Is any point to be skeptical regarding individuals with Down syndrome who are admitted with COVID-19?

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Abstract

SARS-CoV-2 and COVID-19 pandemic may affect susceptible populations such as people with Down's syndrome. People with Down's syndrome are more likely to get infections that cause respiratory problems and auto-inflammation. They also have many comorbidities linked to a worse prognosis compared to the general population.

Introduction:

The most common chromosomal cause of developmental disabilities is Down syndrome (DS), caused by a trisomy of specific gene 21. It has been linked to several co-existing health disorders and immunological dysfunction, all of which can influence the disease symptoms and increase the risk of life-threatening disease from exposure to the emerging severe acute respiratory syndrome coronavirus 2. (SARS-CoV-2) (1). COVID-19 is primarily a respiratory infection, although it can progress to a severe illness with multi-organ failure and mortality (1). Immune dysregulation in people with Down syndrome makes them more susceptible to viral diseases, while structural airway characteristics make them more susceptible to respiratory infections (2-4). Respiratory diseases are a leading cause of death in people with Down syndrome (5, 6). People with the Down syndrome condition appear to be especially vulnerable to COVID-19, with a four-fold increased risk of COVID-19-related hospitalization and an estimated three- to ten-fold more significant risk of COVID-19-related fatality (7-9). Several genetic variants in coordinating immune responses are found on chromosome 21 in Down syndrome, and their amplification causes an increased immune system. Four interferons (IFN) receptors, which function as a sensor, operate for the cytokines interleukin (IL)-10, IL-22, and IL-26, are the primary immunity stabilizers encoded on chromosome 21 (10). Additionally, people with Down syndrome have immunological and non-immune cells vulnerable to IFN activation (11). In people with Down syndrome, persistent immunological dysregulation is frequent. As a result, they are more susceptible to infections, particularly bacterial and virus-related pneumonia (12). T cell lineages in adults with Down syndrome have been demonstrated in previous research to display significant evidence of heightened activity even in the absence of any evident infections, a trait presumed to be driven by persistent IFN hyperactivity (13). As a result, patients with Down syndrome have a strong IFN response, which is vital for elevating antiviral responses and triggering and magnifying the cytokine storm (3, 14). It is unclear how people with Down syndrome may react to the illness. Espinosa provided solid evidence in a recent analysis that people with trisomy 21 have a higher chance of getting more severe symptoms and have higher hospitalization rates, intensive care admission, secondary bacterial infections, and mortality from SARS-CoV-2 infection (3). We

address adults' patients with Down syndrome by reporting the results of COVID-19 who was hospitalized in a private hospital in Chittagong, Bangladesh.

Case history:

A 42-year-old woman with Down's Syndrome, a background of hypothyroidism on L-thyroxine, and diabetes mellitus developed a fever on 10th January 2022, and the next day, she had mild cough associated weakness. She had no history of vaccination against COVID-19. On 12th January 2022, she underwent a COVID-19 test and became positive; the same day, she started tab Azythromycin 500mg once daily, tab Motelukust 10mg once at night and tab paracetamol 500 mg 8 hourly as physician advised. Her vital was within the standard limit the following week except for temperature. She was admitted to the COVID-19 department, Feni hospital, on 21st January 2022, with respiratory distress progressively worsening over the last few days and was accompanied by fever, myalgia, and cough. At the time of the patient's admission, the clinical assessment was done, which revealed neurological stability with a Glasgow score of 15/15, body temperature of 38.2 degrees Celsius with a heart rate of 98 beats per minute, blood pressure (BP) of 130/80 mmHg, peripheral oxygen saturation (SpO2) at ambient air (AA) of 95 per cent with Arterial blood gas test (Table: 01) and underwent routine and relevant investigation (Table: 01). Then she was referred to Chittagong hospital due to better facilities and got admitted on 25th January 2022. Again, they do, the nasopharyngeal swab PCR test for SARS-CoV-2 was negative on that day, but a CT scan (computerized tomography) revealed bilateral ground-glass pneumonia with an estimated 30 per cent parenchymal involvement and no sign of pulmonary embolism (Figure: 01). She again did the blood test and urine test (Table:01) and started the treatment as per protocol (Table:02), including continuous positive airway pressure (CPAP). She was transported to the cabin on 1st February 2022, with oxygen delivery at a rate of 2-3 L per minute through a nasal route due to her improved respiratory status. She was later discharged on 6th February 2022 with medication and respiratory exercise with stable conditions.

Discussion:

This may be the first reported in Bangladesh with this combination of Down syndrome and COVID-19 patients to the best of our knowledge. People with intellectual disabilities the unique issues resulting from the COVID-19 epidemic (15). Down syndrome patients, who have the most typical kind of intellectual impairment(16). With a prevalence of about 1 in 1,000 live births, Down syndrome seems to be the most prevalent chromosomal defect in people around the globe. Considering an estimated prevalence of Down syndrome of around 0.125% in Bangladesh (17). Individuals with Down syndrome have unique socio-demographic potential risks for COVID-19. They are more likely to have complications such as obesity, diabetes, congenital heart disease, and respiratory disorders linked to a worse COVID-19 outcome in the overall population (18). Furthermore, The production of cytokines that are more involved in the triggering of a prothrombotic procoagulant reaction (19) and Down syndrome may be an established risk factor for thromboembolic illness and an increased risk of cardiovascular episodes (20, 21). There is a higher incidence of respiratory infections, immunological dysfunction, systemic inflammation, early ageing, and complications linked with COVID-19 risk, all of which contribute to poor patient outcomes, although it is uncertain they are more prone to SARS-CoV-2 infection (3).

The TMPRSS2 gene is found on chromosome 21q22.3, suggesting that it may be overexpressed in people with Down syndrome. The protein produced by this gene is related to the increase in TMPRSS2 receptors at the molecular level. As a result, it is reasonable to believe that this contribution may account for some of these people's more severe COVID-19 cases. Studies in Down syndrome patients can help researchers learn more about the processes behind the infectious process in COVID-19, which will help them better understand and prioritize treatments for severe instances in the overall population (22).

This case demonstrates the need for more clinical and scientific research into the genetic susceptibilities that influence the severity of COVID-19 and SARS-CoV-2-related problems. While there is an apparent dearth of systematic epidemiological data on COVID-19 in Down syndrome patients, we want to draw attention to this hyperinflammatory and life-threatening presentation of adults with Down syndrome to ensure the early

clinical diagnosis of comparable cases in the ongoing SARS-CoV-2 pandemic.

In one research, hospital individuals with Down syndrome and COVID-19 had a relative risk of mortality of 2.9 compared to controls (23). Since the H1N1 outbreak in Mexico in 2009, the chances of intubation and mortality were 8-fold and 335-fold higher for individuals with Down syndrome than for others (24). The one research of 12 people with Down syndrome and COVID-19 revealed that those admitted with COVID-19 had a worse illness than their age-matched counterparts (25). In these two investigations, people with Down syndrome are identified as a high-risk population for severe COVID-19 with a poor prognosis. Difficulty breathing, fever, coughing, and muscle fatigue were the most common signs and symptoms of COVID-19 in patients with Down syndrome (4). This case report supports this observation. On the other side, patients with Down syndrome had a more severe condition than controls, with a higher risk of sepsis and the need for mechanical breathing, according to a prior study (25). It's possible that in the first wave of the pandemic, people with Down syndrome were hospitalized later due to diagnostic delays, resulting in even worse clinical outcomes. This tendency, however, has not been seen in the overall population who have been treated for SARS-CoV-2 pneumonia(26, 27). This patient was diagnosed as soon as her symptoms began, and she received rapid treatment for her problem and additional investigations. So, this patient outcome, she was discharged from hospital with a stable condition. In COVID-19 individuals with Down syndrome, the main complication for inpatient and death was age, which is in line with evidence from the general population as published in previous ISARIC4C survey data (23). Significantly, we noticed an elevated death rate starting at 40, much younger than the entire populace. Many indications of accelerated ageing have been extensively observed in people with Down syndrome (28). In our case, the patient's age of 42 was a risk factor during admission into the hospital as for COVID-19.

Limitation, we solely focused on hospital admissions; outcomes in the specific community (including asymptomatic and mild COVID-19 cases) might vary.

Effective strategy from both family members and local practitioners is required for individuals with Down syndrome to adhere to the necessary guidelines. To summarize, patients with Down syndrome have multiple risk factors for respiratory infections and poor outcomes due to a high number of comorbidities, anatomical changes in the upper respiratory tract, and immunological dysregulation. Individuals with Down syndrome are among the priority candidates for early immunosuppression, current antiviral treatments, and, once accessible, the SARS-CoV-2 vaccine.

Conclusion:

Our outcomes suggest that patients with Down syndrome should pay special attention to COVID-19 early identification, management and prevention since they are at a higher risk of hospitalization-related complications during the COVID-19 outbreak. Individuals with Down syndrome are high-risk groups for significant COVID-19 infection and should get the vaccine as fast as possible. Additionally, if they become hospitalized due to the disease, they should receive more rigorous support and care.

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Declaration of competing interest

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

Author contributions

The article's first draft was written by MAA and MDH. MAA, IIK, SN, ASB, SA and SD contributed to the literature review and manuscript preparation. All authors contributed to the final version by critically reviewing and editing drafts.

Ethical approval

The article is about a case study. As a result, our Ethics Committee's consent was not required.

Consent

The patient's written informed consent for publishing of this case report, as well as images, was acquired.

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Table and figure

Table 1. Investigation parameters of the cases

Sl No	Name of the test	Date	Findings
01	Blood C/S	02.02.2022	No growth.
02	HRCT of Lung	31.01.2022	Bilateral peripheral & central Pneumonitis. Highly suspicious for COVID-19. CO-RADS:04. About 30% lungs involved. RT-PCR & hematological correlation please. Other findings: bilateral small pleural effusion.
03	Procalcitonin	28.01.2022	1.51 ng/mL
04	Creatinine	24.01.2022	1.2 mg/dl
		27.01.2022	1.10 mg/dl
05	GFR	27.01.2022	57.0 ml/min/.73 m3
06	Troponin-I	27.01.2022	0.64 ng/mL

Sl No	Name of the test	Date	Findings
07	CRP	21.01.2022	126 mg/L
		27.01.2022	72 mg/L
08	D-Dimer	24.01.2022	3.01 ug/mL
		27.01.2022	1.65 ug/mL
09	ALT	25.01.2022	23 U/L
		26.01.2022	22 U/L
10	Iron	25.01.2022	16 ug/ml
11	25 OH-Vitamin-D	24.01.2020	22.5 ng/ml
12	HbA1-c	21.01.2022	7.8 %
13	RBS	21.01.2022	14.75 mmol/L
14	TSH	21.01.2022	6.023 Uiu/mL
15	Urine RME	21.01.2022	Chemical Examination: Albumin-Nil Sugar-Nil Bilirubin-Nil Ketones-Positive Nitrate-Negative Microscopic Examination: RBC-Nil Pus Cells-2-4HPF Epithelial Cells-0-1HPF
16	Febrile Ag/Triple Ag	21.01.2022	Anti-Rickettsia Ab: OX2-1:80 OX19-1:80 OXK-1:80 Anti-brucella Ab: Anti B. Abortus-1.80 Anti B. Melitensis-1.80 Widal test: TO: 1.80 AO: 1.80 BO: 1.80 TH: 1.80 AH: 1.80 BH: 1.80
17	S. Electrolytes		
	S. Sodium (Na)-mmol/L	02.02.2022	141
		28.01.2022	140
		27.01.2022	141
		26.01.2022	144
		24.01.2022	136
	S. Potassium (k)-mmol/L	02.02.2022	3.62
		28.01.2022	4.27
		27.01.2022	4.50
		26.01.2022	4.33
		24.01.2022	3.82
	S. Chloride (Cl)-mmol/L	02.02.2022	94
		28.01.2022	99
		27.01.2022	103
		26.01.2022	102
		24.01.2022	96
	S. Calcium (Ca)-mmol/L	02.02.2022	0.99
		28.01.2022	0.74

Sl No	Name of the test	Date	Findings
		26.01.2022	0.99
		24.01.2022	1.03
18	ABG	02.02.2022	PH:7.45, pCO2-46.9, pO2-48,
		28.01.2022	PH:7.42, pCO2-46.4, pO2-156
		26.01.2022	PH:7.43, pCO2-47.4, pO2-49
		24.01.2022	PH:7.48, pCO2-31.9, pO2-87
19	Hb (g/dL)	21.01.2022	10.1
		27.01.2022	9.4
20	WBC(/L)	21.01.2022	6.21X 10ˆ9
		27.01.2022	7.4X 10ˆ9
21	Platelets	21.01.2022	217X10ˆ9
		27.01.2022	145X10ˆ9
22	Neutrophil %	21.01.2022	63
		27.01.2022	86
23	ESR (mm)	21.01.2022	92
		27.01.2022	80
24	MCV (FL)	21.01.2022	76.5
		27.01.2022	78.7

Table 2. Treatment

Date	Hospital	Treatment	Status
24.01.2022	Feni Diabetes Hospital	Inj. Meropenem (1gm) Inj. Dexamethasone (5mg) Inj. Enoxaparin sodium (60mg) Inj. Actrapid 100 IU Inj. Remdesivir Inj. Levofloxacin (500 mg) Tab. Paracetamol (500mg) Tab. Baricent 2mg Tab. Levothyroxine 50 micrograms Tab. Cholecalciferol (Vitamin D3) Tab. Montelukast (10mg) Inj. Omeprazole (40mg) Tab. Acetylcysteine (600 mg) Inh. Salbutamol and Ipratropium Bromide Tab. Pirfenidone (267 mg)	Refer to CMCH

Date	Hospital	Treatment	Status
30.01.2022	Medical Centre Hospital	Inj. Meropenem (1gm) Inj. Dexamethasone (5mg) Inj. Vitamin complex Inj. Enoxaparin sodium (60mg) Inj. Levofloxacin (500 mg) Inj. Actrapid 100 IU Tab. Baricent 2mg Tab. Acetylcysteine (600 mg) Tab. Levothyroxine 50 micrograms Tab. Omeprazole (40mg) Tab. Montelukast (10mg) 2% Miconazole gel	Ongoing treatment
02.02.2022	Medical Centre Hospital	Cap. Denvar (400mg) Inj. Dexamethasone (5mg) Inj. Enoxaparin sodium (60mg) Inj. Actrapid 100 IU Tab. Paracetamol (500mg) Tab. Baricent 2mg Tab. Levothyroxine 50 micrograms Tab. Cholecalciferol (Vitamin D3) Tab. Montelukast (10mg) Inj. Omeprazole (40mg) Tab. Acetylcysteine (600 mg) Inh. Salbutamol and Ipratropium Bromide Tab. Pirfenidone (267 mg) Tab. Clonazepam 0.5mg Tab. Quetiapine 50mg	Ongoing treatment and later discharge.

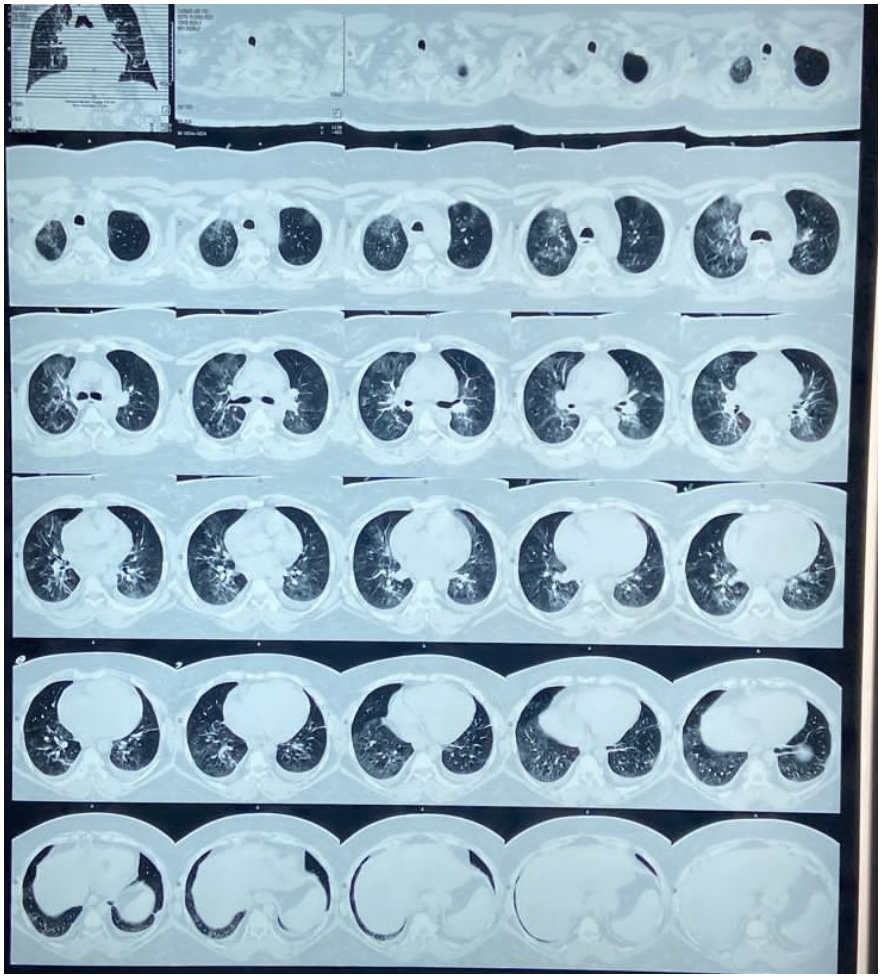

Figure 1: HRCT of the case