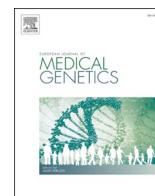




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Clinical research

## Impact of COVID-19 pandemic on patients with rare disease in Hong Kong

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## ABSTRACT

The COVID-19 pandemic has had significant health, social, and economic consequences internationally. While the pandemic has direct implications on infected patients and families, there is a need to examine the pandemic's effect on patients with non-COVID-19-related diseases. This study examines the impact of the COVID-19 pandemic on 272 rare disease patients with 89 distinct rare diseases in Hong Kong using a cross-sectional online survey between April 10 and April 29, 2020 from the patient and caregiver perspective. The pandemic has impacted patient's health status in 46%, service use patterns in 71%, mental health in 79%, daily living in 82%, social life in 92%, and financial status in 81% of patients. Patient's health status, medical and rehabilitation, and mental health were more impacted by the COVID-19 pandemic in the group of patients with any level of dependency according to the Barthel Index for Activities of Daily Living compared with that in the group of patients who are fully independent ( $p < 0.0001$ ;  $p < 0.0001$ ;  $p = 0.0420$ ). This study is the first study to examine the impact of COVID-19 pandemic on the rare disease population in Hong Kong, and demonstrates the pandemic's effect on service and resource utilization, and patient's physical and mental well-being.

## 1. Introduction

With over 25.6 million confirmed Coronavirus disease 2019 (COVID-19) cases worldwide as of September 2, 2020, it is not to our surprise that the COVID-19 pandemic has had significant global impact on infected patients, families, healthcare systems, communities, and the economies. Hong Kong is a Special Administrative Region of China that is located in Southern China, neighboring Guangdong province. COVID-19 was first confirmed to have spread to Hong Kong on January 23, 2020. As of September 2, 2020, Hong Kong has recorded 4823 confirmed COVID-19 cases and 90 deaths, which was the highest in China outside of Hubei. The "Preparedness and response plan for novel infectious disease of public health significance" was raised to emergency response level in healthcare settings on January 25, 2020, in which hospitals were required to suspend all nonessential visits, reduce non-emergency services, and postpone elective surgeries to focus manpower and resources on combating COVID-19. Schools and civil services have been suspended since January 25 and January 29 respectively because of social distancing. There has been a shortage of personal protective equipment (PPE) including face masks and hand sanitizers in the market as people in Hong Kong are worried about

COVID-19 infection and have been stocking up protective gears. Up to 10,000 people were in a queue for hours or even overnight to purchase PPE (Cheung and Lum, 2020).

The impact of the pandemic is beyond patients with COVID-19. This has affected patients with non-COVID-related diseases such as cancer (Rosenbaum, 2020), developmental and epileptic encephalopathies (Aledo-Serrano et al., 2020), and ST-segment-elevation myocardial infarction (Tam et al., 2020). The impact of this pandemic is important to be assessed in the rare disease population, a relatively vulnerable group of patients. Rare disease is defined to affect fewer than 5 per 10,000 people in the European population according to the World Health Organization (World Health Organization). The total number of rare diseases is estimated at 5000 to 8000. They are individually rare, but collectively rare diseases affect 6–8% of the European population (Šimerka, 2009). In Hong Kong, one in 67 is living with at least one rare disease, representing 1.5% of the population (Chiu et al., 2018). With majority of the rare diseases being chronically debilitating or life threatening, healthcare resource reallocation and public gathering restrictions during the pandemic may exacerbate the difficulties this population is facing and pose significant risk on patient's health and social well-being.

Increasing research have been done to assess the impact of the

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### Abbreviations

ADL	Activities of Daily Living
COVID-19	Coronavirus disease 2019
ICD-10	10th version of the International Classification of Diseases and Related Health Problems
RDHK	Rare Disease Hong Kong.

pandemic on different disease populations globally, yet evidence on the rare disease population have been very limited, with the only evidence available in an ongoing study in the European population conducted by the EURORDIS, a non-governmental patient driven alliance of rare disease patient organizations in Europe (EURORDIS Rare Disease Europe, 2020). It is important to assess the impact of the pandemic in each region to guide policy makers in preparing for the possible new wave of COVID-19 infection. The current study sought to prospectively examine the impact of the COVID-19 pandemic in the rare disease population in Hong Kong, a region with the highest number of COVID-19 confirmed cases in China outside of Hubei.

## 2. Methods

### 2.1. Participants

This was a cross-sectional study between April 10 and April 29, 2020, 12–32 days after public gathering restrictions establishment in Hong Kong. Patients with rare diseases or the caregivers of rare disease patients who were at least 18 years of age at the study period were recruited online through Rare Disease Hong Kong (RDHK) and other online social media platforms on a strictly voluntary basis. RDHK is the first and biggest rare disease patient group that was established in 2014 in Hong Kong, comprising 487 members (285 rare disease patients and 153 carers) with over 130 rare diseases as of April 2020. It represents rare disease patients in Hong Kong and it links with Asia Pacific and international rare disease groups. All patients and caregivers were informed of the study's objectives and data confidentiality standards, and informed consent was obtained from all participants from the survey.

### 2.2. Data collection and data analysis

A structured online quantitative survey comprising of 37 questions was distributed to the participants through internet-based sources. For rare disease patients who were under the age of 18 at the time of the study period or who were mentally or physically incapable of survey self-completion, the survey was completed by their parent or caregiver. The survey included questions regarding patient's demographic characteristics, health status, service use patterns, reasons for reduced service use, daily living and social life, and financial status from the patient or caregiver perspective. Participants were also asked to complete the Barthel Index for Activities of Daily Living (ADL) for the patient, which measures a person's ability to perform ten basic activities of daily living and provides a quantitative estimate of the subject's level of dependence. Rare diseases were categorized according to the 10th version of the International Classification of Diseases and Related Health Problems (ICD-10) and were described previously (Chiu et al., 2018). Fisher's exact test was performed to detect any association of health status, medical rehabilitation, mental health, daily life, social life, financial status between the group of patients who are fully independent and the group of patients with any level of dependency according to the Barthel Index for ADL. A p-value of  $\leq 0.05$  was judged to be significant.

## 3. Results

### 3.1. Patient demographics

Between April 10 and April 29, 2020, a total of 272 responses were collected, of which 170 (63%) were from rare disease patients, and 102 (38%) were from caregivers of patients with rare diseases. The rare disease patients and carers are totally independent. The basic demographics of the 272 patients were summarized in Table 1. There are a total of 89 distinct rare diseases included in this cohort, with the most rare diseases being a type of rare neurological disease (55%), followed by rare developmental defect during embryogenesis disease (14%), and

**Table 1**  
Demographic characteristics of the 272 rare disease patients. Impact of COVID-19 on non-COVID-related rare disease patients.

Characteristic		Number of patients (n = 272)
Sex	Male	111 (40.8%)
	Female	161 (59.2%)
Age group	0–2	2 (0.7%)
	2–10	49 (18.0%)
	11–20	16 (5.9%)
	21–40	90 (33.1%)
	41–64	98 (36.0%)
	≥65	17 (6.3%)
Rare disease category	Rare neurologic disease	149 (54.8%)
	Rare developmental defect during embryogenesis disease	37 (13.6%)
	Rare inborn errors of metabolism disease	32 (11.8%)
	Rare hematologic disease	16 (5.9%)
	Rare systemic or rheumatologic disease	12 (4.4%)
	Rare bone disease	6 (2.2%)
	Rare endocrine disease	5 (1.8%)
	Rare eye disease	4 (1.5%)
	Rare respiratory disease	4 (1.5%)
	Rare neoplastic disease	3 (1.1%)
	Rare skin disease	2 (0.7%)
	Rare cardiac disease	1 (0.4%)
	Rare otorhinolaryngologic disease	1 (0.4%)
	Level of independence (Barthel Index for Activities of Daily Living)	Total dependency (score of 0–20)
Severe dependency (score of 21–60)		40 (14.7%)
Moderate dependency (score of 61–90)		77 (28.3%)
Slight dependency (score of 91–99)		24 (8.8%)
Fully independent (score of 100)		98 (36.0%)
Type of disability	Physical disability	135 (49.6%)
	Visceral disability	39 (14.3%)
	Intellectual disability	34 (12.5%)
	Visual problems	32 (11.8%)
	Speech problems	31 (11.4%)
	Specific Learning Difficulties (SpLD)	23 (8.5%)
	Attention Deficit/Hyperactivity Disorder (ADHD)	18 (6.6%)
	Mental disorder/mood disorder	15 (5.5%)
	Autism	14 (5.1%)
	Hearing problems	10 (3.7%)
Main carer's role	No disability	58 (21.3%)
	Self-care	61 (22.4%)
	Relative living in the same household	154 (56.7%)
	Domestic helper	41 (15.1%)
	Caring home workers	9 (3.3%)
	Relative and friends not living in the same household	6 (2.2%)
Others	1 (0.4%)	

rare inborn errors of metabolism disease (12%) (Table 1). Among all patients, 79% have a certain degree of disability, of which, 33% have more than one disabilities. Of those with disabilities ( $n = 214$ ), the top three disabilities were found to be physical disability (63%), visceral disability (18%), and intellectual disability (16%). According to the Barthel Index for ADL, 98 (36%) patients are fully independent (score of 100), 24 (9%) are slightly dependent (score of 91–99), 77 (28%) are moderately dependent (score of 61–90), 40 (15%) are severely dependent (21–60), and 33 (12%) are totally dependent on their carers (score of 0–20). Over half (57%) of the patients are taken care of by their relative(s) living in the same household, followed by self-care (22%), and domestic helper(s) (15%).

There is no reported COVID-19 case within this study population. Among patients who receive care from domestic helper(s) or non-residing relatives and friends ( $n = 61$ ), 66% of the patients claimed that the care was affected by the COVID-19 pandemic, of which, 60% (24/40) were perceived as moderate, severe, or extreme impact. A total of 17 participants provided reason(s) for reduced or paused care provision, reasons included carers being concerned of the risk of COVID-19 infection (35%), infection control regulations launched by hospital or care home (24%), personal reasons (24%), and immigration measures to domestic helpers and overseas relatives (6%).

Of all rare disease patients, 25% are followed-up with at least five different specialties under the Hong Kong Hospital Authority (public healthcare system that provides over 90% of all secondary and tertiary health services in Hong Kong), and 55% of the patients require over five follow-up visits annually. Highest service needs were found to be follow-up visits in specialty clinics, physiotherapy service, and occupational therapy service. Among those who were expected to utilize services offered by the Hospital Authority during the COVID-19 pandemic ( $n = 229$ ), 71% claimed that service use was reduced due to COVID-19, of which, 59% were significantly reduced or completely halted. Medical and rehabilitation services reduction or cancellation were also seen in non-governmental organizations (community 79%, homecare 75%), special education units (77%), and the private sector (63%). The most frequently identified reason for appointment delay or cancellation was the concern of the risk of COVID-19 infection at the service units (67%), followed by being concerned of the risk of COVID-19 infection in public transport (43%), service units unable to provide services (42%), lack of protection gear (22%), financial factors (13%), poor mental health or unstable mood problems (10%), and caregiver unable to accompany the patient (9%).

Health status was impacted in 46% of all patients due to reduced service provision, of which 81% claimed that their health status was slightly worse and 19% claimed that their health status was worse. The fisher exact test demonstrated that there was a significant association of slightly worsen or worse health status during the pandemic in the dependency group compared with that of the fully independent group of patients ( $p < 0.0001$ ) (Table 2). In addition, 79% of the patients claimed that their mental health was affected by the COVID-19 pandemic, especially those who are severely dependent (85%) and totally dependent (97%). Patients' mental health was more impacted in the dependency group compared with that of the fully independent patients ( $p = 0.042$ ). Furthermore, medical and rehabilitation were impacted in 78% of all patients. There was a statistically significant association between affected medical and rehabilitation and patients who are of any level of dependency compared with that in patients who are completely independent ( $p < 0.0001$ ). Among those who claimed that medical and rehabilitation were affected by the COVID-19 pandemic ( $n = 212$ ), 41% claimed that the pandemic had a huge or significant impact on their medical and rehabilitation. The impact was seen to be the most serious in the groups of patients who are severely dependent and totally dependent on their carers, in which 95% and 94% of the their medical and rehabilitation were affected respectively.

Furthermore, patient's daily living, social life, and financial status were also impacted by the pandemic, affecting 89%, 92%, and 81% of

**Table 2**  
COVID-19 pandemic's effect on patients according to the level of independence.

	Level of independence (Barthel Index for Activities of Daily Living)		P-value
	Fully independent (n = 98)	Any level of dependency (n = 174)	
<b>Health status</b>			
Slightly worse/worse	24 (24.5%)	100 (57.5%)	<0.0001
No change	74 (75.5%)	74 (42.5%)	
<b>Medical and rehabilitation</b>			
Impacted	59 (60.2%)	153 (87.9%)	<0.0001
No impact/no comment	39 (39.8%)	21 (12.1%)	
<b>Mental health</b>			
Impacted	71 (72.4%)	145 (83.3%)	0.0420
No impact/no comment	27 (27.6%)	29 (16.7%)	
<b>Daily life</b>			
Impacted	82 (83.7%)	159 (91.4%)	0.0727
No impact/no comment	16 (16.3%)	15 (8.6%)	
<b>Social life</b>			
Impacted	91 (92.9%)	160 (92.0%)	1.0000
No impact/no comment	7 (7.1%)	14 (8.0%)	
<b>Financial status</b>			
Impacted	75 (76.5%)	145 (83.3%)	0.1993
No impact/no comment	23 (23.5%)	29 (16.7%)	

the patients, respectively, though the association between the level of independence and these outcomes were not statistically significant at  $p \leq 0.05$ . Those who are severely dependent or totally dependent on their carers were seen to be affected the most in these areas. In particular, social lives of 100% of the severely dependent and 97% of the totally dependent group of patients were affected. Family income was reduced in 56% of all patients, while expenditure was increased in 57%, with the top three highest expenditure spent in purchasing self-protection resources such as face masks and hand sanitizers, general family expenditure, and study/work-from-home resources. Over 30% and 20% of the patients claimed to be in shortage or extreme shortage of face masks and disinfecting wipes, respectively.

#### 4. Discussion

This study demonstrated the patients and caregivers perception of the pandemic's impact on rare disease patient's health and social well-being in two levels: the effect brought about by the closure of public healthcare services, and the perceived risk of infection from patients and carers. Currently, this serves as the only evidence of COVID-19 in this vulnerable population in Hong Kong. Some of the research findings have been reported in a press release by RDHK (Rare Disease Hong Kong, 2020).

Rare disease patients with appointments in hospitals were experiencing specific difficulties. Getting access to healthcare became more difficult due to patients and carers' perceived risk of COVID infection and healthcare resource allocation to reduce non-emergency services. The impact of COVID-19 on infected patients and the high speed of infection globally have made many to worry about being infected, especially those who are more vulnerable with existing co-morbidities, such as the rare disease population in this study. The ongoing European study by EURORDIS on rare disease patients' experience of COVID-19 reported findings on a similar study period (18–April 28, 2020) across Europe (EURORDIS Rare Disease Europe, 2020). Although the number of confirmed COVID-19 cases in Europe was significantly higher than that in Hong Kong, both the European study and the current Hong Kong study demonstrated patients' and carers' fear of COVID-19

infection at health service providers, with approximately 6 in 10 and 5 in 10 reporting this to be one of the major obstacles in receiving care in Hong Kong and in Europe, respectively (EURORDIS Rare Disease Europe, 2020). On the other hand, in the current study, around 3 in 10 reported that hospitals or medical service units were unable to provide services during the pandemic, in which a similar figure was found in the European cohort (EURORDIS Rare Disease Europe, 2020). Interruptions of care, in particular, cancellation of inpatient medical therapies and rehabilitation services, and delay in surgery and transplantation, pose significant impact on patients' health and social well-being. This was further supported by the findings from the European cohort (EURORDIS Rare Disease Europe, 2020), and even in other non-rare disease populations without COVID-19 (Rosenbaum, 2020; Aledo-Serrano et al., 2020).

To date, a lot of research have been focusing on COVID-related topics such as disease mechanism, public health measures to control infection including social distancing and the use of PPE, and the need for vaccine and population screening. However, this study demonstrated that patients without COVID-19 also face multiple challenges and concerns during the pandemic. There were several limitations acknowledged. Firstly, similar to other studies that aimed to assess the impact of COVID-19 on patients, the results of this study relied on a convenient sample of patients and carers recruited via RDHK or other social media platforms on a strictly voluntary basis. Patients and carers without access to online means or those who are not familiar with electronic devices would not be recruited into this study. Secondly, although patients included in this study covered a wide range of rare diseases in Hong Kong, the sample size was relatively small. Lastly, baseline characteristics such as the Barthel index for ADL were not collected which precluded comparison before and after the pandemic. While this self-reported cross-sectional survey design has its limitations, evidence in delayed emergency consultation, suspended rehabilitation services and management, and the lack of access to PPE warrant policy makers to plan for appropriate service and resource allocation, and to tackle people's fear of infection in the community, especially in the possible resurgence of COVID-19 infection, possibly with co-circulation of the influenza outbreak in the coming winter. Further research from the healthcare system perspective is also warranted to provide a more detailed analysis of the pandemic's impact on the rare disease population.

#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Not applicable.

#### CRedit authorship contribution statement

**Claudia CY. Chung:** Writing - original draft, Data curation, Formal analysis. **Wilfred HS. Wong:** Writing - review & editing, Data curation, Formal analysis. **Jasmine LF. Fung:** Writing - review & editing. **Rare Disease Hong Kong:** Writing - original draft. **Brian HY. Chung:** Supervision, Project administration, Writing - review & editing.

#### Declaration of competing interest

The authors declare that they have no competing interests.

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