Journal of Epidemiology and Public Health (2022), 07(03): 397-409
Masters Program in Public Health, Universitas Sebelas Maret

Meta-Analysis

Meta-Analysis the Impact of Social Restriction during COVID-19 Pandemic on Blood Glucose Control in Type 1 Diabetes Mellitus Patients

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ABSTRACT

Background: The COVID-19 lockdown has an impact on the daily lives of people with type 1 diabetes, including restrictions on physical activity, changes in diet, difficulty contacting health care providers and concerns about drug supplies. The purpose of this study was to analyze the impact of the COVID-19 lockdown on blood sugar control in type 1 diabetes mellitus patients.
Subjects and Method: This research is a meta-analysis study using PRISMA flowchart guidelines. The PICO model used is Population= type 1 diabetes mellitus patients. Intervention = COVID-19 lockdown. Comparison = before the COVID-19 lockdown. Outcome = HbA1c. The article search process was carried out between 2019 and 2022 using online databases from PubMed, Springer Link and Google Scholar. The keywords used in the article search were "Quarantine" OR "Quarantines" OR "Stay at Home Orders" OR "Health Lockdowns" OR "Self-Quarantine" OR "Self-Quarantine" AND "Diabetes Mellitus" OR "Diabetes Insipidus" OR "Diabetic" OR "Glucose Intolerance" AND "Glycemic Control" OR "Blood Glucose Control". The inclusion criteria used in this study were full paper articles with cohort studies, using English or Indonesian, the intervention given was COVID-19 lockdown, and the outcome was blood glucose level (HbA1C) in diabetes mellitus patients.The analysis was performed using RevMan 5.3 software.
Results: A total of 11 articles reviewed in the meta-analysis showed that the impact of the COVID-19 lockdown decreased HbA1c levels by 0.23 compared to before the COVID-19 lockdown in patients with type 1 diabetes mellitus and was statistically significant (SMD= -0.23; 95% CI -0.29 to -0.18; p<0.001).
Conclusion: COVID-19 lockdown reduces HbA1c levels compared to before COVID-19 lockdown in type 1 diabetes mellitus patients.

Keywords: COVID-19 lockdown, type 1 diabetes mellitus, HbA1c.

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Cite this as:
Pratiwi YM, Tamtomo DG, Murti B (2022). Meta-Analysis the Impact of Social Restriction during COVID-19 Pandemic on Blood Glucose Control in Type 1 Diabetes Mellitus Patients. J Epidemiol Public Health. 07(03): 397-409. https://doi.org/10.26911/jepublichealth.2022.07.03.11.

BACKGROUND

Since it was first discovered in Wuhan, China in December 2019, the COVID-19 pandemic caused by the Novel Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV2) has spread to nearly 200 countries worldwide, with more than 4 million people infected and nearly 300,000 deaths in May 2020. With no effective treatment or vaccine yet found, governments and policymakers in most countries are trying to "flatten the curve" by implementing social distancing, including community lockdowns (Anjana et al., 2020). Many countries are implementing precautionary measures including closure of non-essential schools and businesses, cancellation of non-urgent routine health checks, and lockdowns, to reduce the spread of COVID-19 (Wamsley, 2020 in Alharthi et al., 2021).

The modifications implemented by the lockdown strategy carried out in Italy have several consequences on the daily lives of patients with T1DM. The first phase was marked by the suspension of educational activities and the second phase of a complete lockdown in which only essential services were running, has forced children and adolescents with T1DM to reduce physical activity, changes in meal times and food choices (Dalmazi et al., 2020). This agrees with Aragona et al. (2020), namely that the lockdown has had quite an impact on the daily lives of diabetics, including restrictions on physical activity, changes in diet, difficulty contacting health care providers and concerns about drug supplies. The COVID-19 pandemic makes it clear how routine activities, lifestyles and people's access to care can change in rather fast and unpredictable ways

The unprecedented COVID-19 pandemic has caused sudden and unplanned changes in almost all factors, and people living with T1DM are among those most affected by this pandemic. Recent studies have shown the negative impact of lockdowns on the health behavior of diabetics (Khader MA, 2020 in Alharthi et al., 2021). This is in accordance with Rastogi et al. (2020) in Karatas et al. (2020) who reported that lockdowns during the COVID-19 pandemic were associated with worsening glucose control in diabetic patients without COVID-19 infection. Studies show that glycemic control becomes chaotic during the lockdown period. Lifestyle changes, psychological stress, difficulty in getting treatment and medical advice were identified as factors that may be responsible for impaired glycemic control (Khare and Jindal, 2020). Significant worsening of glycemic control in T1DM individuals on previous good glycemic control during the COVID-19 lockdown. The perceived stress associated with the COVID-19 pandemic translates into glucose instability during the lockdown period (Barchetta et al., 2020). Maintaining good glycemic control in patients with T1DM is often challenging during usual times, and becomes even more challenging and important during times of uncertainty and physical and mental stress (Agiostratidou et al., 2017 in Alharthi et al., 2021).

This research is a systematic review and meta-analysis. This study uses secondary data which is data from the results of previous studies. Meta-analysis is a way of summarizing and quantitatively synthesizing the most accurate estimates. Many studies show a decrease in blood sugar control in patients with diabetes mellitus during the COVID-19 lockdown. Most existing studies have small sample sizes. Therefore, researchers are interested in examining the impact of the COVID-19 lockdown on blood sugar control in type 1 diabetes mellitus patients using a meta-analysis.

SUBJECTS AND METHOD

1. Study Design

This research design uses a meta-analysis study, namely the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta Analyses) method. Articles were obtained from online databases, namely Google Scholar, PubMed and Springer Link. The keywords used in the article search were “Quarantine” OR “Quarantines" OR "Stay at Home Orders" OR "Health Lockdowns" OR "Self-Quarantine" OR "Self-Quarantine" AND "Diabetes Mellitus" OR "Diabetes Insipidus" OR "Diabetic" OR "Glucose Intolerance" AND "Glycemic Control" OR "Blood Glucose Control".

2. Inclusion Criteria

The inclusion criteria used in this study were full paper articles with retrospective cohort studies, articles using English or Indonesian, the intervention given was COVID-19 lockdown and the outcome was blood glucose levels (HbA1C) in type 1 diabetes mellitus patients.

3. Exclusion Criteria

Exclusion Criteria The research subjects used in this study were patients with a diagnosis of type 2 DM, gestational DM, and diabetes due to other factors and articles published before 2019.

4. Operational Definition of Variables

Articles included in this study were screened according to the PICO (Population, Intervention, Comparison, & Outcome) model. The PICO model used is Population= type 1 diabetes mellitus patients. Intervention= COVID-19 lockdown. Comparison= before the COVID-19 lockdown. Outcome= HbA1c.

HbA1C is the level or percentage of glucose bound to hemoglobin. The measurement scale is continuous.

COVID-19 Lockdown is the restriction of certain activities of residents in an area suspected of being infected with Corona Virus Disease 2019 (COVID-19) in such a way as to prevent the possible spread of Corona Virus Disease 2019 (COVID-19). The measurement scale is categorical.

5. Study Instruments

Research is guided by PRISMA flow diagrams and article quality/feasibility assessment using the Critical Appraisal Checklist for Cohort Study (CASP, 2018). There are 12 questions, each criterion is given a score of 2 if the answer is yes, a score of 1 if the answer is uncertain, and a score of 0 if the answer is no. The 12 questions used in the check list are as follows:

a. Does this research have a clear research focus?
b. Is the cohort research process clearly defined?
c. Is exposure accurately measured so as to minimize bias?
d. Are results measured accurately to minimize bias?
e. Did the authors identify important confounding factors? Were confounding factors considered in the design or analysis?
f. Was the follow-up on the subject complete? Is the follow-up sufficient?
g. Do the results of the study use the mean value of HbA1C?
h. Are the research results accurate?
i. Do you believe the results of this study?
j. Can this research be applied to the local population?
k. Are the results of this study in accordance with the existing evidence?
l. Do the results of this study have any implications?

6. Data Analysis

The software used to perform the meta-analysis is Review Manager 5.3 (RevMan 5.3). Data processing was carried out by calculating effect sizes and heterogeneity values to determine the combined research model and form the final meta-analysis in the form of forest plots and funnel plots.

RESULTS

The article review process was carried out using the PRISMA flowchart which can be seen in Figure 1. The total articles obtained were 11 articles from 2 continents, namely 9 in Europe and 2 in Asia as shown in Figure 2.

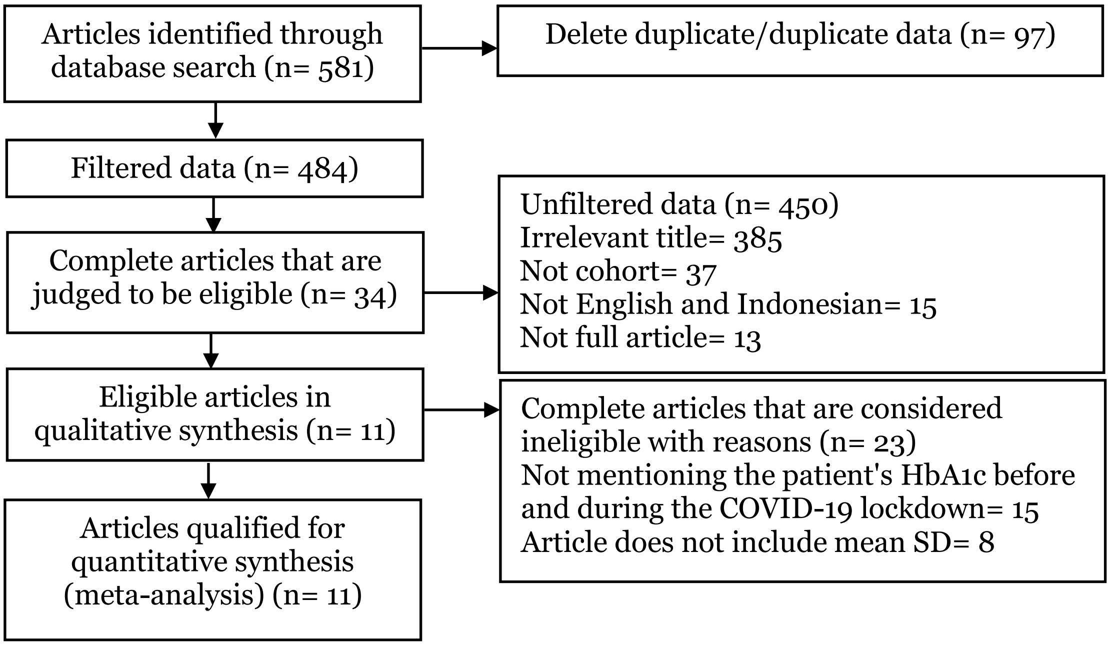

Figure 1. PRISMA Flowchart

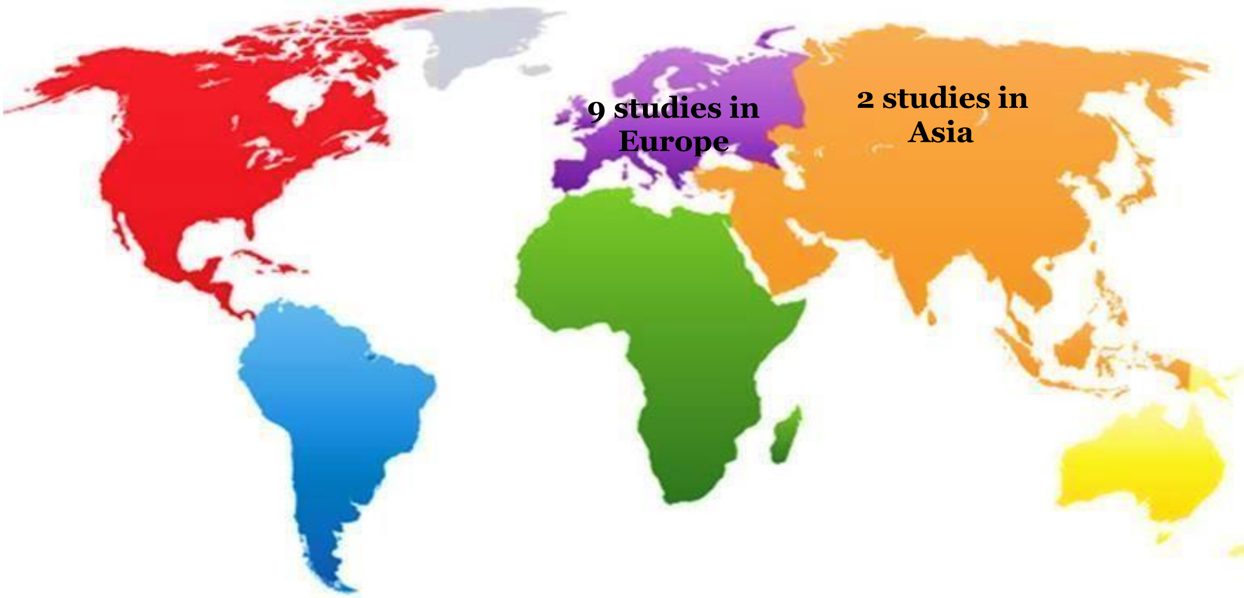

Figure 2. Map of study area

Table 1. Assessment of study quality using the cohort study checklist published by CASP (Critical Appraisal Skills Program)

No	Indicators	Publications (Author and Year)					
		Aragona et al. (2020)	Fernandez et al. (2020)	Mesa et al. (2020)	Minuto et al. (2021)	Potier et al. (2021)	Shah et al. (2020)
1	Does this research address a clearly focused problem?	2	2	2	2	2	2
2	Was the group recruited in an acceptable way?	2	2	2	2	2	2
3	Is exposure accurately measured to minimize bias?	2	2	2	2	2	2
4	Was the outcome accurately measured to minimize bias?	2	2	2	2	2	2
5	Did the author identify all the important confounding factors? Has the author taken into account confounding factors in the design and/or analysis?	2	2	2	2	2	2
6	Was the follow-up subject complete enough? Was the follow-up of the subject long enough?	2	2	2	2	2	2
7	Are the research results accurate?	2	2	2	2	2	2
8	How precise is the result?	2	2	2	2	2	2
9	Do you believe the results of this study?	2	2	2	2	2	2
10	Can this research be applied to the local population?	2	2	2	2	2	2
11	Are the results of this study in accordance with the existing evidence?	2	2	2	2	2	2
12	Do the results of this study have any implications?	2	2	2	2	2	2
	Total	**24**	**24**	**24**	**24**	**24**	**24**

Note: 2: Yes; 1: Can't tell; 0: No

Table 1. Cont.

No	Indicators	Publications (Author and Year)				
		Vinals et al. (2020)	Wu et al. (2021)	Predieri et al. (2020)	Capaldo et al. (2020)	Marigliano et al. (2021)
1	Does this research address a clearly focused problem?	2	2	2	2	2
2	Was the group recruited in an acceptable way?	2	2	2	2	2
3	Is exposure accurately measured to minimize bias?	2	2	2	2	2
4	Was the outcome accurately measured to minimize bias?	2	2	2	2	2
5	Did the author identify all the important confounding factors? Has the author taken into account confounding factors in the design and/or analysis?	2	2	2	2	2
6	Was the follow-up subject complete enough? Was the follow-up of the subject long enough?	2	2	2	2	2
7	Are the research results accurate?	2	2	2	2	2
8	How precise is the result?	2	2	2	2	2
9	Do you believe the results of this study?	2	2	2	2	2
10	Can this research be applied to the local population?	2	2	2	2	2
11	Are the results of this study in accordance with the existing evidence?	2	2	2	2	2
12	Do the results of this study have any implications?	2	2	2	2	2
	Total	**24**	**24**	**24**	**24**	**24**

Note: 2: Yes; 1: Can't tell; 0: No

Table 2. Description of the primary studies included in the meta-analysis

Author (Year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome	Mean	SD
Aragona et al. (2020)	Italy	Cohort Retrospective	63	Type 1 DM patients (44% male and mean age 44 ± 12 years)	Lockdown COVID-19	Before the COVID-19 lockdown	Mean glucose, HbA1c, GMI, TIR, TAR, TBR	I= 7.20 C= 7.20	I= 0.70 C= 0.70
Fernandez et al. (2020)	Spain	Cohort Retrospective	307	Type 1 DM patients (50.2% male and mean age 45.8 ± 12.6 years)	Lockdown COVID-19	Before the COVID-19 lockdown	Mean glucose, HbA1c, TIR	I= 7.10 C= 7.40	I= 1.00 C= 1.00
Mesa et al. (2020)	Spain	Cohort Retrospective	92	Type 1 DM patients (56.52% male and mean age 42.8 ± 3.9 years)	Lockdown COVID-19	Before the COVID-19 lockdown	HbA1c, mean glucose, TIR	I= 7.00 C= 7.20	I= 0.80 C= 0.80
Minuto et al. (2021)	Italy	Cohort Retrospective	202	Type 1 DM patients (53% male and mean age 18.30 ± 6.43 years)	Lockdown COVID-19	Before the COVID-19 lockdown	HbA1c, TIR, TAR, TBR, glucose mean, exercise time	I= 7.56 C= 7.76	I= 1.05 C= 1.04
Potier et al. (2021)	Paris	Cohort Retrospective	1,378	Type 1 DM patients (37.2% male and mean age 45.6 ± 13.6 years)	Lockdown COVID-19	Before the COVID-19 lockdown	BMI, HbA1c, lifestyle changes, TIR	I= 7.50 C= 7.40	I= 17.10 C= 1.00
Shah et al. (2020)	India	Cohort Retrospective	77	Type 1 DM patients (41.6% male and mean age 14 ± 4 years)	Lockdown COVID-19	Before the COVID-19 lockdown	HbA1c, BMI, working time of parents	I= 8.90 C= 9.30	I= 1.50 C= 1.70
Vinals et al. (2020)	Spain	Cohort Retrospective	59	Type 1 DM patients (44.07% male and mean age 46.17 ± 13.0 years)	Lockdown COVID-19	Before the COVID-19 lockdown	HbA1c, mean glucose	I= 6.75 C= 6.94	I= 0.71 C= 0.78

TAR, time above range; TBR, time below range; TIR, time in range; TDD, total daily dose; BMI, Body Mass Index

Table 2. Description of the primary studies included in the meta-analysis

Author (Year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome	Mean	SD
Wu et al. (2021)	China	Cohort Retrospective	43	Type 1 DM patients (53.49% male and mean age 7.45 ± 3.23 years)	Lockdown COVID-19	Before the COVID-19 lockdown	BMI, education level, HbA1c, annual income, diabetes onset, diabetes duration, mean glucose, TIR, time of hyperglycemia, time of hypoglycemia	I= 6.54 C= 6.47	I= 0.72 C= 0.75
Predieri et al. (2020)	Italy	Cohort Retrospective	62	Type 1 DM patients (50% male and mean age 11.1 ± 4.37 years)	Lockdown COVID-19	Before the COVID-19 lockdown	TDD insulin, physical activity, HbA1c, average glucose, TBR, TIR, TAR, sensor usage	I= 7.35 C= 7.45	I= 0.72 C= 0.74
Capaldo et al. (2020)	Italy	Cohort Retrospective	207	Type 1 DM patients (53.62% male and mean age 38.4 ± 12.7 years)	Lockdown COVID-19	Before the COVID-19 lockdown	Mean glucose, HbA1c, TAR, TIR, TBR, Lifestyle changes	I= 7.60 C= 7.70	I= 1.10 C= 1.30
Marigliano et al. (2021)	Italy	Cohort Retrospective	233	Type 1 DM patients (55.7% male and mean age 13.9 ± 4.4 years)	Lockdown COVID-19	Before the COVID-19 lockdown	BMI, Mean glucose, HbA1c, TAR, TIR, TBR,	I= 7.44 C= 7.82	I= 0.83 C= 0.84

TAR, time above range; TBR, time below range; TIR, time in range; TDD, total daily dose; BMI, Body Mass Index

a. Forest Plot

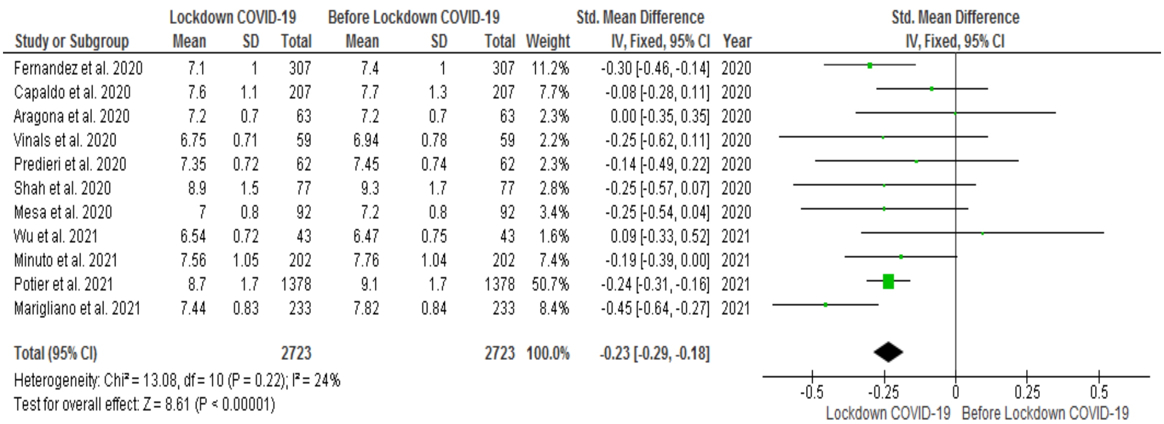

Figure 3. Forest plot of the impact of the COVID-19 lockdown on blood sugar control in type 1 diabetes mellitus

Forest plot in Figure 3. which shows that the impact of the COVID-19 lockdown reduced HbA1c levels by 0.23 compared to before the COVID-19 lockdown in patients with type 1 diabetes mellitus and was statistically significant ($p<0.001$). The heterogeneity value in the forest plot shows I^2= 24%, so the data analysis in the forest plot uses the fixed effect model.

b. Funnel Plot

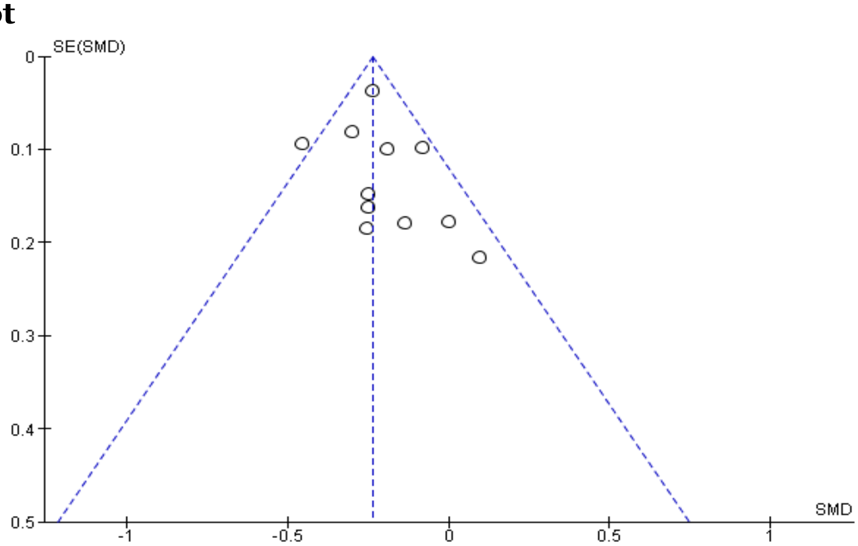

Figure 4. Funnel plot of the impact of the COVID-19 lockdown on blood sugar control in patients with type 1 diabetes mellitus

The funnel plot in Figure 4 shows no publication bias which is indicated by a symmetric distribution between the right and left plots, namely 5 plots each and one plot touching the vertical line. The plot on the right side of the graph has a standard error

(SE) between 0 and 0.3. The plot on the left side of the graph has a standard error (SE) between 0 and 0.2.

DISCUSSION

This meta-analysis investigated the impact of the COVID-19 lockdown on blood sugar control in patients with type 1 diabetes mellitus with a sample size of 2,723 patients from 11 cohort studies conducted in Europe and Asia. The findings of this study explain that the COVID-19 lockdown does not have a negative impact on blood sugar control in patients with type 1 diabetes mellitus. and statistically significant (SMD= -0.23; 95% CI= -0.29 to -0.18, p<0.001).

The results of this study are in accordance with the research of Aragona et al. (2020) where it was stated that the COVID-19 lockdown did not have a negative impact on the glycemic control of type 1 diabetes mellitus patients apart from several potential disturbing factors such as physical activity, diet and psychological stress during the COVID-19 lockdown. The modest but significant improvement in glycemic control which most likely reflects more regular daily activities and reduced work-related distress is the impact of the COVID-19 lockdown on patients with type 1 diabetes mellitus. (2020) in which lifestyle changes in patients with type 1 diabetes mellitus are not only considerations of diet and physical activity but also more regular and less stressful life. Other studies have concluded that while the COVID-19 lockdown is a source of anxiety for many people with type 1 diabetes mellitus, it is also an opportunity to make positive behavioral changes in glycemic control (Potier et al., 2021).

Patients with type 1 diabetes mellitus have been shown to be at high risk for insufficient sleep duration and previous studies have shown that inadequate sleep can affect patients' self-management behavior and glycemic control (Frye et al., 2019). So that it can explain that the COVID-19 lockdown has resulted in fewer dinners being eaten at restaurants where the carbohydrate and calorie content is often higher than what is consumed at home and adequate sleep duration. In addition, the COVID-19 lockdown provides an opportunity for the expansion of telemedicine for high-risk diabetes patients and especially for the management of glycemic control in patients with type 1 diabetes mellitus (Aragona et al., 2020). In the research of Predieri et al. (2020) emphasizes the usefulness of telemdicine in the isolation situation that we now live in a world with internet access that allows easy flow of information between doctors and patients during periods of health crises.

Another factor that may influence the improvement of glycemic control is the fact that diabetes has been reported in various media as a risk factor for the prognosis of COVID-19 which then affects the awareness and self-management of diabetes mellitus patients (Ferna et al., 2020). According to research by Marigliano and Maffeis (2021), the forced COVID-19 lockdown to stay at home provides opportunities for children and adolescents with type 1 diabetes mellitus to get better glucose control from their parents or caregivers, in addition to the awareness that type 1 diabetes mellitus can exacerbate SARS-CoV-2 infection thereby increasing adherence in diabetes medication management. Improved glycemic control emphasizes the importance of a more stable daily routine and a stronger family support system (Shah et al., 2021). To prevent the spread of COVID-19, COVID-19 lockdowns have been imposed in many countries with restrictions on all outdoor activities and also limiting attendance at diabetes clinics. In diabetics the COVID-19 lockdown implies lifestyle changes related to physical activity, stress, and nutrition that may be detrimental and affect glycemic control. On the other hand, during the COVID-19 lockdown, it is expected that patients with type 1 diabetes mellitus have a more regular lifestyle and are more regular on the insulin administration schedule (Capaldo et al., 2020). A healthier lifestyle and stress reduction potential result in significant improvements in glycemic control and diabetes management (Minuto et al., 2021). This is in accordance with the research of Wu et al. (2021) which mention the COVID-19 lockdown provides good awareness of diabetes management and may enhance the stable routine of the patients thereby benefiting from this COVID-19 lockdown. In addition, patients lead a more relaxed and calm lifestyle during the COVID-19 lockdown, with less physical activity, longer study time and sleep duration thereby improving glycemic control.

The meta-analysis in this study showed that the COVID-19 lockdown could reduce HbA1c levels in type 1 diabetes mellitus patients compared to before the COVID-19 lockdown. This may be because the COVID-19 lockdown has provided positive lifestyle changes, reduced stress in life and work, adequate sleep duration, expansion of telemedicine, increased awareness and self-management of diabetic patients as a result of knowing that diabetes can worsen COVID-19 infection.

AUTHORS CONTRIBUTION

Yeocelin Mega Pratiwi is the main researcher who selects the topic, searches for and collects research data. Didik Gunawan Tamtomo and Bhisma Murti who analyzed the data and reviewed the research documents.

FUNDING AND SPONSHORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

ACKNOWLEDGEMENT

We are very grateful to the database providers PubMed, Springer Link and Google Scholar.

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