The Impact of the Indonesian Chronic Disease Management Program (PROLANIS) on Metabolic Control and Renal Function of Type 2 Diabetes Mellitus Patients in Primary Care Setting

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Abstract

Background: Indonesia through its government National Health Insurance System has launched a non-communicable and chronic disease management program named Indonesian Chronic Disease Management Program (PROLANIS), with Type 2 Diabetes Mellitus (T2DM) and hypertension as the main focus. However, study that evaluates the clinical impact of PROLANIS in patients with T2DM is still scarce to this date. This study aims to evaluate the metabolic control and renal function of PROLANIS participants with T2DM every six month within the first 18-months of implementation. **Methods:** This study was a retrospective cohort study conducted at Wates sub-district, East Java using secondary data from PROLANIS group report from April 2018 to October 2019. The study population was T2DM patients who voluntarily joined the PROLANIS group in April 2018. The six-month-evaluation included metabolic parameters [body mass index (BMI), blood pressure, hemoglobin A1C, total cholesterol, high-density lipid, low-density lipid, and triglyceride (TG)] and renal parameters [blood urea nitrogen (BUN), creatinine serum, and urinary microalbumin]. Paired t-test and wilcoxon signed-rank test was used for the analysis, and the P-value was adjusted using Bonferroni correction. A P-value $<.0015$ was considered statistically significant, while a P-value between .0015 and .003 was considered as marginally significant. **Results:** A total of 30 participants were included in the analysis. Following the PROLANIS implementation, the only parameter of metabolic control that showed significant improvement was TG serum level ($P<.001$). Despite the worsening status of other metabolic parameters, the changes were not statistically significant except for BMI that was marginally significant ($P=.002$). From renal function, only BUN serum level was significantly deteriorated ($P<.001$), while the others did not significantly change. **Conclusion:** PROLANIS implementation in our study population seems to be ineffective. Future study with more primary healthcare centers needs to be done to scrutinize the clinical impact of this program nationwide.

Keywords

government program, Indonesia, primary healthcare, PROLANIS, type 2 diabetes mellitus

Introduction

Type 2 Diabetes Mellitus (T2DM), one of the most notable non-communicable and chronic diseases (NCDs), is a growing global problem affecting 463 million people in the world. Western Pacific region, including Indonesia, is listed as the leading region of T2DM global prevalence in the world.[1,2] In Indonesia, the national prevalence of T2DM is steadily increasing from 6.9% in 2013 to 10.9% in 2018.[3] As T2DM is responsible for many deaths and burdens, the World Health Organization recommends every country to establish national policies and plans for the prevention and control of many NCDs including T2DM.[4,5]

The optimization of a primary healthcare facility function is considered vital in the management of T2DM.[4,6] Unfortunately, many problems occur, especially in low- to

middle-income countries including Indonesia. The barriers of T2DM management in Indonesia include the lack of access to healthcare, the availability of antidiabetic drugs in primary and secondary healthcare, and the quality of healthcare workers in disease prevention and management.[7] Many studies have emphasized that a prudent community program is essential in T2DM management.[8] Therefore, there is an urge to strengthen the health systems to address diabetes as clinical entities through primary healthcare services for early detection and management.[9]

Indonesia, through the government National Health Insurance System (NHIS), launched a non-communicable and chronic disease management program named Indonesian Chronic Disease Management Program (PROLANIS) in 2014. The diseases that become the main focus of PROLANIS are T2DM and hypertension.[10,11] This program is an integrated health service program involving the community of patients, healthcare professionals, healthcare facilities, and NHIS. It aims to control the clinical and laboratory outcomes, prevent disease complications, as well as improve patients' quality of life. PROLANIS is specifically designed to be implemented at the primary care level (government-owned community healthcare centers, primary care clinics, or private doctors).

This program gives additional benefits for its participants through some routine activities as follow:[11]

(1) Monthly regular meeting for medical consultation.
(2) Peer group education by healthcare professionals.
(3) Healthcare visit reminder.
(4) Peer-club activities.
(5) Home visit.
(6) Regular health status monitoring (including monthly blood glucose check for T2DM patients).
(7) Laboratory evaluation for metabolic control and renal function every 6 months.

All patients diagnosed with either hypertension or T2DM in the primary care are offered to be enrolled in this program.

If the patients decided not to participate in this program, they will not receive the above-mentioned additional advantages. However, they will still receive the same pharmacological therapies as PROLANIS participants, albeit the quantity is lower (one to two weeks for non PROLANIS participants vs one month for PROLANIS participants).[12] Giving only a half or a quarter of the monthly dose for non PROLANIS participants will force patients to come the healthcare more often. Majority of patients hate it because every visit to the healthcare is considered time-consuming for them.

Unfortunately, published studies that evaluated the impact of PROLANIS in patients with T2DM are still scarce to this date.[13-16] Moreover, those studies did not present all the laboratory evaluation data and only used cross-sectional method. This study aims to analyze all evaluated clinical parameter outcomes of PROLANIS participants with T2DM treated in a primary healthcare center in Wates, East Java, Indonesia every six month during the first 18-months of PROLANIS implementation.

Materials and Methods

Study Design

This study was an observational retrospective cohort study using secondary data from PROLANIS group report at Wates sub-district. Wates sub-district is located in Mojokerto city, East Java province, Indonesia. Although the PROLANIS has been launched since 2014, PROLANIS activities in this sub-district have only been routinely implemented since April 2018 and managed by Wates Primary Healthcare. Wates Primary Healthcare is one of the six government-owned community healthcare centers (Puskesmas) in Mojokerto city.

The study population was all T2DM patients who voluntarily joined the PROLANIS group in April 2018 (T0). The participants who left the PROLANIS, deceased, or did not attend the 6-month-evaluation in October 2018 (T1), April

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2019 (T2), or October 2019 (T3) were excluded from the analysis. This study was conducted according to the Declaration of Helsinki and was approved by the relevant Department of Health. This study also follows the STROBE reporting guideline (Supplemental Table 1).[17]

Evaluated Parameters

The compliance of the PROLANIS participants was measured by their attendance at the monthly routine meeting. Those who missed the meeting more than two times during the study period were categorized as not routine or uncompliant. The 6-month-evaluation consisted of metabolic control and renal function parameters. Evaluated metabolic parameters were body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), hemoglobin A1C (HbA1C), total cholesterol (TC), high-density lipid (HDL), low-density lipid (LDL), and triglyceride (TG). Evaluated renal parameters were blood urea nitrogen (BUN), creatinine serum, and urinary microalbumin. BMI and blood pressure were measured by the healthcare workers from Wates Primary Healthcare, while laboratory evaluation was done by designated third parties laboratory at Mojokerto city. Data of BMI were presented in kg/m^2, blood pressure in mmHg, HbA1C in %, urinary microalbumin in mg/l, and TC, HDL, LDL, TG, and BUN in mg/dl. Creatinine serum was converted to an estimated glomerular filtration rate (eGFR) using the Cockcroft-Gault equation and presented in $ml/min/1.73\,m^2$.[18] The targeted cut-off level for good metabolic control for each parameter was based on recent Indonesian Society of Endocrinology (PERKENI) T2DM guidelines, defined as follows: BMI between 18.5 and $23\,kg/m^2$; $SBP < 140\,mmHg$; $DBP < 90\,mmHg$; $HbA1C < 7\%$; $TC < 200\,mg/dl$; $LDL < 100\,mg/dl$; $TG < 150\,mg/dl$; $HDL > 40\,mg/dl$ for male and $>50\,mg/dl$ for female.[19]

Statistical Analysis

Kolmogorov-Smirnov test was used to evaluate the data distribution. Normally distributed data were presented in mean $\pm$ SD, skewed data were presented in median [IQR], and nominal data were presented in n (%). Paired t-test was used for statistical analysis in normally distributed data and Wilcoxon signed-rank test was used for statistical analysis in skewed data. A P-value $< .05$ was considered significant. However, since we performed multiple (33) paired tests, the P-value was adjusted using Bonferroni correction to reduce the chance of a type I error.[20] Thus, a P-value $< .0015$ was considered statistically significant in the multiple paired test. Meanwhile, the P-value between .0015 and .003 was considered as marginally significant in the same test. Acquired data were analyzed using IBM SPSS Statistics for Windows version 25.0. (IBM Corp., Armonk, NY, USA).

Results

Baseline Characteristics

There were 43 T2DM patients recruited in this study at baseline (T0), however, 13 participants were lost to follow up (Figure 1). The majority of the participants were women with a mean age of 62.83 ± 7.96 years old. The detailed characteristics of the participants including the evaluated parameters at T0 were summarized in Table 1.

Evaluated Parameters

After 18 months of PROLANIS implementation, the only parameter of metabolic control that showed significant improvement was TG serum level ($P < .001$). Despite the worsening status of other metabolic parameters, the changes were not statistically significant except for BMI that was marginally significant ($P = .002$; Table 2). The number of participants reaching the target levels of BMI, DBP, LDL, and HbA1C was reduced. Meanwhile, the number of participants reaching the targeted levels of TG and HDL was increased (Figure 2). From three renal function parameters, all of them were worsened but the statistical significance was only found in BUN serum level ($P = .001$) (Table 2).

There were three different trends from the evaluated metabolic (Figure 3) and renal parameters (Figure 4): (1) deteriorated in the beginning and showed improvement in the end (HbA1C, eGFR, and urinary microalbumin); (2) improvement in the beginning but deteriorated afterward (BMI, SBP, LDL, and HDL after T1; DBP, TC, and BUN after T2); (3) continuous improvement since the beginning (TG). In the first trend, HbA1C was significantly worse while eGFR and urinary microalbumin were marginally worse in T2 than T0. After the improvement from T2 to T3, all the differences become insignificant albeit the worse serum level compare to T0. Similar condition was also noticed in the second trend, where T3 was worse compared to T0 despite the improvement in the beginning. Nonetheless, statistically different finding was only seen in BUN, and only BMI parameter that showed marginal significance. TG was the only parameter that showed significant improvement in T3 and always showed improvement since the implementation of PROLANIS.

Discussion

We found that TG serum level was the only parameter that significantly improved, while BUN was the only parameter that significantly deteriorated and BMI was marginally deteriorated after 18 months of PROLANIS implementation. Meanwhile, the rest of the evaluated parameters were worsened but not statistically significant. We also found that the number of participants that achieved the targeted
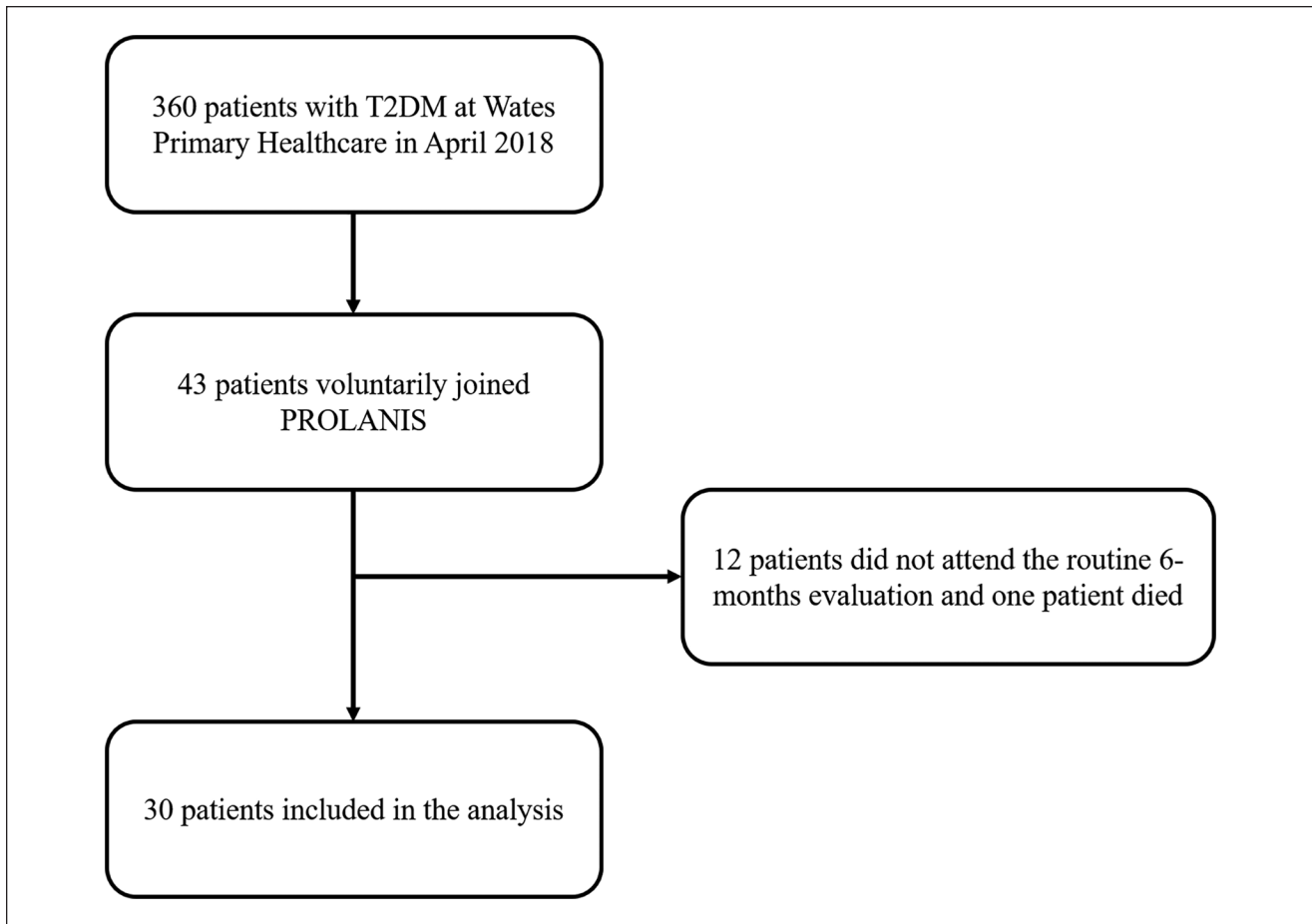
Figure 1. Flow chart of the study population selection.

levels of BMI, DBP, LDL, and HbA1C was decreased, while the number of participants that achieved the targeted levels of TG and HDL was increased.

In T0, there were 53.3% of PROLANIS participants that had achieved HbA1C targeted level. This prevalence was higher than the Indonesia national data.[21] However, after 18 months of PROLANIS implementation, those who achieved the HbA1C targeted level declined to 40%. The failure of maintaining glycemic control among T2DM in this study indicated the ineffectiveness of PROLANIS in Wates Primary Healthcare in controlling the main metabolic parameter of T2DM management. There was only one previous study in Indonesia that assessed the HbA1C among PROLANIS participants. The data showed merely 12.9% of the PROLANIS participants who successfully achieved HbA1C serum level < 7%.[15] The low percentage of achieved HbA1C was also observed in a study in Brazil with only 18.6% subjects with HbA1C serum level < 7%.[22] The percentage of poor glycemic control among T2DM subjects were also common globally. In a GUIDANCE study involving eight countries in Europe which evaluated

the metabolic control parameters in primary healthcare showed that the subjects who had satisfying HbA1C level ranged from 35.7% to 70.5%.[23] A recent meta-analysis consisting of 24 studies from 20 countries and 369 251 participants revealed the proportion of people achieving HbA1C targets was 42.8%,[24] which was comparable to the result of our study.

In our study, BMI, SBP, and DBP levels were increased and the percentage of those who achieved the targeted cut-off level was lower after 18 months of PROLANIS implementation. The GUIDANCE study explicitly showed that only 14.7% of the subjects with T2DM had BMI < 25 kg/m^2. This number was exaggerated with only 15.4% men and 5% women who had waist circumference below recommended levels, increasing the magnitude of body composition problems in subjects with T2DM.[23] Other study in Brazil with similar SBP and the DBP target with our study demonstrated that more T2DM subjects met DBP target than subjects who met the SBP target (72.5% vs 58.2%).[22] The number fell when tighter criteria were used for evaluating blood pressure control as SBP < 130 mmHg and

Table 1. Baseline Characteristics of Study Population.

Parameter	N = 30
Age (year, mean ± SD)	62.83 ± 8.0
Women, n (%)	25 (83.3)
Family history of type 2 diabetes mellitus, n (%)	10 (33.3)
Hypertension, n (%)	16 (53.3)
Routine PROLANIS attendance, n (%)	16 (53.3)
Drug therapy	
Single oral drug, n (%)	17 (56.7)
Double oral drug, n (%)	11 (36.7)
Insulin injection, n (%)	1 (3.3)
Mix of oral and injection, n (%)	1 (3.3)
Type 2 diabetes mellitus duration	
<5 years, n (%)	16 (53.3)
5-10 years, n (%)	7 (23.3)
>10 years, n (%)	7 (23.3)
Education level background	
No formal education, n (%)	2 (6.7)
Elementary school graduates, n (%)	6 (20.0)
Junior high school graduates, n (%)	10 (33.3)
Senior high school graduates, n (%)	10 (33.3)
University graduates, n (%)	2 (6.7)
BMI (kg/m^2, mean ± SD)	24.8 ± 3.3
SBP (mmHg, median [IQR])	125.0 [117.5-140.0]
DBP (mmHg, median [IQR])	80.0 [80.0-90.0]
HbA1C (%, mean ± SD)	6.4 ± 1.8
TC (mg/dl, mean ± SD)	216.4 ± 40.1
LDL (mg/dl, mean ± SD)	136.5 ± 37.0
TG (mg/dl, median [IQR])	161.5 [104.2-232.7]
HDL (mg/dl, median [IQR])	47.5 [45.5-55.2]
eGFR (ml/min/1.73 m^2, mean ± SD)	62.2 ± 21.9
BUN (mg/dl, median [IQR])	27.6 [19.0-35.8]
Urinary microalbumin (mg/l, median [IQR])	33.5 [8.0-124.8]

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1C, hemoglobin A1C; TC, total cholesterol; LDL, low-density lipid; TG, triglyceride; HDL, high-density lipid; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen.

DBP < 80 mmHg. Only 19% to 35.3% achieved SBP target and 22.4% to 59.2% achieved DBP target T2DM.[23]

In addition to worse glycemic, blood pressure, and BMI control, our study also highlighted the unmet LDL target among the participants. From all metabolic control parameters, the achievement of the LDL target was the worst since the beginning. Together with increased TC, it was the lipid parameter that became worse after 18 months of PROLANIS implementation. This showed the failure of PROLANIS in Wates Primary Healthcare in managing LDL treatment targets in T2DM patients. On the contrary to LDL and TC worsening, HDL and TG showed promising improvements. HDL improvement was found to be statistically significant in T1

compared to T0 but not in T3. On the other hand, TG showed the most assuring improvement consistently from T0 to T3.

Previous PROLANIS studies in Indonesia were also lack of LDL data.[13-16] Only one study showed the data of TC level, but this seems did not provide any insight in assessing the effectivity of PROLANIS in meeting the target of lipid profile in T2DM management.[13] According to a study in Indonesia, primary care physician's adherence to statin prescription was the least among many recommendations in T2DM management.[25] In addition, the regulation does not support the management of LDL in T2DM. Based on the government recommendation, the only available statin in primary healthcare is simvastatin, and it is only allowed to be given to T2DM patients if the LDL > 130 mg/dl.[26] Meanwhile, according to Indonesian clinical guidelines and also the various clinical international guidelines, the desired LDL target is < 100 mg/dl.[19,27,28] We argued that the above-mentioned reasons could be the cause of unmet LDL and TC target in our participants.

One study also observed an increase of HDL level among T2DM subjects who were more physically active, even though this finding was only significant in men.[29] We postulated the improvement of HDL after PROLANIS implementation was because of the increased physical activity as one part of the PROLANIS routine meeting. Unfortunately, we could not confirm this finding because we did not have any objective record of our subjects' physical activity level.

A lower-carbohydrate diet was associated with a significant reduction of the TG level.[30] Thus, we suspected that our subjects were more adhered to lower carbohydrate consumption, resulting to lower the TG serum. However, a lower-carbohydrate diet should also reduce the HbA1C level, but on the contrary, it is significantly increasing in our findings. We could not explain this phenomenon because we did not evaluate the daily nutrition intake of our subjects. In addition, we also did not have the data regarding what kind of education has been given to the PROLANIS participants during the monthly regular meeting. Nevertheless, reflecting on the findings that the TG parameter was improved while the HbA1C parameter was deteriorated, we believe that the education given to the participants was more focused on TG-related management than other topics. To our knowledge, there was no guideline from the national government about what kind of education should be given to the PROLANIS participants. It is up to every healthcare center to determine education topics every month.

The implementation of the PROLANIS was associated with worsened renal function. Sub-group analysis based on participants' attendance showed that patients who routinely attended PROLANIS activities have better ΔT3-T0 of eGFR and urinary microalbumin but worse BUN than patients who were not routinely attended PROLANIS

Table 2. Routine 6-Month-Evaluation of Metabolic Control and Renal Function.

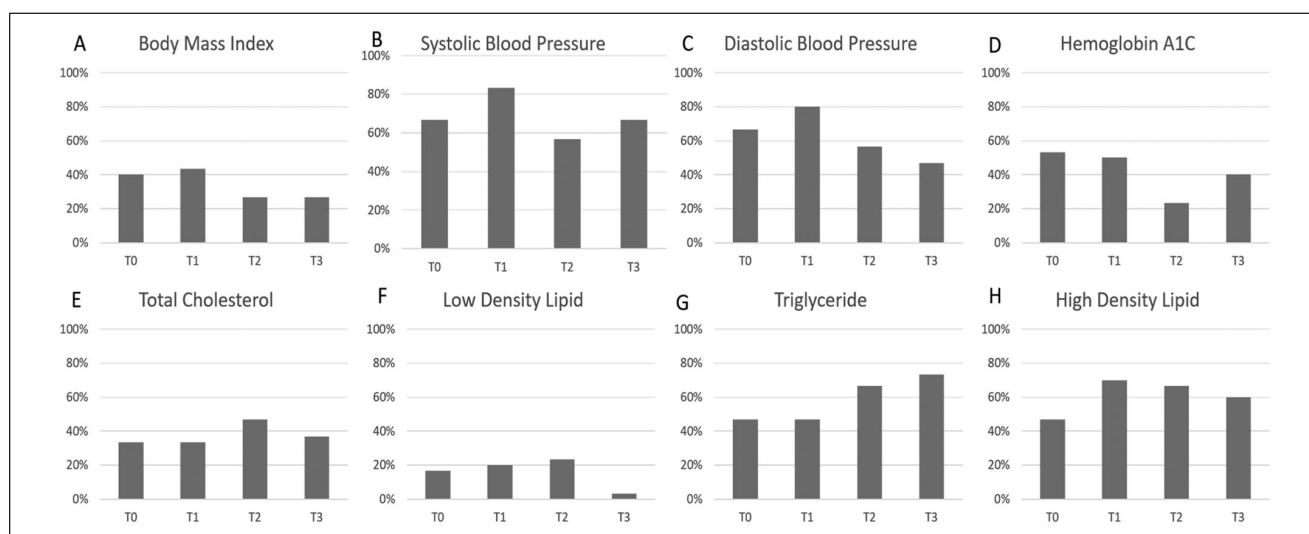| Parameters	N = 30			
	T0	T1	T2	T3
BMI (kg/m²), mean ± SD¶	24.78 ± 3.35	24.68 ± 3.59 P=.693	25.56 ± 3.61 P=.007	25.86 ± 3.75 P=.002#
SBP (mmHg), median [IQR]‡	125 [117.5-140]	120 [120-130] P=.871	130 [127.5-150] P=.002#	130 [120-140] P=.059
DBP (mmHg), median [IQR]‡	80 [80-90]	80 [80-90] P=.142	80 [80-90] P=.399	90 [80-90] P=.090
HbA1C (%), mean ± SD¶	6.65 ± 1.70	7.56 ± 2.29 P=.014	7.69 ± 1.16 P=.001*	7.35 ± 1.35 P=.022
TC (mg/dl), mean ± SD¶	216.37 ± 40.12	210.93 ± 33.21 P=.390	200.4 ± 32.27 P=.024	220.77 ± 35.58 P=.533
LDL (mg/dl), mean ± SD¶	136.53 ± 37.04	124.8 ± 25.62 P=.030	127.03 ± 30.2 P=.189	147.37 ± 31.16 P=.079
TG (mg/dl), median [IQR]‡	161.5 [104.25-232.75]	156.5 [91.5-206.75] P=.719	130 [79.5-166.5] P=.006	99 [74-156] P<.001*
HDL (mg/dl), median [IQR]‡	47.5 [45.5-55.25]	53.5 [47-58.25] P=.002#	51.5 [45-56] P=.083	49.5 [45-56.25] P=.361
eGFR (ml/min/1.73 m²), mean ± SD¶	62.17 ± 21.93	57.03 ± 21.50 P=.004	56.6 ± 20.09 P=.003#	58.97 ± 23.47 P=.114
BUN (mg/dl), median [IQR]‡	27.6 [19.02-35.84]	24.29 [17.92-34.13] P=.349	21.82 [17.12-30.11] P=.094	30.38 [25.46-42.04] P=.001*
Urinary microalbumin (mg/l), median [IQR]‡	33.5 [8-124.75]	65.32 [11.18-165.53] P=.06	85.29 [34.00-206.65] P=.002#	39.86 [18.28-156.93] P=.066

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1C, hemoglobin A1C; TC, total cholesterol; LDL, low-density lipid; TG, triglyceride; HDL, high-density lipid; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen.
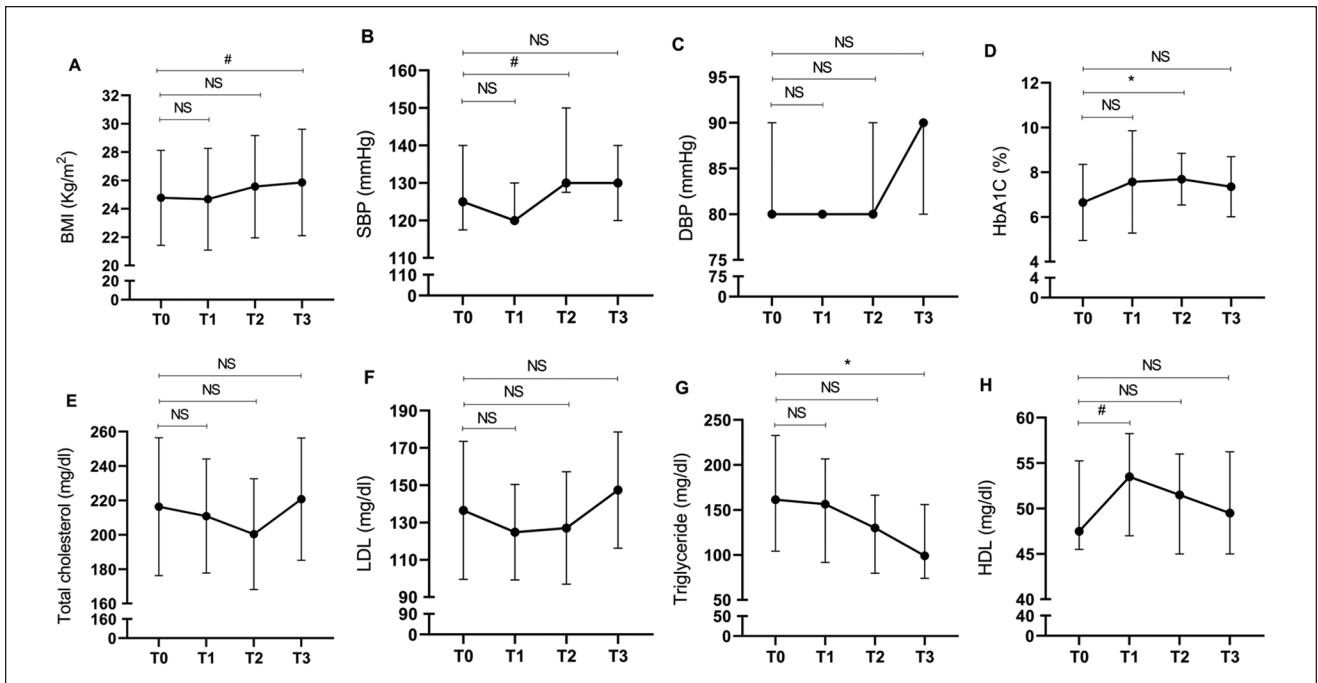*P*-value was adjusted using Bonferroni correction.
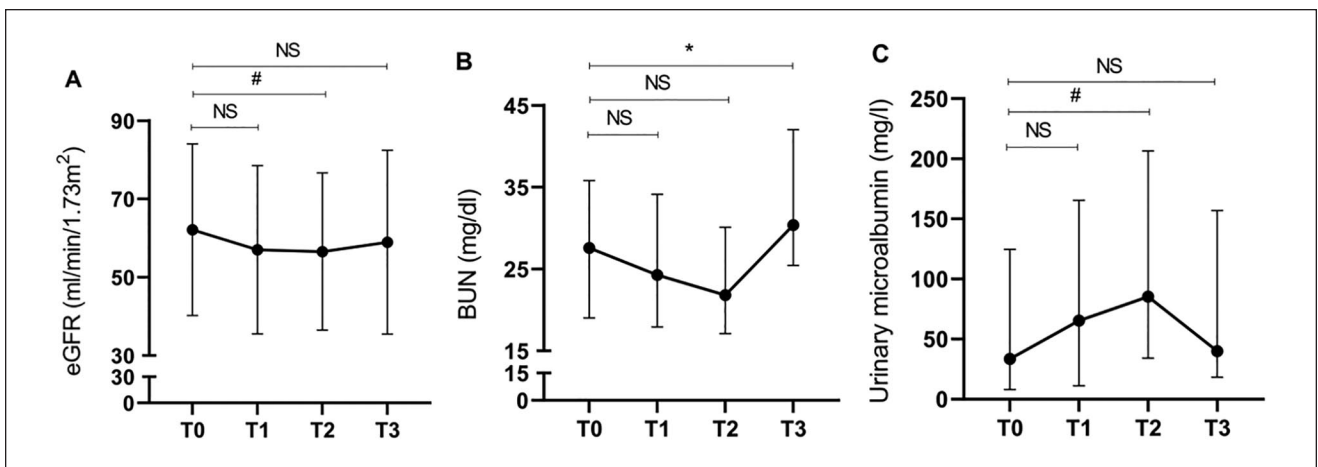¶Paired *T*-test was used.
‡Wilcoxon signed-rank test was used.
P-value < .0015 was considered statistically significant. #*P*-value between .0015 and .003 was considered marginally significant.

Figure 2. Proportion of metabolic control parameters achievement in T2DM management. The proportion of metabolic target parameter in T2DM management describes the percentage of the number of subjects who had successfully achieved metabolic control. The targeted cut-off level for good metabolic control for each parameter was based on recent Indonesian Society of Endocrinology (PERKENI) T2DM guidelines in 2015,[19] defined as follows: (A) Body Mass Index between 18.5 and 23 kg/m², (B) Systolic Blood Pressure < 140 mmHg, (C) Diastolic Blood Pressure < 90 mmHg, (D) Hemoglobin A1C < 7%, (E) Total Cholesterol < 200 mg/dl, (F) Low Density Lipid < 100 mg/dl, (G) Triglyceride < 150 mg/dl, and (H) High Density Lipid > 40 mg/dl for male and > 50 mg/dl for female.

Figure 3. Routine 6-month-evaluation of metabolic control parameters. The routine 6-month-evaluation of metabolic parameters includes: (A) body mass index (BMI), (B) systolic blood pressure (SBP), (C) diastolic blood pressure (DBP), (D) hemoglobin A1C (HbA1C), (E) total cholesterol (TC), (F) high-density lipid (HDL), (G) low-density lipid (LDL), and (H) triglyceride (TG). Data are displayed in mean ± SD for BMI, HbA1C, TC, and LDL, and in median [IQR] for SBP, DBP, TG, and HDL. *P*-value was adjusted using Bonferroni correction. *P-value < .0015 was considered statistically significant, #P-value between .0015 and .003 was considered marginally significant, NS = not statistically significant.

Figure 4. Routine 6-month-evaluation of renal function parameters. The routine 6-month-evaluation of renal function parameters includes: (A) estimated glomerular filtration rate (eGFR), (B) blood urea nitrogen (BUN), and (C) urinary microalbumin. Data are displayed in mean ± SD for eGFR and in median [IQR] for BUN and urinary microalbumin. *P*-value was adjusted using bonferroni correction. *P-value < .0015 was considered statistically significant, #P-value between .0015 and .003 was considered marginally significant, NS = not statistically significant.

activities, although all the differences are not statistically significant (Supplemental Table 2). However, even though BUN could be used as an indicator for renal function, eGFR is a more reliable parameter to represent renal function because BUN is influenced by other factors such as intake and catabolism of proteins or hydration status.[31,32] In this study, we found a declining level of eGFR and higher percentage of patients with eGFR below 60 ml/min/1.73 m^2.

This percentage was considerably high compared to other studies.[33-35] According to a large prospective observational study and randomized controlled trial studies, tight glycemic control was associated with better renal function and less microvascular complications.[36-38] Thus, it can be suggested that the worse glycemic control finding explains the deterioration of the eGFR level and the proportion of subjects with low eGFR in our study.

According to a review by Nam et al,[39] there are two main factors that become the barriers in diabetes management in general, patient factors and healthcare provider factors. The main contributing factor from patients is adherence to treatment. In addition, health education in PROLANIS participants was significantly correlated with systolic blood pressure and fasting blood glucose levels.[14] Another study showed that by educating the PROLANIS participants regarding medication administration, their blood glucose level is significantly improved.[40]

Participants' adherence to attend PROLANIS activities is also important to improve the clinical outcome. In our study, we found that 53% of our subjects adhered to PROLANIS activities. Moreover, those who routinely attended the PROLANIS activities showed better outcomes in most of the metabolic control and renal complication parameters compared to those who did not routinely attend the activities (Supplemental Figures 1 and 2). Nevertheless, all of the changes in participants who routinely attended PROLANIS were not different statistically compared to participants who did not routinely attend it (Supplemental Table 2). We argued that these statistically insignificant findings were because of the low number of subjects. A prior study found that the HbA1C serum level was significantly correlated with participants' adherence to PROLANIS activity.[15] Another study found that T2DM patients who routinely attended PROLANIS activities had significantly more controlled fasting blood glucose compared to patients who did not attend PROLANIS activities.[16]

From healthcare provider barriers, primary healthcare has limitations to achieve the treatment goals for patients with T2DM due to limitations in laboratory facilities and medicines.[41] In addition, primary care physicians in Indonesia are also more likely not to adhere to the national T2DM guideline even though they are aware of it. This will lead to clinical inertia and poor outcome in T2DM management in Indonesia.[25] However, these factors were not directly assessed in our study.

In this study, there were only two out of 30 PROLANIS participants that received insulin prescriptions for their T2DM management, and none of them received the prescription from primary healthcare. Previous studies from other countries showed that the prescription of insulin is significantly lower in primary healthcare.[42,43] In Indonesia, insulin prescription is not covered by the NHIS in primary healthcare, preventing T2DM patients to access insulin regimen.[26] Thus, it is important to increase the coverage of essential drugs to improve the capability of primary healthcare workers in managing T2DM patients.[7]

PROLANIS has several activities, and funding from the government was needed to conduct all activities effectively. However, the cost per individual for PROLANIS participants was found to be reduced by 50% within the first 2 years of program implementation because of the increasing number of participants.[44] The lack of funding might affect the quality of PROLANIS activities. Unfortunately, we were not able to evaluate all the activities, whether they have been conducted properly and achieved all the desired targets as indicated in the PROLANIS guidebook.[11]

There were several limitations to this study. This study was a single-center study with data from only 30 participants. Meanwhile, latest data in 2016 showed that the registered PROLANIS participants in the province where this study was conducted was 44 999 and the nationwide participants was 260 364.[44] Thus, our study did not entirely reflect the impact of PROLANIS nationwide. We also could not provide complete medical drug consumption other than the type of anti-diabetic drugs and the daily food intake which might affect the evaluated metabolic control parameters. The reason that affected the participants' compliance also could not be evaluated. Nevertheless, this was the first study that evaluated serial metabolic control and renal complication parameters outcome of PROLANIS participants with T2DM every 6 month during the first 18-months of PROLANIS implementation.

Conclusion

PROLANIS implementation in our study population seems to be ineffective. Future study with more in-depth analysis combining qualitative and quantitative approach as well as involving more primary healthcare centers and participants needs to be done to scrutinize the clinical impact of this program nationwide.

Ethical Approval

This study was approved by the Department of Health of Mojokerto City (Approval number: 072/29/417.405/2020)

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Supplemental Material

Supplemental material for this article is available online.

References

1. International Diabetes Federation. *IDF Diabetes Atlas*. International Diabetes Federation; 2019.
2. World Health Organization. *Noncommunicable Diseases Country Profiles 2018*. 2018.
3. Badan Penelitian dan Pengembangan Kesehatan. *Hasil Utama RISKESDAS 2018*. Kementerian Kesehatan Republik Indonesia; 2018.
4. World Health Organization. *2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Non-communicable Diseases: Prevent and Control Cardiovascular Diseases, Cancers, Chronic Respiratory Diseases and Diabetes*. 2008.
5. Bommer C, Heesemann E, Sagalova V, et al. The global economic burden of diabetes in adults aged 20-79 years: a cost-of-illness study. *Lancet Diabetes Endocrinol*. 2017;5:423-430.
6. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care*. 2019;42(suppl 1):S1-S192.
7. Soewondo P, Ferrario A, Tahapary DL. Challenges in diabetes management in Indonesia: a literature review. *Global Health*. 2013;9:63.
8. Nissinen A, Berrios X, Puska P. Community-based noncommunicable disease interventions: lessons from developed countries for developing ones. *Bull World Health Organ*. 2001;79:963-970.
9. World Health Organization. *Prevention and Control of Noncommunicable Diseases: Guidelines for Primary Health Care in Low Resource Settings*. 2012.
10. Agustina R, Dartanto T, Sitompul R, et al. Universal health coverage in Indonesia: concept, progress, and challenges. *Lancet*. 2019;393:75-102.
11. Indonesian National Health Insurance System. *Practical Guideline for Non Communicable and Chronic Disease Management (Panduan Praktis Program Pengelolaan Penyakit Kronis)*. Badan Penyelenggara Jaminan Sosial Kesehatan; 2014.
12. Putri LP, Mawarni D, Trisnantoro L. Challenges of shifting diabetes mellitus care from secondary- to primary-level care in urban and rural districts: a qualitative inquiry among health providers. *J Prim Care Community Health*. 2020;11:2150132720924214.
13. Ahmad M, Rachmawaty R, Sjattar EL, Yusuf S. Prolanis implementation effective to control fasting blood sugar, HBA1C and total cholesterol levels in patients with type 2 diabetes. *Jurnal Ners*. 2017;12:88-98.
14. Pradyta AD, Masfiah S, Gamelia E, Maqfiroch AFA. Relationship between utilization of PROLANIS with health status of diabetes mellitus patient in Purwokerto (Article in Indonesia). *Jurnal Kesmas Indonesia*. 2017;9:63-72.
15. Syuadzah R, Wijayanti L, Prasetyawati AK. Adherence to PROLANIS acitvity in type 2 diabetes mellitus's patients with HBA1C Levels (Article in Indonesia). *Nexus Kedokteran Komunitas*. 2017;6:24-30.
16. Tanty HN, Anggriani Y, Saragi S. Effects of PROLANIS on clinical outcome of type 2 diabetes mellitus patients in puskesmas kecamatan pulogadung (Article in Indonesia). *Farmasains*. 2019;6:11-19.
17. von Elm E, Altman DG, Egger M, et al. The Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Bull World Health Organ*. 2007;85:867-872.
18. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16:31-41.
19. Soelistijo SA, Novida H, Rudijanto A, et al. *Konsensus Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 di Indonesia*. Pengurus Besar Perkumpulan Endokrinologi Indonesia (PB PERKENI); 2015.
20. Armstrong RA. When to use the Bonferroni correction. *Ophthalmic Physiol Opt*. 2014;34:502-508.
21. Cholil AR, Lindarto D, Pemayun TGD, Wisnu W, Kumala P, Puteri HHS. DiabCare Asia 2012: diabetes management, control, and complications in patients with type 2 diabetes in Indonesia. *Med. J. Indones*. 2019;28:47-56.
22. Simão CCAL, Costa MB, Colugnati FAB, de Paula EA, Vanelli CP, de Paula RB. Quality of care of patients with diabetes in primary health services in Southeast Brazil. *J Environ Public Health*. 2017;2017:1709807.
23. Stone MA, Charpentier G, Doggen K, et al. Quality of care of people with type 2 diabetes in eight European countries: findings from the guideline adherence to enhance care (GUIDANCE) study. *Diabetes Care*. 2013;36:2628-2638.
24. Khunti K, Ceriello A, Cos X, De Block C. Achievement of guideline targets for blood pressure, lipid, and glycaemic control in type 2 diabetes: a meta-analysis. *Diabetes Res Clin Pract*. 2018;137:137-148.
25. Widyahening IS, van der Graaf Y, Soewondo P, Glasziou P, van der Heijden GJMG. Awareness, agreement, adoption and adherence to type 2 diabetes mellitus guidelines: a survey of Indonesian primary care physicians. *BMC Fam Pract*. 2014;15:72.
26. Decree of the Minister of Health of The Republic Indonesia Number HK.01.07/MENKES/813/2019 on National Formularium. 2019.
27. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020;41:111-188.
28. Jellinger PS, Handelsman Y, Rosenblit PD, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease. *Endocr Pract*. 2017;23(suppl 2):1-87.
29. Yates T, Davies MJ, Gray LJ, et al. Levels of physical activity and relationship with markers of diabetes and cardiovascular disease risk in 5474 white European and South Asian adults screened for type 2 diabetes. *Prev Med*. 2010;51:290-294.

30. Kirk JK, Graves DE, Craven TE, Lipkin EW, Austin M, Margolis KL. Restricted-carbohydrate diets in patients with type 2 diabetes: a meta-analysis. *J Am Diet Assoc*. 2008;108: 91-100.

31. Salazar JH. Overview of urea and creatinine. *Lab Med*. 2014;45:e19-e20.

32. Jujo K, Minami Y, Haruki S, et al. Persistent high blood urea nitrogen level is associated with increased risk of cardiovascular events in patients with acute heart failure. *ESC Heart Fail*. 2017;4:545-553.

33. Jitraknatee J, Ruengorn C, Nochaiwong S. Prevalence and risk factors of chronic kidney disease among type 2 diabetes patients: a cross-sectional study in primary care practice. *Sci Rep*. 2020;10:6205.

34. van der Meer V, Wielders HP, Grootendorst DC, et al. Chronic kidney disease in patients with diabetes mellitus type 2 or hypertension in general practice. *Br J Gen Pract*. 2010;60:884-890.

35. DEMAND investigators, Parving HH, Lewis JB, Ravid M, Remuzzi G, Hunsicker LG. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. *Kidney Int*. 2006;69:2057-2063.

36. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321:405-412.

37. Group AC, Patel A, MacMahon S, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2008;358:2560-2572.

38. Wong MG, Perkovic V, Chalmers J, et al. Long-term benefits of intensive glucose control for preventing end-stage kidney disease: ADVANCE-ON. *Diabetes Care*. 2016;39:694-700.

39. Nam S, Chesla C, Stotts NA, Kroon L, Janson SL. Barriers to diabetes management: patient and provider factors. *Diabetes Res Clin Pract*. 2011;93:1-9.

40. Rahem A, Utami W, Sukorini AI, Effendi MH. The effect of advocacy on understanding and levels of blood glucose in diabetes mellitus patients. *Asian J Pharm*. 2019;13:375-380.

41. Arifin B, van Asselt ADI, Setiawan D, Atthobari J, Postma MJ, Cao Q. Diabetes distress in Indonesian patients with type 2 diabetes: a comparison between primary and tertiary care. *BMC Health Serv Res*. 2019;19:773.

42. Seo DH, Kang S, Lee YH, et al. Current management of type 2 diabetes mellitus in primary care clinics in Korea. *Endocrinol Metab (Seoul)*. 2019;34:282-290.

43. Diabcare (Taiwan) Study Group, Tai TY, Chuang LM, Tsai ST, Huang BY. Treatment of type 2 diabetes mellitus in a primary care setting in Taiwan: comparison with secondary/tertiary care. *J Formos Med Assoc*. 2006;105:105-117.

44. Khoe LC, Wangge G, Soewondo P, Tahapary DL, Widyahening IS. The implementation of community-based diabetes and hypertension management care program in Indonesia. *PLOS ONE*. 2020;15:e0227806.