survey team randomly chose willing participants of all age groups from each sampling area. A minimum ofthirty individuals were enrolled from each random location and a total of 250 individuals were enrolled from each subpopulation. Healthcare workers who were willing to take part in the study were recruited from among doctors, nurses, paramedical staff, and support staff ofChristian Medical College (CMC), Vellore.

Procedure:

Individuals who agreed to participate answeredan interviewer-based semi-structured questionnaireafter providing a written informed consent or assent as applicable. The questionnaire comprised of questions related to socio-demographic variables including age, gender, socioeconomic status, comorbidities, respiratory symptoms or fever inthe 6 months prior to enrolment in the study, hospitalisation for COVID-19 since March 2020, and mask usage in the workplace and public places. Vaccination statusby the second wave was also included in the questionnaire at the end of wave 2. After administration of the questionnaire, a 5 ml blood samplewas drawn from the participants and transportedin a sample carrier box with gel packs to the laboratory where they were centrifuged.Plasmasamples were collected and stored at -70 °C untilIgGELISAtesting wasdone.

Journal Pre-proof

SARS-CoV-2 serological testing was done using SCoV-2 Detect™ IgG ELISA kit (InBios International, Seattle, USA), an indirect ELISA that detects the presence of IgG antibodies against SARS-CoV-2 S proteins on human serum. The incurred sample reanalysis values above 1.1 were considered positive. The specificity of the SCoV-2 Detect™ IgG ELISA kit is reported to be 97.6%(Deshpande et al., 2021). Similarly, Recombivirus TM Human Anti-Human Coronavirus NL63/OC43 Spike 1 IgG ELISA Kit (Alpha International diagnostics, USA) was used on human serum or plasma for quantifying IgG antibody specific for S1 subunit of the spike protein of the HCoV [NL63 (alpha coronavirus) and OC43 (betacoronavirus)] viruses, which are etiologic agents for human endemic respiratory disease. The incurred sample optical density values above 3.5 were considered positive.

The primary outcome assessed was seropositivity (seroprevalence)to SARS-CoV-2 antibodies overall and in different subgroups. The secondary outcomes included the various factors associated with seropositivity, symptomatic and asymptomatic infection, seropositivity to HCoV,and vaccination status.

The study was approved by the Institutional Review Board and Ethics Committee of CMC Vellore (Number: 13165).

Statistical analysis:

A target sample size of 1000 participants was estimated for each time point to detect the differences by subpopulations (approximately 2,000 participants for both waves), assuming a seroprevalence in the general population of 20% at the end of wave 1, with an α error of 0·05 and power of 80%to detect at least a 12% difference in seroprevalence which gives a sample size of 225 per subpopulation. In order to account for a 10% loss to follow-up, from different subpopulations, 250 samples were targeted at each sampling period. The actual sample size that was sampled was 2,433 for both waves (1,228 for wave 1 and 1,205 for wave 2),which was slightly higher than the target sample size and, hencecontributed to a gain in power.

Journal Pre-proof

The summary measures of participants, seroprevalence, and odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated by subpopulation, time period, and participant characteristics. The seroprevalence estimates were calculatedby subpopulation and previously known test performances.The overall seropositivity for each wave was weighted using the Vellore population. Post-stratification weighting was used to align the composition of the respondents' sampling fraction with the known distribution of the whole population's subgroup proportions, thereby reducing sampling error. Weights were computed based on the expected proportion of the population ofeach location.

Therisk factors for seropositivity were assessed by univariatemixed-effects logistic regression analysisclustered by time period.A p-value less than 0.05 were considered statistically significant. Multivariablemixed-effects logistic regression analysis was done to adjust for potential confounding factors and clustering effects. Statistically significant risk factors identified in univariate analysis were selected as variables for the multivariable analysis. Statistical analyses were performed in SPSS version 21 and Stata 16College Station, Texas 77845 USA.

Results

A total of 2,433 willing participants from four subpopulations namely Rural, Urban slums, Urban affluent, and Healthcare workers were included in this study. Sampleswere collected from these four subpopulations at the end of wave 1 in January 2021 and wave 2 in July 2021 to give a total of756 samples fromrural, 645 from the urban slum, 534 from urban affluent, and 498 from healthcare workers. The sample population constituted 56.6% females with a mean age of 37 years (SD± 17.5). Of the participants,18.7% were less than 20 years, 41.8% were between 21-40 years, 28.7% were between 41-60 years, and 10.9% were above 60 years. The most commonly reported comorbidities were diabetes (11.1%),hypertension (10.7%), chronic obstructive pulmonary disease (COPD)/asthma (2.1%), and heart diseases (1.4%). The subpopulation

Journal Pre-proof

specific baseline demographic characteristics including education, occupation, and socioeconomic class aresummarised in Table 1.

A total of 588 participants (24.2%) reported symptoms suggestive of acute respiratory infection or fever during the six months preceding sample collection. Symptoms were reported by 46.2% of healthcare workers,28.3% of the urban affluent group, 16.1% of the urban slum, and 13.4% of the rural group. Overall symptoms reported among participants were similar during wave 1(27.6%)and wave 2(20.7%). Among the SARS-CoV-2 positive participants,30.7%and 22.5% were symptomaticduring wave 1 and wave 2, respectively. Notably, only 4.1% of the study population had symptomatic infection requiring hospitalisation,most of which were for infection control purposes. In public places, cloth maskremained the most common type of mask used (58.1%)followed by surgical mask (35.1%), and N95(6.8%), respectively. Other human coronavirus antibodies (NL63, OC43) were detected in almost all the participants:99.6% of participants who were seronegative for SARS-CoV-2 and 100% of the participants who were seropositive for SARS-CoV-2 antibodies, respectively.

The overall weighted prevalence of SARS-CoV-2 antibodies adjusted for the population of Vellore was 28.5% (95% CI: 22.3%-33.7%) at the end of wave 1 and 71.6% (95% CI: 62.8%-80.5%) at the end of wave 2. At the end of wave 1, seroprevalence was found to be the maximum among individuals from urban slums (43.7%; 95% CI: 38.1%-49.4%) followed by healthcare workers (31.6%; 95% CI: 26.5% -37.0%), rural (26.8%; 95% CI: 22.9%-32.2%), and urban affluent (24.7%; 95% CI: 20.0%-30.0%). At the end of wave 2, seropositivity was the maximum among healthcare workers (95.5%; 95% CI: 91.3%-98.0%) with a high vaccination rate of 91.6%(95% CI: 86.5%-95.2%). The urban affluent had similar high seropositivity of 85.4%(95% CI: 80.2%-89.6%) with 65.7%(95% CI: 59.3%-71.7%)of the participants being vaccinated. The urban slums and rural areas also had a high seroprevalence of 75.1%(95% CI: 70.2%-79.7%)and 67.8%(95% CI: 63.1%-71.9%), respectively, with only 6.6%(95% CI: 4.2%-9.8%) and

10.4%(95% CI: 7.7%-13.5%) of respective participants being vaccinated.The community seropositivity for IgG at the end of wave 1 and wave 2 for the four different subpopulations is tabulated in Table 2 and Figure 2. The seroprevalence along with the vaccination status in different subpopulations at the end of wave 2 is depicted in Figure3. Seropositivity by different characteristics and time periods are depicted in Table 3.There was a slight shift in seropositivity noted from older age groups (above 60 and 40-60) in wave 1 to younger age groups (20-40 years and 1-20 years) in wave 2. This may be because of the larger proportion of the population who got infected during the second wave which is a reflection of the younger population in the country.

Mixed-effects logistic regression analysis of factors associated with seropositivity was adjusted for the clustering of time periods (Table 4). Healthcare workers and individuals among the urban affluent showed 2.1 and 1.5 times higher odds for seropositivity as compared to the rural populationin the univariate analysis. However, these were not found to be significant in the multivariable analysis. People living in urban slums showed about 2 times higher odds for seropositivity as compared to those living in rural areasin both univariate and multivariable analysis with an OR of 2.02(95% CI: 1.57-2.60; p<0.001]. Middle socioeconomic class based on the modified Kuppuswamy scale (Kattula et al., 2016) showed higher oddsfor seropositivity as compared to upper class in univariate analysis with an OR of 1.40 (95% CI: 1.05-1.86; p=0.024) and in multivariable analysis with an OR of 1.77 (95% CI: 1.17-2.67; p=0.007). Although skilled workers showed a 30% lower risk of seropositivity in univariate analysisas compared to professional workers, it was not found to be significant on multivariable analysis. Among the comorbidities, diabetes and hypertension showed 1.5- and 1.3-times higher odds for seropositivity in univariate analysis, respectively, as well asin multivariable analysis with an OR of 1.70(95% CI: 1.15-2.58; p=0.009) and 1.75(95% CI: 1.16-2.64; p=0.008), respectively. There was no significant difference in protection noted between the use of N95 mask and the use of

Journal Pre-proof

cloth masks in public places. However, usage of surgical masksshowed slightly higher odds for seropositivity of 1.38(95% CI:1.13 – 1.28; p-value=0.001) compared to cloth mask in univariate analysis.This was not found to be significant on multivariable analysis. Smoking habits and alcohol consumption were not found to be potential risk factors for seropositivity. The presence of symptoms suggestive of recent respiratory infection in the past 6 months and close contact with confirmed cases were not found to be an independent risk factor for COVID-19 infection. Close contact with confirmed SARS-CoV-2 positive cases was also insignificant.

Discussion

Our results reporteda high community seroprevalence of SARS-CoV-2in Vellore, India and it demonstrated the variability in transmission dynamics and vaccine utilisation in different subpopulations. The overall weighted seroprevalence for Vellore district increased almost three-folds from 28.5% at the end of wave 1 in January 2021 to 71.6% at the end of wave 2in July 2021 suggesting thatpopulation immunity was achieved. The transmission dynamics varied in different subpopulations. The seroprevalence was highest among the urban slum population both at the end of wave 1 (43.7%)and wave 2(75.1%). As the transmission progressed, the lower seroprevalences at the end of wave 1 among the rural and urban affluent increased rapidly at the end of wave 2 to 67.6% and 85.4%, respectively, and probably reachedconsiderable population immunity. The high seroprevalence achieved among the healthcare workers and the urban affluent perhaps is largely due to the high vaccination rate of 91.6% and 65.7%, respectively.Whereas it is likely the natural infection that caused the high seroprevalence among the rural and urban slum populationsince vaccination rates were low (10.4% and 6.6%, respectively) in these populations.The majority of individuals (75%) with positive SARS-CoV-2 antibody did not report any symptoms in the six months prior to sample collection, suggesting significant asymptomatic transmission in the community.

Journal Pre-proof

Achieving populationimmunity either by natural infection or vaccination is a major goal for future prevention of the pandemic(Papachristodoulou et al., 2021).Emergingdata from different parts of India suggest that this goal is reached or is not far (George et al.,2021,Laxminarayan et al.,2021, Dyer et al.,2021). The heterogeneous nature of transmission dynamics in the community was clear by the end of wave 1. High seroprevalence was reported among the urban slum population with overcrowding, where social distancing and diligent personal hygiene, such as frequent hand washing were virtually impossible.(George et al.,2021, Malaniet al.,2021). The subsequent spread of infection among other subpopulations followed, resulting in a large second wave in India between April and June 2021(Gupta et al.,2021).The majority of transmissions in India were due to the prevalent Delta variant (Sarkar et al.,2021, Adamoskiet al.,2021). However, a similar large second wave in Brazil was predominantly due tothe Gamma variant with the Delta variant only contributing to a small proportion (De Souza et al., 2021, Singh et al.,2021). This evidence suggests that, although SARS-CoV-2 variants play a role in the transmission dynamics in the community, other factors such as overcrowding and personal hygiene play bigger roles.

Living in the urban slum population, a surrogate for overcrowding was strongly associated with SARS-CoV-2 infection and had a twice higher risk for seropositivity as compared to the other subpopulations on multivariable analysis. Our study findings are similar to the multi-state serosurvey conducted by the Indian Council of Medical Research reporting the highest seroprevalence in urban slum areas followed by urban non-slum and rural areas(Murhekar et al.,2021).Our observationsthat low and middle socioeconomic status and co-morbidities such as diabetes mellitus and hypertension showeda higher risk for seropositivity in both univariate and multivariable analysisare noted in other studies as well(Roy, Soumya 2020,Royo et al.,2021).As Diabetes is an important risk factor for viral, bacterial, and fungal infections, presumably these emerging data may suggest that there is an increased risk for SARS CoV-2 infection.

Journal Pre-proof

The disease transmission among different age groups varied based on their exposure to infection at different time points during the pandemic. We found that there has been a shift in the seroprevalence among theage groups between wave 1 and wave 2which is similar to other observations(Laxminarayan et al.,2021,Miragliaet al.,2021). Among urban slum, rural, and urban affluent subpopulations maximum seropositivity was seen in the 40–60years and above 60 years age groups after wave 1 but at the end of wave 2 slightly higher seropositivity rates were seen in the 1-20years and 20-40years age groups. An age-stratified regional modelling study from France predicted that wave 2 will affect the middle age groups and the younger population more, which is similar to our observations (Roederer et al.,2021).

The vast majority of infections were asymptomatic. Among the individuals with SARS-CoV-2 antibodies, only 24.9% reported any symptoms during the recall period of 6 months. Several other studies from India and other parts of the world reported similar high proportions of asymptomatic infection (Purkayastha et al.,2021, George et al.,2021, Feaster, Goh 2020, Varghese, John 2020).Although there is a possibility of recall bias, a high proportion of asymptomatic seroprevalence reported worldwide underscores the limitations of widely used syndromic surveillance for COVID-19. The asymptomatic transmission in the community coupled with the high exposure ratio questions the utility of contact tracing and surveillance measures. Therefore, mitigation strategies to target individuals with risk factors for severe disease, such as medical co-morbidities and the elderly, might be more pragmatic and effective (Khan et al., 2021).

The reported infection fatality rate for COVID-19 in India of 0.04% is lower than what is reported from several other countries which could be attributed to the young median age of the population in our demographic dividend. (Laxminarayan et al., 2021, Pei et al., 2020 ,Wagner et al., 2021, Yang et al., 2020).Cross protective immunity due to other human coronaviruses (HCoV) are postulated to be contributing to this lower-than-expected IFR(Huang et al., 2020).

Journal Pre-proof

To answer this question, we evaluated IgG antibodies against two endemic strainsof HCoV (NL63 and OC43) to analyse possible cross-protection against the current SARS-CoV-2 infection. We found almost 100% of participants were positive for HCoV antibodies. A similar estimate of high antibody titres due to acquisition of infection in early childhood is common. (Hovi et al., 1979,Ukkonenet al.,1984). Infection by the endemic HCoV strains has little cross-protection with SARS CoV. Afteran acute infection with endemic HCoV, no neutralizing antibodies against SARS CoV are produced (Che et al., 2005,Liang et al.,2013). Whether endemic HCoV infections are will impact COVID-19 severity and if there is variation in antibody response between HCoV strains, remains to be studied.

The healthcare worker grouphad seropositivity of 31.6% at the end of wave 1 which was comparable to the community seroprevalence in Vellore indicating that the nosocomial acquisition of infection was the same as acquisition of infection in the community if appropriate personal protective measures were taken. The seropositivity in this group rose to 95.5% at the end of wave 2 which can be attributed to the mandatory vaccination drive among healthcare workers.In our study, 91.6% of health workers were vaccinated. A good vaccination utilisation was also found among the urban affluent with a vaccination rate of 65.7% by the second sampling in July 2021.

Multiple factors have played a role in driving the massive second wave of COVID-19 in a diverse country like India. Firstly, a large proportion of asymptomatic transmission occurred in a huge,susceptible population of the country.This corresponded to the time after travel restrictions were relaxed following the first wave. It was further fuelled by mass gatherings for various religious festivals and election campaigns(Patel et al.,2021). Secondly, the commonly prevalent Delta variant may have contributed to the larger second wave. India failed to vaccinate the majority and takingthe advantage that flattening the epidemiological curve gained during the initial period through enforced social distancing and strict lockdown. Vaccine supply and

Journal Pre-proof

acceptance have been issues(Wouters et al., 2021).As of 13 October2021,only 19.9% ofIndia's 1·4 billion population werefully vaccinated(Hannah et al.,2020).

The major limitation of our study was that this data may not be representative of the rest of the country. However, observations from the nationwide serosurvey had a similar seroprevalence and hence this study adds value and provides deeper insight. The simple random sampling used in our study for convenience may have caused minimal estimation error. This method is what was practical and feasible as the apprehension among the general public to the COVID 19 pandemic posed a major hindrance to the willingness to participate in the study.

Our results have important implications for making future health policies. The considerable population immunity achieved predominantly by natural infections and vaccination in certain sub populations, makes large-scale future epidemics less likely. It is known that patients who had natural infections compared to those who are vaccinated are reported to have comparable immune protection (Lumley et al., 2021, Khoury et al., 2021). While massive vaccine drives have their place, focussed vaccination of susceptible populations among vulnerable groups to decrease morbidity and mortality should be a priority. The high seroprevalence also encourages most activities, including business, tourism, and education to remain open. However, the benefits of a high seroprevalence can be thwarted by the emergence of SARS CoV-2 variants. The virus has unusually large genomic RNA, error-prone proofreading mechanisms, and continues to mutate during infections. Therefore, well-coordinated genomic surveillance for emerging SARS CoV-2 variants is important.

In conclusion, our results confirm the high seroprevalence of SARS-CoV-2in Vellore and provide insights into the heterogeneity and various factors associated with transmission of infection. We also found that urban slum and rural subpopulations needed to be targeted for preventive strategies as they had the least vaccination status. Going forward, improved vaccination strategies among unreached subpopulations, particularly focussed vaccination in high-

Journal Pre-proof

risk individuals are suggested for better preparedness in future. Additionally, a rational approach of single dose of vaccine for the majority who are already infected with positive antibodies and natural immunity could be considered. The meaningful inferences drawn can be utilised to target high-risk groups that warrant attention and to be better prepared to address challenges in future.

Funding

Wellcome Trust/DBT India Alliance fellowship (IA/CPHS/16/1/502679) to GMV and Capgemini Technology Services India Limited & Fluor Daniel IndiaPrivate Limited as COVID grants to IIT Madras. Funding sources had no role in the design and conduct of the study, in the collection, management, analysis, and interpretation of the data, or in the preparation, review, and approval of the manuscript.

Ethical approval

The study was approved by the Institutional Review Board of Christian Medical College, Vellore (IRB minute 13165 dated 22.7.2020)

Conflict of interest

The authors have no conflicts of interest to declare.

Acknowledgements

We gratefully acknowledge Rohini Karthikeyan, S. Suresh Kumar, Merylin Sebastian, Emily Devasagayam, Vivegh V, Priyanka Gautam and Mithun Mohan Georgefor their technical helpand support.

Journal Pre-proof

References

1. Adamoski D, de Oliveira JC, Bonatto AC, Wassem R, Nogueira MB, Raboni SM, et al; SCB-UFPR COVID-19 team,2. Large-Scale Screening of Asymptomatic Persons for SARS-CoV-2 Variants of Concern and Gamma Takeover, Brazil. Emerg Infect Dis. 2021 Sep 17;27(12). doi: 10.3201/eid2712.211326.
2. Anand A, Sandefur J, Subramanian A. Three new estimates of deaths in India during the pandemic. Center for Global Development. 20 Jul 2021. https://www.cgdev.org/blog/three-new-estimates-deaths-during-pandemic.
3. Anderson EM, Goodwin EC, Verma A, Arevalo CP, Bolton MJ, Weirick ME, et al; UPenn COVID Processing Unit, Betts MR, Wherry EJ, Meyer NJ, Cherry S, Bates P, Rader DJ, Hensley SE. Seasonal human coronavirus antibodies are boosted upon SARS-CoV-2 infection but not associated with protection. Cell. 2021 Apr 1;184(7):1858-1864.e10. doi: 10.1016/j.cell.2021.02.010. Epub 2021 Feb 9. PMID: 33631096; PMCID: PMC7871851.
4. Che XY, Qiu LW, Liao ZY, Wang YD, Wen K, Pan YX, et al. Antigenic cross-reactivity between severe acute respiratory syndrome-associated coronavirus and human coronaviruses 229E and OC43. J Infect Dis. 2005 Jun 15;191(12):2033-7. doi: 10.1086/430355.
5. Covid19India.org. (accessed on 30 September, 2021).
6. Deshpande K, Pt U, Kaduskar O, Vijay N, Rakhe A, Vidhate S, et al. Performance assessment of seven SARS-CoV-2 IgG enzyme-linked immunosorbent assays. J Med Virol. 2021 Jul 31:10.1002/jmv.27251. doi: 10.1002/jmv.27251. Epub ahead of print. PMID: 34331713; PMCID: PMC8426713.
7. de Souza UJB, Dos Santos RN, Campos FS, Lourenço KL, da Fonseca FG, Spilki FR, Corona-Ômica Br/McTi Network. High Rate of Mutational Events in SARS-CoV-2

Journal Pre-proof

Genomes across Brazilian Geographical Regions, February 2020 to June 2021. Viruses. 2021 Sep 10;13(9):1806. doi: 10.3390/v13091806.

8. Dyer O. Covid-19: Two thirds in India carry antibodies, while research suggests country's death toll is 10 times official figure. BMJ. 2021 Jul 21;374:n1856. doi: 10.1136/bmj.n1856.
9. George CE, Inbaraj LR, Chandrasingh S, de Witte LP. High seroprevalence of COVID-19 infection in a large slum in South India; what does it tell us about managing a pandemic and beyond? Epidemiol Infect. 2021 Feb 4;149:e39. doi: 10.1017/S0950268821000273.
10. Feaster M, Goh Y-Y. High proportion of asymptomatic SARS-CoV-2 infections in 9 long-term care facilities, Pasadena, California, USA, April 2020. Emerg Infect Dis 2020; 26: 2416–19.
11. Feehan AK, Denstel KD, Katzmarzyk PT, Velasco C, Burton JH, Price-Haywood EG, Seoane L. Community versus individual risk of SARS-CoV-2 infection in two municipalities of Louisiana, USA: An assessment of Area Deprivation Index (ADI) paired with seroprevalence data over time. PLoS One. 2021 Nov 30;16(11):e0260164. doi: 10.1371/journal.pone.0260164.
12. Gupta N, Kaur H, Yadav PD, Mukhopadhyay L, Sahay RR, Kumar A, et al. Clinical Characterization and Genomic Analysis of Samples from COVID-19 Breakthrough Infections during the Second Wave among the Various States of India. Viruses. 2021 Sep 7;13(9):1782. doi: 10.3390/v13091782.
13. Hannah Ritchie, Edouard Mathieu, Lucas Rodés-Guirao, Cameron Appel, Charlie Giattino, Esteban Ortiz-Ospina, et al (2020) - "Coronavirus Pandemic (COVID-19)". Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/coronavirus' [Online Resource]
14. Hovi T, Kainulainen H, Ziola B, Salmi A. OC43 strain-related coronavirus antibodies in different age groups. J Med Virol. 1979;3(4):313-20. doi: 10.1002/jmv.1890030410.

Journal Pre-proof

15. Huang AT, Garcia-Carreras B, Hitchings MDT, Yang B, Katzelnick LC, Rattigan SM, et al. A systematic review of antibody mediated immunity to coronaviruses: kinetics, correlates of protection, and association with severity. Nat Commun. 2020 Sep 17;11(1):4704. doi: 10.1038/s41467-020-18450-4. PMID: 32943637; PMCID: PMC7499300.

16. JHU CSSE Coronavirus COVID-19 Global Cases: https://arcg.is/0fHmTX (accessed on 31 August, 2021).

17. Kattula D, Venugopal S, Velusamy V, Sarkar R, Jiang V, S. MG, et al. (2016) Measuring Poverty in Southern India: A Comparison of Socio-Economic Scales Evaluated against Childhood Stunting. PLoS ONE 11(8): e0160706. https://doi.org/10.1371/journal.pone.0160706

18. Khan SMS, Qurieshi MA, Haq I, Majid S, Ahmad J, Ayub T, et al. Seroprevalence of SARS-CoV-2-specific IgG antibodies in Kashmir, India, 7 months after the first reported local COVID-19 case: results of a population-based seroprevalence survey from October to November 2020. BMJ Open. 2021 Sep 23;11(9):e053791. doi: 10.1136/bmjopen-2021-053791.

19. Khoury DS, Cromer D, Reynaldi A, Schlub TE, Wheatley AK, Juno JA, Subbarao K, Kent SJ, Triccas JA, Davenport MP. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nat Med. 2021 Jul;27(7):1205-1211. doi: 10.1038/s41591-021-01377-8.

20. Kshatri JS, Bhattacharya D, Kanungo S, Giri S, Palo SK, Parai D, et al; ICMR-RMRC [OdiSHA-COVID-19] Serosurvey Team. Serological surveys to inform SARS-CoV-2 epidemic curve: a cross-sectional study from Odisha, India. Sci Rep. 2021 May 18;11(1):10551. doi: 10.1038/s41598-021-89877-y.

21. Laxminarayan R, B CM, G VT, Arjun Kumar KV, Wahl B, Lewnard JA. SARS-CoV-2 infection and mortality during the first epidemic wave in Madurai, south India: a

Journal Pre-proof

prospective, active surveillance study. Lancet Infect Dis. 2021:S1473-3099(21)00393-5. doi: 10.1016/S1473-3099(21)00393-5.

22. Liang FY, Lin LC, Ying TH, Yao CW, Tang TK, Chen YW, et al. Immunoreactivity characterisation of the three structural regions of the human coronavirus OC43 nucleocapsid protein by Western blot: implications for the diagnosis of coronavirus infection. J Virol Methods. 2013 Feb;187(2):413-20. doi: 10.1016/j.jviromet.2012.11.009.
23. Lumley SF, Rodger G, Constantinides B, Sanderson N, Chau KK, Street TL, O'Donnell D, Howarth A, Hatch SB, Marsden BD, Cox S, James T, Warren F, Peck LJ, Ritter TG, de Toledo Z, Warren L, Axten D, Cornall RJ, Jones EY, Stuart DI, Screaton G, Ebner D, Hoosdally S, Chand M, Crook DW, O'Donnell AM, Conlon CP, Pouwels KB, Walker AS, Peto TEA, Hopkins S, Walker TM, Stoesser NE, Matthews PC, Jeffery K, Eyre DW. An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status. Clin Infect Dis. 2021 Jul 3:ciab608. doi: 10.1093/cid/ciab608.
24. Malani A, Shah D, Kang G, Lobo GN, Shastri J, Mohanan M, et al. Seroprevalence of SARS-CoV-2 in slums versus non-slums in Mumbai, India. Lancet Glob Health. 2021 Feb;9(2):e110-e111. doi: 10.1016/S2214-109X(20)30467-8.
25. Miraglia JL, NascimentoMonteiro C, GiannecchiniRomagnolo A, Xavier Gomes R, PitangueirasMangueira C, AparecidaRosseto-Welter E, et al. A seroprevalence survey of anti-SARS-CoV-2 antibodies among individuals 18 years of age or older living in a vulnerable region of the city of São Paulo, Brazil. PLoS One. 2021 Jul 29;16(7):e0255412. doi: 10.1371/journal.pone.0255412.
26. Mora AM, Lewnard JA, Kogut K, Rauch SA, Hernandez S, Wong MP, Huen K, Chang C, Jewell NP, Holland N, Harris E, Cuevas M, Eskenazi B; CHAMACOS-Project-19 Study Team. Risk Factors Associated With SARS-CoV-2 Infection Among Farmworkers in Monterey

Journal Pre-proof

County, California. JAMA Netw Open. 2021 Sep 1;4(9):e2124116. doi: 10.1001/jamanetworkopen.2021.24116.

27. Murhekar MV, Bhatnagar T, Thangaraj JWV, Saravanakumar V, Kumar MS, Selvaraju S 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.
28. Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review. Ann Intern Med. 2020 Sep 1; 173(5):362-367. doi: 10.7326/M20-3012. Epub 2020 Jun 3. PMID: 32491919; PMCID: PMC7281624.
29. Papachristodoulou E, Kakoullis L, Parperis K, Panos G. Long-term and herd immunity against SARS-CoV-2: implications from current and past knowledge. *Pathog Dis*. 2020;78(3):ftaa025. doi:10.1093/femspd/ftaa025
30. Patel AK, Mukherjee S, Leifels M, Gautam R, Kaushik H, Sharma S, et al. Mega festivals like MahaKumbh, a largest mass congregation, facilitated the transmission of SARS-CoV-2 to humans and endangered animals via contaminated water. Int J Hyg Environ Health. 2021 Aug;237:113836. doi: 10.1016/j.ijheh.2021.113836.
31. Purkayastha S, Kundu R, Bhaduri R, Barker D, Kleinsasser M, Ray D, et al. Estimating the wave 1 and wave 2 infection fatality rates from SARS-CoV-2 in India. BMC Res Notes. 2021 Jul 8;14(1):262. doi: 10.1186/s13104-021-05652-2.
32. Pei S, Yamana TK, Kandula S, Galanti M, Shaman J. Burden and characteristics of COVID-19 in the United States during 2020. Nature. 2021 Aug 26. doi: 10.1038/s41586-021-03914-4.
33. Roederer T, Mollo B, Vincent C, Nikolay B, Llosa AE, Nesbitt R, et al. Seroprevalence and risk factors of exposure to COVID-19 in homeless people in Paris, France: a cross-sectional

Journal Pre-proof

study. Lancet Public Health. 2021 Apr;6(4):e202-e209. doi: 10.1016/S2468-2667(21)00001-3.

34. Roy, Soumya. "Low-income countries are more immune to COVID-19: A misconception." Indian Journal of Medical Sciences vol. 72,1 5–7. 30 Apr. 2020, doi:10.25259/IJMS_26_2020.
35. Royo-Cebrecos, C, Vilanova, D., López, J, Arroyo, V., et al. Mass SARS-CoV-2 serological screening, a population-based study in the Principality of Andorra. The Lancet Regional Health - Europe, 2021 May 20, 100119. doi:10.1016/j.lanepe.2021.100119.
36. Sarkar A, Chakrabarti AK, Dutta S. Covid-19 Infection in India: A Comparative Analysis of the Second Wave with the First Wave. Pathogens. 2021 Sep 21;10(9):1222. doi: 10.3390/pathogens10091222.
37. Singh BB, Ward MP, Lowerison M, Lewinson RT, Vallerand IA, Deardon R, et al. Meta-analysis and adjusted estimation of COVID-19 case fatality risk in India and its association with the underlying comorbidities. One Health. 2021 Dec;13:100283. doi: 10.1016/j.onehlt.2021.100283.
38. Song G, He WT, Callaghan S, Anzanello F, Huang D, Ricketts J, et al. Cross-reactive serum and memory B-cell responses to spike protein in SARS-CoV-2 and endemic coronavirus infection. Nat Commun. 2021 May 19;12(1):2938. doi: 10.1038/s41467-021-23074-3.
39. Ukkonen P, Hovi T, von Bonsdorff CH, Saikku P, Penttinen K. Age-specific prevalence of complement-fixing antibodies to sixteen viral antigens: a computer analysis of 58,500 patients covering a period of eight years. J Med Virol. 1984;13(2):131-48. doi: 10.1002/jmv.1890130204.
40. Varghese GM, John R. COVID-19 in India: Moving from containment to mitigation. Indian J Med Res. 2020 Feb & Mar;151(2 & 3):136-139. doi: 10.4103/ijmr.IJMR_860_20.

Journal Pre-proof

41. Wagner R, Peterhoff D, Beileke S, Günther F, Berr M, Einhauser S, et al. Estimates and Determinants of SARS-Cov-2 Seroprevalence and Infection Fatality Ratio Using Latent Class Analysis: The Population-Based Tirschenreuth Study in the Hardest-Hit German County in Spring 2020. Viruses. 2021 Jun 10;13(6):1118. doi: 10.3390/v13061118.

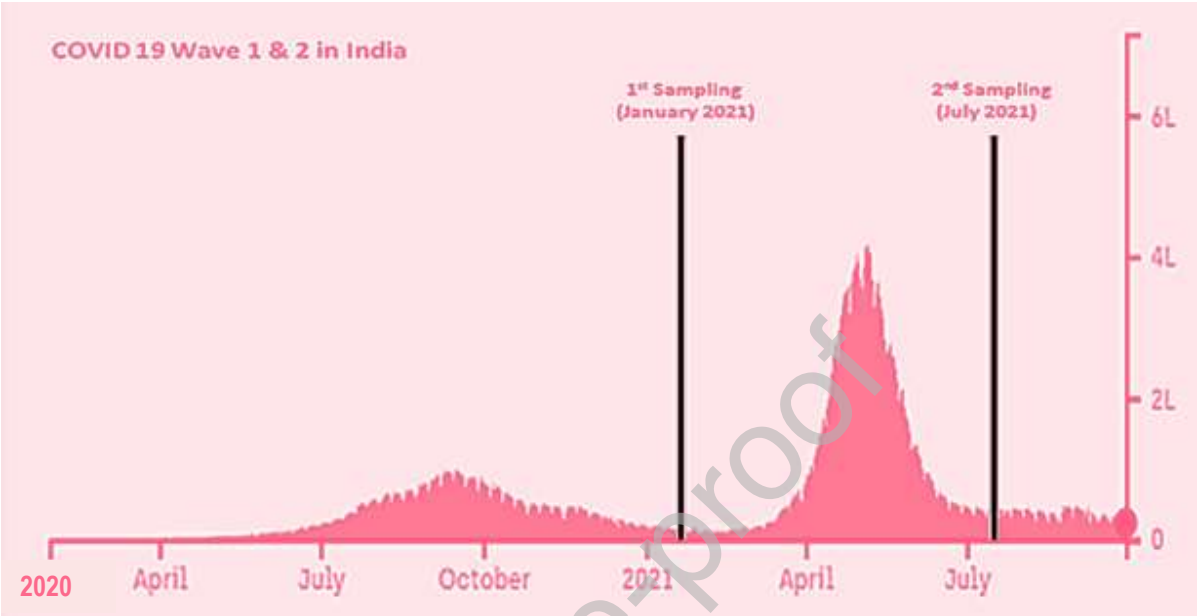
42. Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, et al. Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. Lancet. 2021 Mar 13;397(10278):1023-1034. doi: 10.1016/S0140-6736(21)00306-8. Epub 2021 Feb 12. PMID: 33587887; PMCID: PMC7906643.

43. Wu D, Wu T, Liu Q, Yang Z. The SARS-CoV-2 outbreak: What we know. Int J Infect Dis. 2020 May;94:44-48. doi: 10.1016/j.ijid.2020.03.004. Epub 2020 Mar 12. PMID: 32171952; PMCID: PMC7102543.

44. Yang W, Kandula S, Huynh M, Greene SK, Van Wye G, Li W, et al. Estimating the infection-fatality risk of SARS-CoV-2 in New York City during the spring 2020 pandemic wave: a model-based analysis. Lancet Infect Dis. 2021 Feb;21(2):203-212. doi: 10.1016/S1473-3099(20)30769-6.

Journal Pre-proof

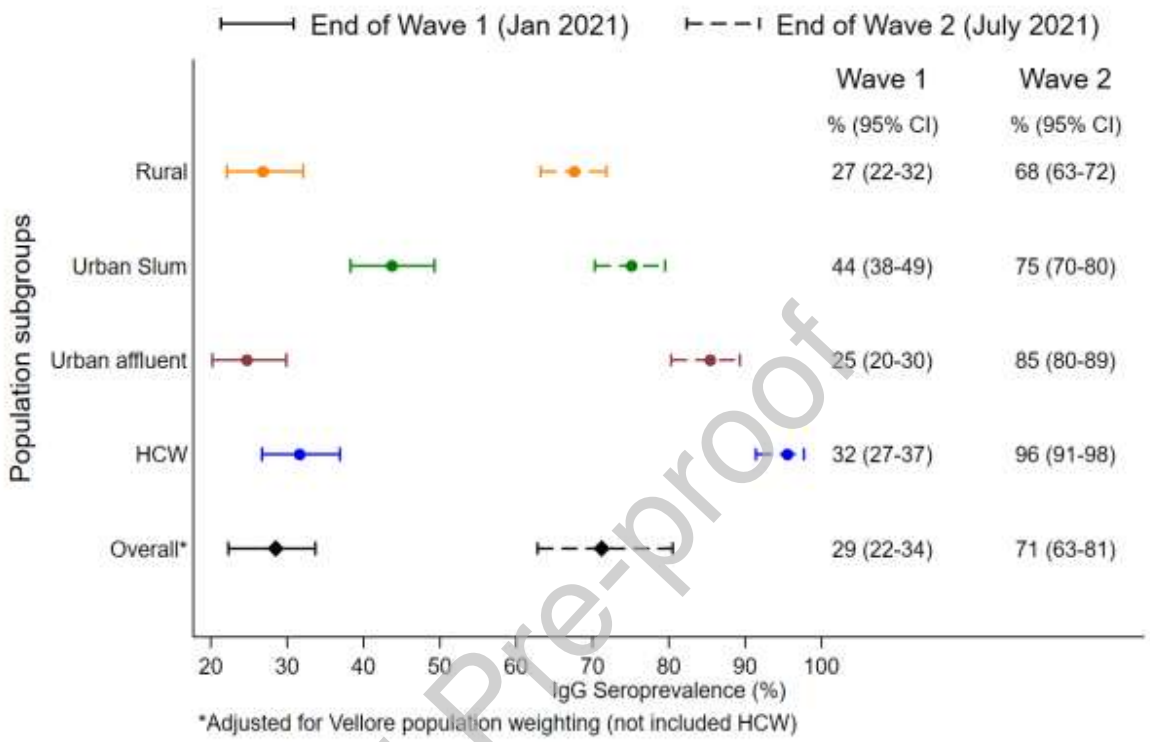
Figure 1: Wave 1 & wave 2 in India with two sampling periods (modified from Covid 19 India.org 2021**)**



This figure represents the Covid 19 peaks in India during wave 1 and wave 2. The X axis depicts the time line in months and the Y axis depicts the number of infected cases in lakhs. The study samples at the end of wave 1 were collected in January 2021 and the study samples at the end of wave 2 were collected in July 2021.

Journal Pre-proof

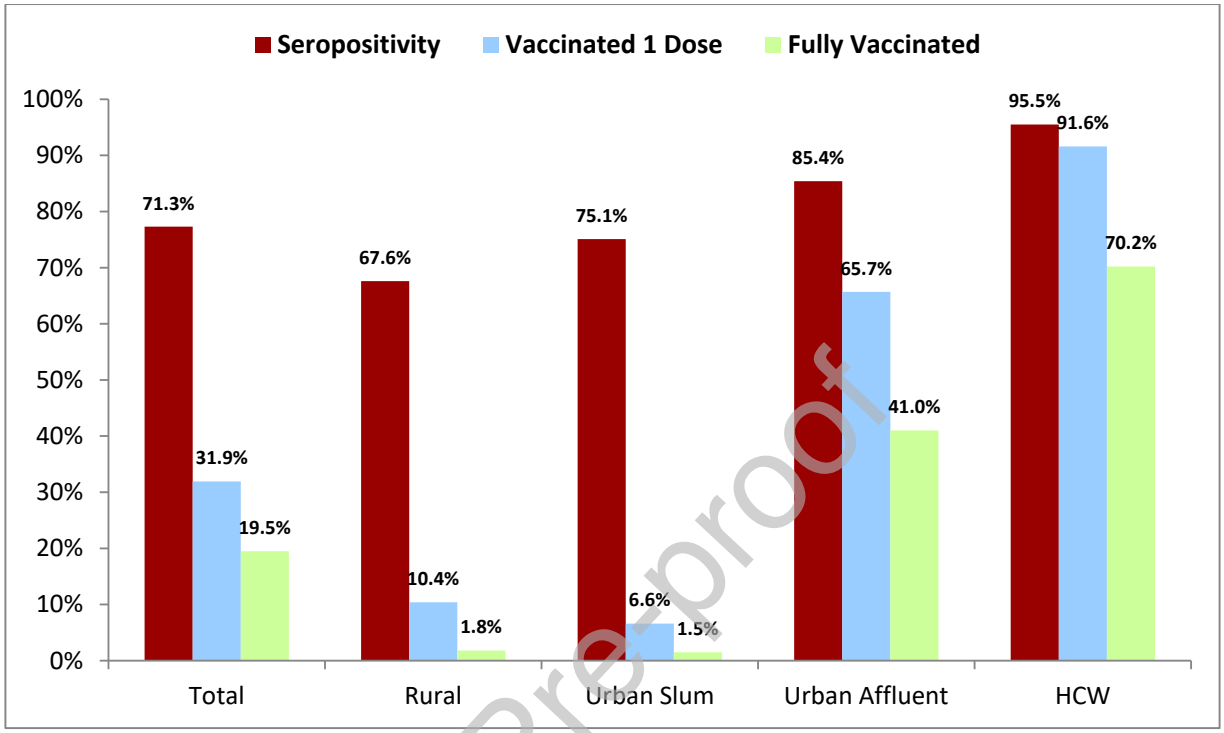
Figure 2 - Community seroprevalence in different subpopulations



This figure gives a visual representation of the community seroprevalence with the 95% confidence interval in various subpopulations at the end of wave 1 and wave 2. The X axis depicts the IgG seropositivity as a percentage and the Y axis describes the various sub populations.

Journal Pre-proof

Figure 3 - Distribution of Vellore Population by Seroprevalence and Vaccination status



This figure represents the seropositivity and vaccination status (Participants who received 1 dose and fully vaccinated) in the total study population and the various subpopulations. The rural and urban slums had the least vaccination status of 10.4% and 6.6% respectively. Healthcare workers had the highest vaccination status of 91.6% followed by urban affluent subpopulation who reported a vaccination status of 65.7% respectively.

Journal Pre-proof

Table 1 -Demographic characteristics

Demographics	Categories	Total N=2,433, n (%) or n/N (%)	Rural N=756, n (%) or n/N (%)	Urban Slum N=645, n (%) or n/N (%)	Urban Affluent N=534, n(%) or n/N (%)	Healthcare Workers N=498, n (%) or n/N (%)
Age	<20 years	454 (18.7)	159 (21)	198 (30.7)	92 (17.2)	5 (1)
	21-40 years	1,017 (41.8)	220 (29.1)	198 (30.7)	181 (33.9)	418 (83.9)
	41-60 years	698 (28.7)	253 (33.5)	185 (28.7)	188 (35.2)	72 (14.5)
	>60 years	264 (10.9)	124 (16.4)	64 (9.9)	73 (13.7)	3 (0.6)
Gender	Male	1,055 (43.4)	273 (36.1)	255 (39.5)	298 (55.8)	229 (46)
	Female	1,378 (56.6)	483 (63.9)	390 (60.5)	236 (44.2)	269 (54)
Education	Illiterate	194 (8)	107 (14.2)	87 (13.5)	0 (0)	0 (0)
	Primary to High school*	1,361 (55.9)	573 (75.8)	517 (80.2)	213 (39.9)	58 (11.6)
	Graduate	878 (36.1)	76 (10.1)	41 (6.4)	321 (60.1)	440 (88.4)
Occupation	Professional	514 (21.1)	8 (1.1)	2 (0.3)	126 (23.6)	378 (75.9)
	Semi professional	231 (9.5)	28 (3.7)	14 (2.2)	107 (20)	82 (16.5)
	Skilled worker	528 (21.7)	272 (36)	116 (18)	102 (19.1)	38 (7.6)
	Unskilled/Daily wage laborers	174 (7.2)	89 (11.8)	85 (13.2)	0 (0)	0 (0)
	Housewife/ Unemployed/ Students	986 (40.5)	359 (47.5)	428 (66.4)	199 (37.3)	0 (0)
Socioeconomic class	Upper	313 (12.9)	0 (0)	0 (0)	116 (21.7)	197 (39.6)
	Middle	923 (37.9)	144 (19)	75 (11.6)	418 (78.3)	286 (57.4)
	Lower	1,197 (49.2)	612 (81)	570 (88.4)	0 (0)	15 (3.0)
Comorbidities	Diabetes	271 (11.1)	93 (12.3)	82 (12.7)	83 (15.5)	13 (2.6)
	Hypertension	261 (10.7)	99 (13.1)	66 (10.2)	73 (13.7)	23 (4.6)
	COPD***/Asthma	51 (2.1)	11 (1.5)	5 (0.8)	10 (1.9)	25 (5)
	CAD/Heart Disease	34 (1.4)	13 (1.7)	2 (0.3)	16 (3)	3 (0.6)
Presence of symptoms**		588 (24.2)	103(13.4)	104(16.1)	151(28.3)	230(46.2)
Symptomatic infection requiring hospitalisation		99 (4.1)	0(0)	6 (0.9)	18 (3.4)	75 (15.1)
Mask usage in public places	Cloth	1,414 (58.1)	606 (80.2)	584 (90.5)	164 (30.7)	60 (12)
	Surgical	855 (35.1)	150 (19.8)	57 (8.8)	300 (56.2)	348 (69.9)
	N95	164 (6.8)	0(0)	4 (0.6)	70 (13.1)	90 (18.1)
HCoV antibodies positivity among SARS-CoV-2 + ve		391/391 (100)	81/81 (100)	136/136 (100)	73/73 (100)	101/101 (100)
HCoV antibodies positivity among SARS-CoV 2 – ve		834/837 (99.6)	221/221 (100)	172/175 (98.2)	222/222 (100)	219/219 (100)

**<12 years of formal education*

*** suggestive of recent respiratory infection in the last 6 months*

Journal Pre-proof

****COPD*, chronic obstructive pulmonary disease

Table 2 -Community seroprevalence and vaccination status in different subpopulations

Subpopulation	End of Wave 1 (Jan 2021) (N=1,228)		End of Wave 2 (July 2021) (N=1,205)			
	Serology IgG, n/N (%) or %	95% CI	Serology IgG, n/N (%) or %	95% CI	Vaccination status[#], n/N (%)	95% CI
Rural	81/302 (26.8)	22.9 - 32.2	307/454 (67.6)	63.1 - 71.9	47/454 (10.4)	7.7 - 13.5
Urban Slum	136/311 (43.7)	38.1 - 49.4	251/334 (75.1)	70.2 - 79.7	22/334 (6.6)	4.2 - 9.8
Urban affluent	73/295 (24.7)	20.0 - 30.0	204/239 (85.4)	80.2 - 89.6	157/239 (65.7)	59.3 - 71.7
Healthcare workers	101/320 (31.6)	26.5 - 37.0	170/178 (95.5)	91.3 - 98.0	163/178 (91.6)	86.5 - 95.2
Overall weighted prevalence adjusted for Vellore population	**28.5**	**22.3 - 33.7**	**71.6**	**62.8 - 80.5**	20.3	0 - 46.7

[#]received at least 1 dose of vaccine

n- seropositives, N - Total number of participants sampled, CI - Confidence Interval

Journal Pre-proof

Table 3: Seropositivity by characteristics and time period.

Demographics	Categories	Seropositivity, n/N (%)		
		End of Wave 1	End of Wave 2	Overall
Subpopulation	Rural	81/302 (26.8)	307/454 (67.6)	388/756 (51.3)
	Urban Slum	136/311 (43.7)	251/334 (75.1)	387/645 (60.0)
	Urban affluent	73/295 (24.7)	204/239 (85.4)	277/534 (51.9)
	Healthcare workers	101/320 (31.6)	170/178 (95.5)	271/498 (54.4)
Age	<20 years	75/237 (31.6)	162/217 (74.7)	237/454 (52.2)
	21-40 years	166/540 (30.7)	385/477 (80.7)	551/1,017 (54.2)
	41-60 years	105/317 (33.1)	294/381 (77.2)	399/698 (57.2)
	>60 years	45/134 (33.6)	91/130 (70.0)	136/264 (51.5)
Gender	Male	168/558 (30.1)	379/497 (76.3)	547/1,055 (51.8)
	Female	223/670 (33.3)	553/708 (78.1)	776/1,378 (56.3)
Education	Graduate	161/534 (30.1)	307/344 (89.2)	468/878 (53.3)
	Primary to High school*	199/616 (32.3)	552/745 (74.1)	751/1,361 (55.2)
	Illiterate	31/78 (39.7)	73/116 (62.9)	104/194 (53.6)
Occupation	Professional	94/332 (28.3)	170/182 (93.4)	264/514 (51.4)
	Semi professional	31/109 (28.4)	111/122 (91.0)	142/23 1(61.5)
	Skilled worker	71/214 (33.2)	222/314 (70.7)	293/528 (55.5)
	Unskilled/Daily wage laborers	29/63 (46.0)	71/111 (64.0)	100/174 (57.5)
	Housewife/ Unemployed/ Students	166/510 (32.5)	358/476 (75.2)	524/985 (53.1)
Socioeconomic	Upper	41/197 (20.8)	106/116 (91.4)	147/313 (47.0)

Journal Pre-proof

	Middle	188/554 (33.9)	319/369 (86.4)	507/923 (54.9)
	Lower	162/477 (34.0)	507/720 (70.4)	669/1,197 (55.9)
Smoking Habit	Smoker	14/38 (36.8)	0/0 (NA)	14/38 (36.8)
	Non-smoker	377/1,190 (31.7)	932/1,205 (77.3)	1,309/2,395 (54.7)
Alcohol Consumption	Alcohol consumer	14/41 (34.1)	2/2 (100.0)	16/43 (37.2)
	Non-consumer	377/1,187 (31.8)	930/1,203 (77.3)	1,307/2,390 (54.7)
Comorbidities	No comorbidities	301/989 (30.4)	749/976 (76.7)	1,050/1,965 (53.4)
	Diabetes	33/70 (47.1)	56/72 (77.8)	89/142 (62.7)
	Hypertension	28/70 (40.0)	54/65 (83.1)	82/135 (60.7)
	Asthma/ chronic obstructive pulmonary disease	3/30 (10.0)	12/14 (85.7)	15/44 (34.1)
	CAD/ Heart Disease	3/4 (75.0)	6/8 (75.0)	9/12 (75)
	Any two or more comorbidities	23/65 (35.4)	55/70 (78.6)	78/135 (57.8)
Presence of symptoms**	Yes	120/339 (35.4)	210/249 (84.3)	330/588 (56.1)
	No	271/889 (30.5)	722/956 (75.5)	993/1,845 (53.8)
Close contact with confirmed cases	Yes	102/320 (31.9)	171/182 (94.0)	273/502 (54.4)
	No	289/908 (31.8)	761/1,023 (74.4)	1,050/1,931 (54.4)
Mask usage In public places)	Cloth	218/645 (33.8)	552/769 (71.8)	770/1,414 (54.5)
	Surgical	148/473 (31.3)	333/382 (87.2)	481/855 (56.3)
	N95	25/110 (22.7)	47/54 (87.0)	72/164 (43.9)

**<12 yrs of formal education*

***suggestive of recent respiratory infection in the last 6 months*

Journal Pre-proof

Table 4: Univariate and Multivariable Analysis of factors associated with seropositivity adjusted for clustering effects of time periods

Demographics	Categories	Univariate Odds Ratio (OR) (95 confidence interval)	p-value	Multivariable (Adjusted) OR (95 confidence interval)	p-value
Subpopulation	Rural	(ref)		(ref)	
	Urban Slum	1.95 (1.52-2.49)	<0.001	2.01 (1.57-2.59)	<0.001
	Urban affluent	1.51 (1.17-1.95)	0.002	0.95 (0.65-1.39)	0.786
	Healthcare workers	2.13 (1.64-2.78)	<0.001	1.472 (0.93-2.33)	0.099
Age [a]	<20 years	(ref)			
	21-40 years	1.13 (0.88-1.45)	0.342		
	41-60 years	1.10 (0.84-1.44)	0.482		
	>60 years	0.93 (0.66-1.31)	0.695		
Gender [a]	Male	(ref)			
	Female	1.14 (0.95-1.36)	0.163		
Education	Graduate	(ref)			
	Primary to High school*	0.76 (0.63-0.93)	0.006	0.92 (0.66-1.29)	0.641
	Illiterate	0.62 (0.44-0.89)	0.009	0.77 (0.48-1.25)	0.295
Occupation	Professional	(ref)		(ref)	

Journal Pre-proof

	Semi professional	1.13 (0.79-1.60)	0.516	0.85 (0.53-1.36)	0.496
	Skilled worker	0.70 (0.53-0.93)	0.012	0.72 (0.42-1.23)	0.223
	Unskilled/Daily wage laborers	0.69 (0.47-1.04)	0.074	0.81 (0.43-1.53)	0.510
	Housewife/ Unemployed/ Students	1.81 (0.64-1.03)	0.089	0.86 (0.51-1.47)	0.584
Socioeconomic class	Upper	(ref)		(ref)	
	Middle	1.39 (1.05-1.86)	0.024	1.77 (1.17-2.67)	0.007
	Lower	0.90 (0.68-1.19)	0.471	1.04 (0.59-1.83)	0.900
Smoking Habit [a]	Smoker	1.25 (0.64-2.45)	0.509		
	Non-smoker	(ref)			
Alcohol Consumption [a]	Alcohol consumer	1.16 (0.61-2.21)	0.65		
	Non-consumer	(ref)			
Comorbidities	No comorbidities	(ref)		(ref)	

Journal Pre-proof

	Diabetes	1.46 (1.03-2.08)	0.034	1.72 (1.15-2.58)	0.009
	Hypertension	1.35 (0.94-1.93)	0.101	1.75 (1.16-2.64)	0.008
	Asthma/ chronic obstructive pulmonary disease	0.56 (0.28-1.13)	0.104	0.49 (0.24-1.02)	0.056
	CAD/ Heart Disease	2.21 (0.52-9.33)	0.281	2.46 (0.59-10.23)	0.216
	Any two or more comorbidities	1.19 (0.79-1.76)	0.395	1.46 (0.97-2.21)	0.073
Presence of symptoms**, [a]	Yes	1.09 (0.91-1.32)	0.329		
	No	(ref)			
Close contact with confirmed cases [a]	Yes	1.00 (0.82-1.22)	0.998		
	No	(ref)			
Mask usage (Public places)	Cloth	(ref)		(ref)	
	Surgical	1.38 (1.13-1.28)	0.001	1.15 (0.89-1.47)	0.271
	N95	0.97 (0.67-1.39)	0.868	0.80 (0.52-1.23)	0.316

**<12 years of formal education*

*** suggestive of recent respiratory infection in the last 6 months*

[a]*This factor was not included in the multivariable analysis because it was not significant in univariate analysis.*

Journal Pre-proof