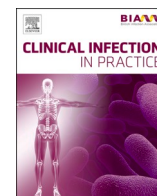




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Asymptomatic RT-PCR positive COVID-19 patients in orthopaedic pre-operative evaluation during the peak of the second wave

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ABSTRACT

Introduction: Asymptomatic COVID-19 patients are the most challenging and feared obstacles in resuming these surgical procedures. The purpose of this study was to evaluate the proportion of asymptomatic carriers detected by RT-PCR in pre-operative orthopaedic evaluation during the peak of the second wave.

Methods: 514 asymptomatic COVID-19 patients, negative for TOCC (Travel, Profession, Cluster, Contact) risk factors were observed retrospectively. A nasopharyngeal RT-PCR test was obtained 48 to 72 h before the surgery in all cases. Possible risk factors for a positive test was identified.

Results: The detected asymptomatic COVID-19 infection rate during the peak of the second wave among the pre-operative orthopaedic patients was 12.3%. Younger age, female gender, longer duration of admission to RT-PCR test interval were found to be significant ($p < 0.05$) risk factors for asymptomatic RT-PCR to be positive. The hazard ratio (HR) for being asymptomatic RT-PCR positive was 4.3 ($p = 0.025$), while the RT-PCR was performed at 14 days, but the HR increased to 9.2 ($p = 0.049$) when the test was performed after 45 days.

Conclusion: According to our findings, pre-operative testing to rule out COVID-19 should be regarded as a critical step in preventing the disease clusters in hospitals.

Introduction

A novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) has caused catastrophic, life-threatening respiratory illness, known as coronavirus disease 2019 (COVID-19), which has never been seen before in human history. The ever-evolving nature, extended incubation period, and asymptomatic transmission have rendered it almost unstoppable, culminating in wave after wave of attacks. (Kavitha et al., 2021; Nakai et al., 2021) The crisis has put enormous strain on healthcare systems. Hospital resources have been primarily focused on the care of COVID-19 patients, causing thousands of orthopedic procedures to be postponed throughout the world if they were not deemed to cause substantial harm to the patient or outcome. (Mouton et al., 2020)

The illness has a wide spectrum of symptoms, from asymptomatic infection to mild, moderate or severe pneumonia and even mortality. Because of the wide range of manifestations and the long incubation period, 20–70% of all patients are asymptomatic carriers, transmitting

the disease silently. (Wang et al., 2020) This group of asymptomatic individuals poses a great threat to the healthcare system, as both patients and healthcare workers. According to prior research, the incidence of asymptomatic carriers among healthcare professionals is between 0.76 and 3%. (Rivett et al., 2020; Zhou et al., 2020; Lombardi et al., 2020; Olmos et al., 2021) Data regarding the asymptomatic infection in orthopaedic admitted cases are sparse and primarily refer to the 1st wave, with reported incidences ranging from 7 to 9%. (Kumar et al., 2021; Gruskay et al., 2020)

The second wave, which began in September 2020 in the Indian subcontinent, has a much steeper slope than the first, with a large number of asymptomatic people and a more infectious viral variant, resulting in a 50% higher infection rate. (Kavitha et al., 2021) The COVID-19 detection rate in our country had been steadily declining to 2.3% by February 2021, but a sudden surge in COVID-19-positive cases began in early March 2021, resulting in a positive rate of 3 to 13%. It jumped to 21.02% by April 6, 2021, in just two weeks. This definitely

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denotes the arrival of the second wave. (Daria and Islam, 2021) It has been claimed that during the study period our country was the second-worst-affected country in South Asia affected by at least eight SARS-CoV-2 variants of concern (VOC) and the clades or lineages: 20A, 20B, 20C, 20H (Beta, V2), 20I (Alpha, V1), 20 J (Gamma, V3), 21A (Delta), 21D (Eta), and six GISAID clades: four main (G, GH, GR, GRY) and two minors (GV, O) with an introduction of VOC B.1.1.7/Alpha, B.1.351/Beta and B.1.617.2/Delta. In particular, VOC B.1.617.2/Delta has surpassed all previous VOCs in Bangladesh, posing a major threat to country's current disease control strategies. (Afrin et al., 2022; Saha et al., 2021)

Governments all around the globe have been attempting to figure out how to resume elective medical interventions and surgical procedures while protecting both the caregivers and the patients. The big concern is that COVID-19 may exist in the pre-or asymptomatic transmission phase. Moreover, a 30-day mortality rate of 21.2% was observed among patients who tested positive for SARS-CoV-2 within seven days pre-operative, with respiratory complication death rates reaching 40%. (Price et al., 2020) Being the country's highest orthopaedic referral center, we were unable to postpone; instead, we modified the strategy, performing only essential cases, lowering the surgical load of elective cases to 30 to 40%, reduce the operating time, and making services available to other hospitals around the country as an emergency trauma care referral facility. Furthermore, dedicated floors were set up for orthopaedic COVID-19 patients. For all non-emergency cases, we routinely obtained a RT-PCR (Reverse Transcription-polymerase Chain Reaction) from nasopharyngeal-swab 48 to 72 h before the surgery. (Mouton et al., 2020) In the event of an absolute emergency, we proceeded without RT-PCR following sufficient precautionary measures, including complete PPE protection. The purpose of this study was to evaluate the proportion of asymptomatic carries detected by RT-PCR while pre-operative orthopaedic evaluation, notably when the country is experiencing the devastation of the second wave. Thus, a reduction in viral nosocomial transmission risk, safety of the surgical team, and a decrease in post-operative mortality rates are all possible benefits from avoiding surgery on orthopaedic patients who already have asymptomatic COVID-19 infection.

Methods

This was a retrospective, single-center, observational cohort study conducted at a tertiary care orthopaedic hospital. Our hospital is the highest orthopaedic referral center at the Government level and is situated in the capital of the country. 514 consecutive patients who were selected for elective orthopaedic surgery between June 01, 2020, and July 31, 2021, and who were negative for COVID-19 symptoms and did not have any TOCC (Travel, Profession, Cluster, Contact) risk factors were included. In all the cases, an RT-PCR (from nasopharyngeal swab) was obtained 48 to 72 h before the surgery. Orthopaedic emergencies such as infection/septic arthritis, vascular injury, severe crush injury with an unstable patient, widely displaced supracondylar fractures, replants and revascularizations cases, cauda equina syndrome, or unstable spinal fracture/trauma were considered to be excluded. Protocol of this retrospective study was approved by the institutional review board of our institution, and the requirement for written informed consent was removed in the face of a pandemic scenario.

For every individual, a history of TOCC risk factors was gathered. The assessment for COVID-19 symptoms (cough, fever, dyspnea, sputum production, tiredness or myalgia, headache, anosmia, ageusia, diarrhea, or vomiting) was also performed. If patients presented with TOCC risk indicators and/or positive symptoms, they were sent to the COVID-19 specialized unit of this hospital for further management. Thus, there were no TOCC risk factors or COVID-19 symptoms among the study subjects. Demographic characteristics with associated co-morbidities and admission to RT-PCR test interval (in days) were also recorded. These asymptomatic individuals who underwent RT-PCR from

nasopharyngeal-swab 48 to 72 h before the surgery were classified into either asymptomatic RT-PCR positive or asymptomatic RT-PCR negative cohorts, and a comparison of their demographic and clinical characteristics was performed. Risk factors for the asymptomatic RT-PCR positive cases were also analyzed.

Statistical analyses were done using the Statistical Package for the Social Sciences (SPSS) version 23 (IBM). Data are represented as the mean, percentage, and standard deviation (SD). Significance was set at $p < 0.05$. The unpaired *t*-test was used to produce *p*-values for quantitative data, while the chi-square test was performed to determine the relationship between qualitative variables. Univariate and multivariate logistic regression was also performed with hazard ratio to observe the risk factors. Statistical significance was defined as $p < 0.05$.

Results

Out of 514, male patients were 363 (63.4%), and the male to female ratio was 1:0.41. About half of the patients were in the > 60 age group. The mean age of the study population was 61.17 ± 16.73 . The most common co-morbidity present among the study population was hypertension (HTN) (46.7%). Diabetes mellitus (DM), being the second-highest, was present in 31.9% of patients, while bronchial asthma (BA) in 9.5% and ischemic heart disease (IHD) in 7.3% of individuals. Chronic kidney disease (CKD), carcinoma, chronic obstructive pulmonary disease (COPD), liver disease, or inflammatory bowel disease (IBD) was present in only 0.5 to 3% of the cases. When evaluating the admission to RT-PCR test interval before surgery, half of the people (49.9%) did the test 30 to 45 days following the hospital admission. In 63 patients, RT-PCR positive for COVID-19 was identified, suggesting a 12.3% asymptomatic positive rate [Table 1]. A brief overview of the different elective surgeries that were performed during the study period showed hip surgery was the topmost surgery performed during the study period, followed by knee procedures [Table 2]. Comparison of asymptomatic RT-PCR positive with asymptomatic RT-PCR negative cohorts showed a significant difference in mean age and sex ($p = < 0.05$). The RT-PCR positive group was comparatively younger (47.35 years versus 60.53 years), and the male to female ratio revealed that the proportion of females was greater (1:0.70) among asymptomatic RT-PCR positive participants than in the negative group (1:0.38). The asymptomatic positive individuals had the RT-PCR test at a significantly later date (46 ± 7.32) than the asymptomatic RT-PCR negative group (29 ± 11.62). Except for bronchial asthma, which was significantly higher (17.4%) in the asymptomatic RT-PCR positive group, there was no difference in co-morbidities between the two groups [Table 3]. In univariate analysis, age < 50 years (OR = 3.81) and female sex (OR = 1.13) was risk factor for becoming asymptotically RT-PCR positive. However, in multivariate analysis, longer duration (> 30 days) in performing RT-PCR was also a risk factor ((OR = 7.05), in addition [Table 4]. In this study, the hazard ratio (HR) for being asymptomatic RT-PCR positive when compared with being asymptomatic RT-PCR negative was 4.3 ($p = 0.025$) while the RT-PCR was performed at 14 days, but the HR increased to 9.2 ($p = 0.049$) when the test was performed after 45 days. [Table 5].

Discussion

The high prevalence of asymptomatic infected individuals, as well as their infectivity, are the primary reasons why COVID-19 has become a pandemic. According to WHO (World Health Organization), laboratory diagnosis is the only way to identify and confirm these invincible hidden drivers of disease transmission. (Siegel and Shadduck, 1987) On the other hand, these asymptomatic patients are the most challenging and feared obstacles in resuming elective surgical procedures. We are presenting our data when our country is at the peak of the second wave. The study evaluated the proportion of asymptomatic COVID-19 patients detected by RT-PCR (from nasopharyngeal-swab) while pre-operative orthopaedic evaluation in our center.

Table 1
Clinicodemographic characteristics of the patients (n = 514).

Characteristics	Group	Mean ± SD	Ratio	n(%)
Age (in years)	<20			12(2.3)
	21–40	61.17 ± 16.73		97(18.8)
	41–60			154 (29.9)
	>60			251 (48.8)
Sex	Male			363 (63.4)
	Female			151 (36.5)
Male:Female ratio		1:0.41		
Co-morbidities	HTN			183 (36.7)
	DM			164 (31.9)
	BA			49(9.5)
	IHD			38(7.3)
	CKD			17(3.3)
	Carcinoma			13(2.5)
	COPD			10(1.9)
	Liver Disease			9(1.7)
	IBD			3(0.5)
	Others			5(0.9)
	Admission to RT-PCR test interval	07 Days		
14 Days				161 (31.3)
30 Days				149 (28.9)
45 Days				108 (21.0)
RT-PCR test result	Positive			63(12.3)
	Negative			451 (87.7)

Values are presented as frequency, percentage (in the parenthesis), mean ± Standard Deviation (SD), hypertension (HTN), diabetes mellitus (DM), bronchial asthma (BA), ischemic heart disease (IHD), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), Inflammatory Bowel Disease (IBD)

Our study revealed an asymptomatic COVID-19 infection rate of 12.3% among patients during pre-operative orthopaedic evaluation from nasopharyngeal RT-PCR testing. An article from Bangalore, India, and another research from a specialized orthopaedic hospital in New York showed that the asymptomatic positive rate was 3% to 4% lower than ours. (Kumar et al., 2021; Gruskay et al., 2020) Both studies were carried out during the first wave of COVID-19, which was less destructive than the present. We conducted our study when our country had seen the highest case detection rate of the more catastrophic second wave, which might explain this greater asymptomatic rate. Furthermore, recent research shows that the second wave contains a higher proportion of asymptomatic patients with a more infectious viral variant. (Kavitha et al., 2021)

The age and gender of the asymptomatic RT-PCR positive and asymptomatic RT-PCR negative groups were found to be significantly different in this investigation. Asymptomatic individuals were comparatively younger. Moreover, both multivariate and univariate analysis revealed age < 50 years was a risk factor to be asymptomatic COVID-19 positive. Various epidemiological studies previously confirmed that the asymptomatic patients of SARS-CoV-2 were relatively younger. (Oran and Topol, 2020; Tan et al., 2020; Hu et al., 2020) In a Study on pre-operative orthopaedic patients from New York, the mean age of asymptomatic COVID-19 patients was likewise reported to be lower than that of symptomatic one. (Gruskay et al., 2020) In our research, the ratio between men and women indicates that the proportion of women in the asymptomatic RT-PCR positive cohort was significantly higher (1:0.70)

Table 2
Types elective orthopaedic procedures performed (n = 514).

Elective orthopaedic procedures performed	No. of cases	Sex	
		Male	Female
Hip			
Primary hip arthroplasty	148	99	49
Revision hip arthroplasty	4	3	1
Excision of trochanteric bursa	2	1	1
Knee			
Primary knee arthroplasty	4	1	3
Revision knee arthroplasty	1	0	1
Unicompartmental knee arthroplasty	1	1	0
Knee arthroscopic procedures	127	104	23
Excision of cystic swelling around the knee	3	2	1
Foot & Ankle			
Tendo-Achilles reconstruction	7	3	4
Tibiotalocalcaneal fusion	3	2	1
Metatarsophalangeal joint fusion with osteotomy	2	1	1
Zadek's procedure (great toe)	2	1	1
Shoulder			
Shoulder arthroscopic procedures	66	54	12
Latarjet procedure	23	17	6
Primary shoulder arthroplasty	4	3	1
Revision shoulder arthroplasty	1	1	0
Pectoralis major repair	1	1	0
Manipulation under anaesthesia (MUA)	2	2	0
Wrist and Hand			
Carpel tunnel decompression	24	8	16
Release of trigger finger	11	5	6
De Quervain's release	7	4	3
Spine			
Spinal decompression with/without discectomy	19	13	6
Epidural injection	7	5	2
Removal of fixation devices			
Upper limb	7	6	1
Lower limb	11	8	3
All other procedures	27	18	9
Total	514	363	151

Table 3
Comparison of demography, symptoms and co-morbidity between asymptomatic RT-PCR positive and RT-PCR Negative cases (n = 514).

Characteristics	Asymptomatic RT-PCR positive (n = 63)		Asymptomatic RT-PCR Negative (n = 451)		p value
	n	%	n	%	
Age (Mean ± SD)	47.35 ± 14.37		60.53 ± 14.32		^a 0.001 ^s
Sex					
Male	37	58.7	326	72.1	^b 0.026 ^s
Female	26	41.3	125	27.9	
Male:Female	1:0.70		1:0.38		^c 0.025 ^s
Admission to RT-PCR test interval					
Days (Mean ± SD)	46 ± 7.32		29 ± 11.62		^a 0.001 ^s
Co-morbidity					
HTN	19	30.1	184	40.7	^b 0.335 ^{ns}
DM	14	22.2	150	33.2	^b 0.078 ^{ns}
BA	11	17.4	38	8.4	^b 0.022 ^s
IHD	8	12.6	30	6.6	^b 0.119 ^{ns}
CKD	4	6.3	13	2.8	^b 0.149 ^s
Carcinoma	3	4.7	10	2.2	^b 0.228 ^{ns}
COPD	2	3.1	8	1.7	^b 0.450 ^{ns}
Liver Disease	3	4.0	6	1.3	^b 0.051 ^{ns}
IBD	1	1.5	2	0.4	^b 0.264 ^{ns}
Others	2	3.1	3	0.6	^b 0.057 ^{ns}

s = significant, ns = not significant, ^a p-value from Unpaired t-test, ^b p-value from Chi-square test.

hypertension (HTN), diabetes mellitus (DM), bronchial asthma (BA), ischemic heart disease (IHD), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), inflammatory bowel disease (IBD)

^c p-value from z test of proportion, ReverseTranscription-polymerase Chain Reaction (RT-PCR),

Table 4
Factor predicting asymptomatic RT-PCR for COVID-19 positive case.

Factors	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age						
< 50 Years	3.81	1.31–13.07	0.005 _s	1.207	0.923–2.988	0.001 _s
Sex						
Female	1.13	0.64–1.99	0.065 _{ns}	8.081	1.326–49.572	0.025 _s
Admission to RT-PCR test interval						
>30 days	0.54	0.83–1.09	0.045 _s	7.058	1.234–36.743	0.034 _s

s = significant, ns = not significant

Coronavirus Disease 2019 (COVID-19)

Reverse Transcription–polymerase Chain Reaction (RT-PCR)

Factor analysis was done by logistic regression

Table 5

Risk measurement (hazard ratios) for being COVID-19 Positive among asymptomatic RT-PCR positive compared to asymptomatic RT-PCR negative patients at 7,14,30 and 45 Days after admission.

Duration of riskmeasure	Hazard Ratio Value	95% CI	p-Value
07 Days	3.4	0.11–76.0	0.385
14 Days	4.3	1.3–19.8	0.025
30 Days	4.1	1.1–15.9	0.056
45 Days	9.2	0.9–91.2	0.049

Reverse Transcription–polymerase Chain Reaction (RT-PCR)

Coronavirus Disease 2019 (COVID-19)

than in the RT-PCR negative cohort (1:0.38). Female gender was also a risk factor for being an asymptomatic carrier in multivariate regression analysis of our data. Previous studies indicate that infected men have more severe symptoms and a greater mortality rate. In contrast, infected women have less symptomatology and mortality. (Jin et al., 2020; Haitao et al., 2020) A surveillance testing of hospitalized patients for SARS-CoV-2 from Louisville, Kentucky, USA found 76% of female gender among the asymptomatic cases. (Arnold et al., 2021)

The most frequent co-morbidities among all research participants were hypertension (HTN) and diabetes mellitus (DM). Bronchial asthma (BA), ischemic heart disease (IHD), and chronic renal disease (CKD) were notable among the other associated diseases. However, there was no significant difference among the associate co-morbidities between the asymptomatic RT-PCR positive and asymptomatic RT-PCR negative cohort, except, bronchial asthma (BA), which was significantly associated with the asymptomatic positive group. A recent article from Madrid, Spain, claimed the risk of severe COVID-19 infection is small in BA patients. In addition, they stated that BA seems to be protective against SARS-CoV-2 infection (Fernández-de-las-Peñas et al., 2021). This factor might have a role in making COVID-19 illness less severe or asymptomatic in our BA patients. To validate or reject this finding, a large randomized population-based research would be necessary.

After hip surgeries, operations around the knee were the most commonly performed procedures. Researchers from University College London in the United Kingdom revealed a similar result. (Chang et al., 2020) A half of the participants (49.9%) completed the RT-PCR test 30 to 45 days after being admitted to the hospital suggests that surgery was delayed with a prolonged pre-operative period. This might be owing to a huge referral burden from other centers, as a result of their closure or conversion to a COVID-19 facility, and a decline in the number of elective orthopaedic surgery performed, resulting in a substantial backlog and waiting time. (Wang et al., 2020; Green et al., 2021) One

important observation of our research longer duration (>30 days) in performing RT-PCR was a risk factor for becoming asymptomatic RT-PCR positive. When the RT-PCR was done after 45 days of admission, the hazard of becoming asymptomatic RT-PCR positive was almost doubled compared to when it was done after 14 days. This means patients are being infected while staying at the hospital. A surveillance study of hospitalized trauma and labor patients revealed a gradual increase in the rate of SARS-CoV-2 infection from 20% to 70% during their stay in the hospital (Arnold et al., 2021). According to another study from Italy, the incidence of SARS-CoV-2 hospital-acquired infection is 12–15%. (Barranco et al., 2021)

A recent article on the second wave from Japan among orthopaedic patients has strongly recommended RT-PCR screening before elective surgery (Nakai et al., 2021). We have a similar opinion from our research. However, present work had several limitations, including the use of only RT-PCR for the detection of asymptomatic disease, where the false-negative rates of this testing modality are high and hence may result in a large number of cases being under-reported. (Kumar et al., 2021; Ai et al., 2020) Chest CT scans could supplement for further evaluation of the negative cases to increase asymptomatic case detection, but in this resource-hungry situation the use of CT for the large RT-PCR negative asymptomatic individual was questionable. Further, we evaluated only the patients planned for surgery, but cases with non-operative plans or outdoor orthopaedic patients were not included. Nevertheless, the identification of risk factors for being asymptotically COVID-19 positive by RT-PCR is an important aspect of this research. Additional investigations, such as a chest CT scan that focuses on the smaller group of at-risk persons among asymptomatic RT-PCR negative patients, may be beneficial in better detecting the under-reported cases.

Conclusion

The detected asymptomatic COVID-19 infection rate during the peak of the second wave among the pre-operative orthopaedic patients was 12.3%, which appears to be slightly higher than the prior detection rate. We are in the opinion of doing RT-PCR evaluation in orthopaedic pre-operative patients before elective surgery. Younger age, female gender, longer duration of admission to RT-PCR test interval, and thereby long hospital stay were found to be risk factors for asymptomatic RT-PCR to be positive. Further, additional investigations focused on at-risk individuals may be useful in identifying asymptomatic cases that could be missed by RT-PCR evaluation.

CRediT authorship contribution statement

Md. Samiul Islam: . **Sultana Parvin:** . **Mohammad Mahbubur Rahman Khan:** . **G.M. Jahangir Hossain:** . **A.K.M. Zahiruddin:** Resources. **Md Jahangir Alam:** Methodology. **Monaim Hossen:** . **Md Wahidur Rahman:** Methodology. **Syed Shahidul Islam:** Conceptualization. **Md Abdul Gani Mollah:** Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical Approval statement

Ethical Approval of the research was obtained from author's affiliated institution

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