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Meta-analysis

Meta-Analysis of the Effects of Diet and Physical Activity on HbA1c in Type II Diabetes Mellitus Patients

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ABSTRACT

Background: Type II Diabetes Mellitus is still a global health problem. The prevalence of diabetes has increased over the decades due to the increased incidence of Type II DM. This study aims to analyze the effectiveness of diet therapy and physical activity on HbA1c levels in type II DM patients.
Subject and Method: This study is a systematic and meta-analysis study, with the following PICO Population = Patients diagnosed with type II DM. Intervention= High physical activity and diet therapy. Comparison = Low physical activity and no diet. Outcome= HbA1c level. The articles used in this study were obtained from several databases, including PubMed, Science Direct, Scopus, Clinical Key, and Google Scholar. The keywords used were: "tertiary prevention and DM", "diet", "physical activity", "diet and DM" "physical activity and DM", "diet and tertiary prevention and DM". The inclusion criteria were full-text articles, experimental study design using randomized controlled trial (RCT). Articles were collected using PRISMA flow diagram. Articles were analyzed using Review Manager 5.3 application.
Results: A meta-analysis of 9 articles on the effectiveness of diet therapy on HbA1c levels from Spain, the United States, Japan, the United Kingdom, and Israel concluded that Type II DM patients on diet therapy had an HbA1c level of 0.49 units compared to Type II DM patients without treatment, and the results were statistically significant (SMD= -0.49; 95% CI= -0.56 to -0.42; $p < 0.001$). A meta-analysis of 9 articles on the effectiveness of physical activity on HbA1c levels from the United States, Australia, Italy, and India concluded that Type II DM patients with high physical activity had HbA1c levels by 0.81 units lower than Type II DM patients with low physical activity, and the results were statistically significant (SMD= -0.81; 95% CI= -1.20 to -0.43; $p < 0.001$).
Conclusion: Diet therapy and high physical activity reduce HbA1c levels in type II DM patients.

Keywords: Physical activity, diet, HbA1c, type II DM

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BACKGROUND

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction and abnormalities of organs, especially the eyes, kidneys, nerves, heart, and blood vessels (ADA, 2014; WHO, 2016).

The prevalence of diabetes for decades has increased dramatically due to the conti-

nuous increase in the incidence of Type II DM (Danaei et al., 2011). According to WHO (2016) that as many as >422 million adults suffered from DM in 2014. This increase is expected to continue to grow. The International Diabetes Federation predicts that this number will increase to 642 Million by 2040 (Andrew et al., 2013).

Diet therapy in DM patients is to reduce or control body weight in addition to controlling sugar or cholesterol levels. All this is done to improve the patient's quality of life and prevent at least delay the occurrence of acute and chronic complications. Weight loss in diabetes mellitus patients who are obese will generally reduce insulin resistance. Thus, weight loss will increase glucose uptake by cells and improve blood glucose control (Mirza, 2019).

Physical exercise has a small, but detectable effect on glycemic control and cardiovascular risk factor control for type II diabetes (Downes, 2015; Micha et al., 2017). The combination of aerobic and resistance training is more effective than aerobic exercise. The effect of exercise training on glucose control is clinically necessary and can be attributed to effects on body weight and body composition (Mannuci, 2021; Rahati et al., 2014).

Various studies have been carried out with mixed results around the world, but further analysis needs to be carried out in order to reach more convincing conclusions. Therefore, researchers were interested in analyzing using a systematic approach to relevant studies by conducting a meta-analysis to identify the magnitude of the effect of diet therapy and physical activity on HbA1c levels in type II DM patients.

SUBJECTS AND METHOD

1. Study Design

This study is a systematic study and meta-analysis, with the following PICO Population = Patients diagnosed with type II DM. Intervention = High physical activity and diet therapy. Comparison = Low physical activity and no diet. Outcome = HbA1c level. The articles used in this research were obtained from several databases, including PubMed, Science Direct, Scopus, Clinical Key, and Google Scholar. The keywords used are: “tertiary prevention and DM”, “diet”, “physical activity”, “diet and DM” “physical activity and DM”, “diet and tertiary prevention and DM”. The inclusion criteria were articles. full-text experimental study design with randomized controlled trial (RCT). Articles were collected using PRISMA flow diagram. Articles were analyzed using Review Manager 5.3 application.

2. Inclusion Criteria

The inclusion criteria in this study were a full paper article on the design of an RCT study with an HbA1c outcome.

3. Exclusion Criteria

Exclusion criteria were articles with a quasi-experimental, cohort, case-control and cross-sectional study design and using languages other than English and Indonesian.

4. Operational Definition of Variable

Type II DM is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Instrument: glucometer with categorical measuring scale.

Diet is the regulation of patterns and consumption of foods and beverages that are prohibited, modified or allowed in certain amounts for the purpose of treating illness, health, or weight loss. Instrument: UKDDQ with continuous measuring scale.

Physical activity is any bodily movement produced by skeletal muscles that requires energy. Physical activity involves biochemical and biomechanical processes. Instru-

ment: IPAQ with continuous measurement scale.

5. Instrument

The study was guided by the PRISMA flow chart and quality assessment using the assessment of a randomized controlled trial (RCT) published by the CEBM (Centre for Evidence-Based Medicine)

6. Data Analysis

The data in the study were analyzed using the Review Manager application (RevMan 5.3). Forest plots and funnel plots were used to determine the size of the relationship and heterogeneity of the data. The fix effect model was used for homogeneous data, while the random effect model was used for heterogeneous data across studies.

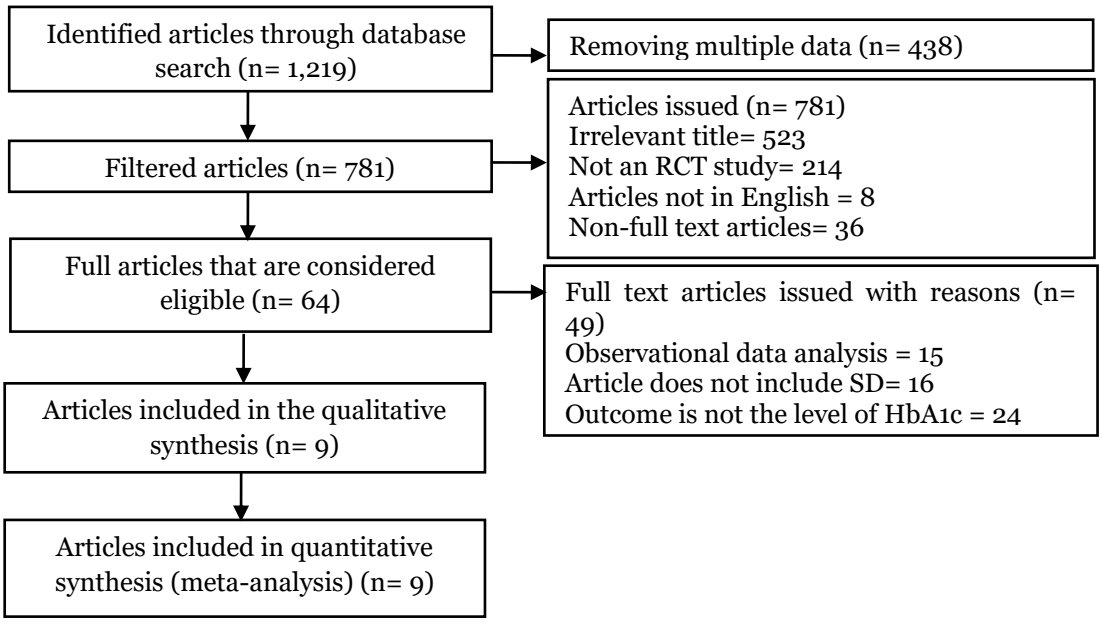

Figure 1. PRISMA Flow Diagram of the Effectiveness of Physical Activity on HbA1c Levels

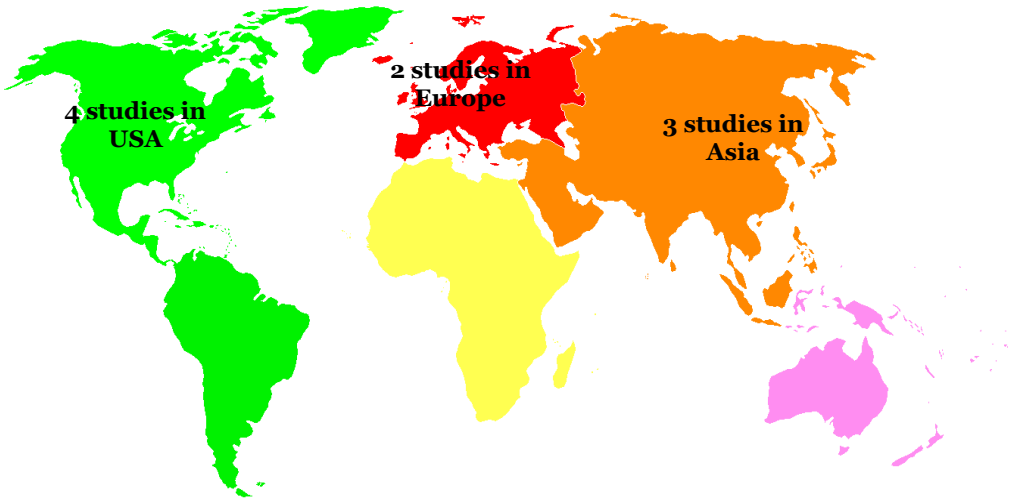

Figure 3. Map of the study area on the effectiveness of physical activity on HbA1c levels

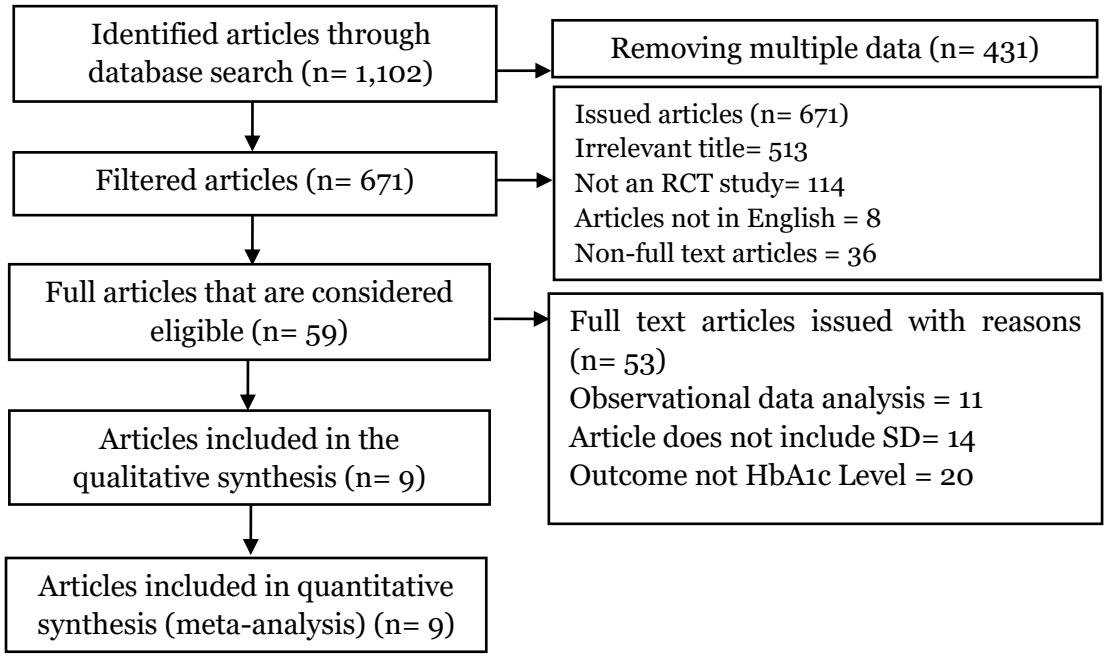

Figure 3. PRISMA Flow Diagram of the Effectiveness of Diet Therapy on HbA1c Levels

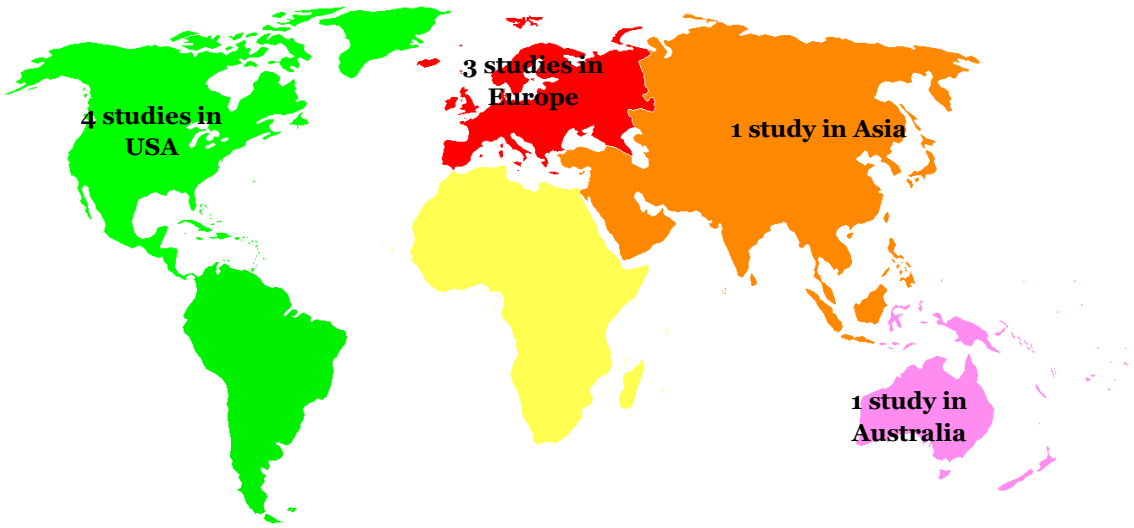

Figure 4. Map of study areas on the effectiveness of diet therapy on HbA1c levels

Table 1. The Results of Quality Assessment on physical activity on HbA1c levels in type II DM DM patients

No	Questions	Publication (Author and Year)								
		Castaneda et al. (2002)	Crunch et al. (2010)	Dustan et al. (2002)	Goldhaber-Fiebert et al. (2003)	Kadoglou et al. (2007)	Kadoglou et al. (2010)	Middlebrooke et al. (2006)	Sigal et al. (2016)	Sridhar et al. (2010)
1	Does this study address a clear research focus?	2	2	2	2	2	2	2	2	2
2	Is the Randomized Controlled Trial research method appropriate to answer the research question?	2	2	2	2	2	2	2	2	2
3	Are there enough subjects in the study to establish that the findings are not coincidental?	2	2	2	2	2	2	2	2	2
4	Are the subjects randomly divided into the experimental and control groups? If not, can this be biased?	2	2	2	2	2	2	2	2	2
5	Does the study use inclusion/exclusion criteria?	2	2	2	2	2	2	2	2	2
6	Are the two groups comparable at the start of the study?	2	2	0	2	2	2	2	2	2
7	Are objective and unbiased outcome criteria used?	2	2	2	2	2	2	2	2	2
8	Is the measurement method used objective and valid to measure the results? If not, is there any blinding in the study?	2	2	2	0	2	2	2	2	2
9	Is effect size practically relevant?	2	2	2	2	2	2	2	2	2
10	Is the estimated effect correct? Is there a confidence level interval?	2	1	1	2	2	2	2	2	2
11	Are there any confounding factors that have not been taken into account?	1	2	2	2	2	2	2	2	2
12	Can the results be applied to your research?	2	2	2	2	2	2	2	2	2
	Total score	**23**	**23**	**21**	**22**	**24**	**24**	**24**	**24**	**24**

Description: 2= Yes; 1= Uncertain; 0= No

Table 2. Description of the primary study on dietary therapy for controlled HbA1c levels in type II DM patients

No	Questions	Publication (Author and Year)								
		Goday et al. (2016)	Saslow et al. (2012)	Westman et al. (2008)	Morris et al. (2019)	Sato et al. (2012)	Iqbal et al. (2010)	Yamada et al. (2014)	Goldstein et al. (2011)	Maharani et al. (2015)
1	Does this study address a clear research focus?	2	2	2	2	2	2	2	2	2
2	Is the Randomized Controlled Trial research method appropriate to answer the research question?	2	2	2	2	2	2	2	2	2
3	Are there enough subjects in the study to establish that the findings are not coincidental?	2	1	2	2	2	2	2	2	2
4	Are the subjects randomly divided into the experimental and control groups? If not, can this be biased?	2	2	2	2	2	2	2	2	1
5	Does the study use inclusion/exclusion criteria?	1	2	2	2	2	2	2	2	2
6	Are the two groups comparable at the start of the study?	2	2	1	2	2	2	2	2	2
7	Are objective and unbiased outcome criteria used?	2	2	2	2	2	2	2	1	1
8	Is the measurement method used objective and valid to measure the results? If not, is there any blinding in the study?	1	2	2	1	2	2	2	2	2
9	Is effect size practically relevant?	2	2	2	2	2	2	1	2	2
10	Is the estimated effect correct? Is there a confidence level interval?	2	2	2	2	2	2	2	2	2
11	Are there any confounding factors that have not been taken into account?	2	2	2	2	2	2	2	2	2
12	Can the results be applied to your research?	2	2	2	2	2	2	2	2	2
	Total score	**23**	**23**	**23**	**23**	**22**	**24**	**23**	**23**	**22**

Description: 2= Yes; 1= Uncertain; 0= No.

Table 3. Description of the primary study on physical activity on HbA1c levels in type II DM patients

Author (Year)	Country	Study Design	Total sample		Population	Intervention	Compa-rison	Outcome	Mean		SD	
			Physical Activity	Control					High Physical Activity	Low Physical Activity	Physical Activity	Low Physical Activity
Castaneda et al. (2002)	USA	RCT	31	31	DM patients aged 66 years old, consisting of 40 women and 22 men	High physical activity	Low physical activity	Decreased HbA1c levels	7.6	8.3	0.2	0.5 (SE)
Crunch et al. (2010)	Louisiana, USA	RCT	31	24	DM patients aged 58 years old	High physical activity, endurance training, and a combination of physical and endurance training	Low physical activity	Decreased HbA1c levels	7.64	8.18	0.10	0.12 (SE)
Dunstan et al. (2002)	Melbourne, Australia	RCT	16	13	Male and female DM patients aged 60 to 80 years old	High physical activity	Low physical activity	Decreased HbA1c levels	-1.2	-0.4	1.0	0.8
Goldhaber-Fiebert et al. (2003)	Costa Rica, Central America	RCT	33	28	A total of 61 DM patients aged 59 years old	High physical activity	Low physical activity	Decreased HbA1c levels	-1.8	-0.4	2.3	2.3
Kadoglou et al. (2007)	Italy, South Europe	RCT	30	30	A total of 60 DM patients consisted of 26 men and 34 women aged 64 years old	High physical activity	Low physical activity	Decreased HbA1c levels	-0.63	-0.31	0.41	0.10
Kadoglou et al. (2010)	Finland, Europe	RCT	25	25	A total of 50 DM patients aged >18 years old	High physical activity, therapy with anti-diabetic drugs, and a combination of physical activity and anti-diabetic drug therapy	Low physical activity	Decreased HbA1c levels	-0.29	0.51	0.57	0.61

Author (Year)	Country	Study Design	Total sample		Population	Intervention	Compa-rison	Outcome	Mean		SD	
			Physical Activity	Control					High Physical Activity	Low Physical Activity	Physical Activity	Low Physical Activity
Middlebro oke et al. (2006)	United Kingdom, Europe	RCT	22	30	A total of 59 DM patients consisted of 32 men and 27 women aged 63 years old	High physical activity	Low physical activity	Decreased HbA1c levels	6.9	7.2	1.1	0.9
Sigal et al. (2016)	Canada	RCT	59	62	A total of 251 DM patients aged 39 to 70 years old	High physical activity, endurance training, combination of physical exercise and endurance	Low physical activity	Decreased HbA1c levels	6.98	7.41	1.50	1.50
Sridhar et al. (2010)	India	RCT	50	55	A total of 105 DM patients aged 60 years	High physical activity	Low physical activity	Decreased HbA1c levels	6.40	8.61	0.45	0.74

Table 4. Description of the primary study on dietary therapy for controlled HbA1c levels in type II DM patients

Author (Year)	Country	Study Design	Total Sample		Population	Intervention	Comparison	Outcome	Mean		SD	
			I	C					Diet	Without diet	Diet	Without diet
Goday et al. (2016)	Spain	RCT	45	44	A total of 89 DM patients aged 60 to 65 years old	Diet	Without Diet	Decreased HbA1c levels	6.0	6.4	0.7	0.8
Saslow et al. 2012	USA	RCT	16	16	A total of 32 DM patients aged 55 to 64 years old	Diet	Without Diet	Decreased HbA1c levels	6.0	6.9	0.3	1.1
Westman et al. (2008)	USA	RCT	21	21	A total of 42 DM patients aged 52 years old	Diet	Without Diet	Decreased HbA1c levels	7.2	7.5	1.2	1.7
Morris et al. 2019	England	RCT	21	12	A total of 33 DM patients aged 64 to 69 years old	Diet	Without Diet	Decreased HbA1c levels	-16.13	-0.7	13.3	4.5
Sato et al. (2012)	Japan	RCT	32	30	A total of 62 DM patients with a mean age of 58 to 61 years old	Diet	Without Diet	Decreased HbA1c levels	-0.81	-0.06	1.21	0.87
Iqbal et al. (2010)	USA	RCT	70	74	A total of 114 DM patients aged 35-75 years old	Diet	Without Diet	Decreased HbA1c levels	-0.2	0.3	-0.1	0.2
Yamada et al. (2014)	Japan	RCT	12	12	A total of 24 DM patients aged 64 years old	Diet	Without Diet	Decreased HbA1c levels	7.0	7.5	0.7	1.0
Goldstein et al. (2011)	Israel	RCT	20	20	A total of 40 DM patients aged 35 to 37 years old	Diet	Without Diet	Decreased HbA1c levels	1.1	1.5	1.0	1.0
Mahara ni et al. (2015	USA	RCT	14	10	A total of 24 DM patients aged >18 years old	Diet	Without Diet	Decreased HbA1c levels	-0.3	-0.18	0.49	0.42

RESULTS

The initial search process in the database obtained 1,219 articles for activity on controlled HbA1c levels, and 1,102 articles for dietary therapy for controlled HbA1c levels in DM patients. After the process of deleting published articles, 9 of them fulfilled the requirements for a full text review.

Figure 3 shows that a study related to the effectiveness of physical activity on controlled HbA1c levels in type II DM patients consisted of 9 articles from 4 Americas, 3 from Europe, 1 from Asia, and 1 from Australia. Figure 4 shows that studies related to the effectiveness of dietary therapy on controlled HbA1c levels in patients with type II diabetes consist of 9 articles from 4 Americas, 2 from Europe, and 3 from Asia.

1. Correlation between Physical Activity on HbA1c Level

The forest plot in Figure 5 shows that high physical activity can reduce HbA1c levels in type II DM patients. Type II DM patients with high physical activity had HbA1c levels by 0.81 units lower than type II DM patients with low physical activity, and the results were statistically significant (SMD = -0.81; 95% CI = -1.20 to - 0.43; $p < 0.001$). The heterogeneity of the research data showed I2 = 96%, which mean that the estimated effect between the primary studies in this meta-analysis was highly variable. Thus, the calculation of the average effect estimate was carried out using a random effects model approach.

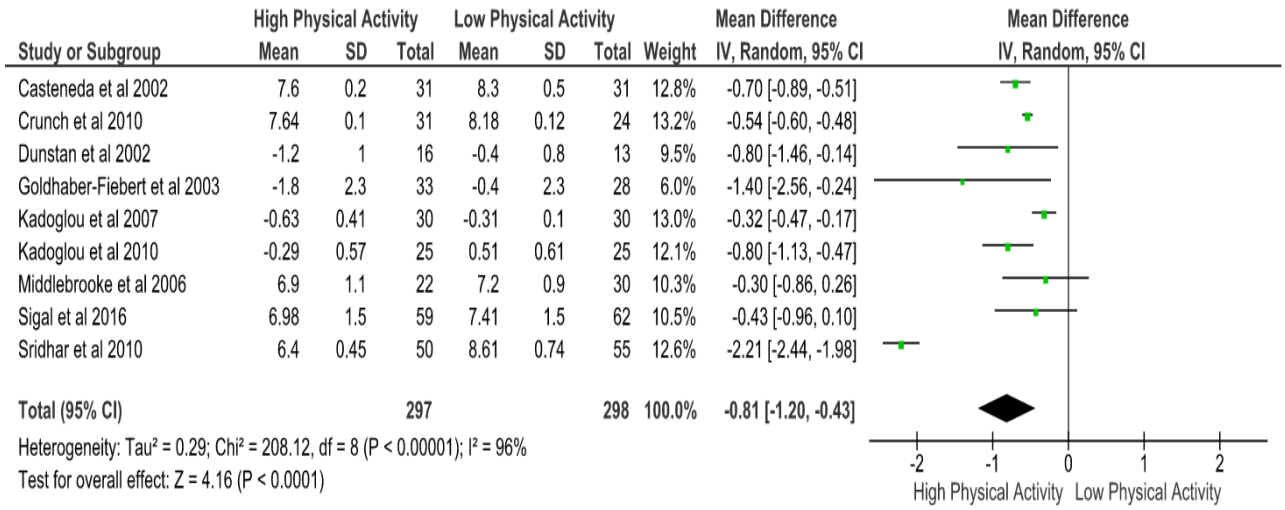

Figure 5. Forest Plot of Physical Activity on HbA1c Level

The funnel plot in Figure 6 shows that the distribution of effect estimates from the primary study of this meta-analysis were placed more to the right of the vertical mean line of the estimate than to the left, indicating publication bias. Because the publication bias tends to the right of the vertical mean line in the same direction as the diamond shape in the forest plot, the publication bias tends to reduce the effect of actual physical activity on HbA1c (under-estimate).

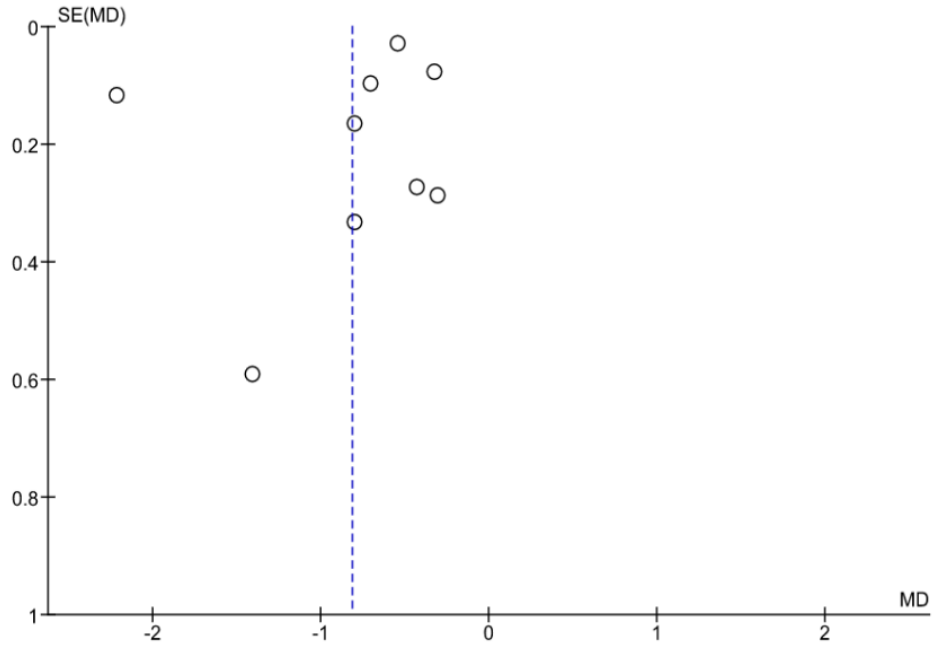

Figure 6. Funnel Plot of Physical Activity on HbA1c Level

2. Correlation between Diet on HbA1c Level

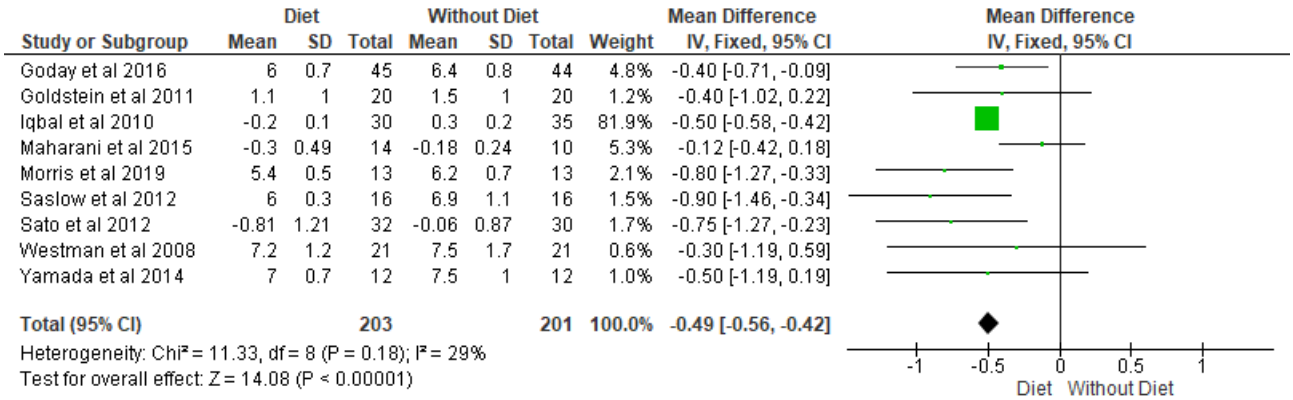

Figure 7. Forest Plot of Diet on HbA1c Level

The forest plot in Figure 7 shows that high dietary therapy can reduce HbA1c levels in type II DM patients. Type II DM patients on diet therapy had an HbA1c level of 0.49 units compared with type II DM patients without treatment, and the results were statistically significant (SMD= -0.49; 95% CI= -0.56 to -0.42; $p < 0.001$). The heterogeneity of the research data showed I^2= 29%, which mean that the estimated effect between the primary studies in this meta-analysis did not vary. Thus, the calculation of the average effect estimate is carried out using a fixed effect model approach.

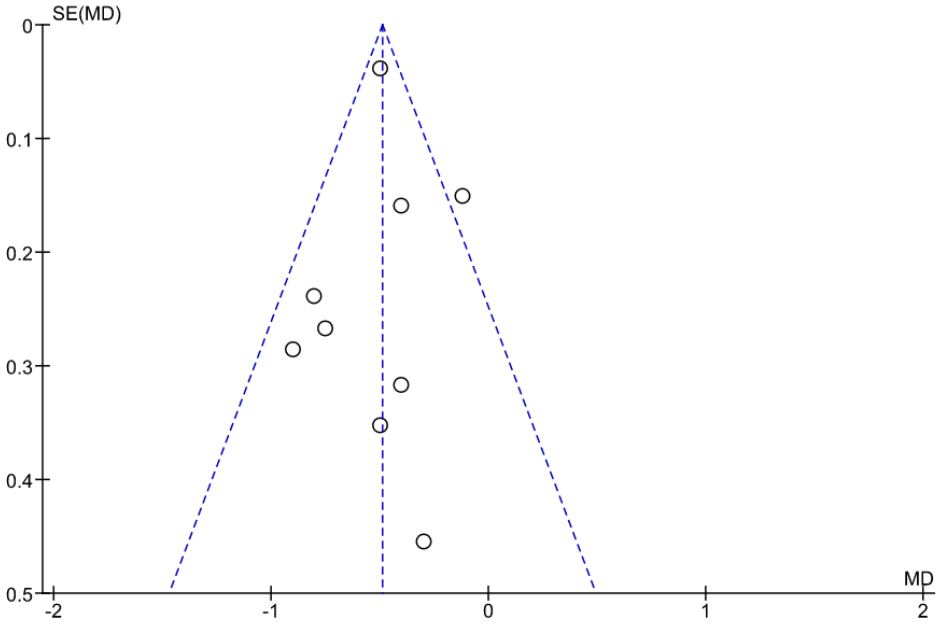

Figure 8. Funnel Plot of Diet Therapy on HbA1c Level

The funnel plot in Figure 8 shows that the distribution of effect estimates from the primary study of this meta-analysis were placed more to the right of the vertical mean line of the estimate than to the left, indicating publication bias. Because the publication bias tends to the right of the mean vertical line in the same direction as the diamond shape in the forest plot, it tends to reduce the effect of actual diet therapy on HbA1c (underestimate).

DISCUSSION

Systematic review and meta-analysis in this study was conducted with the aim of increasing the generalizability of the findings and obtaining convincing conclusions from the results of various similar studies regarding the effectiveness of physical activity and diet therapy in reducing HbA1c levels.

A total of 9 experimental research articles with RCT as a source of meta-analysis of the effectiveness of physical activity and diet therapy on reducing HbA1c levels were obtained. This study showed that physical activity and diet therapy reduced HbA1c levels in type II DM patients, and it was statistically significant. The forest plot results showed that type II DM patients with high physical activity could reduce HbA1c levels by 0.81 units lower than type II DM patients with low physical activity, and the results were statistically significant (SMD= -0.81; 95% CI= -1.20 to -0.43; $p < 0.001$). The results of the forest plot related to diet therapy showed that type II DM patients with diet therapy decreased HbA1c levels by 0.49 units lower than type II DM patients without diet therapy, and the results were statistically significant (SMD = -0.49; 95% CI = - 0.56 to -0.42; $p < 0.001$).

Physical activity has an important role in regulating blood glucose, protein and fat metabolism, increasing insulin action, preventing diabetes complications, increasing muscle flexibility and strength, and having a good effect on the cardiovascular system (ADA, 2014). Low physical activity is known to be associated with a 25-70% increased risk of cardiovascular disease and mortality in type II DM patients with a median age of 60 years when followed for 5 years (Zethelius et al., 2014). Increased physical activity

is also known to reduce the risk of progression from Gestational Diabetes (GDM) to type II diabetes. In addition, regular physical activity can also improve blood circulation, and reduce risk factors for type II diabetes (Damayanti, 2016).

Regular and regular physical activity management is very necessary in order to improve insulin sensitivity, glycemic control, and metabolic profile of patients and individuals who are at risk of experiencing type II DM (Aune et al., 2015; ADA, 2018; Nurayati and Adriani , 2017). Light physical activity with high intensity and a minimum duration of 30 minutes is sufficient for the prevention of type II DM (Lisiswanti, 2016).

The results of this study showed that diet therapy reduced HbA1c levels by 0.49 times compared to no diet. The results of Abidah's research (2016) show that there is a significant relationship between the consumption of sweet and fatty foods with the incidence of type II diabetes. Foods with a sweet, fatty, and salty taste trigger an unbalanced intake and will lead to obesity (Nuraini and Surpriatna, 2016). Obesity is a trigger for various diseases, especially type II diabetes, besides the habit of consuming high-risk foods has three times the chance of having uncontrolled blood sugar levels (Werdani and Triyanti, 2014). This study concluded that diet therapy and physical activity were effective in reducing HbA1c levels in type 2 BM patients.

AUTHOR CONTRIBUTION

Utari Kusumaningrum is the main researcher who selected the topic, explored and collected the data. Bhisma Murti and Hanung Prasetya played a role in analyzing data and reviewing research documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTERESTS

There is no conflict of interest in this study.

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