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The impact of SARS-CoV2 on the anxiety levels of subjects and on the anxiety and depression levels of their parents

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ARTICLE INFO

Keywords:

Anxiety
Depression
Multiple sclerosis (MS)
Severe acute respiratory syndrome (SARS-CoV2)
Hospital Anxiety and Depression Scale (HADS)

ABSTRACT

Background: The Severe Acute Respiratory Syndrome-CoV2 outbreak was announced a pandemic by the World Health Organization on March 11th, 2020. Both the pandemic itself and the restrictions were thought to create some psychological problems especially in patients with chronic illnesses such as Multiple Sclerosis (MS). This study was conducted to evaluate the impact of SARS-CoV2 pandemic on daily lives of children with MS, and the anxiety status of these patients and anxiety - depression status of their parents.

Methods: This study was performed on a group of pediatric MS patients aged 8–18 years in Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, and Child Neurology Department. Thirty patients with MS and their 30 parents were enrolled to the study. The control group consisted of 49 healthy, age- and sex-matched children and their 49 parents. The patients (and their parents) were asked to complete a web-based survey evaluating access to health care and other changes in daily life between March 11th, 2020 and June 1st, 2020. The State-Trait Anxiety Inventory (STAI) [which is composed of two parts; S-anxiety (STAI-S) and T-anxiety (STAI-T)] was administered to the patients and healthy controls and the results were compared between the two groups to assess their anxiety levels. The Hospital Anxiety and Depression Scale (HAD) [which is composed of two parts; HAD-anxiety (HAD-A) and HAD-depression (HAD-D)] was also given to all parents. The results of the HAD tests were compared between the two groups statistically.

Results: The results of the web-based survey showed that 4 of 9 (44.4%) patients, who had a regular workout program, left the program and 13 (43.3%) patients put on weight during the pandemic. Twenty-two patients (73.3%) could not get direct exposure to sunlight because of the curfew. Therefore, approximately half of the patients started to take vitamin D supplement. Most of the patients (80%) thought that they had higher risk and believed that they would have severe symptoms compared to healthy people. Twenty one (70%) patients disrupted their regular health checks and the most frequent causes were identified as closure of polyclinics to routine patient care (33%) and concerns of getting SARS-CoV2 infection (26,6%). Two of 3 patients who had an MS attack did not go to the doctor during this period. The mean STAI-S scores in MS patients were significantly higher compared to the healthy controls ($p < 0.001$). The level of S-anxiety in all patients was higher compared to the cut off value. The mean HAD A score was found to be significantly higher in them compared to the parents of healthy individuals ($p = 0.001$).

Conclusion: Our results showed that children with MS had negative changes in daily life and high anxiety levels during the pandemic. Since MS patients have also psychiatric comorbidities, they may need psychosocial support especially in this period. Besides, establishment of separate health centers to be used during pandemics for children with chronic illnesses such as MS may be recommended to facilitate access to health care.

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<https://doi.org/10.1016/j.msard.2020.102595>

Received 3 July 2020; Received in revised form 7 October 2020; Accepted 20 October 2020

Available online 26 October 2020

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1. Introduction

The World Health Organization (WHO) declared the Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV2) outbreak a global pandemic on March 11th, 2020. As of May 15th, WHO reported 4.248.389 cases and 292.046 deaths due to SARS-CoV2 infection in 216 countries (Organization, n.d.). SARS-CoV2 infections have caused high mortality in the elderly and those with chronic infections (Lu et al., 2020). However, children seem to have milder clinical course and fewer complications compared to adults; rather children may be carriers of the disease without any symptoms and infect older people. According to a systematic review in 2020, asymptomatic individuals had a high proportion among the children infected with SARS-CoV2, and this condition contributed to spread of the virus (Baojia et al., 2020). However pediatric outcomes are usually excellent due to milder clinical course, complications such as septic shock, renal failure, acute respiratory distress syndrome and multiple organ damage were reported in a small number of pediatric patients (Yu and Chen, 2019). Recently, multi-systemic inflammatory syndrome, which was initially named Kawasaki like-disease due to similarity in terms of clinical course, was reported in children. The disease renamed as pediatric multisystem inflammatory syndrome and onset is usually preceded by gastrointestinal symptoms, which are followed by systemic vasculitis with prolonged, nonresponsive fever associated with rash, palmar erythema, conjunctivitis, oral mucositis, and laterocervical lymphadenopathy, and sometimes complicated with myocarditis and/or severe coronaritis (Schroeder et al., 2020). Therefore, several countries have imposed various restrictions such as curfew and abandoning social life especially for young and old people.

In Turkey, the first case of SARS-CoV2 infection was reported on March 11th, 2020. The Turkish Ministry of Health declared a curfew restriction for individuals under 20 years and over 65 years on April 3rd to prevent physical contact between these groups, so that the risk of spread and mortality could be decreased. For this, schools were closed, social contacts were restricted, most public and leisure places, except vital services, were closed down, staying at home was highly recommended, and the whole community was recommended to obey the rules of social isolation and 14 rules announced by The Turkish Ministry of Health (See Appendix) to avoid the spread of SARS-CoV2 infection (<http://en.istanbul.gov.tr/14-rules-against-new-coronavirus-risk>).

These quick actions decelerated the spread of new cases of infection in Turkey. However, such a sharp change in children's life might have led to adverse psychological effects (Liu et al., 2020).

Such a change in people's life brought along other problems as well. Large numbers of patients with SARS-CoV2 infection were admitted to the hospitals. As a result, people avoided going to the hospital out of fear of infection. Therefore, people with chronic diseases had some problems such as reaching the doctor and obtaining medications and treatment during the pandemic. In addition, some chronic diseases have potential risks in terms of infectious diseases due to both nature of the disease and immunosuppressive treatment. Multiple sclerosis is one of the chronic diseases, which may be activated by infections and may include immunosuppressive agent as a treatment choice. Therefore, it is thought that adverse psychological effects of the pandemic would be more severe in patients with MS and their parents compared to healthy people. On the other hand, psychiatric comorbidities have long been recognized as a concern in the MS population. Many studies revealed that anxiety and depression are the most common psychiatric disorders in all individuals with MS. In a current systematic review, the prevalence rates of depression and anxiety were reported to be 31% and 22, respectively, in MS patients including adults (Boeschoten et al., 2017). Results of the studies conducted with pediatric patients showed similarities with those of the adults and the levels of anxiety and depression in children were 19% and 14.3, respectively (Ostojic et al., 2016).

In this study, we aimed to evaluate the impact of SARS-CoV2 pandemic on daily lives of children with MS, and the anxiety status of

these patients and anxiety - depression status of their parents.

2. Materials and methods

2.1. Subjects and controls

This prospective and cross-sectional study was performed on a group of patients with MS and their parents in Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Child Neurology Department. A total of 60 individuals including thirty patients who met the inclusion criteria and their 30 parents (one parent of each patient) were enrolled to the study as the subject group. The study inclusion criteria were as follows: 1. having a definite diagnosis of MS based on 2017 Mc Donald Criteria (Thompson et al., 2018), 2. being aged between 8 and 18 years, 3. having been followed up by our clinics for at least one year 4. having adequate intellectual ability and educational background (for both patients and their parents) 5. having been informed and given verbal consent for participation in the study.

Also, 49 healthy (without any chronic and acute disease), age- and sex-matched children and their healthy parents, including one parent of each healthy child, were included in the study as the control group. All 98 controls had adequate intellectual ability and education to fill the survey.

2.2. Investigation

This study was carried out in two stages.

In the first stage, MS pediatric patients (and their parents) were asked to complete a web-based survey evaluating access to health care and other changes in daily life between March 11th, 2020 and June 1st, 2020. Disease flares, problems about reaching the hospitals, and medication, any history of contact with confirmed SARS-CoV2 infections of self or family members, encounters with digital screen, workout program, caring about diet, use of vitamins, direct exposure to sunlight, obeying the 14 rules recommended by the Ministry of Health and similar issues were questioned in the survey. In the second stage, surveys were administered to the patients, healthy controls and also the parents of patients and controls to assess their anxiety and depression status.

One of the surveys, the State-Trait Anxiety Inventory (STAI), is a questionnaire that measures anxiety. It was developed by Spielberger et al. (Spielberger et al., 1983) and adapted to Turkish by Le Compte and Öner (LeCompte and Envanterinin, 1975). The test assesses anxiety levels under two subscales within this measure: First, the State anxiety scale evaluates the current state of anxiety; and secondly, the trait anxiety scale evaluates relatively stable aspects of anxiety proneness including general states of calmness, confidence, and security. Respectively, STAI is formed of two parts including 20 questions for S-anxiety (STAI-S) and 20 questions for T-anxiety (STAI-T). The range of scores for each subtest is 20–80, higher scores indicating greater anxiety. The cut off point is accepted as 41 for STAI-S and 45 for STAI-T (Ercan et al., 2015). We accepted cases as positive if their scores were higher than the cut off point. The patient and control groups were compared according to STAI scores to investigate the anxiety status during SARS-CoV2 pandemic.

The other survey, Hospital Anxiety and Depression Scale (HAD) test which assesses depression and anxiety level in one test, was also given to the parents of both the study and control groups. The test is composed of 14 questions, 7 of which assess anxiety [HAD-anxiety (HAD-A)] and 7 of which assess depression [HAD-depression (HAD-D)]. The cut off value is 10 for anxiety and 7 for depression. We accepted cases as positive if their scores were higher than the cut off point. The HAD test was adapted to Turkish by Aydemir who showed that HAD was an appropriate instrument for Turkish people. The Cronbach Alpha Internal Consistency Coefficient of the scale was 0.8525 and 0.7784 for anxiety and depression subscales, respectively (Aydemir et al., 1997).

The results of the HAD tests were compared between the parents of the patients and healthy children to investigate anxiety and depression

states of the parents of our patients with MS; Also, the correlations between anxiety status of MS patients and anxiety-depression status of their parents were examined statistically. Same correlations were also analyzed in the controls and their parents.

2.3. Statistical analyses

The results were analyzed by the Statistical Package for Social Sciences ver. 15. The parametric data were presented as Mean and Standard Deviation (SD). The student's T-test was used to compare the parametric data, and the Mann-Whitney U Test was used for comparison of non-parametric data. Spearman's RHO Correlation Coefficient 'r' was used to determine the relationship between different variables. For all these tests, a probability (p) value of < 0.05 was considered significant.

2.4. Ethics

This study was approved by the Ethics Committee of Istanbul University- Cerrahpaşa Faculty of Medicine. The study was carried out in accordance with the Helsinki Declaration.

3. Results

3.1. Data groups

The study group consisted of 30 pediatric MS patients (Female/Male; 19/11), who had been followed up for 1–5 years at our child neurology department and were aged between 8 and 18 years (15.6 ± 2.1 years), and their 30 parents. In the study group, the age at onset of the disease was 12.9 ± 2.7 years, and the duration of the disease was 2.5 ± 1.3 years.

Also 49 controls (Female/Male; 29/20) aged between 8 and 15 years (15.6 ± 2.1), and their parents were included in the study. There were no significant differences between the pediatric MS patients and healthy children in terms of age ($p = 0.153$) and gender ($p = 0.114$). Demographics and clinic features of the patients with MS are shown in [Table 1](#).

3.2. Subjects

The results of the first stage showed that 9 patients (30%) had regular workout program before the pandemic, but 4 of them (44.4%) left

Table 1
Demographic and Clinical Features of Patients with Multiple sclerosis.

Features	n (n:30)	%
Medications DP		
Interferon 1A	10	33.3
Interferon 1B	10	33.3
Mycophenolatmofetil	2	6.6
Fingolimod	2	6.6
Dimethylfumarat	2	6.6
Natalizumab	2	6.6
Rituximab	2	6.6
Regular medication intake		
Before pandemic	29	96.6
During the pandemic	26	86.7
Regular Workout/Physical Exercise		
Before pandemic	9	30
During pandemic	5	16.6
Regular Balanced Diet DP	19	63.3
Weight Gain DP	13	43.3
Concern of Risk Increase DP	24	80
Disruption of Doctor Checks DP	21	70
Decrease in Exposure to Sunlight DP	22	73.3
Vitamin D intake – starting in DP	13	43.3
Increased exposure to smoking DP	3	10
Having attack DP	3	10

DP: During Pandemic.

regular workout program during the pandemic. Only 19 (63.3%) patients reported that they cared for their recommended diet during the curfew. In total, 13 (43.3%) patients put on weight despite the fact that 6 (46,1%) of them cared for their diet. The children who put on weight had significantly higher STAI-S and STAI-T scores compared to the ones who did not put on weight ($p = 0,03$ and $p = 0,009$ respectively). Twenty-two patients (73.3%) could not get direct exposure to sunlight because of the curfew. Therefore, approximately half of the patients (13 patients; 43.3%) started to take vitamin D supplement during this period. All patients and their parents obeyed the rules of social isolation and 14 rules recommended by the Ministry of Health.

The number of patients who disrupted their regular health checks was 21 (70%). Causes of disruptions were identified as closure of polyclinics to routine patient care in 10 patients (33%), concerns of getting SARS-CoV2 infection in 8 patients (26,6%), problems about inter-city travel in 2 patients (6.6%) and curfew in 1 patient (%3.3).

STAI-S and STAI-T were not found to be significantly different between the patients who could and could not have regular health checks ($p:0,235$, $p:0,212$).

During the curfew, 26 patients (86.7%) took their medications regularly. Two patients (6.6%) using interferon 1A, 1 patient (3.3%) using interferon 1b, and 1 patient (3.3%) using dimethylfumarate did not take their medications regularly due to reasons not related with the pandemic.

During the pandemic period, 24 patients (80%) thought that they had higher risk, and believed that they would have more severe symptoms compared to healthy people. Eleven patients (36.7%) reported that they thought their medication would increase the risk of SARS-CoV2 infection, but the anxiety of these 11 patients did not differ from the other 19 patients in terms of state-anxiety and trait-anxiety status ($p: 0,56$ and $p:0,93$).

Three of 30 patients (10%) had an MS attack during this period. One of them applied to hospital and received attack treatment, but the other 2 patients did not apply to the hospital due to their fear of SARS-CoV2 infection. The patients who had attacks had no regular workout program, and less direct exposure to sunlight, but they were taking vitamin D supplement. Demographic features of these patients are shown in [Table 2](#).

3.3. STAI and had results

In the second stage, the STAI scores in MS patients and healthy controls were compared statistically. The level of S-anxiety of all patients was higher than the cut off value (normal <45). All MS patients were accepted as positive cases. In the control group, individuals who had high S-anxiety levels constituted 34.7% of the group, and they were accepted as positive cases.

The mean value of S-anxiety was significantly higher in the patient group compared to the controls ($p=<0.001$). However, there was no significant difference in terms of the mean T-anxiety value between the two groups ($p = 0.763$) ([Table 3](#)).

Upon analyzing the HAD scales of the parents, it was observed that 53.3% of the parents of the MS patients had higher HAD-A scores and 80% had higher HAD-D scores than the cut off value. In the control group, 28.6 and 49% of the parents had higher HAD A and HAD D scores, respectively. The mean HAD A score was found to be significantly higher in the parents of the MS patients compared to the parents of the healthy individuals ($p = 0.001$). The mean HAD-D score was also higher in the parents of the patients, but the difference was not statistically significant ($p = 0.095$).

Finally, the correlations between anxiety levels of MS patients and anxiety-depression levels of their parents were examined statistically. Same correlations were also analyzed in the controls and their parents.

For the correlations, STAI-S and STAI-T scores and HAD-A and HAD-D scores were taken either as positive (higher than the cut off point) or as negative (lower than the cut off point).

Table 2
Demographic Features of the Patients who had attacks.

	Patient 1	Patient 2	Patient 3
Age (year)	16	14.4	12.5
Gender	F	F	F
BMI	22	26.6	26.2
Regular medication intake DP	Yes	Yes	Yes
Medication	Interferon 1B	Interferon 1A	Interferon 1A
Symptoms during attack of MS	Diplopia	Numbness in right hand	Back pain and Paresthesia on legs
Duration of attack	2 days	6 days	9 days
Application to hospital during attack	Yes	No	No
Workout/Physical Exercise			
Before pandemic	negative	negative	Negative
During pandemic	negative	negative	Negative
Balanced diet DP	Yes	No	Yes
Weight gain DP	None	None	None
Vitamin D intake DP	Yes	Yes	Yes
STAI-S score	62	56	59
STAI-T score	42	42	42
HAD-A score of the parent	12	6	9
HAD-D score of the parent	7	7	7

BMI: Body Mass Index DP: During Pandemic.

The correlations between the STAI-S and STAI-T scores of MS patients and HAD-A and HAD-D scores of their parents were found to be significant (Table 4).

In the healthy group, there was no significant correlation between the STAI-S and STAI-T scores of controls and HAD-A scores of their parents ($p = 0.285$, $p = 0.489$). There was also no correlation between STAI-T and STAI-S scores of healthy children and HAD-D scores of their parents ($p = 0.247$, $p = 0.115$).

4. Discussion

Multiple sclerosis is a chronic inflammatory and degenerative disorder of the central nervous system. Although its pathogenesis is still unclear, the underlying pathogenesis is thought to be related to autoimmune characteristics influenced by environmental or infectious factors in genetically susceptible individuals (Duquette et al., 1987; Donati, 2020). Infections may contribute to relapses and a worsening of neurological symptoms as well as leading to morbidity (Willis and Robertson, 2020). Although there are limited data about the relationship between SARS-CoV2 infection and MS, people may think that MS patients who already have an immune-related disease can be more susceptible to infectious diseases- here- SARS-CoV2, which may bring adverse psychological effects.

In our study we expected that the changes such as curfew, social isolation and closure of schools may also lead to an increase in the level of anxiety in patients with MS. In other words, these subjects may be affected to a greater extent during the pandemic due to their vulnerability towards psychiatric comorbidities. Considering that the risk of attack for MS patients always exists and is not predictable, their existing

anxiety burden may be heightened due to the effects of SARS-CoV2 pandemic. Little knowledge about the SARS-CoV2 infection, the risks of contamination, and changes in daily life may lead to anxiety. Consistent with expectation, we observed that anxiety symptoms of MS patients seemed to be more remarkable compared to healthy controls. Our results showed that 100% of MS patients had pathological state anxiety, whereas this ratio was 34,6% in the control group . However, the subjects and controls were similar in terms of trait anxiety levels. One of the causes of the striking difference in rates between the two types of anxiety may be related to the pandemic. In other words, the higher levels of state anxiety, which shows current anxiety, may indicate that these young children with MS were more vulnerable compared to healthy children during the pandemic. We do not know the pre-pandemic anxiety status of our patients. In previous reports, psychiatric comorbidities such as anxiety and depression, which may be attributable to several factors such as having chronic illnesses, using disease modifying drugs and immunological and inflammatory changes have been noted in MS patients. In 2015, a systematic review including population-based studies showed that anxiety and depression both affected > 20% of the MS population (Marrie et al., 2015). The results of the studies including pediatric patients with MS are similar to the studies including adults with MS; the prevalences of depression and anxiety were found to be 19% and 14.3, respectively (Ostojic et al., 2016). Therefore, it could be thought that pre-pandemic levels of depression and anxiety in our patients had been higher than those in healthy children.

We found out that 3 of 30 patients had an attack during the curfew and 2 of them could not apply to hospital due to their fear of getting SARS-CoV2 infection. Even though we were following up these patients, we could only learn that they had attacks during the curfew when they mentioned this in the survey. Regular health checks were disrupted in 70% of the patients due to various problems related to SARS-CoV2 infection. Four patients did not use their medications regularly, although the Ministry of Health provided patients with chronic diseases with the opportunity to obtain their medications directly from pharmacies upon their previous patient records without having to go to the hospitals. Due to imposed restrictions, 80% of the patients thought that they would have higher risk, and 36.7% thought that their medications would increase the risk of SARS-CoV2 infection. Although the proportion of those who had regular workout program was low (30%) before the pandemic, this proportion decreased even more during the pandemic (16.6%).

During the curfew, 43.3% the patients put on weight. While 73.3% of

Table 4
Correlation Analysis Between Anxiety Scores of MS patients and Hospital Anxiety/Depression Scores of Parents.

	HAD-A of parents		HAD-D of parents	
STAI-S	Correlation	1	Correlation	0.733
	Coefficient		Coefficient	
	Sig. (2-tailed)	<0.001	Sig. (2-tailed)	<0.001
	N	30	N	30
STAI-T	Correlation	0.733	Correlation	0.738
	Coefficient		Coefficient	
	Sig. (2-tailed)	<0.001	Sig. (2-tailed)	<0.001
	N	30	N	30

Table 3
The Mean Value of STAI and HAD Scores in the Study and Control Groups.

Tests	Patients/Parents of Patients	Controls /Parents of Controls	*P value
S-anxiety	60.6 ± 3.4	40.7 ± 9.6	<0.001
T-anxiety	43.0 ± 2.8	43.4 ± 7.3	0.763
HAD-A	10.6 ± 3.4	7.8 ± 3.6	0.001
HAD-D	8.0 ± 2.8	6.6 ± 3.8	0.095

*Descriptive statistic and Mann Whitney U test were performed.

the patients had less exposure to sunlight, 43.3% took vitamin D supplement. As a pleasing result, all the patients obeyed the rules of social isolation and 14 rules recommended by the Ministry of Health.

Strong positive correlations were found between the anxiety scores of the MS patients and both anxiety and depression scores of their parents. However, we did not find any correlations within the healthy group. One of the possible causes of high anxiety status of parents of MS patients may be that having a child with a chronic disease at a time which heightened public awareness of possible risk for these children. In addition, this might have arisen from the emotional/mental interaction between the child and the parent (i.e. parent's mood can affect child's mood or vice versa). Similarly, Neda Razaz et al. also found that there was a relationship between the parents who were MS patients and their controls in terms of mental health disorders (e.g. anxiety and depression), (Razaz et al., 2016).

4.1. Limitations

There are several limitations to our results. The findings of the study should be interpreted cautiously before replication on larger groups of children, because the sample size was small and the group of children with MS was heterogeneous especially with respect to attack rates. Furthermore, this is a cross-sectional study, preventing an analysis of cause and effect.

We do not have any data about basal anxiety levels of our sample. Therefore, more studies need to be conducted with onset subjects out of pandemic time so that we can have a better understanding of the anxiety symptoms of these children.

5. Conclusion

In our study, children with MS had negative changes in daily life such as disruption of workout program, weight-gain, less exposure to sunlight, and difficulty in accessing health care service. Since disruption of routine health checks was an important problem for patients with chronic illnesses such as MS, establishment of separate health centers to be used during such epidemic/pandemic periods for these children may be recommended.

Our results showed that children with MS were affected to a greater extent compared to healthy children in terms of anxiety symptoms, and highlighted their need for psychiatric evaluation and psychosocial support especially during the pandemic. Psychiatric assessment and symptom control in their parents seem to be an important component considering the interaction between them.

CRedit authorship contribution statement

Tugce Damla Dilek: Conceptualization, Writing - original draft, Visualization. **Zehra Boybay:** Writing - review & editing. **Nursena Kologlu:** Investigation, Writing - review & editing. **Oguzhan Tin:** Investigation, Writing - review & editing. **Serhat Güler:** Conceptualization, Methodology, Writing - original draft, Visualization. **Sema Saltık:** Conceptualization, Formal analysis, Visualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

None

Appendix

- 1 Wash your hands frequently with soap and water for at least 20 s.
- 2 Keep at least 3–4 steps away from people who show symptoms of common cold.
- 3 Ventilate your environments frequently.
- 4 Wash your clothes with normal detergent at 60–90 °C.
- 5 If you have complaints of such as fever, cough and shortness of breath, wear a mask and consult a healthcare provider.
- 6 Do not touch your eyes, mouth, and nose with your hands.
- 7 Spend the first 14 days at home on your return from abroad.
- 8 Cover your mouth and nose with disposable tissues when coughing or sneezing, and use inside of your elbow in absence of tissues.
- 9 Cancel or postpone your overseas journey.
- 10 Clean your frequently used surfaces, such as door handles, fixtures and sinks with water and detergent daily.
- 11 Avoid close contact, such as shaking hands and hugging.
- 12 If you have cold symptoms, do not contact with elders and patients with chronic diseases, do not go out without wearing a mask.
- 13 Do not share any personal belongings (casual items such as towels) in common.
- 14 Drink plenty of fluids, eat a balanced diet, and pay attention to your regular sleep pattern.

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