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Research Article

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A Retrospective Clinico-demographic Study of SARS-CoV-2 Patients at a Tertiary Care Centre, Assam, North-East India during the Second Wave of the Pandemic

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Abstract

Assam along with the entire country of India experienced an unprecedented rise in SARS-CoV-2 infections and its fatal repercussions. Our earlier study during the first wave of the pandemic provided insight into the relationship between age and gender in COVID-19 cases. The present follow-up study is a retrospective Clinico-demographic Study of 1110 SARS-CoV-2 Patients during the Second Wave of the Pandemic. Out of the 1110 positive cases studied during the peak of the COVID-19 second wave, a total of 624 (56.21%) infected individuals were male, and 486 (43.7%) individuals were female. However, individuals in the age group 18-30 showed significant infection of COVID-19 cases (p>0.00001) suggesting higher susceptibility in this age group irrespective of gender. In addition, the highest number of positive symptomatic cases in males were seen in the age group of 31-40 years followed by the age group of 18-20 years. The clinical profiles of all COVID-19-infected symptomatic patients were also analyzed. While females were more likely to experience symptoms like nausea, bodily aches, and abdominal pain (p< 0.0001). Male patients were substantially more likely than female patients to experience chest pain (p = 0.0006) and diarrhea (p <0.0001*). Additionally, throughout the duration of the study, 115 samples were sent over for sequencing in which the delta variant [B.1.617.2] was found to be the most common strain during the Second Wave. Our research will add to the body of information that might help develop data-driven North-East India-centric recommendations to improve the preparedness to respond to similar future emergencies.*

Keywords: SARS-CoV-2, Clinico-Demographic, Symptomatic, Delta Variant, Susceptibility

List of Abbreviations used:

1. COVID-19: Coronavirus Disease 19
2. WHO: World Health Organisation
3. NE India: North-East India
4. ICMR: Indian Council of Medical Research
5. MoH&FW: Ministry of Health and Family Welfare
6. VTM: Virus transport medium
7. RNA: Ribonucleic acid
8. NGS: Next-Generation Sequencing
9. RGSL: Regional Genome Sequencing Laboratories

10. PCR: Real-time reverse-transcriptase polymerase chain reaction
11. INSACOG: Indian SARS-CoV-2 Genomics Consortium
12. (VoC) & (VoI): Variant of Concern and Variant of Interest
13. ACE-2: Angiotensin converting enzyme-2

1. Introduction

Just over two years ago, a new coronavirus called SARS-CoV-2, which caused the coronavirus disease 19 (COVID-19) pandemic, unleashed an unanticipated attack on the world. On December 31, 2019, reports of COVID-19 in people were made for the first time. The coronavirus (COVID-19) disease was classified as a worldwide pandemic by the World Health Organisation (WHO) on March 11, 2020 [1]. SARS-CoV-2 is a Coronaviridae virus with the genus Betacoronavirus, the subgenus Sarbecovirus, and the species severe acute respiratory syndrome-related coronavirus [2]. The word "wave," which has a specific technical meaning, is used to describe a disease's rising and declining tendencies over an extended period. Over the past two years, there have been two different waves of COVID-19 infections in India. In September 2020, the first wave's peak was attained. Beginning in March-April 2021, the second wave peaked in the first week of May 2021. The World Health Organisation (WHO) reports that during the first week of May 2021, India recorded an average of 390,000 new cases, with a peak of 414,188 cases reported on May 7th, 2021. Following that, there was a sharp decline in the number of new cases from June on, with just 7,495 instances recorded on December 20, 2021, until a new upsurge in cases began in the first week of January, which may have been the third wave and quickly waned [3].

Developing measures intended to reduce transmission throughout the population as a whole and estimating the anticipated global burden both depend on understanding the role of age in transmission. Preliminary shreds of evidence point to an age-dependent sensitivity to and risk of clinical symptoms following SARS-CoV-2 infection [4, 5]. Our earlier study during the first wave of the pandemic provided insight into the relationship of age and gender with COVID-19 cases, particularly when it showed that the most affected age group in both men and females was in the younger age range. Although males were affected more than females [6].

Considering the importance of the above study during the first wave of the pandemic, it was pertinent to follow up the exercise to understand the clinico-demographic profile of patients affected during the second wave. In addition to comprehending the disease pattern, the data obtained by this study may be employed in various mathematical models to develop credible future forecasts of the anticipated surges of infection and identify sensitive population proportions. Our research will expand on the body of information and might help local health authorities develop North-East (NE) India-centric recommendations that are data-driven and increase their readiness to respond to future emergencies of a similar nature.

2. Materials and Methods

2.1. Study population:

The data for the study were collected and analyzed as part of outbreak investigations during the second wave of the Covid-19 public health emergency. Considering the processing of COVID-19 data is essential for public interest in the sphere of public health, such as protection against serious cross-border health threats or ensuring high quality and safety of health care, this study was exempted from institutional review board approval. India was one of the most affected nations in the world during the initial wave of the COVID-19 pandemic. As a result, when cases began to rise in April 2021, spatially focused restrictions like a ban on mass gatherings and the installation of quarantined zones around the most vulnerable towns were promptly reinstated. Non-essential productive activity in quarantined zones was suspended, and strong individual mobility restrictions were implemented.

We examined the close contacts of COVID-19 cases found in the Sonitpur, Biswanath, and Udalguri districts of Assam during contact tracing operations carried out by regional health authorities between April 2021 and August 2021. Through standardized epidemiological investigations, close connections of cases with laboratory confirmation were found to ascertain the course of each person's exposure. Close contacts of those who could not take part in the contact tracing interview were identified through their emergency contacts. Close contacts of the patients were informed of their possible exposure within 24 hours following a positive test result for the index cases. All identified contacts were confined and monitored after 7 days of positive tests. Regardless of any clinical signs, all contacts with confirmed COVID-19 infections were screened using RTPCR from April to August 2021. Positive people were isolated, and their information was recorded in a database of laboratory-confirmed infections.

2.2 Sample Description

Study participants were selected from an initial database of 72403 individuals suspected of Covid-19 of which a total of 1110 confirmed SARS-CoV-2 positive cases were identified. Individuals tested after August 31, 2021, were excluded to avoid biases caused by delays in symptom development, or potential exposure after the gradual lifting of imposed restrictions during the national lockdown.

2.3 Data Collection:

All patients' epidemiological and clinical information was obtained from the COVID-19 SRF created by the Indian Council of Medical Research (ICMR). For each patient who had a SARS-CoV-2 test, the appropriate information was filled out on the form, which also inquired about the patient's age, gender, occupation, testing methods, clinical signs and symptoms, history of contact with COVID- 19 patients, medical history, including co-morbidities, quarantine, and travel history. Throughout the pandemic, this form was modified and changed several Times to reflect new testing techniques, clinical indications, and symptoms, and the most recent edition noted the level of immunization [7].

2.4. Classification of COVID-19-infected patients:

All patients were classified using the most recent WHO and Ministry of Health and Family Welfare (MoH&FW) criteria. Asymptomatic patients were those who had no symptoms. Furthermore, for the objective of comparing individuals with severe illness, patients who were asymptomatic or were classified

as having mild or moderate disease were grouped as nonsevere COVID-19.

2.5 Laboratory Confirmation:

Standard methods were used to collect samples from the throat and/or nasopharynx. The samples were then placed into a single virus transport medium (VTM), transferred to the microbiology lab while preserving cold chain, and kept there at -20 °C until being processed. Ribonucleic acid (RNA) was extracted from the samples in the lab using a variety of ICMR approved kits during the entire course of the pandemic. The extraction process strictly followed the manufacturer's directions. The RNA elute was subjected to a multiplex qRT-PCR test to identify targets unique to SARS-CoV-2. Genes unique to SARS-CoV-2 such as the E gene, ORF 1ab, N gene, and RdRp gene were amplified. The manufacturer's instructions were strictly followed during the preparation of the master mix, the programming of the real-time PCR thermocycler, the subsequent assay run validation, and the interpretation of the results. Samples with an exponential amplification profile for the target genes' cycle threshold (Ct) were classified as positive and documented.

2.5 Sequencing of Samples:

Next-generation sequencing (NGS) was done on samples from individuals with severe illnesses, lengthy recoveries, other abnormal clinical presentations, and patients with a history of overseas travel. According to the instructions of the regional health authorities, a representative sample set from these individuals was forwarded to authorized regional genome sequencing laboratories (RGSL) for sequencing. According to the region, the government portal's sequencing data was updated. Sequencing data, however, was not individually distributed to the institute or other laboratories [8].

2.6 Data analysis:

The data were analyzed by using XLSTAT (version 23.1.1094.0). Descriptive statistics and Chi-square tests were done and the significance of the tests was decided at P=0.0

3. Results

3.1 Study Design:

For this retrospective, single-center study, patients were recruited at the peak of the 2nd wave in India from April 2021 to August 2021, at Viral Research and Diagnostic Laboratory (VRDL), Tezpur Medical College and Hospital (TMCH), Assam. Patient details were collected from the hospital facility. During this period, a total of 72,403 samples suspected of COVID-19 were tested by Real-time reverse-transcriptase polymerase chain reaction (PCR) and a total of 1110 participants tested positive for COVID-19.

3.2 Males were more susceptible to Covid-19 as compared to females:

TOTAL POSITIVE SAMPLES	**1110**	Percentage
MALE	624	56.21%
FEMALE	486	43.70%

Table 1: Gender-wise Distribution of Covid-19 Positive Cases at the Study Centre

Out of the 1110 positive cases during the peak of the COVID-19 second wave, a total of 624 (56.21%) infected individuals were male and 486 (43.7%) individuals were female (Table 1). While females still contracted the disease less than males, the positivity of females was markedly high as compared to the first wave of the disease (81% males and 19% females).

3.3 Individuals in the younger age groups were more susceptible to Covid-19:

While conducting the details analysis of age group distributions, the age groups of 0-9 and 10-17 were taken together. In addition, the overall infected cases in the age groups of 18-30, 31-40, 41-50, 51-60, and ≥60 were analyzed. Interestingly, individuals aged 18-30 (312 cases, 27.32%) and 31-40 (236 cases, 20.66%) were the only two age groups showing maximum positive cases (Figure 1). It may be noted that individuals in the age group 18-30 showed significant infection of COVID-19 cases ($p>0.00001$) suggesting higher susceptibility in this age group irrespective of gender. No significant difference was observed in the other age groups.

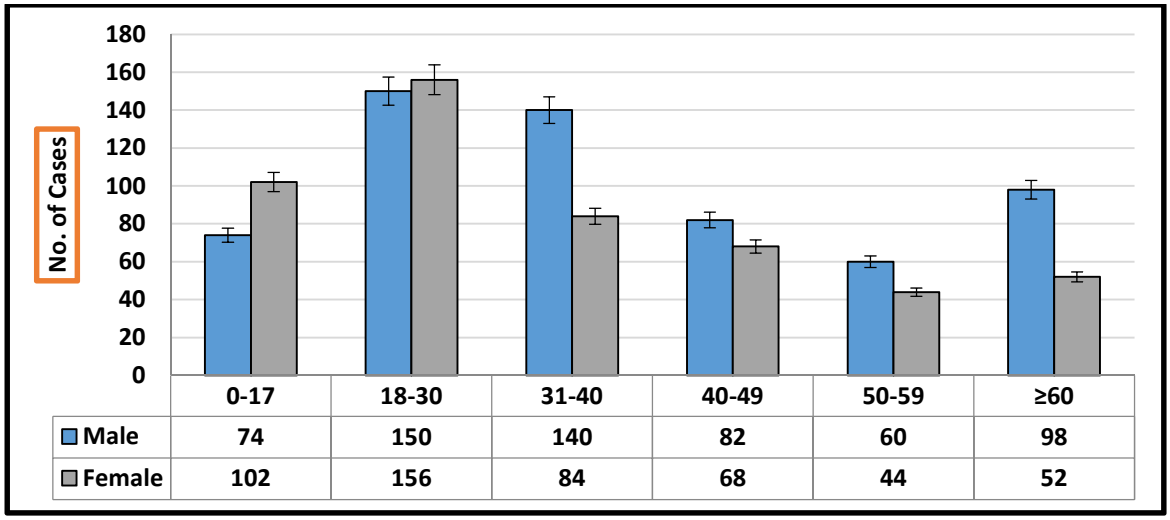

Figure 1: Gender Wise Distribution of COVID-19 cases in different age groups

3.4 Prevalence of Asymptomatic COVID-19 cases to that of symptomatic cases:

Symptomatic COVID-19 cases accounted for only 120 (10.8%) cases out of the total 1110 positive cases included in the study. Asymptomatic cases were markedly higher 990 (89.1%) than the symptomatic cases (Figure 2).

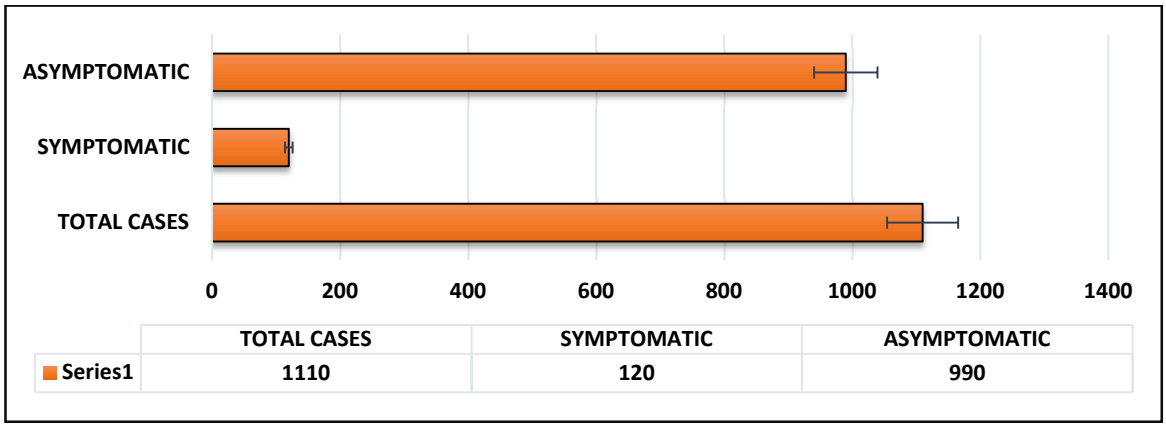

Figure 2: Distribution of Symptomatic and Asymptomatic Covid-19 Positive Cases at the Study Centre

Further analysis of symptomatic and asymptomatic Covid-19 cases of both genders was undertaken. The positive cases were stratified according to age group and gender (Table 2). Most of the transmissions took place from male patients. The highest number of positive symptomatic cases in males were seen in the age group of 31-40 years followed by the age group of 18-20 years. The total number of symptomatic male patients accounted for 12.26% of the total cases (Table 2-A). In contrast, the highest number of positive symptomatic in females was seen in the age group of 50-59 years. Further, the total number of symptomatic female patients accounted for just 8.3% of the total cases (Table 2-B)

(A) Male Age Group	Symptomatic	Asymptomatic	**(B)** Female Age Group	Symptomatic	Asymptomatic
0-17	4	70	**0-17**	6	96
18-30	16	134	**18-30**	8	148
31-40	26	114	**31-40**	6	78
40-49	12	70	**40-49**	2	66
50-59	8	52	**50-59**	16	28
≥60	12	86	**≥60**	4	48
Total	**78**	**526**	**Total**	**42**	**464**

Table 2: Distribution of Symptomatic and Asymptomatic Covid-19 COVID-19-positive cases at the study Centre (A) Different Male age groups (B) Different Female age groups

3.5 The district of Sonitpur showed the highest load of confirmed positive cases:

Samples from 3 districts of Assam namely Sonitpur, Biswanath, and Udalguri districts were tested at the VRDL, TMCH laboratory during the second COVID-19 wave. Out of the 1110 positive cases taken in the present study, a total of 582 cases were from the Sonitpur district which was followed by the districts of Biswanath (398 cases) and Udalguri (130 cases). It is worth noting that a total of 16.1% out of the 582 cases in the Sonitpur district were symptomatic cases. In contrast, symptomatic cases from Biswanath and Udalguri districts accounted for only 3.5% and 6.1% respectively.

Districts	Total	Symptomatic	Asymptomatic
Sonitpur	582	94 (16.1%)	488 (83.8%)
Biswanath	398	14 (3.5%)	384 (96.4%)
Udalguri	130	8 (6.1 %)	122 (93.8%)

Table 3: District-wise distribution of Positive patients (Symptomatic and Asymptomatic) tested at the Study Centre.

3.6 Clinical characteristics of symptomatic individuals tested at the hospital screening site as well as hospitalized patients:

Symptoms	Male (%) n=72	Female (%) n=42	p-value*
Fever	56 (77.7)	32 (76.1)	0.8
Body Ache	22 (30.5)	27 (64.2)	**< 0.0001***
Sore Throat	48 (66.6)	29 (69.0)	0.9
Nasal Discharge	45 (62.5)	25 (59.5)	0.84
Cough	44(61.1)	26 (61.9)	0.58
Abdominal pain	16 (22.2)	24 (57.1)	**< 0.0001***
Diarrhea	23 (31.9)	7 (16.6)	**< 0.0001***
Vomiting	18 (25.0)	20 (47.6)	**< 0.0001***
Chest Pain	30 (41.6)	8 (19.0)	**0.0006***
Loss of smell	15 (20.8)	9 (21.4)	0.52
Loss of Taste	16 (22.2)	9 (21.4)	0.43

Table 4: Comparison of clinical profile of symptomatic COVID-19 infected patients (Male and Female).

*Each of the symptomatic patients had one or more symptoms; n: number of patients, when $p < 0.05$, the two proportions differ significantly.

The clinical profiles of all COVID-19-infected symptomatic patients tested at the hospital's screening point as well as of hospitalized patients (Both male and female) together with their statistical significance are listed in Table 4. The majority of the symptoms reported during both the first and second waves of the study were found to be similar. Interesting as it may be, some of the symptoms were significantly higher in men and vice versa. While females were more likely to experience symptoms like nausea, bodily aches, and abdominal pain ($p< 0.0001$*). Male patients were substantially more likely than female patients to experience chest pain ($p = 0.0006$) and diarrhea ($p <0.0001$*). The proportion of other symptoms was the same for both genders, and the difference was not statistically significant.

3.7 Sequencing Results:

Throughout the duration of the study, 115 samples were sent over for sequencing. According to the week-by-week sequencing data for the North East Indian region posted on the website of the Indian SARS-CoV-2 Genomics Consortium (INSACOG), the delta variant [B.1.617.2] was the most common strain circulating in this region during the Second Wave. The major strains circulating during the First Wave, in contrast, belonged to the 'other lineage' category, which comprises strains other than those classified by WHO as Variant of Concern (VoC) and Variant of Interest (VoI) [8, 9].

4. Discussion

SARS-CoV-2, along with MERS, is one of the most virulent infections causing severe acute respiratory disease in humans. In accordance with initial case studies from China, COVID-19 was demonstrated as a respiratory illness with a spectrum of symptoms that can range from moderate sickness (81%), severe respiratory distress (14%), and critical illness in 5% of cases, with a case fatality rate of roughly 2.4 percent. Additionally, there are significant differences in demographic and clinical trends between nations on different continents [10]. The fact that there have been regional variations in health literacy, healthcare equity, and general public risk perceptions in India, a country with a

sizable population, highlights the significance of having access to regionspecific epidemiological data that will help local health authorities develop guidelines and policies to prevent and control a future COVID-19 infection surge. In addition, the genetic makeup, environment, traditions, and geography of NE India are noticeably different from those of the rest of the nation [7, 9, 11]. Assam is one of the seven sisters of North-East India, sharing international borders that have multiple neighboring countries, including Tibet in the north, Myanmar in the east, and Bangladesh, Bhutan, and Nepal in the west, all of which were affected by the pandemic. As a result, Assam as well as the rest of the NE Indian states stands vulnerable to future breakouts [12-15].

Our investigation revealed intriguing COVID-19 case trajectories in individuals based on gender, age groupings, and clinical presentation. Our study was consistent with previous studies as well as study from our group during the first wave in which males were more susceptible to Covid-19 disease as compared to females [16, 17]. At all ages, there are differences between the prevalence and course of infectious diseases based on gender, with males generally carrying a heavier burden of bacterial, viral, fungal, and parasitic infections [18, 19]. In coronavirus outbreaks in the past, both SARS and MERS-CoV, men have been observed to contract CoV at higher rates than women [20, 21]. The strong sex bias seen in the COVID-19 pandemic is likely caused by basic disparities in the immune response between males and females, notwithstanding the possibility that socioeconomic variables are impacting some elements of the pandemic. In terms of the adaptive immune system, females produce more B cells and immunoglobulin than males, have more CD4+ T cells than males, and have stronger CD8+ T cell cytotoxic activity. The X chromosome and sex hormones, which have been demonstrated to play a role in innate and adaptive immunity, may be responsible for women being less susceptible to infection [22-24].

Further, Age groups 18 to 30 years and 31 to 40 years had the highest percentages of positive cases. It must be highlighted that people between the ages of 18 and 30 years demonstrated a considerable COVID-19 infection rate ($p>0.00001$), indicating increased vulnerability in this age range regardless of gender. In the other age categories, there was no significant difference. Interestingly, our data was consistent with other studies from North India [25, 26]. Contrarily, a small number of studies from China, New York, and Italy reported a median age (59–63 years) that was higher and more susceptible to the disease [17, 27, 28].

The current study investigated whether there exists any gender bias in the development of symptoms in symptomatic patients. It was learned that general symptoms such as fever, sore throat, nasal discharge, cough, and loss of smell and taste occurred in almost equal proportions in men and women. This could be attributable to the delta strain, which was prevalent in the country, including NE India, during the second wave [29, 30]. WHO classed it as a VoC since it had been identified to be highly transmissible and virulent, with certain distinctive clinical hallmarks? Interestingly, females were found more likely to experience symptoms like nausea, bodily aches, and abdominal pain ($p< 0.0001$*). Male patients were substantially more likely than female patients to experience chest pain ($p = 0.0006$) and diarrhea ($p <0.0001$*). While studies regarding the mechanisms employed by the virus during the infection are still in their naive phases, preliminary studies have shown that Angiotensin converting enzyme-2 (ACE-2) receptors are the entrance point for SARS-CoV-2, potentially with the aid of transmembrane serine protease-2. Since ACE2 is known to play a significant role in regulating intestinal inflammation, therefore, the mechanism has been postulated to be the cause of diarrhea in COVID-19 patients [31]. It may also contribute to the virus's potential trans-neuronal propagation to the olfactory bulb, which would cause anosmia [32].

While much emphasis has been placed on symptomatic patients of all ages, it would be unwise to ignore the asymptomatic Covid-19 positive individuals, as increasing evidence has shown that people who are asymptomatic spread the virus effectively, and the growing number of these silent SARS-CoV-2 spreaders hampered the pandemic control [33, 34]. However, our knowledge of the clinical characteristics and immunological responses of asymptomatic patients infected with SARS-CoV-2 is still remarkably limited and requires further research.

Furthermore, due to a lack of funding, manpower, and technical competence, we were unable to undertake sequencing at our Institute. However, Given North-East India's particular regional significance and the global requirement to produce and share genomic and serological profiles of SARS-CoV-2 transmission and evolution, our samples were forwarded to authorized regional genome sequencing laboratories (RGSL) for sequencing [8]. The devastating second wave of COVID-19 cases in India in 2021 corresponds with the prevalence of B.1.617.2 (Delta variant) and its other major sub-lineages AY.4/AY.x16. Delta outbreaks may be correlated to their high transmissibility, capacity to escape immune responses within the human body, and diagnostic detection failure. Increased viral replication and mutation are the prime evolutionary mechanisms that result in the emergence of more transmissible and deadly virus variants [35-37].

5. Conclusion

In conclusion, the data obtained from the study will contribute to our understanding of SARSCoV-2 infections in the population of Assam, North-East India. The data produced by this study may be used in various mathematical models to develop reliable future projections of anticipated surges of infection and identify sensitive population proportions. Our research will add to the body of knowledge and may assist local health authorities in developing data-driven recommendations for North-East (NE) India and increasing their readiness to respond to future catastrophes of a similar sort.

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References

1. Ghinai, I., McPherson, T. D., Hunter, J. C., Kirking, H. L., Christiansen, D., et al. (2020). First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA. The Lancet, 395(10230), 1137-1144.
2. Gorbalenya, A. E., Baker, S. C., Baric, R. S., De Groot, R. J., Drosten, C., et al. (2020). The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol. 2020; 5: 536–44. Clinical Nutrition, 39, 2324.
3. World Health Organization. (2020). Coronavirus disease (COVID-19), 12 October 2020.
4. Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., et al. (2020). Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine, 382(18), 1708-1720.
5. Mueller, A. L., McNamara, M. S., & Sinclair, D. A. (2020). Why does COVID-19 disproportionately affect older people?. Aging (albany NY), 12(10), 9959.
6. Alam, S. T., Biswas, S., Bezborah, K., Begum, S., Pathak, M., et al. (2021). A Retrospective Study of COVID-19 Cases Based on Age and Gender in Patient's Visiting Tertiary Care Centre, Tezpur Medical College and Hospital, Tezpur, Assam. Int. J. Curr. Microbiol. App. Sci, 10(09), 128-139.
7. Kumar, K. R., Mufti, S. S., Sarathy, V., Hazarika, D., & Naik, R. (2021). An update on advances in COVID-19 laboratory diagnosis and testing guidelines in India. Frontiers in public health, 9, 568603.
8. Mlcochova, P., Kemp, S., Dhar, M. S., Papa, G., Meng, B., et al. (2021). SARS-CoV-2 B. 1.617. 2 Delta variant emergence, replication and sensitivity to neutralising antibodies. BioRxiv, 2021-05.
9. Prasad, A. K., Khyriem, A. B., Lyngdoh, W. V., Lyngdoh, C. J., Phukan, A. C., et al. (2023). Clinico-demographic profile of COVID-19 positive patients-first wave versus second wave–an experience in north-east India. The Journal of Infection in Developing Countries, 17(02), 166-177.
10. Wu, Z., & McGoogan, J. M. (2020). Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. jama, 323(13), 1239-1242.
11. Majumder, P. P., & Basu, A. (2015). A genomic view of the peopling and population structure of India. Cold Spring Harbor perspectives in biology, 7(4), a008540.
12. Samarasekera, U. (2021). Bhutan: small nation, big ideas affecting respiratory health. The Lancet Respiratory Medicine, 9(7), e67-e68.
13. Shrestha, U. K. (2021). B. 1.617. 2 variant and increasing surge of COVID-19 in Nepal. Nepal Mediciti Medical Journal, 2(1), 1-4.
14. Win, A. (2020). Rapid rise of COVID-19 second wave in Myanmar and implications for the Western Pacific region. QJM: An International Journal of Medicine, 113(12), 856-857.
15. Xu, J., & Cao, B. (2021). Letter from China: managing the second-wave COVID-19 outbreak in Beijing. Respirology (Carlton, Vic.), 26(3), 275-276.
16. Ortiz-Prado, E., Simbaña-Rivera, K., Barreno, L. G., Diaz, A. M., Barreto, A., et al. (2021). Epidemiological, socio-demographic and clinical features of the early phase of the COVID-19 epidemic in Ecuador. PLoS neglected tropical diseases, 15(1), e0008958.
17. Richardson, S., Hirsch, J. S., Narasimhan, M., Crawford, J. M., McGinn, T., Davidson, K. W., ... & Northwell COVID-19 Research Consortium. (2020). Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. Jama, 323(20), 2052-2059.
18. Park, M. D. (2020). Sex differences in immune responses in COVID-19. Nature Reviews Immunology, 20(8), 461-461.
19. Fischer, J., Jung, N., Robinson, N., & Lehmann, C. (2015). Sex differences in immune responses to infectious diseases. Infection, 43, 399-403.
20. Flanagan, K. L., Fink, A. L., Plebanski, M., & Klein, S. L. (2017). Sex and gender differences in the outcomes of vaccination over the life course. Annual review of cell and developmental biology, 33, 577-599.
21. Takahashi, T., Ellingson, M. K., Wong, P., Israelow, B., Lucas, C., et al. (2020). Sex differences in immune responses that underlie COVID-19 disease outcomes. Nature, 588(7837), 315-320.
22. Abdullah, M., Chai, P. S., Chong, M. Y., Tohit, E. R. M., Ramasamy, R., et al. (2012). Gender effect on in vitro lymphocyte subset levels of healthy individuals. Cellular immunology, 272(2), 214-219.
23. Mori, M., Adland, E., Paioni, P., Swordy, A., Mori, L., et al. (2015). Sex differences in antiretroviral therapy initiation in pediatric HIV infection. PloS one, 10(7), e0131591.
24. Shepherd, R., Cheung, A. S., Pang, K., Saffery, R., & Novakovic, B. (2021). Sexual dimorphism in innate immunity: the role of sex hormones and epigenetics. Frontiers in immunology, 11, 604000.
25. Soni, S. L., Kajal, K., Yaddanapudi, L. N., Malhotra, P., Puri, G. D., et al. (2021). Demographic & clinical profile of patients with COVID-19 at a tertiary care hospital in north India. The Indian journal of medical research, 153(1-2), 115.
26. Gupta, N., Agrawal, S., Ish, P., Mishra, S., Gaind, R., et al. (2020). Clinical and epidemiologic profile of the initial COVID-19 patients at a tertiary care centre in India. Monaldi archives for chest disease, 90(1).
27. Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., et al. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet, 395(10229), 1054-1062.
28. Grasselli, G., Zangrillo, A., Zanella, A., Antonelli, M., Cabrini, L., et al. (2020). Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. Jama, 323(16), 1574-1581.
29. Sarkar, P., Banerjee, S., Saha, S. A., Mitra, P., & Sarkar, S. (2023). Genome surveillance of SARS-CoV-2 variants and their role in pathogenesis focusing on second wave of COVID-19 in India. Scientific Reports, 13(1), 4692.
30. Wahengbam, R., Bharali, P., Manna, P., Phukan, T., Singh, M. G., et al. (2023). Seroepidemiological and genomic investigation of SARS-CoV-2 spread in North East region of India. Indian Journal of Medical Microbiology, 43, 58-65.

31. Ong, J., Young, B. E., & Ong, S. (2020). COVID-19 in gastroenterology: a clinical perspective. Gut, 69(6), 1144-1145.
32. Yadav, V., Bhagat, S., Sharma, D. K., Sibia, R. P. S., Pandav, R., et al. (2021). Olfactory and gustatory dysfunction in COVID-19 patients: a tertiary care institute experience in India. Indian Journal of Otolaryngology and Head & Neck Surgery, 1-8.
33. Hu, Z., Song, C., Xu, C., Jin, G., Chen, Y., et al. (2020). Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Science China Life Sciences, 63, 706-711.
34. Gao, Z., Xu, Y., Sun, C., Wang, X., Guo, Y., et al. (2021). A systematic review of asymptomatic infections with COVID-19. Journal of Microbiology, Immunology and Infection, 54(1), 12-16.
35. Tareq, A. M., Emran, T. B., Dhama, K., Dhawan, M., & Tallei, T. E. (2021). Impact of SARS-CoV-2 delta variant (B. 1.617. 2) in surging second wave of COVID-19 and efficacy of vaccines in tackling the ongoing pandemic. Human Vaccines & Immunotherapeutics, 17(11), 4126-4127.
36. Singh, J., Rahman, S. A., Ehtesham, N. Z., Hira, S., & Hasnain, S. E. (2021). SARS-CoV-2 variants of concern are emerging in India. Nature medicine, 27(7), 1131-1133.
37. Singh, J., Rahman, S. A., Ehtesham, N. Z., Hira, S., & Hasnain, S. E. (2021). SARS-CoV-2 variants of concern are emerging in India. Nature medicine, 27(7), 1131-1133.