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A COMPARATIVE EXAMINATION OF TEMPORAL PATTERNS IN COVID-19 WAVES: INSIGHTS FROM A TERTIARY CARE HOSPITAL IN JAMSHEDPUR, INDIA

KEY WORDS: SARS-CoV-2, Pandemic, Lymphopenia, Thrombocytopenia, D-dimer, CRP

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ABSTRACT

Background: In December 2019, an outbreak of pneumonia cases emerged in China, caused by a novel coronavirus, later named SARS-CoV-2. This virus spread rapidly worldwide, resulting in a global pandemic. **Materials And Methods:** This retrospective observational study investigates the impact of COVID-19 across three distinct waves in a tertiary care hospital located in Jamshedpur, India. Data from 2,906 confirmed COVID-19 cases were collected and analysed for demographic shifts, clinical presentations, treatment modalities, and their outcomes. **Results:** The third wave exhibited a higher proportion of elderly patients with evolving symptom profiles. While the prevalence of comorbidities like hypertension and diabetes remained relatively stable, conditions such as chronic obstructive pulmonary disease and heart disease showed an increased susceptibility. Laboratory parameters displayed distinct patterns, with inflammatory markers peaking during the second wave. Treatment strategies evolved over time, with shorter hospital stays observed during the third wave. Although mortality rates initially increased from the first to the second wave, there was a slight decrease noted in the third wave. **Conclusion:** Analyzing COVID-19 waves in a tertiary care hospital provides valuable insights into the pandemic's dynamic evolution. Changes in demographics, clinical characteristics, treatment modalities, and outcomes underscore the adaptable nature of the virus, emphasizing the importance of flexible healthcare responses. Further research on a larger scale is crucial for informing targeted public health interventions and effectively combating the ongoing pandemic.

INTRODUCTION:

On December 31, 2019, a group of patients in Wuhan, Hubei province, China, presented with severe pneumonia of unidentified origin, as reported [1]. Subsequently, within a fortnight, a novel viral strain known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified, leading to the outbreak of Coronavirus Disease 2019 (COVID-19) in Wuhan, China, and its rapid global dissemination [1].

Before the identification of SARS-CoV-2, six coronaviruses were recognized as human pathogens, including those of the beta coronavirus family, which includes SARS-CoV2 [2]. While four coronaviruses typically cause mild, seasonal respiratory illnesses and contribute significantly to the global burden of upper respiratory tract infections, the other two, namely SARS-CoV and MERS-CoV, led to severe epidemics with respiratory illness-associated mortality [2-4]. On March 11, 2020, the World Health Organization declared COVID-19 a global pandemic [1].

India recorded its first COVID-19 case on January 30, 2020, in Kerala [1]. A nationwide serosurvey conducted in May-June 2020 found a SARS-CoV-2 IgG antibody seroprevalence of 0.73% among adults aged 18 years or older in India [5]. Common symptoms associated with mild to moderate COVID-19 include troublesome dry cough, fever exceeding 37.8°C, diarrhoea, headache, breathlessness upon light exertion, muscle pain, fatigue, and loss of smell and taste. Symptoms indicating severe disease or pneumonia include breathlessness at rest, loss of appetite, confusion, chest pain or pressure, and temperature exceeding 38°C [5].

India witnessed a significant surge in COVID-19 cases starting in mid-March 2021, marking the onset of the second wave. By the first week of April, the highest number of cases (144,829) was reported, severely straining the healthcare infrastructure [6]. Hospitals were converted into COVID-19 care facilities, with non-COVID-19 services being scaled down. Many makeshift facilities were established to cope with the crisis, yet many patients struggled to secure hospital beds, resulting in fatalities due to oxygen shortages [6].

Lymphopenia is the most frequently reported blood count abnormality, occurring in 35%-83% of COVID-19 patients [7]. Lymphopenia is more prevalent and the absolute lymphocyte count significantly lower in severe cases [8]. Additionally, severe cases exhibit lower CD8+ lymphocytes, with subsequent increases positively correlated with improved outcomes [8]. Mild thrombocytopenia (100-150 x 10^9/L) has been reported in up to 20-36% of cases, while severe thrombocytopenia (<50 x 10^9/L) is rare [9]. Hospitalized COVID-19 patients often experience blood hypercoagulability, with venous thromboembolic events being more frequent in critically ill patients admitted to the ICU [9,10]. Elevated D-dimers, fibrinogen, and other acute phase markers like CRP, procalcitonin, ESR, and ferritin are associated with increased mortality [11]. Severe cases often exhibit elevated proinflammatory markers, indicating a dysregulated immune response known as the cytokine storm [7].

In the Indian context, the pandemic has significantly strained the healthcare infrastructure, particularly during peak infection periods [5]. The experiences in Jamshedpur, an industrial hub in eastern India, provide insights into the broader national response to the pandemic. The Tertiary Care

Hospital in Jamshedpur serves as a crucial healthcare institution, offering valuable insights into the impact of COVID-19 on local healthcare systems, patient demographics, treatment strategies, and public health interventions [5]. Analyzing the temporal patterns of COVID-19 waves within this hospital setting can offer nuanced perspectives on the challenges faced and the strategies employed to mitigate the virus's impact.

MATERIAL AND METHODS:

This retrospective observational study was conducted at a tertiary care hospital located in Jamshedpur, Jharkhand, India, with the objective of comparing demographic, clinical, and laboratory characteristics among confirmed COVID-19 cases during three distinct periods: the third wave (November 2022 to March 2023), the second wave (March 2021 to May 2021), and the first wave (July 2020 to January 2021). The study aimed to examine various parameters, including patient demographics such as age and gender, clinical manifestations, presence of underlying health conditions, requirement for intensive care unit (ICU) admission and tracheal intubation, duration of hospital stay, and outcomes upon discharge from the hospital.

Inclusion Criteria-

All COVID-19 RT-PCR- positive patients above 12 years admitted to the hospital.

Exclusion Criteria-

RT PCR Negative patients with Covid like symptoms & Patients below 12 years.

Data for the research were gathered from both the hospital's Health Management Information System (HMIS) portal and individual patient case files. Ethical clearance was obtained from the hospital's Ethical Committee, ensuring adherence to the ethical standards outlined in the Declaration of Helsinki. Confirmed cases of COVID-19 were identified through positive results from real-time polymerase chain reaction (RT-PCR) testing of nasopharyngeal or oropharyngeal specimens for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA. Additionally, the study utilized computed tomography (CT) severity scores to evaluate the severity of the disease.

The primary source of data was the hospital's electronic medical records of COVID-19 patients. Statistical analysis was conducted using SPSS 27 software, incorporating chi-square and logistic regression tests. A significance level of $P < 0.05$ was utilized. Stepwise multivariate logistic regression analysis was employed to determine odds ratios for non-invasive ventilation and mortality, while adjusting for various factors.

RESULTS:

During the first, second, and third waves at TMH, Jamshedpur, Jharkhand, a tertiary care hospital accredited by NABH with 983 beds, there were 644, 1836, and 426 confirmed cases of COVID-19 admitted, respectively.

Among the 644 confirmed cases in the first wave, 434 (67.39%) were male and 210 (32.59%) were female. In the second wave, the proportion of male cases was 1161 (63.23%), while in the third wave, it was 291 (68.30%). There was no significant difference in the proportion of male cases across the waves ($P = 0.37$). The mean age of patients was 58.11 ± 12.43 years in the first wave, 56.31 ± 14.19 years in the second wave, and 62.11 ± 17.23 years in the third wave, with a statistically significant difference ($P < 0.001$).

Table 1 presents a comparison of demographic and clinical characteristics of COVID-19 patients across the three waves. The third wave predominantly consisted of older patients, with a mean age of 62.11 years, showing significant variations in age distribution. Common symptoms included fever, cough, and breathlessness, although the third wave had lower rates of fever but higher rates of sore throat, running nose, and nausea. Fatigue was less prevalent in the third wave. Physiological parameters exhibited minor differences. Pharmacotherapy usage varied, with a higher utilization of Remdesivir and steroids in the earlier waves. Oxygenation and ventilator support were less frequently required in the third wave. Hospital stays were shorter during the third wave, but the duration of oxygen therapy was longer. Overall, discernible trends in demographics, symptoms, and treatment modalities were observed across the waves.

Table 1: Demographic and clinical characteristics of patients admitted with COVID-19 during the first, second & third outbreak

Characteristics	First wave n= 644	Second wave n= 1836	Third wave n= 426	P-value
Age in years				
Mean±SD	58.11 ± 12.43	56.31 ± 14.19	62.11 ± 17.23	0.000
Age group				
<40	104 (16.1)	332 (18.1)	65 (15.2)	0.000
40-59	297 (46.1)	697 (37.9)	80 (19.2)	
60+	243 (50.2)	807 (43.9)	281 (65.9)	
Total	644	1836	426	
Male	434 (67.4)	1161 (63.2)	291 (68.3)	0.290
Symptoms				
Fever	586 (81.1)	1542 (83.9)	214 (50.2)	0.000
Cough	551 (85.5)	1532 (83.4)	247 (57.9)	0.000
Breathlessness	491 (76.2)	1156 (62.9)	255 (59.8)	0.550
Sore throat	30 (4.6)	182 (9.9)	38 (8.9)	0.000
Running nose	8 (1.2)	29 (1.5)	21 (4.9)	0.000
Nausea	28 (4.3)	67 (3.6)	14 (3.2)	0.000
Vomiting	34 (5.2)	60 (3.2)	18 (4.2)	0.012
Diarrhoea	21 (3.2)	18 (0.9)	8 (1.8)	0.628
Headache	60 (9.3)	110 (5.9)	13 (3.0)	0.000
Joint pain	24 (3.72)	29 (1.5)	11 (2.5)	0.517
Loss of appetite	64 (9.9)	228 (12.4)	48 (11.2)	0.000
Chest pain	32 (4.9)	71 (3.8)	44 (10.3)	0.000
Fatigue	181 (28.10)	997 (54.3)	88 (20.6)	0.00
Physical examination				
Blood pressure (systolic)	130.1± 14.66	129.96± 16.21	128.50± 20.17	0.565
Blood pressure (diastolic)	78.34± 10.24	79.12± 11.24	75.13± 11.66	0.001
Pulse rate	87.17± 13.08	88.52± 15.29	91.85± 17.96	0.001
Pharmacotherapy				
Remdesivir	392 (60.8)	1377 (75.0)	293 (68.7)	0.000
Antibiotic	615 (95.4)	1780 (96.9)	397 (93.6)	0.030
Steroid	625 (97.0)	1626 (88.5)	255 (64.0)	0.000
Tocilizumab	05 (0.7)	35 (1.9)	02 (0.4)	0.011
Oxygenation	381 (59.1)	1144 (62.3)	132 (30.9)	0.001
Non-invasive ventilator	132 (20.5)	497 (27.0)	29 (6.8)	0.000
Invasive ventilator	24 (3.7)	187 (10.1)	12 (2.8)	0.000
Hospital stays (in days)				
Mean±SD	6.55±4.18	8.32±6.61	4.87±4.81	0.000
Avg. day on ventilator	1.33±0.58	4.97±4.67	4.75±2.87	0.403
Avg. day on oxygen	3.71±2.44	5.70±5.29	4.08±3.11	0.000
Avg. day on non-invasive ventilation	3.78±3.14	4.76±3.57	4.63±6.18	0.080

Table 2 presents the prevalence of co-morbid conditions

among hospitalized COVID-19 patients across three waves:

Systemic Hypertension: The prevalence showed an increase from the first wave (42.0%) to the third wave (51.2%), indicating a higher association with systemic hypertension in later waves.

Type 2 Diabetes Mellitus: The prevalence remained relatively stable, with a slight increase noted in the third wave (36.8%), suggesting a consistent impact of diabetes across the outbreaks.

Chronic Obstructive Pulmonary Disease (COPD): There was a notable rise in prevalence during the third wave (18.4%), highlighting an increased vulnerability of individuals with COPD during this period.

Bronchial Asthma: The prevalence increased in the third wave (8.0%), emphasizing a higher impact of bronchial asthma among COVID-19 patients during that phase.

Heart Disease: A substantial increase in prevalence was observed in the third wave (25.6%), indicating a heightened risk for individuals with pre-existing heart conditions.

Thyroid Disease: The prevalence significantly increased in the third wave (12.0%), suggesting an elevated risk for individuals with thyroid disorders during this outbreak.

Table 2: Co-morbid disorders in hospitalized patients with confirmed COVID-19 during the two COVID-19 outbreaks

Co-morbidities	First wave n=644	Second wave n=1836	Third wave n=426
Systemic hypertension	271 (42.0)	706 (37.9)	218 (51.2)
Type 2 diabetes mellitus	225 (34.9)	559 (30.0)	157 (36.8)
Chronic obstructive pulmonary disease	32 (4.9)	41 (2.2)	78 (18.4)
Bronchial asthma	38 (5.9)	89 (4.8)	34 (8.0)
Heart disease	64 (9.9)	170 (9.1)	109 (25.6)
Thyroid disease	29 (4.5)	67 (3.6)	51 (12.0)

Table 3 provides an overview of laboratory parameters observed in COVID-19 cases across three waves, alongside normal reference values:

Haematology Parameters:

White Blood Cells (WBC): No significant difference was noted among waves (p = 0.075).

Hemoglobin (Hb): Significant variations were observed, with lower levels detected in the second and third waves compared to the first (p = 0.000).

Biochemical Parameters:

Serum Glutamic Oxaloacetic Transaminase (SGOT): No significant discrepancies were found among waves (p = 0.326).

Serum Glutamic Pyruvic Transaminase (SGPT): Similarly, no significant differences were observed among waves (p = 0.246).

Serum Creatinine: A notable increase was identified in the third wave (p = 0.006).

Serum Bilirubin: No significant variations were noted among waves (p = 0.835).

Inflammatory Markers:

Interleukin-6 (IL-6): Substantial elevations were observed in the second and third waves compared to the first (p = 0.000).

Serum Ferritin: Significant variations were noted, with a noticeable decrease in the third wave (p = 0.063).

Lactate Dehydrogenase (LDH): Marked increases were detected in the second wave compared to both the first and third waves (p = 0.000).

C-Reactive Protein (CRP): Significant differences were observed, with higher levels detected in the second wave (p = 0.001).

Table 3: Laboratory parameters of the COVID-19 cases in the first, second & third wave

Investigator parameters	Normal values	First wave n=644	Second wave n=1836	Third wave n=426	P-value
Haematology parameter					
WBC (10^9 cells/L)	4.5-11×10^3 cells/mcL	7.11± 4.19	7.36± 7.94	8.15± 5.40	0.075
Hb	>12-14 g/dL	13.11± 1.80	12.56± 2.1	12.34± 2.31	0.000
Biochemical parameters					
SGOT	<35 U/L	44.94± 88.87	52.78± 62.84	40.24± 59.13	0.326
SGPT	<35 U/L	43.44± 66.19	43.75± 54.11	32.13± 34.01	0.246
Serum creatinine	<1.2 mg/dL	1.05± 0.48	1.11± 0.69	1.24± 0.85	0.006
Serum bilirubin	<1.2 mg/dL	0.61± 0.41	0.30± 0.47	0.39± 0.56	0.835
Inflammatory marker					
IL-6	<500 ng/mL	726.96± 1024.82	1659.42± 2168.25	2031.89± 2368.35	0.000
Serum ferritin	<7 pg/mL	87.07± 212.44	471.72± 3352.83	155.90± 718.63	0.063
LDH	<300 ng/mL	430.10± 544.41	682.13± 533.42	429.66± 508.98	0.000
CRP	<160 U/L	51.56± 61.14	90.48± 133.82	75.63± 84.01	0.001

Overall, hemoglobin levels displayed a consistent decline in the second and third waves, while serum creatinine levels showed an increase in the third wave, indicating potential renal involvement. Notable elevations in inflammatory markers (IL-6, LDH, and CRP) were observed during the second wave. Conversely, serum ferritin exhibited a decrease in the third wave, suggesting a potential alteration in the inflammatory profile.

Table 4 outlines the patient outcomes observed during the first, second, and third waves of COVID-19, categorized into mortality, recovery, and referrals/discharge on request:

Mortality: In the first wave, 13 patients (2.01%) succumbed to the virus. During the second wave, the mortality rate increased to 8.4%, with 155 patients not surviving. However, in the third wave, the mortality rate significantly decreased to 0.9%, with only 4 reported deaths.

Recovery: A significant majority of patients recovered from COVID-19 across all waves. In the first wave, 95.3% (614 patients) successfully overcame the infection. The recovery rate decreased to 84.9% in the second wave, with 1560 patients recovering. Nevertheless, in the third wave, the recovery rate increased to 94.8%, with 404 patients successfully recovering.

Referred/LAMA/Discharge on Request: A small percentage of patients were either referred, left against medical advice (LAMA), or discharged on request. In the first wave, this category comprised 2.6% of patients (17 individuals), which increased to 6.6% in the second wave (121

patients). However, in the third wave, this percentage decreased to 4.2%, involving 18 individuals.

Overall, the mortality rate showed an increase from the first to the second wave but significantly decreased in the third wave. Recovery rates exhibited a decrease from the first to the second wave but rebounded in the third wave. The percentage of patients referred, leaving against medical advice, or discharged on request demonstrated fluctuations, with the second wave showing the highest percentage in this category. These outcomes offer valuable insights into the pandemic's progression, the efficacy of medical interventions, and potential shifts in patient management strategies across successive waves.

Table 4: Outcome in first and second wave in terms of mortality, recovery and referrals

Outcomes	First wave n=644	Second wave n=1836	Third wave n=426
Mortality	13 (2.01)	155 (8.4)	04 (0.9)
Recovery	614 (95.3)	1560 (84.9)	404 (94.8)
Referred/LAMA/ Discharge on request	17 (2.6)	121 (6.6)	18 (4.2)

DISCUSSION:

The study provides a thorough examination of the COVID-19 waves observed in a tertiary care hospital in Jamshedpur, India, offering insights into the changing landscape of the pandemic. From the data analysis, significant findings emerge, covering shifts in demographics, clinical presentations, treatment approaches, and patient outcomes across three distinct waves.

Demographic and Clinical Characteristics: The profile of patients admitted during the third wave suggests an older average age, with a mean age of 62.11 years. This differs from the demographics observed in the first and second waves, indicating a possible alteration in the demographic composition of affected individuals.

Singh et al. [12] reported that in the first wave of COVID-19, 68.8% of confirmed cases were males and 31.2% were females. In the second wave, this proportion slightly decreased to 66.6% for males. The mean ages in the first, second, and third waves were 58.21 ± 13.63 years, 56.38 ± 15.89 years, and 63.11 ± 18.03 years, respectively. Tendulkar et al. (reference [13]) found that the mean age of patients was 55 years in the first wave and 56.81 years in the second wave, with no statistically significant difference between the groups. Symptoms such as sore throat, running nose, and nausea showed increased prevalence in the third wave, while fatigue exhibited a significant reduction. Singh et al. [12] summarized clinical manifestations, noting that fever, cough, sore throat, headache, fatigue, loss of appetite, and chest pain were more common in the second wave compared to the first and third waves. Runny nose and chest pain were predominant in the third wave. Analysis of co-morbidities revealed stable prevalence of systemic hypertension and type 2 diabetes mellitus but a substantial increase in chronic obstructive pulmonary disease (COPD), bronchial asthma, and heart disease during the third wave, emphasizing the importance of tailored interventions for patients with specific comorbidities. Heart disease, chronic obstructive pulmonary disease, and thyroid disorders were the most common co-morbidities during the third wave (Singh et al. [12])

Hematological and biochemical parameters showed distinct trends across the waves. A consistent decline in hemoglobin levels during the second and third waves suggested potential implications for oxygen-carrying capacity. Elevated levels of inflammatory markers such as CRP, IL-6, and ferritin in the second wave indicated a more pronounced inflammatory response, potentially contributing to disease severity. In our study, we observed significantly higher levels of CRP, IL-6, and ferritin in the second wave compared to the first and third waves [14-15].

Recent research suggests that uncontrolled inflammation contributes to the severity of COVID-19, alongside direct viral damage. Consistent with this idea, patients with severe illness have shown high levels of inflammatory markers, including CRP, ferritin, and cytokines [16-18]. This pathogenic inflammation, akin to a cytokine storm, resembles what was observed in patients infected with other severe coronaviruses like SARS-CoV and MERS-CoV, as well as cytokine release syndrome in certain cancer treatments [19]. Interestingly, although IL-6 levels were elevated in all three waves, there was no significant difference, and IL-6 inhibitors like Tocilizumab have not proven effective in countering cytokine storms induced by COVID-19 [20]. Thus, the correlation between IL-6 and disease severity remains uncertain, a finding also noted in our study.

Regarding treatment strategies, pharmacotherapy use varied across waves, with increased utilization of Remdesivir and steroids in earlier waves. Oxygenation and ventilator support were less common in the third wave, indicating potential adaptations in treatment approaches. Additionally, hospital stays were shorter in the third wave, suggesting improved management efficiency or potentially milder disease manifestations.

Outcomes: Analysis of patient outcomes reveals a fluctuating trend. Mortality rates increased from the first to the second wave but notably decreased in the third wave. Recovery rates followed a similar pattern, indicating potential advancements in clinical management (Singh et al., 12). The proportion of patients referred, leaving against medical advice, or discharged on request varied across waves, with the second wave showing the highest percentage in this category. These findings highlight the evolving nature of the pandemic and the importance of adaptive healthcare strategies (Singh et al., 12).

Limitations And Implications: This study has inherent limitations, including its retrospective design and reliance on electronic medical records. Additionally, focusing solely on a single tertiary care hospital may limit generalizability. Nevertheless, the results have implications for healthcare professionals and policymakers, emphasizing the necessity for targeted interventions based on demographic shifts, evolving clinical characteristics, and treatment dynamics.

CONCLUSION:

The comparative analysis of COVID-19 waves within a tertiary care hospital context provides valuable insights into the nuanced progression of the pandemic. The observed demographic changes, clinical manifestations, treatment strategies, and outcomes underscore the dynamic nature of the virus and the importance of adaptive healthcare responses. Future research should explore these trends on a broader scale to inform more effective and targeted public health interventions.

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