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Zero COVID-19 infection in inflammatory bowel disease patients: Findings from population-based inflammatory bowel disease registries in Hong Kong and Taiwan

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Introduction

The novel coronavirus infection (COVID-19) caused by Severe Acute Respiratory Syndrome coronavirus (SARS-CoV)-2 virus have affected more than 8 million people worldwide. Elderly subjects and those with chronic underlying conditions have more severe disease and higher mortality with SARS-CoV-2 infection.^{1,2} Patients with immune-mediated diseases are at increased risk of viral infections.^{3,4} Through April 30, 877 inflammatory bowel disease (IBD) patients with COVID-19 were included in the Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE)-IBD worldwide registry (<https://covidibd.org/>) based on voluntary physician reporting. Self-reported registries may be associated with under-reporting, and in North America and Europe, individuals with suspected COVID-19 symptoms are advised to self-isolate without testing. In the early phase of outbreak, single-center studies in Wuhan and Northern Italy have reported that none of their IBD patients had COVID-19 infection.^{5,6} A multicenter study in Spain reported that 40 IBD patients were infected with SARS-CoV-2, but none required intensive care unit admission or mechanical ventilation.⁷ Hong Kong and Taiwan were amongst the first two regions in the world to be affected by COVID-19 since the initial outbreak in Wuhan. Three months into the pandemic, we utilized population-based registries in Hong Kong and Taiwan to determine the risk of COVID-19 infection amongst IBD patients.

Abstract

Background and Aim: It is unsure whether inflammatory bowel disease (IBD) is a risk factor for novel coronavirus infection (COVID-19).

Methods: IBD patients were identified from population-based databases in Hong Kong and Taiwan from January 21, 2020, until April 15, 2020.

Results: Total 2954 and 2554 IBD patients were identified in Hong Kong and Taiwan, respectively. None had COVID-19. Pooled analysis showed that 65.3%, 39.1%, 4.3%, and 12.8% IBD patients in Hong Kong and 75.8%, 51.4%, 26.1%, and 52.3% in Taiwan were on 5-aminosalicylates, immunomodulators, corticosteroids, and biologics, respectively.

Conclusion: There were no reported cases of COVID-19 infection amongst IBD patients in Hong Kong and Taiwan. IBD patients should continue their usual medications during the COVID-19 pandemic.

Methods

In Hong Kong, patients with IBD were identified from Clinical Data Analysis and Reporting System (CDARS), an electronic health-care database covering patient's demographics, diagnoses, procedures, drug prescription, laboratory results, and mortality from all public hospitals and clinics under the management of Hospital Authority in Hong Kong. Hospital Authority is the sole public health-care provider in Hong Kong, serving 7.5 million population. We further confirmed findings from Clinical Data Analysis and Reporting System with information from the Nixon-TAM Hong Kong IBD registry, a territory-wide registry developed in 2013, covering >95% of IBD patients in Hong Kong. In Taiwan, National Health Insurance (NHI) provided by Ministry of Health and Welfare, Taiwan, is a compulsory program with coverage of 99.7% of 2.3 billion population in Taiwan, and data were updated until 2015. From 2000 to 2015, there were 3806 IBD registered as catastrophic illness. Since there is a 3-year gap for NHI data availability, lack of disease phenotype and severity recording, Taiwan Society of IBD set up a web-based registration, which included one retrospective registration since 2015 and prospective registration since 2017. So far, registered cases covered >80% of those registered in NHI database. The diagnosis of SARS-CoV-2 infection was confirmed by positive RT-PCR testing of nasopharyngeal swabs.

Results

A total of 2954 (59.7% male, mean age: 53.36 ± 16.12 years, 62.3% ulcerative colitis (UC)) and 2,554 (63.1% male, mean age: 44.95 ± 16.34 years, 65.9% UC) IBD patients were identified in Hong Kong and Taiwan, respectively. Pooled analysis showed that 65.3%, 39.1%, 4.3%, and 12.8% IBD patients in Hong Kong and 75.8%, 51.4%, 26.1%, and 52.3% in Taiwan were on treatment with 5-aminosalicylates, immunomodulators, corticosteroids, and biologics, respectively. (Table 1). As of April 15, 2020, 75 210 and 60 956 COVID-19 tests were performed, and 1017 and 429 subjects, in Hong Kong and Taiwan, respectively, were tested positive for SARS-CoV-2. None of these subjects had IBD. In Hong Kong, 40 IBD patients were tested for COVID-19 due to suspected symptoms, contact with suspected cases and travel history, and none were detected positive for SARS-CoV-2. Twenty-eight (70%) were symptomatic, and one had a travel history to mainland China. Thirty (75%) were on 5-aminosalicylates acid, 15 (37.5%) on immunosuppressants (14 thiopurine and 1 tacrolimus), 11 (27.5%) on corticosteroids, and 7 (17.5%) on biologics (3 infliximab, 1 adalimumab, 2 vedolizumab, and 1 ustekinumab). One IBD patient on ustekinumab in Taiwan was a close contact with confirmed COVID-19 case and tested negative for COVID-19.

Discussion

Three months into the first cases of laboratory-confirmed COVID-19 in Hong Kong and Taiwan in January 21 and 22, respectively, we reported zero-infection rate with COVID-19 amongst IBD patients. Hong Kong and Taiwan have one of the lowest numbers of SARS-CoV-2 infected people, and mortality rates (0.39% Hong Kong; 1.40% Taiwan) remain extremely low. These two regions have effectively reduced COVID-19 transmission, measured by

the average number of people each infected individual infects, through swift surveillance, active contact tracing, quarantine for returning residents, and social distancing including universal face masks and school closures.⁸ Transmissibility of COVID-19 (R_t) remained at approximately 1 in Hong Kong.⁹ So far, there is no evidence that IBD patients are at increased risk of COVID-19 unless they also have other comorbidities including increased age, cardiovascular diseases, or diabetes mellitus.¹⁰ Data from SECURE-IBD Registry showed an overall 4% mortality rate amongst IBD patients with COVID-19.¹¹ In Hong Kong and Taiwan, patients with stable IBD are recommended to continue their treatment, which is consistent with recommendations from the International Organization of IBD. Up to 6% adult and 22% pediatric IBD patients who delayed immunosuppressants or biologic treatment had experienced disease flare.^{5,12} Tumor necrosis factor (TNF) antagonists do not appear to be associated with severe COVID-19 outcomes, and it has been suggested that anti-TNF could potentially be protective against COVID-19 although further data are required. The pro-inflammatory cytokine, TNF- α , was found to be increased in various pulmonary inflammatory conditions including acute respiratory distress syndrome.¹³ Data from the SECURE-IBD registry showed that corticosteroids (adjusted odds ratio 6.9; 95% confidence interval 2.3–20.5), but not anti-TNF (adjusted odds ratio 0.9; 95% confidence interval 0.4–2.2), were associated with adverse outcomes in patients with COVID-19 infection.¹¹ Corticosteroids have been consistently shown to be associated with worse clinical outcomes in COVID-19 in both IBD and rheumatology patients.^{5,14} There was a high rate of steroids usage in the Taiwan cohort (55.6% for the retrospective cohort and 26.1% in the prospective cohort); it is thus recommended that physicians should wean off steroids in a timely manner and avoid unnecessary use of steroids unless there are no other alternatives.

To our knowledge, these are the first and only population-based cohorts to report COVID-19 incidence in IBD. Besides, both Hong

Table 1 Characteristics of IBD patients in Hong Kong and Taiwan

	Hong Kong (<i>n</i> = 2954)	Taiwan TSIBD retrospective cohort (<i>n</i> = 2554)	Taiwan TSIBD prospective cohort (<i>n</i> = 537)
Age [†]	53.36 \pm 16.12	43.33 \pm 18.03	43.87 \pm 16.26
Male, <i>n</i> (%)	1766 (59.7%)	1614 (63.1%)	354 (65.9%)
Disease phenotype, <i>n</i> (%)			
• Crohn's disease	1115 (39.1%)	871 (34.1%)	229 (42.6%)
• Ulcerative colitis/IBD-Undifferentiated	1839 (62.3%)	1685 (65.9%)	308 (57.4%)
Medical therapy for IBD, <i>n</i> (%)			
• Corticosteroids [‡]	126 (4.3%)	1421 (55.6%)	140 (26.1%)
• 5-Aminosalicylate acid	1928 (65.3%)	2381 (93.2%)	407 (75.8%)
• Thiopurines	1070 (36.2%)	906 (35.4%)	267 (49.7%)
• Methotrexate	57 (1.9%)	44 (1.7%)	7 (1.3%)
• Tacrolimus	17 (0.6%)	18 (0.7%)	2 (0.4%)
• Biologics			
○ Infliximab	150 (5.1%)	24 (0.94%)	13 (2.4%)
○ Adalimumab	130 (4.4%)	347 (13.6%)	66 (12.3%)
○ Vedolizumab	46 (1.6%)	30 (1.2%)	198 (36.9%)
○ Ustekinumab	49 (1.7%)	0 (0%)	4 (0.7%)

IBD, inflammatory bowel disease; TSIBD, Taiwan Society of Inflammatory Bowel Disease Registry.

[†]Age was expressed as mean \pm standard deviation.

[‡]Corticosteroids include prednisolone (oral), budesonide and budesonide MMX (oral), and hydrocortisone (intravenous).

Kong and Taiwan governments recommend COVID-19 testing in symptomatic subjects and those returning from overseas or had close contacts with confirmed COVID-19 cases. Our rates are applicable to the symptomatic population. Currently, only 1% and 0.3% of population in Hong Kong and Taiwan had received COVID-19 testing, so asymptomatic cases might be missed, but we believe these numbers are small. To detect the true prevalence of COVID-19 amongst IBD and/or the general population, Hong Kong is currently offering serology test for viral antibody as a pilot trial and such data will allow us to identify the “silent” positive subjects.

Nonetheless, both regions need to be prepared for the second wave of the COVID-19 outbreak. In fact, there has been resurgence of COVID-19 cases in certain parts of Asia, like Beijing and Seoul since early June 2020. Continuation of mask policy and maintaining good personal and environmental hygiene should still be enforced. Ensuring adequate supply of surgical masks and personal protective equipment is essential in order to prepare for the possible second wave of COVID-19. Effective contact tracing strategy should be implemented once there is a sign of resurgence of COVID-19.

In conclusion, our population-based data revealed that there were no IBD patients who developed COVID-19 infection during the study period. We should continue to stay alert and be prepared for the possible second wave of COVID-19 infection.

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