THERAPY COMPLIANCE OF TYPE-2 DIABETES MELLITUS PATIENTS BEFORE AND DURING THE COVID-19 PANDEMIC: A SYSTEMATIC REVIEW

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ABSTRACT

Medical compliance is a key aspect in the management of multiple-modalities therapies, such as those found in patients with type-2 diabetes mellitus. Aspects such as healthcare accessibility, complications or secondary ailments, lifestyle, socioeconomic status, and academic status can affect a patient's compliance, thus their therapeutic outcomes. The Covid-19 pandemic brought various observable shifts toward these aspects which raises the need for further evaluation regarding type-2 diabetes mellitus therapy compliance during the Covid-19 pandemic. This study is a systematic review that uses secondary data gathered from articles published in Pubmed, ScienceDirect, and Google Scholar with publication dates ranging from January 2018 until October 2021. Using the PRISMA algorithm and JBI critical appraisal questionnaire, we selected 10 controlled studies that discussed therapy compliance of Type-2 Diabetes Mellitus patients before the Covid-19 pandemic and 7 studies that discussed therapy compliance of Type-2 Diabetes Mellitus during the Covid-19 pandemic. There was a notable difference between the therapy compliance profile of Type-2 Diabetes Mellitus patients before and during the Covid-19 pandemic. Pharmacotherapy compliance during the Covid-19 pandemic showed a moderate-high trend whereas the trend before the Covid-19 pandemic was moderate-low. Compliance of physical activity and diet modification related to Type-2 Diabetes Mellitus respectively showed a moderate-high and moderate-low trend during the Covid-19 pandemic, whereas the trend before Covid-19 pandemic was low. A notable shift was found between the therapy compliance profile of Type-2 Diabetes Mellitus patients before and during the Covid-19 pandemic. Further meta-analysis study is required to measure the significance of this shift as well as their correlations. Additional studies are also required to isolate the factors that may contribute to this shift.

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INTRODUCTION

The Covid-19 pandemic is a worldwide phenomenon that has been ongoing for well over a year. By July 2021, around 190 million confirmed cases and over 4 million confirmed deaths were reported globally[1]. The pandemic had also affected various sectors and aspects of life, such as healthcare access, the economy, education, and mental health, just to name a few[2,3,4,5]. Among those affected by the Covid-19 pandemic, patients with Type 2 Diabetes Mellitus are a group that deserves extra consideration and attention. Several studies had already shown the vulnerability of these patients to Covid-19's morbidity and mortality[6, 7].

While further studies are needed to determine the direct correlation between Covid-19 and Type 2 Diabetes Mellitus, several studies have already suggested the significance of Type 2 Diabetes Mellitus as a notable comorbid factor for patients infected with the SARS-COV-2 virus[8,9]. It is difficult to determine the exact mechanisms that correlate the two conditions together due to the complexity and multidimensional nature of Type 2 Diabetes Mellitus. Aspects such as heredity, ethnicity, dietary pattern, lifestyles, and the affliction of other underlying diseases are but a few factors that may affect patients with Type 2 Diabetes Mellitus[10,11,12].

Adherence to diabetic treatment is crucial for effectively managing diabetes and preventing complications. It involves following the prescribed medication regimen, adopting a healthy lifestyle, monitoring blood sugar levels, and attending regular medical appointments. Consistent adherence helps regulate blood sugar levels, reducing the risk of short-term complications like hyperglycemia (high blood sugar) or hypoglycemia (low blood sugar). It also lowers the chances of long-term complications such as heart disease, kidney problems, nerve damage, and vision loss. The Covid-19 pandemic has posed challenges to adherence to diabetic treatment. The pandemic has disrupted healthcare systems, leading to limited access to healthcare facilities and resources. Some individuals with diabetes might face difficulties in obtaining their medications, glucose monitoring supplies, or medical consultations due to lockdowns, supply chain disruptions, or overwhelmed healthcare systems. Moreover, the fear of contracting Covid-19 has discouraged people from visiting hospitals or clinics, resulting in missed or delayed medical appointments. Social distancing measures and quarantine restrictions have also impacted the ability to engage in physical activity and maintain a healthy lifestyle, which is essential for diabetes management. Overall, Covid-19 conditions have influenced adherence to diabetic treatment by disrupting healthcare services, limiting access to medications and supplies, hindering physical activity, and impacting mental health. It is crucial for individuals with diabetes to seek alternative means of obtaining medications, utilize telemedicine options for remote consultations, prioritize self-care practices, and seek support from healthcare professionals to maintain adherence despite the challenges posed by the pandemic.

Adding to the complexity of its already complex and multidimensional aspects was the multimodalities characteristic of Type 2 Diabetes Mellitus treatments[13,14]. Consisting of oral drugs, insulin therapy, lifestyle modification, glucose monitoring, and various

complication management, Type 2 Diabetes Mellitus therapy requires a significant amount of medical adherence from the afflicted patients as a patient's compliance can significantly determines the outcome of Type 2 Diabetes Mellitus therapy[15,16,17,18]. More research about the therapy compliance of Type 2 Diabetes Mellitus patients is needed to further determine the missing correlation between Covid-19 morbidity and mortality among patients with Type 2 Diabetes Mellitus. Therefore, the objective of this research was to compare type 2 diabetes mellitus patients' therapy compliance before and during the Covid-19 pandemic.

MATERIALS AND METHODS

This research used a systematic review method. Studies relevant to the systematic review were filtered using a specific keyword and boolean operators following the Medical Subject Heading (MeSh) protocol. Literature sources were obtained and selected through a methodological process. Data collection was taken from PubMed, Google Scholar, and ScienceDirect. The keywords used in the database were: ((Diabetes Mellitus OR DM Type 2 OR DMT2) AND (Covid-19 Pandemic OR Covid-19 OR N SARS COV 2 Pandemic OR N SARS COV 2) AND (Compliance Therapy OR Medical Compliance OR Adherence Therapy)). A similar search was done through the PROSPERO database to avoid duplication of previous reviews. Studies included in this systematic review consisted of cross-sectional, case-control, and cohort studies that discussed the therapy compliance of Type 2 Diabetes Mellitus patients before and during the Covid-19 pandemic. Studies obtained from the databases were then filtered from duplications, selected by article type, and screened accordingly by their abstracts and, later, full text using the PICO framework.

Table 1. PICO and search keyword

PICO	Keyword
Population	Diabetes type 2 patients
Intervention	Treatment and Management
Comparator	Before and after a pandemic
Outcomes	Patient's compliance

Using this selection method, 17 articles were obtained and were deemed compatible for the systematic review. Each selection step was conducted by 5 researchers of a medical background using the PRISMA flowchart protocol.

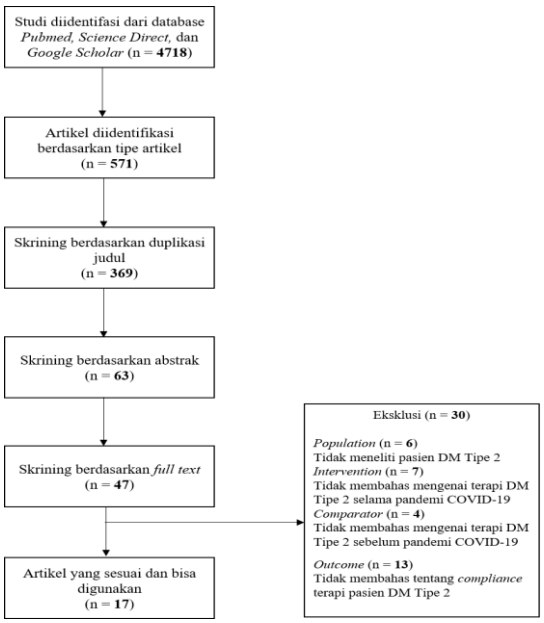

Figure 1. PRISMA flowchart protocol

After a preliminary selection process, 47 studies were further reviewed for compatibility with the systematic review based on their population, intervention, comparators, and outcomes component.

Based on their population component, studies that include Type 1 Diabetes Mellitus, Gestational Diabetes Mellitus, and Diabetes Mellitus as comorbid to other diseases were excluded. Based on their intervention and comparator component, studies that failed to describe the Type 2 Diabetes Mellitus therapy modalities used (drugs, insulin, physical activity, or dietary modification) were excluded. Based on their outcome component, studies that did not include the therapy compliance of Type 2 Diabetes Mellitus patients were also excluded. All 17 studies used in this systematic review were identified and sorted by their article types. Studies were then assessed for quality control using The Joanna Briggs Institute (JBI) Critical Appraisal checklist. Studies with scores of 50% or higher were then included in the systematic review while studies that score lower than 50% were removed. The studies included in this systematic review consisted of 2 cohort studies and 15 cross-sectional studies. Details regarding each study's critical appraisal scores are shown in Table 2 and Table 3.

A descriptive analysis was then conducted from the data gathered and synthesized from the selected articles. Data relevance was reviewed based on the article's author, country, year, background, theoretical framework, research goal, research design, sample size, sample collection method, inclusion/exclusion criteria, quality and validity, measuring instrument, statistical method and analysis, therapy outcome of Type 2 Diabetes Mellitus patients before and during the Covid-19 pandemic, and analysis of the study's result. A narrative approach was used in synthesizing the data gathered in this study, primarily aiming to gather credible references and compare studies regarding the difference in Type 2 Diabetes Mellitus therapy adherence before and during the Covid-19 pandemic.

RESULTS

All 17 screened studies showed significant data analysis and testing results and were then included in this systematic review. Studies that depicted the therapy compliance of Type 2 Diabetes Mellitus patients prior to the Covid-19 pandemic were 10, while those during the pandemic were 7. A notable bias risk was addressed in this systematic review due to the non-heterogenized data and result analysis found in the 17 studies included in this systematic review.

In this systematic review, there were 3 studies conducted in Saudi Arabia and India, 2 studies conducted in Ethiopia, and 9 other studies conducted in the USA, Ghana, China, Cameroon, United Arab Emirates, Malaysia, Poland, Lebanon, and Nepal. The goal of this systematic review was to portray an overall picture of the therapy adherence level of Type 2 Diabetes Mellitus patients before and during the Covid-19 pandemic. The population scope was every patient with Type 2 Diabetes Mellitus with ongoing therapy of either pharmacotherapy (oral antidiabetic agents or insulin therapy), physical activity, and dietary modification. The number of samples in each study varied between 257 patients to 419 patients, all with Type 2 Diabetes Mellitus. There was no significant difference in sample size between both male and female samples in all the studies used in this review. Seventeen articles were found through literature search and screenings and were included in this review to analyze the therapy compliance of Type 2 Diabetes Mellitus before and during the Covid-19

pandemic. Data collected from said articles were compiled through a systematic review protocol.

Table 2. Critical appraisal score of cohort studies included in the systematic review using *The JBI critical appraisal tools*

Article	Criteria											Score
	1	2	3	4	5	6	7	8	9	10	11	
Fisher L, *et al*., 2020	√	√	√	√		√	√	√	√		√	9/11 (81.8%)
Rastogi A, *et al*., 2020	√	√	√	√	√	√	√	√			√	9/11 (81.8%)

Table 3. Critical appraisal score of cross sectional studies included in the systematic review using *The JBI critical appraisal tools*

Article	Criteria								Score
	1	2	3	4	5	6	7	8	
Mroueh L., *et al*., 2018	√	√	√	√	√	√	√	√	8/8 (75%)
Alqarni A., *et al*., 2019	√	√	√	√	√		√	√	7/8 (87.5%)
Aminde L.N., *et al*., 2019	√	√	√	√			√	√	6/8 (75%)
Jannoo Z. & Khan N.M., *et al*., 2019	√	√	√	√	√	√	√	√	8/8 (100%)
Afaya R.A., *et al*., 2020	√	√	√	√	√	√	√	√	8/8 (100%)
Alhaiti A.H., *et al*., 2020	√	√	√	√			√	√	6/8 (75%)
Alshareef R, *et al*., 2020	√	√	√	√	√	√	√	√	8/8 (100%)
Bonger Z., *et al*., 2020	√	√	√	√	√	√	√	√	8/8 (100%)
Ghosh A, *et al*., 2020	√	√	√	√	√		√	√	7/8 (87.5%)
Grzywacz A. & Śliż S., 2020	√	√	√	√			√	√	6/8 (75%)
Nandini H., *et al*., 2020	√	√	√	√			√	√	6/8 (75%)
Tao J, *et al*., 2020	√	√	√	√	√	√	√	√	8/8 (100%)
Asheq A, *et al*., 2021	√	√	√	√	√	√	√	√	8/8 (100%)
Baral I.A. & Baral S., 2021	√	√	√	√	√	√	√	√	8/8 (100%)
Mekonnen C, *et al*., 2021	√	√	√	√	√	√	√	√	8/8 (100%)

DISCUSSION

Therapy compliance and homecare are two of the most important factors that determine the outcome of diabetes management, with both aspects can be somewhat challenging for several patients. Patients with higher education levels, good glycemic control, an ongoing marital status, and over 5 years of history of diabetes are suggested to have a higher

compliance tendency when it comes to oral antidiabetic drugs[19]. Another study suggested that there is no significant correlation between a patient's knowledge and medication compliance, while also claiming that patients of younger age tend to have less compliance level than patients over the age of 70. It was suggested that the latter was due to busier daily schedules of younger patients to keep track of their health-oriented lifestyle and medications[20]. It is important to increase and maintain the patient's awareness of their condition, especially when it comes to medication compliance, glycemic control, and diet management. Age, education level, and occupational or socioeconomic status all play a significant role in determining a patient's compliance level.[21] Other studies suggested that bad adherence level is attributed to young age, usage of insulin as an alternative therapy, and alcohol consumption. Forgetfulness, poor economic status, and a busy work schedule are among the most commonly reported excuses for a patient's neglect of their medications[22]. Too many drugs consumed (both for diabetes, their complications, and another underlying disease), as well as the complexity of the treatments prescribed, are among other common reasons reported by patients that may affect a patient's medication compliance[23]. A study shows that patients with Type 2 Diabetes Mellitus in general have about an average level of medication compliance, with some patients intentionally or unintentionally stopping their medication without a physician's suggestion. Patients with low compliance levels are shown to have a longer duration of diabetes, a higher body mass index, and a higher level of HbA1c on average. Low compliance levels can also be found in patients who are practicing a specific diet, believing that the specific diet would allow them to reduce their need for medication. On the other hand, good control over their diabetes complications and their blood glucose level may suggest a high level of compliance[24].

During the Covid-19 pandemic, it was found that patients with Type 2 Diabetes Mellitus have worse glycemic control levels due to the lack of physical activity and increased calorie intake. The compliance level of Type 2 Diabetes Mellitus was reported to be around 77.,8% with a significant correlation with blood glucose level. Patients with low compliance levels were shown to have poor glycemic control, while patients with high compliance levels had significantly better glycemic control ($p<0.05$)[25]. Meanwhile, another study shows that patients treated with oral antidiabetic agents were shown to have an increase in compliance level when compared to patients treated with insulin[26]. Studies suggested that the overall compliance level had dropped during the Covid-19 pandemic due to lockdown regulation that was set in place in various areas globally[27]. Age was also found to be a significant factor in a patient's compliance level during the pandemic. This was especially noticeable in patients with Type 2 Diabetes Mellitus when compared to patients with Type 1 Diabetes Mellitus. HbA1c level has also shown an increase in average during the Covid-19 pandemic, mostly attributed to stress, but also due to the spike of hypoglycemia cases and the decrease of the overall management of Type 2 Diabetes Mellitus during the pandemic. Meanwhile race, education level, and marriage status seem to have

little to no effect on compliance levels during the Covid-19 pandemic[28].

Physical activity is one of the key components for Type 2 Diabetes Mellitus patients' lifestyle modification. WHO recommended at least 150 minutes of light exercise or 75 minutes of intense exercise per week to achieve a healthy lifestyle. A cross-sectional study found that Type 2 Diabetes Mellitus patients, on average, have a moderate level of compliance with physical activity. Poor general condition and physical attributes, such as an amputated leg due to diabetic neuropathy, were found to be the most common factor in rudimentary lifestyle in patients with Type 2 Diabetes Mellitus[29]. Another cross-sectional study found that only 34.7% and 46.3% of patients with Type 2 Diabetes Mellitus exercise regularly, both showing a low and moderate level of physical activity compliance respectively. The social, economic, and cultural status was suggested to have some influence over a patient's compliance with physical activity[30,31]. An example of this case is the low compliance level of physical activity in Saudi Arabia due to patient's unwillingness to exercise outdoor in Saudi Arabia hot climates.[32] Educational level also seems to play a role in physical activity compliance, showing patients with lower educational levels to have less compliance for physical activity compared to patients with higher educational levels. Patients with other comorbid were also shown to exercise less than patients with Type 2 Diabetes Mellitus with no other comorbids[33].

During the Covid-19 pandemic, patients with Type 2 Diabetes Mellitus tend to spend less time performing outdoor exercises and spend more time indoors. A cross-sectional study suggested that patients also spend less time exercising due to being "home-bound" during the Covid-19 pandemic[25]. The impact of Covid-19 lockdowns and social distancing also affect patient's activity levels due to the suspension of public facilities such as outdoor parks and fitness centers which ultimately further reduces the number of exercise done by patients with Type 2 Diabetes Mellitus[27, 34]. The increased level of anxiety and depression during the pandemic lockdown also plays a role in the management of Type 2 Diabetes Mellitus and other chronic diseases by lowering the amount of time patients spend on physical activities and exercises.28 Though one cohort study shows a promising moderate level of compliance for physical activities and an improvement of glycemic control in patients with Type 2 Diabetes Mellitus, despite the various regulations on outdoor activities when indoor activities are taken into account and patients are educated to limit their sitting time[35].

In various studies, the elimination of processed meat products and simple carbohydrates was recommended for patients with Type 2 Diabetes Mellitus[29,30,32]. A study by Grzywacz A. & Śliż S. in 56 patients with Type 2 Diabetes Mellitus shows that 70% of the respondents do not follow their recommended diet plan. Among these patients, 52% consume fast food regularly and 82% regularly take sweetened food, while only 52% regularly consume the recommended amount of vegetables and 92% consume meat at least once a day[29]. Another study by Mroueh L., *et al*. on 245 respondents with Type 2 Diabetes Mellitus shows that only 20.4% follow the dietary plan recommended by their corresponding physicians.[30] In contrast, a study in Malaysia shows a mean SDSCA score of

5.04 (+1.88) in terms of dietary awareness in a study conducted among 750 respondents with Type 2 Diabetes Mellitus.[24] An SDSCA survey conducted in Saudi Arabia shows that 75% of the respondents followed a low-fat diet, with 58.5% avoiding complex carbohydrates, 57.3% managing a daily calories deficit while 51.5% having little dietary fibers intake, 63.1% taking little fruit and vegetables in their diet, and 54.4% preferring sweetened food and beverages[32]. In Nepal, while only 54% of the 139 respondents show decent homecare management, 67.6% of the respondents show decent compliance in their diet therapy[33]. In Ethiopia, only 24% of the respondents show good compliance with their dietary modification. This was attributed to the lack of knowledge to differentiate foods with high and low carbohydrate content, the custom of preferring takeout foods as opposed to homemade ones, and the socioeconomic gap between each respondent that may play some roles in their dietary preferences and food availability[31].

During the Covid-19 pandemic, a study by Fisher L. *et al* in the USA shows that a third of the respondents show concern regarding the food availability necessary to maintain their diet[28]. A compliance level of 48.3% [95% CI (44.1-52.4)] was reported in a study in Ethiopia by Mekonnen C. *et al*. In the same study, the compliance shift due to the Covid-19 pandemic was also attributed to the respondent's perspective of diet and food accessibility[36].

CONCLUSION

In conclusion, prior to the Covid-19 pandemic, Type 2 Diabetes Mellitus therapy compliance exhibited a moderate-low tendency, with moderate-high compliance in pharmacotherapy, and low compliance in physical activity and dietary modification. However, some studies presented exceptions to this trend. During the Covid-19 pandemic, overall therapy compliance for Type 2 Diabetes Mellitus showed a relatively moderate-high trend. While there were inconsistencies in pharmacotherapy compliance, it leaned towards the moderate-high end. Physical activity compliance was moderate-high, and dietary modification compliance was moderate-low. This systematic review and the included studies indicate an increase in therapy compliance for Type 2 Diabetes Mellitus during the Covid-19 pandemic from January 2020 to October 2021. Notably, physical activity compliance improved from low to moderate-high, and dietary modification compliance improved from moderate-low. Further research is necessary to understand the significance of this trend and the correlation between these factors.

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CONFLICT OF INTEREST

All Authors have no conflict of interest.

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AUTHOR CONTRIBUTION

All authors have contributed to all processes in this research, including preparation, data gathering, and analysis, drafting and approval for publication of this manuscript.

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