Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.63, No.4(2023). p.298-303; DOI: https://doi.org/10.14238/pi63.4.2023.298-303

Original Article

The effects of large-scale social restriction during the COVID-19 pandemic on glycemic control and occurrence of complications in children with type-1 diabetes mellitus

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Abstract

Background The global pandemic of severe acute respiratory syndrome caused by the coronavirus-2 (SARS-CoV-2) infection has resulted in a national large-scale social restriction (LSSR) to limit the spread of the virus.

Objective To determine the impacts of LSSR on glycemic control-sand the occurrence of complications in type-1 diabetes mellitus (T1DM) children.

Methods A retrospective longitudinal study was carried out in Dr. Sardjito Hospital, Yogyakarta. Subjects were 0-18 years old T1DM patients diagnosed before the LSSR with at least six months of disease. Data on demographics, T1DM status, HbA1c level, and complications pre-LSSR, and during LSSR, were taken from medical records. Paired T-tests were used to assess the difference in HbA1c level between the two-time points

Results We included information on 21 children based on the inclusion and exclusion criteria. Their median (range) age was 13.9 (1.42-17.3) years, with a median (range) diabetes duration of 2.6 (0.0-10.92) years. Glycemic control improved in 76% of the children. The mean HbA1c before and during LSSR was 10.9 (SD 2.7) and. 9.7 (SD 2.3), respectively; $P<0.05$. The glycemic control was not associated with sex, age, duration of diabetes, travel time to the clinic, or a total daily insulin dose. There was also no significant difference in the occurrence of complications.

Conclusion Despite limitations during LSSR, glycemic control improves in most patients with T1DM. This might be related to improved health awareness during the pandemic, more regular meals, and better parental control. **[Paediatr Indones. 2023;63:298-303; DOI: https://doi.org/10.14238/pi63.4.2023.298-303].**

Keywords: *large social scale restriction; type 1 diabetes mellitus; HbA1c; complication*

Diabetes mellitus is a complicated metabolic disorder characterized by high blood glucose levels and changes in carbohydrate, lipid, and protein metabolism. According to data from *Riset Kesehatan Dasar Indonesia 2013* (*Riskesdas*/Indonesia Basic Health Research), the number of diabetes mellitus (DM) cases in Indonesia was roughly 12 million with 52 million having impaired blood glucose tolerance (IGT) and 64 million having impaired fasting blood glucose (IFG).[1] In developed countries, 90% of all diabetes in children was T1DM. Unlike type 2 diabetes, T1DM is marked by a lack of insulin produced by the pancreatic beta cells due to autoimmune destruction.

In type 1 diabetes patients, reasonable glycemic control is achieved through the self-monitoring of blood glucose and HbA1c testing. In younger children, HbA1c level should be checked 4-6 times yearly, whereas in older children it should be checked 3-4

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Submitted August 9, 2022. Accepted August 16, 2023.

times yearly. For all age groups, a healthy HbA1c target is less than 7.5% (5.8 mmol/L).[2] This regiment aims to lower the risk of short- as well as long-term complications[2] while also assuring normal growth and development.[3]

The COVID-19 pandemic that started in 2019 has caused a significant number of deaths in adult patients with diabetes mellitus. In order to curb and limit the spread of COVID-19, governments around the world issued instructions to limit the mobility of people and to prohibit large groups of people from congregating and spreading the virus. The instructions included work-from-home and online schooling.[4] Indonesia's government was one of the countries that imposed serial lockdowns (large social scale restriction/ LSSR) during the COVID-19 pandemic. This policy is estimated to interfere with diabetes management in children by making it difficult to attend diabetes consultations as well as disrupting patients' routines through restrictions against outside activities and school attendance.[5] While many countries try to mitigate these challenges by providing telehealth consultation, not all parts of Indonesia are ready for remote consultation.[6]

A study in Brazil showed no significant change in HbA1c level in children with T1DM during lockdowns.[7] In contrast, studies in India found improvement in HbA1c values during the lockdowns, [8,9] while a study in Egypt found deterioration of HbA1c values.[9] Ethnicity, cultural values, advancement in management (e.q. CGM), and other social aspects may influence glucose control in children with T1DM. There are yet any data on the impact of LSSR on the management of T1DM children in Indonesia. This study aims to determine the impact of LSSR on glycemic control and the occurrence of complications in type-1 diabetes mellitus (T1DM) children.

Methods

This retrospective longitudinal study was conducted in Dr. Sardjito General Hospital, Yogyakarta. Data were obtained from medical records of T1DM (ICD10 E.10) children who attended Dr. Sardjito General Hospital from January 1, 2019 to December 31, 2021. We excluded incomplete data, interrupted control or death before the pandemic era, and also new cases with less than six months of observation.

Since Indonesia implemented multiple types of LSSR during the pandemic, we chose to study the strictest type, which consisted of 100% closing of non-essential institutions otherwise known as emergency response that happened two times; between March 20, 2020 to February 8, 2021, and between July 3, 2021 to September 8, 2021. We used the time before and after LSSR as the comparison, i.e., between January 1, 2019 to March 19, 2020, and between September 9, 2021 to December 31, 2021. Demographic data collected were HbA1c value, presence of complications, gender, age, duration since diagnosis of T1DM, contraction of COVID-19 infection, daily insulin requirement (DIR), duration of travel time from home to the hospital, and accuracy of hospital visit schedule recorded at two points (pre lockdown data and during lockdown). These data were analyzed using paired T-test to calculate a P-value.

The dependent variables in this study were the HbA1c value and the incidence of complications in children with T1DM. The independent variables were the LSSR, gender, age, duration since diagnosis, COVID-19 infection, daily insulin requirement, and travel time to the hospital. Secondary data from physical and electronic medical records were entered and processed using computerized statistical data processing software.

Numerical data presented mean and standard deviation (SD) for normal distribution and median and range value for non-normal distribution. Categorical data were presented in the form of frequency and percentage. The normality test was evaluated with the Shapiro-Wilk test because the number of the samples was less than 50. Bivariate analysis to determine the change in the value of each dependent variable between two measurement time points was conducted by paired T-test since the data met the requirement of the normality test. Otherwise, bivariate analysis to determine the mean difference between two categories at the same point (during LSSR) was conducted with an independent T-test. The value of significance was set at $P<0.05$. This study had received ethical clearance from the Research Ethics Committee of the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada.

Results

Sixty-six (66) subjects of type 1 DM patients were recorded in the medical record. Forty-five out of 66 were excluded from the study because of no hospital visit before the pandemic era and no data on HbA1c value (24 subjects), new cases diagnosed less than six months (5 cases), death before LSSR (2 cases), and incomplete data (14 cases) (**Figure 1**). The 21 remaining subjects (12 girls and 9 boys) had a median age of 13.9 (range 1.42-17.3) years; 57.1% were teenagers. The median duration since diagnosis was 2.58 (range 0.55-10.92) years. Most of them (38,1%) were diagnosed between pre-school and school age (6-12 years). The median travel time from home to the hospital was 35 (range 8-95) minutes; 13/21 of subjects had less than 35 minutes travel time to the hospital. The most common complications observed during LSSR were diabetic ketoacidosis (DKA) and diabetic nephropathy (4/21), followed by diabetic retinopathy (2/21). Three subjects contracted COVID-19 infection during LSSR (**Table 1**).

We found significant improvement in the mean HbA1c level from before LSSR [10.88 (SD 2.69] to during the LSSR [9.72 (SD 2.33)] (P=0.048) (**Table 2**). The decrease in HbA1c level was found in all age groups, with the greatest decline in infants to the pre-school age group (mean difference: 1.55 (SD 0.14). There was no statistically significant difference of HbA1c between subjects diagnosed <5 years (P=0.177) and >5 years (P=0.056). There were no significant difference in the mean total daily dose insulin (TDDI) (P=0.85) and delay of hospital visits [47.81 (SD 105.51) *vs.* 52.71 (SD 76.36) months; P=0.69]. Delay of laboratory and complications evaluations also showed no significant differences on HbA1c test [5.62 (SD 9.12) *vs.* 5.05 (SD 5.72) months; (P=0.985)], kidney function test [4.81 (SD 8.47) *vs.* 5.38 (SD 7.03) months; (P=0.531)], and eye check-up [13.52 (SD 26.38) *vs.* 12.67 (SD 12.13) months; (P=0.248)].

To predict factors interfering with the improvement of HbA1c value during LSSR, we divided samples into two groups using the median

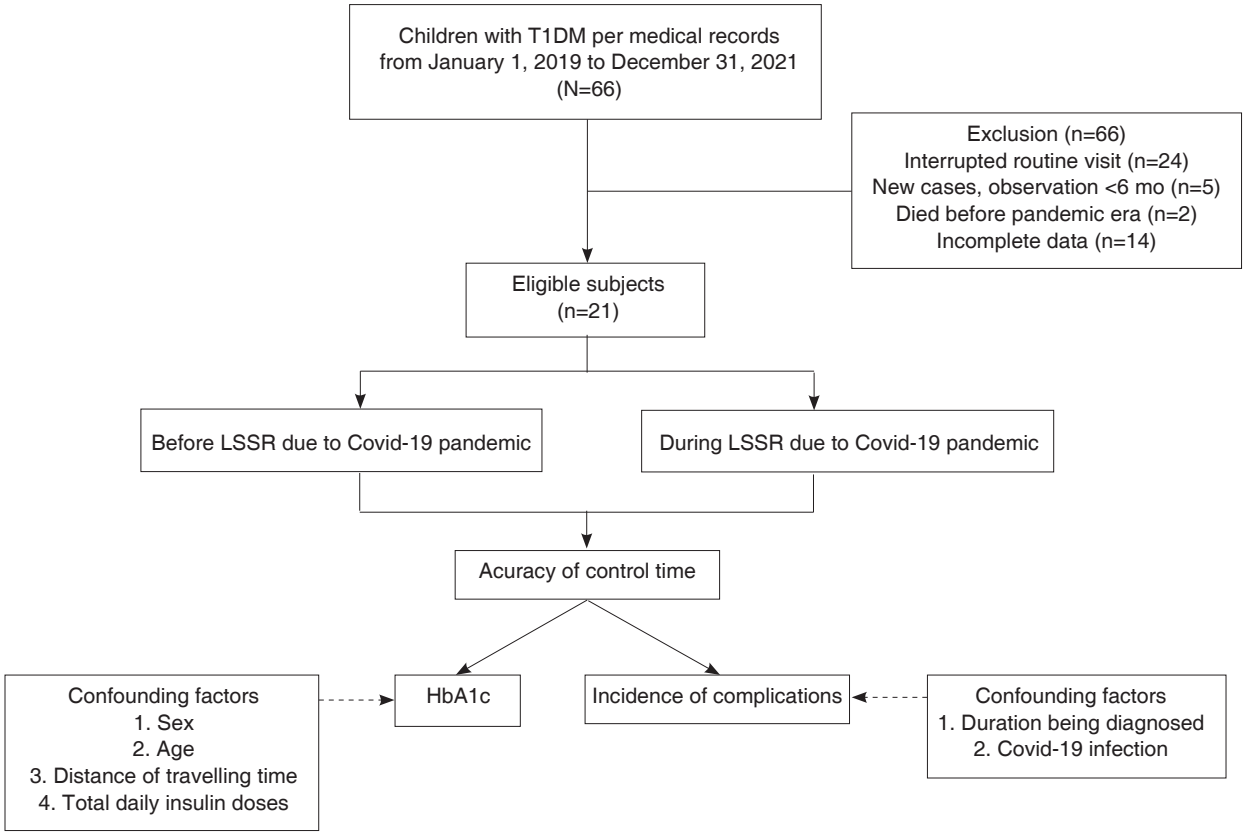

Figure 1. The flow of taking research subjects

HbA1c value before LSSR as the cut-off; i.e., below or above the median (HbA1c 10%). Children with previously poorly-controlled diabetes (HbA1c>10%) experienced the most significantly improved HbA1c post LSSR, ranging from HbA1c -2.58 (SD 1.71) % to +0.74 (SD 2.15) %; (P<0.001). The mean daily insulin requirement was significantly different between the two groups. For those with better-controlled diabetes before the pandemic, the variation in daily insulin requirement increased up to +0.25 (SD 0.33) IU/kg BW/day, P=0.019 (**Table 3**).

Table 1. Basic characteristics of study subjects

Characteristics	(N=21)
Sex, n	
Male	9
Female	12
Median age (range), years	13.92 (1.42-17.33)
Onset of diagnosis, n	
Toddler (0-6 years)	6
School age (6-12 years)	8
Adolescent (12-18 years)	7
Age, n	
Toddler (0-6 years)	2
School age (6-12 years)	7
Adolescent (12-18 years)	12
Contracted Covid-19 , n (%)	
Yes	3
No	18
Travel time to the hospital*	
>35 minutes	8
≤35 minutes	13
Complications during LSSR, n	
Diabetic ketoacidosis	4
Diabetic nephropathy	4
Diabetic retinopathy	2

*median travel time to the hospital was 35 minutes (8-96) minutes

In comparing pre- and during LSSR data, the occurrence of complications was not significantly different between males and females. Travel time to the hospital, age groups, COVID-19 infection, duration of diagnosis, and daily insulin requirement were not significantly associated with complication occurrence. However, the occurrence of DKA was more frequent in patients with poor compliance in attending diabetes consultation during LSSR than in patients with good compliance. There were also no statistically significant differences in complications (DKA, diabetic retinopathy, diabetic nephropathy) before and during the LSSR period, P=0.59; P=0.57; P=0.59, respectively.

Discussion

Our study found an improvement in HbA1c value of 76% from all participants. Despite all limitations and increased sedentary life during the LSSR period, the COVID-19 pandemic suggested that there was more family support and increased parental supervision to monitor meals and regular insulin injection, less stress from school and less meals away from home.[10] The result was the same in a previous study in UK, Scotland, Italy, Spain, and India. According to a study in India, children whose parents were at home during the lockdown/ LSSR period showed improved glycemic control as compared to children whose parents continued to work during lockdown .[8,10,11]

Table 2. Hba1c level and daily insulin requirement pre-LSSR and during the LSSR period

Parameters	Pre-LSSR	During LSSR	P value
Mean HbA1c (SD)	10.88 (SD 2.69)	9.72 (SD 2.33)	0.048
Mean DIR (SD)	1.31 (SD 0.48)	1.29 (SD 0.34)	0.850

Data were analyzed with paired T-test; HbA1c=glycated hemoglobin; DIR=daily insulin requirement; LSSR= large-scale social restriction

Table 3. Comparison of range of HbA1c value and range of daily insulin requirement between patients with HbA1c values lower than 10% and higher than 10% before the LSSR period

Parameter	HbA1c >10%	HbA1c <10%	P value
Overall HbA1c before LSSR period, n	12	9	
Mean variation on HbA1c (SD), %	-2.58 (SD 1.71)	0.74 (SD 2.15)	0.001
Mean variation on DIR (SD), IU/kgBW/day	-0.22 (SD 0.47)	0.25 (SD 0.33)	0.019

Median HbA1c level before LSSR period: 10%

In our study, the most significant reduction of HbA1c level occurred in the group with previously poorly-controlled diabetes (HbA1c > 10%) with P<0.01. It was suspected that an increase of vigilance and health awareness among the parents of children with T1DM occurred due to widely broadcasted educational materials on national television and media about the higher risk of mortality in those with diabetes who contract COVID-19. This may have crystallized the importance of better glycemic control within families.[12]

A large-scale retrospective cohort study in the Netherlands[13] showed only a slight improvement in HbA1c level during LSSR/lockdown. Moreover, there was no significant difference in HbA1c level results from the study in Brazil. This might be because the study used CGM as measurement, which was already familiar to their children with T1DM, unlike TIDM patients in Indonesia. A previous UK study showed no difference in HbA1c levels among CGM users pre-and-post lockdown. However, there was a significant improvement among T1DM children that were non-CGM users who self-monitored their blood glucose with manual glucose strip.[10]

We also found that hospital visit delay before the LSSR period and during LSSR was just the same in our study. Poor compliance among children with T1DM in our hospital may be due to a lack of adequate information about maintaining reasonable glycemic control to avoid the short-term and long-term complications in T1DM patients. A previous study stated that higher attendance to manage diabetes was related to the achievement of glycemic target in T1DM patients.[14]

The occurrence of diabetic complications such as DKA in this study was higher in the poor compliance group even though it was not statistically significant; possibly due to a small study sample. This study did not observe long-term complications like retinopathy and nephropathy for long enough. Retinopathy and nephropathy may need 5-15 years from diagnosis to appear as a clinical manifestation in patients with T1DM.[15] A previous study in the USA did not find any significant impacts of LSSR on hospitalization frequency during the LSSR period in T1DM patients. This might be due to CGM use and telemedicine as an alternative response to pandemic conditions in a developed country.

Our work had several limitations. The data was taken only from medical records; consequently, we were not able to evaluate some information. These were psychosocial aspects such as a change in dietary habits, physical exercise, duration of parental presence in the home, duration of screen time, sleep pattern, and parent concerns during the pandemic. Therefore, in this study we could only predict factors related to the improvement of HbA1c value during the LSSR period. Our observation was not carried out long enough to find the impact of LSSR on long-term diabetic complications such as retinopathy and nephropathy. We assessed only one hospital center in Yogyakarta; therefore, it is not representative of the general population.

Ours was the first study about the impact of the COVID-19 pandemic on glycemic control of T1DM in Indonesia. Under unique conditions in Indonesia (multiple periods of LSSR, unfamiliarity with CGM, and difficulties in the implementation of telemedicine) there was a significant improvement in HbA1c level during the LSSR period. As a developing country, Indonesia faces a significant challenge in overcoming diabetes even before the pandemic. Technology in diabetes management such as insulin pumps and CGM were not widely used due to limited insurance coverage, lack of facilities and knowledge in society to use telemedicine, and the focus on tertiary and secondary levels hospitals. At the same time, primary care services are still far from optimal with lack of expertise, diagnostic equipment, and drug availability.[6] Economic problems are also obstacles to maintaining excellent diabetic management in Indonesia. Facility upgrades, further data analysis, and more advanced technology are expected to be able to improve diabetic management in Indonesia.

Despite the limitations implemented during LSSR in Indonesia, this study showed improved glycemic control in most patients with T1DM. In this study, the patient group with an HbA1c value higher than the median range before pandemic COVID-19 had a significantly improved HbA1 level during LSSR than the other group with the better pre-pandemic HbA1c value. The LSSR might have increased health awareness during the pandemic, also allowed for more regular meals, and better parental control.

Further study should observe deeper the psychosocial aspects that may have roles in improving

glycemic control in children with T1DM. Involvement of multiple types of hospital centers would show a wider range of conditions of T1DM patients during the lockdown. We recommend a mentoring program or T1DM club to improve understanding of T1DM management and better daily glycemic monitoring for hospital service improvement. We also recommend that children with T1DM receive a check-up at least once every three months at a tertiary hospital since HbA1c laboratory evaluation is unavailable in most district hospitals in Indonesia.[16]

Conflict of interest

None declared.

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