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Complications of type 2 diabetes mellitus in Ramallah and al-Bireh: The Palestinian Diabetes Complications and Control Study (PDCCS)

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a growing pandemic that will lead, if not managed and controlled, to frequent complications, poor quality of life, and high rates of disability and death. Little is known about T2DM complications in Palestine. The aim of this study is to estimate the prevalence of T2DM complications in Ramallah and al-Bireh governorate of Palestine.

Methods: The study was conducted in eleven primary healthcare clinics offering services for persons with T2DM. Macrovascular complications were assessed using the Diabetes complication index. Microvascular complications were measured by physical examinations and laboratory tests. Questionnaires, laboratory tests, and physical examinations were used to assess socio-demographic characteristics, co-morbidities and other risk factors.

Results: 517 adult men and nonpregnant women participated in the study (166 men, 351 women). The response rate was 84%. Mean age and mean duration of diabetes were 58.1 and 9.4 years respectively. Prevalence of diagnosed microvascular and macrovascular complications was 67.2% and 28.6% respectively. 78.2% of the participants had poor glycemic control (HbA1c ≥ 7.0%).

Conclusion: Significant proportions of persons with T2DM had macro- and microvascular complications and poor metabolic control. These findings are important for policy development and the planning of health services.

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1. Introduction

In 2014, 422 million people aged 18 years and above were living with diabetes worldwide. This accounts for 8.5% of the world's population. Prevalence was highest in the Eastern Mediterranean region (EMR) increasing from 5.9% (6 million) in 1980 to 13.7% (43 million) in 2014. Of diabetes-related deaths, 43% occurred before the age of 70, with the highest proportion occurring in low- and middle-income countries (LMIC) [1].

Diabetes is a chronic disease; if not detected, managed and controlled it may lead to disability, poor quality of life and a high mortality burden [2,3]. Diabetes is considered the 7th leading cause of disability worldwide and accounts for more than 2 million deaths annually [4]. Age-standardized mortality rates reach up to 140 per 100,000 population in the EMR region [1]. Diabetes complications can be microvascular including neuropathy, nephropathy, and retinopathy, or macrovascular including coronary artery disease (CAD), cerebrovascular disease (CVA) and peripheral vascular disease (PVD) [5,6]. Type 2 diabetes mellitus (T2DM) is the leading cause of retinopathy, lower limb amputation and end-stage renal diseases (ESRD), and almost half of persons with T2DM die from cardiovascular complications [6]. Furthermore, diabetes and its complications exert a large economic burden on health systems, persons with diabetes, and their families. This cost can be direct medical expenditures, or indirect through disability and premature death [1,4]. A recent systematic review estimated the global economic burden of diabetes and its complications to be US$ 825 billion, more than 60% of these costs bared in LMIC [4].

The majority of T2DM complications studies come from high-income countries and results vary greatly between countries [1]. In Palestine, previous studies have shown a high burden of T2DM. Diabetes prevalence in the West Bank was 10% in 2000 and 15% in 2010 and projected to reach 20.8% in 2020 and 23.4% in 2030 [7]. In 2015, diabetes was the fifth leading cause of death [8]. Despite this high burden in Palestine, little is known about diabetes mellitus complications and its determinants. A review published in The Lancet in 2009 indicated the scarcity of data on complications of diabetes in Palestine [9]. In a recent study conducted in the southern part of the West Bank, relatively high levels of T2DM complications were reported (39% for microvascular complications and 16% for microvascular complications) [10].

It is important to identify the burden of T2DM complications and understand their associated factors to contribute to the policy and decision-making process regarding the prevention, management, and control. The aim of this study is to identify the burden and patterns of diabetes complications among persons with T2DM in Ramallah and al-Bireh governorate of Palestine.

2. Methods

This is a cross-sectional study of diabetes complications in Ramallah and al Bireh governorate — Palestine (The Palestinian Diabetes Complications and Control Study (PDCCS)). The general objective of the PDCCS is to assess the prevalence and determinants of T2DM complications in 2012. Ramallah and al Bireh governorate is located in the center of the West Bank with 319,418 inhabitants (2012 estimates), and consists of the cities of Ramallah, al-Bireh and Beitunia with approximately 165,703 inhabitants living in urban areas, and 135,159 in the surrounding villages, in addition to 18,557 in camp dwellings [11].

2.1. Study sample

The sample size was calculated using standard sample size calculation formula: ($SS = (1.96)^2 \times (0.5) \times (0.5)/(0.05)^2 = 384$ participants) with $P = 0.5$ and 95% confidence interval.

Rose [12] had indicated that if the sample represents significant proportion of the total population, (e.g. over 5%), it can be corrected for finite population. Our total population size was estimated to be 5000, so the calculated sample size of 384 was more than 7% of the population size. So the sample was corrected for finite population using the formula:

$$(\text{Sample Size} = n/[1 + (n/\text{population})])$$

The corrected sample was 357 participants ($384/[1 + (384/5000)]$).

Furthermore, as this is a clinic bases survey stratified by health care provider, the sample size was multiplied by 1.4 ($357 \times 1.4 = 500$) to account for design effect [13] resulting in a calculated sample size of 500 persons with diabetes.

All primary health care clinics offering diabetes services in Ramallah and al Bireh governorate were identified. Those were 16 clinics; five clinics were excluded because they served less than 100 persons with diabetes. A total of eleven clinics were included: five clinics were operated by the Palestinian ministry of health (MoH), four by the United Nations Relief and Working Agency (UNRWA) and two by non-governmental organizations (NGOs) in Ramallah and al Bireh governorate. All persons with T2DM receiving care routinely at the selected clinics were eligible to participate in the study (regardless of their age). A sample proportional to the size of each clinic was selected based on the number of persons with diabetes' records at each clinic. All persons with T2DM were invited to participate in the study in-person or by phone. Type 1 diabetes, currently pregnant women, and/or persons with communication problems were excluded from the study.

2.2. Data collection

Data collection was divided into 5 sections: interviews with persons with T2DM, anthropometric measurements, physical examination, blood and urine tests, and eye examination. The first 4 sections were conducted in the same session at the clinic, and then participants were referred to an ophthalmologist for the eye exam. Results from the eye exam will be published separately.

2.3. Persons with T2DM interviews

The instrument was based on selected standardized and validated questionnaires. Those included the Diabetes complication index (DCI) [3], the Summary of diabetes self-care activities (SDSCA) [14], the Audit of Diabetes-Dependent Quality of life (ADDQoL-19) [15], and selected questions on socio-demographic characteristics and disease history from the Palestinian Central Bureau of Statistics (PCBS) surveys and the Stepwise survey [16]. Approvals to use the standardized questionnaires were obtained. Validated Arabic translations were available for the SDSCA, ADDQol and socio-demographic data. The DCI was translated locally taking into consideration the WHO guidelines [17].

2.4. *Anthropometric measures*

Weight (kilograms) was measured in light clothing using a portable scale (Seca 780/783). The scale was calibrated daily at the study site. Height (cm) was measured using portable stadiometer (Seca 220) mounted on the scale. Participants stood up steady with bare feet. Waist circumference (cm) was measured using a tape placed midway between the top of the hip bone and the bottom of the ribs and then wrapped around the waist.

2.5. *Physical examination*

Blood pressure was measured using upper arm electronic blood pressure monitor: Tensoval duo control (HARTMANN) [18]. Participants were allowed to rest for 5 min and then 3 measurements were conducted, the average of the last 2 was considered. Foot examination included inspection of both feet for ulcers and amputations, in addition to a vibration test using 128-Hz tuning fork (the on-off method) and the Semmes-Weinstein monofilament examination (SWME) using 10 g monofilament test as described by the International Working Group on the diabetic foot [19].

2.6. *Blood and urine tests*

Blood tests included HbA1c (% and mmol/mol), lipid profile (triglycerides, total cholesterol, HDL, and LDL cholesterol) (mg/dl). Spot urine tests included micro-albumin and urine creatinine to measure albumin/creatinine ratio (ACR) (mg/g) and estimated glomerular filtration rate (eGFR) using the MDRD equation [20]. All samples were collected at the participants' ordinary clinics from persons with T2DM fasting for at least 12 h. The samples were sent to Birzeit University medical lab for analysis after proper centrifugation and storage.

2.7. *Fieldwork*

Fieldwork was conducted by a team of 6 trained field workers. Blood was sampled by a nurse. All team members had intensive training for 2 days before starting the fieldwork. The fieldwork was conducted between March and May 2012.

2.8. *Diabetes complications*

Data on complications were either based on persons with T2DM reports or measurements (physical, anthropometric, blood and urine tests). Both macro- and micro-vascular complications were assessed. Macro-vascular complications included CAD, PVD and CVA, and were based on the diabetes complications index (DCI) (see supplement). The DCI relies on persons with T2DM reports of both doctor's diagnosis as well as symptoms related to various complications [3]. Microvascular complications included retinopathy, nephropathy, and neuropathy. Neuropathy was identified based on positive vibration test using tuning fork, monofilament test, the presence of foot ulcers or foot amputations based on the physical exam, or reported slipping slipper sign — where the person with T2DM will not feel losing the slipper while walking [21]. Nephropathy was based on blood or spot urine tests and was defined as low estimated glomerular filtration rate (eGFR) <60 ml/min or microalbuminuria >30 mg/g [22].

2.9. *Independent variables*

HbA1c was defined as controlled (<7% or 53 mmol/mol), fair (≥7–8% or 53–64 mmol/mol), poor (>8–10% or >64–86 mmol/mol) and uncontrolled (> 10% or 86 mmol/mol). Dyslipidemia was measured as high triglycerides (>150 mg/dl) and low HDL cholesterol (men < 40 mg/dl and women < 50 mg/dl) (based on the definition of dyslipidemia among persons with diabetes [23,24]. Furthermore, LDL was measured (LDL ≥ 100 mg/dl) [23]) but not included in the dyslipidemia index. Hypertension (HTN) was defined as having a blood pressure measurement >140 mmHg for SBP or >90 mmHg DBP or being on antihypertensive medication. Persons with diabetes were then classified in three categories, no HTN (normal BP and no medications), having HTN but controlled (normal BP and on medications) and having HTN and not controlled (high BP and on medications). Persons with diabetes reporting at least 30 min continuous exercise 3 times per week were characterized as physically active. BMI was calculated from the measured height and weight and coded into obese (BMI ≥ 30) and non-obese. The waist circumference cutoff point was 88 cm for women and 102 cm for men [25].

2.10. *Data analysis*

Data was entered using IBM SPSS data entry software® and analyzed using Statistical package for Social Sciences (SPSS)® version 24. To better understand the distribution and determinants of T2DM complications, three (yes/no) indices were built: (1) microvascular complications index: nephropathy and/or neuropathy; (2) macrovascular complications index: participant's reported doctor's diagnosis of CAD, CVA and/or PVD; (3) Any complications index: having (1) and/or (2). Three logistic regression models were built using the three indices as dependent variables aiming to better understand the demographic, social and biological determinants of these complications. All variables that were significant in the bivariate analysis for any of the indices were entered into the regression models.

2.11. *Ethical considerations*

Ethical approval on the project was obtained from the ethical committee at the Institute of Community and Public Health–Birzeit University. In addition, approvals to collect data were obtained from the health officials at MoH, UNRWA, and the participating NGOs. Witnessed verbal informed consent was obtained from the participating persons with diabetes. All interviews and tests were done in a private space to ensure participant's confidentiality. Results of blood and urine tests

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Table 1 – Socio-demographic, health and biological characteristics of persons with T2DM in Ramallah and al Bireh governorate (N = 517).

		Men N(%)	Women N(%)	Total N(%)
Age (years)**	24–49	19(11.4)	79(22.6)	98(19.0)
	50–59	65(39.2)	127(36.4)	192(37.3)
	Above 60	82(49.4)	143(41.0)	225(43.7)
Education***	Illiterate and acquainted (can read and write)	6(3.6)	83(23.7)	89(17.2)
	Elementary school (up to 10 years)	86(51.8)	190(54.3)	276(53.5)
	Secondary school and above (11 years and above)	74(44.6)	77(22.0)	151(29.3)
Locality type*	Urban	93(56.0)	161(45.9)	254(49.1)
	Rural	51(30.7)	110(31.3)	161(31.1)
	Camp	22(13.3)	80(22.8)	102(19.7)
Diabetes family history		133(80.1)	284(80.9)	417(80.7)
Smoking***	Currently smoking	61(36.7)	17(4.8)	78(15.1)
	Ex-smoker	58(34.9)	20(5.7)	78(15.1)
	Never smoked	47(28.3)	314(89.5)	361(69.8)
Physically active*		61(36.7)	94(26.9)	155(30.0)
High waist circumference***		106(66.3)	320(93.0)	426(84.5)
Obese***		69(42.3)	246(71.3)	315(62.0)
HbA1c	Controlled	31(20.1)	77(22.6)	108(21.8)
	Fair	26(16.9)	75(22.0)	101(20.4)
	Poor	52(33.8)	111(32.6)	163(32.9)
	Uncontrolled	45(29.2)	78(22.9)	123(24.8)
Hypertension	No	37(22.3)	72(20.8)	109(21.3)
	Yes, controlled	46(27.7)	100(28.9)	146(28.5)
	Yes, uncontrolled	83(50.0)	174(50.3)	257(50.2)
Dyslipidemia*		127(81.9)	302(88.8)	429(86.7)
Low HDL***		146(94.2)	272(79.8)	418(84.3)
High LDL**		88(56.8)	238(69.8)	326(65.7)
High triglycerides		90(58.1)	200(58.7)	290(58.5)
Duration of diabetes (years)	0–10	100(60.2)	227(64.9)	327(63.4)
	>10	66(39.8)	123(35.1)	189(36.6)

Significance level for the variation between men and women: * sig. at <0.05, ** sig. at <0.005, *** sig. at <0.001.

and eye exams were shared with each person with diabetes in his/her respective clinic.

3. Results

We invited 621 persons with T2DM and 517(83.8%) participated in the study. Mean age, age at diagnosis and duration of T2DM were 58 ± 9.8, 49 ± 9.9 and 9 ± 7.5 years respectively. Sixty-eight percent of the participants were women. As shown in Table 1, this study highlighted the high levels of socioeconomic, biological and behavioral risk factors for diabetes complications among the study population. Those included around 80% who had family history of diabetes, 30% were current or ex-smokers, 62% were obese and 85% with high waist circumference. In addition to 78% having a HbA1c level higher than 7% (53 mmol/mol) (mean + SD HbA1c was 8.8% (73 mmol/mol) ±2.0%), 89% had high blood pressure or were on anti-hypertensive medications, and 87% had dyslipidemia (high triglycerides or low HDL).

Some risk factors varied significantly between men and women. Those included smoking with 37% and 5% current smokers for men and women respectively. The proportion of women with high waist circumference was much higher than men (93% vs. 66%). The same applies to obesity were 71% of women were obese compared to 42% of men. A higher proportion of men had low HDL while more women tended to have high LDL, overall, more women tended to have dyslipidemia. No significant variation between men and women was observed in terms of HbA1c and hypertension.

Medication utilizing patterns are described in Table 2. For diabetes management, only 2% were not on any medication. Metformin was used by 86% of persons with diabetes.

Our study reflected a high burden of T2DM complications. Fig. 1 presents the prevalence of a set of T2DM complications (objectively measured, reported doctor's diagnosis and reported patient's symptoms). Table 3 presents the prevalence of microvascular and macrovascular complications (objectively measured and reported doctor's diagnosis). Table 3 demonstrates that over three-quarters of the participants had at least one complication (either macrovascular or microvascular), 67% had at least one microvascular complication and 29% had at least one macrovascular complication. Around 20% had both micro- and macrovascular complications. Men tend to have significantly higher levels of macrovascular complica-

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Table 2 – Medication utilization patterns among persons with T2DM in Ramallah and al Bireh governorate.

Type of medication	N(%)
T2DM medications	
No medication	12(2.3)
Oral hypoglycemics only	296(57.3)
Insulin only	49(9.5)
Combined oral hypoglycemics and insulin	160(30.9)
Other medications	
Anticoagulant	408(78.9)
Antihypertensive	350(67.7)
Dyslipidemia	214(41.4)
Cardiac	880(17.0)

tions compared to women (41% compared to 23% respectively) but not microvascular complications.

Using the definitions of both microvascular and macrovascular complications presented in Table 3, different patterns of associations were observed in the bivariate analysis and the multivariate logistic regression for different complications' groups. The bivariate analysis results are detailed in Table 4. All variables showing a statistically significant association with the outcome measures were included in the logistic regression models.

The logistic regression analysis showed that microvascular complications tended to increase with age, lower level of education, living in rural areas and having uncontrolled diabetes (HbA1c higher than 10). A higher risk for macrovascular complications was observed in men, ex-smokers, persons with T2DM and uncontrolled hypertension, and those with longer duration of diabetes. Having at least one complication (regardless of its type) was significantly higher among men, tended to increase with age and lower education, living in rural areas, having HbA1c higher than 10, and having uncontrolled hypertension. Odds ratios (OR) and confidence intervals are detailed in Table 4.

4. Discussion

The current study represents a detailed analysis of T2DM complications in the central region of the West Bank of Palestine. We found a high prevalence of complications accompanied by poor glycemic control. Three-quarters of the study sample had at least one complication and one fifth had at least one microvascular and one macrovascular complication. Dyslipidemia, hypertension, and obesity were major comorbidities among persons with diabetes. Similar results were also reported in a recent study in the southern part of the West Bank. However, it reported lower levels of microvascular and macrovascular complications compared to the PDCCS (39% and 16% respectively). Such differences may be explained by the higher mean duration of diabetes in the current study (9 years) compared to 7 years in the southern part study, and using different definitions for these complications [10].

Some regional studies reported relatively comparable levels of diabetes complications. In 2005–2006 a study conducted in the United Arab Emirates revealed a prevalence of nephropathy and neuropathy was 40.8% and 34.7% respectively; PVD was 11.1% and CAD was 10.5% [26]. The questions and tests used were closely related to the PDCCS. In a follow up study in Iraq for 1079 participants in 2008, 16% had CVD events defined as a history of CAD or stroke, and 44% had hypertension [27], representing relatively lower estimates than the PDCC, however the Iraqi study showed a lower level of glycemic control with only 5.5% having HbA1c less than 7%. This variation in the level of complications might be due to the duration of diabetes were the Iraqi study reported a T2DM mean duration of 7.4 years and only 22.6% having duration more than 10 years compared to 35% in our study. In an Omani study of diabetic nephropathy using ACR, a very close estimate to the PDCCS was found (42.5%) [28]. A national study in Lebanon in 2009 found relatively comparable levels of macrovascular complications of 27.8%, 9.6% and 15.0% for heart disease, stroke, and PVD respectively; however, rates of microvascular complications were much lower, with 7.0% and 8.6% for nephropathy and foot ulcers respectively [29]. All estimates in the Lebanese study were self-reported. All the studies mentioned above included adult populations. Estimates from the developed countries were not far away. In a retrospective cohort in Germany, the prevalence of hypertension was 77.0%, CAD was 23.0% and CVA was 4.2% among persons with T2DM [30]. In another retrospective cohort in Australia, the prevalence of macrovascular complications was 23.7% and mean HbA1c was 8% [31]. In the US, the prevalence of diabetic nephropathy was 34.5% for the years 2005–2008 [32]. In a 4-year screening program in the UK, the prevalence of clinical neuropathy was 21.7% and PVD was 20.8% [33].

As discussed above, different studies have shown different levels of T2DM complications, although some were very close to the current study. This could be a real variation or might be due to variable definitions and tools used in measuring these complications, different study settings including clinic-based, hospital-based or community households, different age group, different glycemic control levels, and variations in access and quality of healthcare services. This was clearly reflected in the literature highlighting inconsistencies in definitions, tools, and settings used in different studies [6]. Regardless of these variations, the PDCCS showed a high burden of T2DM complications, as well as high levels of modifiable behavioral, and biological risk factors. Targeting these risk factors is crucial in controlling the growing burden of diabetes complications and its subsequent effects.

Some gender differences were observed in levels of T2DM complications (Table 3), where men tend to have higher levels in general; however, the small sample size did not allow further exploration of the associated factors and limited the generalizability of the results. Living in rural areas was significantly associated with higher levels of microvascular and total complications. This might be related to access to health care, as people living in rural areas in Palestine tend to have several barriers to access. These barriers include the political situation (separation wall and checkpoints), financial and geographical accessibility factors as well as the perceived health status and the willingness to seek health care [34–36]. Both age and duration of T2DM were major risk factors for developing diabetic microvascular complications [5]. Additionally, diabetes duration was independently associated with both microvascular and macrovascular complications, regardless of age or age at diagnosis in some studies [37,38]. In the PDCCS, the logistic

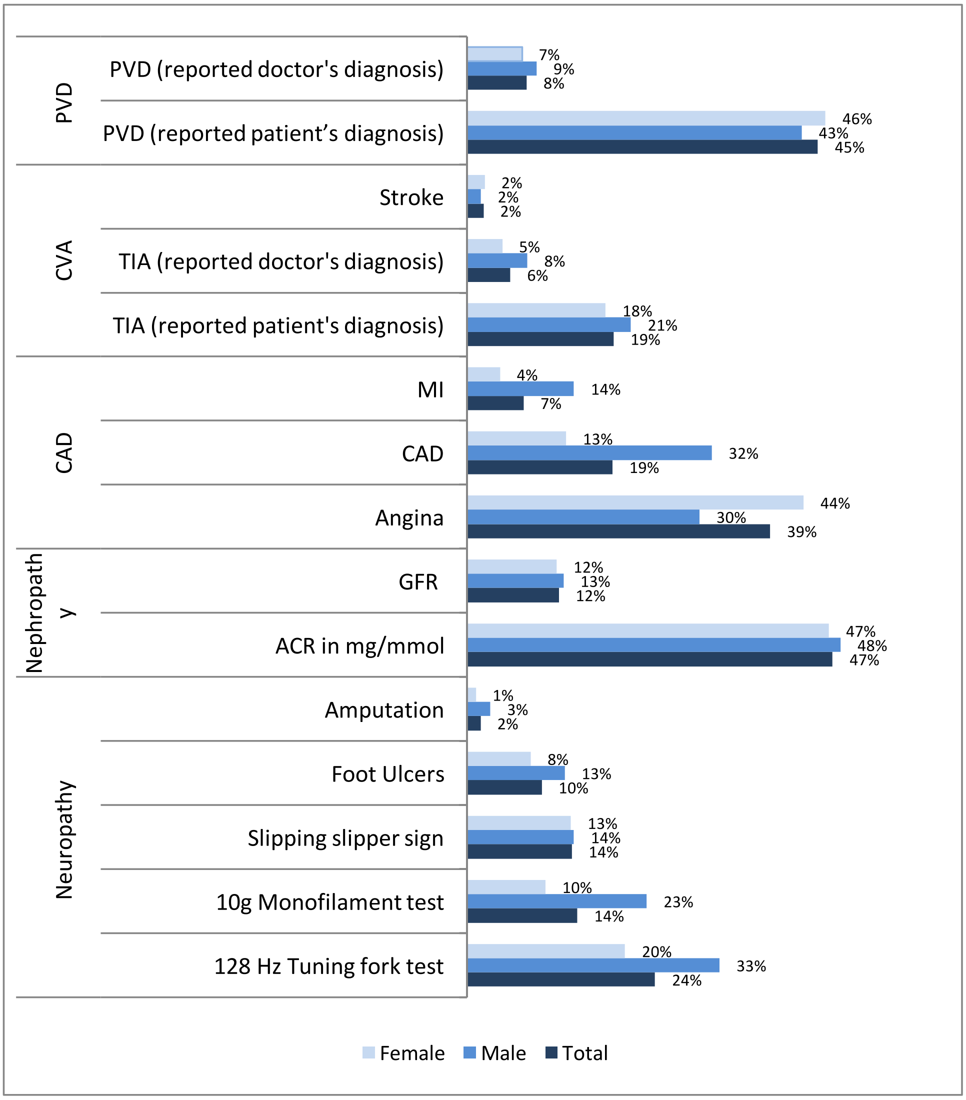

Fig. 1 – Distribution of different complications subcategories among persons with T2DM in Ramallah and al Bireh governorate — Palestine 2012*.
***Macrovascular complications is based on DCI, microvascular complications were measured.**

Table 3 – Prevalence of chronic complications among persons with T2DM in Ramallah and al Bireh governorate-2012.

Category	N(%)	Men N(%)	Women N(%)	Total
Any microvascular complications (N = 481)		108(72.0)	215(65.0)	323(67.2)
Nephropathy (N = 486)		79(52.0)	171(51.2)	250(51.4)
Neuropathy (N = 502)*		73(45.9)	119(34.7)	192(38.2)
Any macrovascular complications (N = 514)***		67(40.9)	80(22.9)	147(28.6)
CAD (reported doctor's diagnosis) (N = 515)***		57(34.8)	50(14.2)	107(20.8)
CVA (Reported doctor's diagnosis) (N = 516)		14(8.4)	19(5.4)	33(6.4)
PVD (Reported doctor's diagnosis) (N = 517)		15(9.0)	25(7.1)	40(7.7)
General (N = 479)	Persons with T2DM with at least one micro- and at least one macrovascular complication***	37(24.8)	80(24.2)	117(24.4)
	Persons with T2DM with at least one complication***	129(86.6)	236(71.5)	365(76.2)

N: total N for this category (N was variable depending on the assessment tool (persons with T2DM reports, physical exam and lab tests)).
Note: macrovascular complications were based on DCI and only reported doctor's diagnosis were considered.
Significance level for the variation between men and women: *sig. at <0.05, ***sig. at <0.001.

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Table 4 – Bivariate analysis and logistic regression for T2DM complications in Ramallah and al Bireh governorate – Palestine 2012.

		Any microvascular				Any macrovascular				Any complication			
		Bivariate		Logistic regression		Bivariate		Logistic regression		Bivariate		Logistic regression	
		N(%)	p-Value*	OR[a]	95%CI	N(%)	p-Value*	OR[a]	95%CI	N(%)	p-Value*	OR**	95% CI
Sex	Women	215(65.0)	0.13	1		80(22.9)	<0.001	1		236(71.5)	<0.001	1	
	Men	108(72.0)		1.75	[0.946–3.259]	67(40.9)		1.89	[1.037–3.453]	129(86.6)		2.26	[1.093–4.698]
Age	24–49 years	52(54.7)	0.13	1		15(15.5)	<0.001	1		55(58.5)	<0.001	1	
	50–59 years	113(62.4)		1.21	[0.690–2.122]	48(25.0)		1.29	[0.648–2.583]	134(74.0)		1.71	[0.946–3.125]
	Above 60 years	158(77.1)		2.10	[1.119–3.959]	84(37.7)		1.68	[0.826–3.445]	176(86.3)		2.82	[1.405–5.692]
Education	Illiterate or acquainted	60(77.9)	0.04	2.22	[1.045–4.717]	29(33.0)	0.38	1.55	[0.764–3.178]	65(84.4)	0.13	2.34	[0.992–5.561]
	Elementary	176(67.4)		1.76	[1.085–2.855]	72(26.2)		1.15	[0.696–1.911]	198(76.2)		1.99	[1.147–3.471]
	Secondary and above	87(61.3)		1		46(30.7)		1		102(72.3)		1	
Locality type	Urban	151(64.0)	0.04	1		77(30.7)	0.02	1		175(74.8)	<0.01	1	
	Rural	113(75.3)		1.66	[1.006–2.742]	52(32.3)		1.09	[0.676–1.760]	128(85.3)		2.00	[1.099–3.653]
	Camp	59(62.1)		0.89	[0.517–1.559]	18(17.6)		0.56	[0.296–1.075]	62(65.3)		0.66	[0.370–1.210]
Smoking	Never smoked	226(67.1)	0.92	1		83(23.1)	< 0.001	1		243(72.5)	<0.01	1	
	Currently smoking	46(65.7)		0.76	[0.378–1.544]	27(35.1)		1.45	[0.726–2.906]	57(81.4)		1.26	[0.559–2.873]
	Ex-smoker	51(68.9)		0.65	[0.326–1.317]	37(47.4)		1.93	[1.019–3.687]	65(87.8)		1.49	[0.613–3.644]
Physically active	No	238(70.4)	0.02	1		101(28.2)	<0.001	1		264(78.6)	0.01	1	
	Yes	85(59.9)		0.63	[0.406–1.000]	46(29.7)		0.98	[0.611–1.587]	101(71.1)		0.59	[0.360–0.990]
BMI categories	Non-obese	129(72.9)	0.04	1		60(31.4)	0.33	1		144(81.8)	0.35	1	
	Obese (BMI ≥ 30)	194(63.8)		0.76	[0.479–1.217]	86(27.4)		1.15	[0.717–1.846]	221(72.9)		0.74	[0.435–1.263]
HbA1c	Controlled	59(55.1)	<0.001	1		26(24.3)	0.72	1		72(67.9)	<0.01	1	
	Fair	57(60.0)		1.06	[0.581–1.966]	28(28.0)		1.04	[0.532–2.043]	66(70.2)		0.84	[0.428–1.674]
	Poor	105(66.5)		1.29	[0.746–2.238]	48(29.4)		0.92	[0.499–1.727]	120(75.9)		1.03	[0.554–1.925]
	Uncontrolled	101(84.2)		3.81	[1.933–7.530]	38(30.9)		1.0	[0.529–2.026]	106(88.3)		3.06	[1.392–6.734]
Hypertension	No	62(60.8)	< 0.01	1		17(15.6)	<0.01	1		67(65.7)	<0.01	1	
	Yes controlled	82(59.9)		0.84	[0.473–1.517]	45(31.0)		1.89	[0.960–3.759]	97(71.3)		1.14	[0.611–2.161]
	Yes uncontrolled	178(73.9)		1.50	[0.862–2.636]	85(33.3)		2.10	[1.112–4.002]	200(83.3)		2.38	[1.283–4.441]
Dyslipidemia	Normal	44(68.8)	0.76	1		28(42.4)	<0.01	1		51(79.7)	0.476	1	
	Abnormal	278(66.8)		1.03	[0.548–1.956]	112(26.2)		0.57	[0.317–1.037]	313(75.6)		0.89	[0.427–1.860]
Diabetes duration	0–10 years	189(61.4)	<0.001	1		71(21.8)	<0.001	1		218(71.0)	<0.001	1	
	>10 years	133(77.3)		1.25	[0.763–2.069]	76(40.6)		1.73	[1.077–2.795]	146(85.4)		1.20	[0.671–2.168]

* Unadjusted.
[a] Adjusted.

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regression model showed an increased risk for microvascular complications with increasing age but not with the duration of diabetes. The latter was only significantly associated with macrovascular complications. With the PDCCS study being a cross-sectional study, it is hard to further explore this association, longitudinal studies are needed to better understand the association between complications and duration of diabetes, may be assessing the year of onset of complications might reflect a more precise association. In the current study educational attainment was associated with both general and microvascular complications. No association was observed with macrovascular complications. Education is generally correlated with socioeconomic status, income, awareness, and access to healthcare services, which may partially explain such association. The association between education and diabetes complications was observed in several studies [39–41].

Smoking is known to be a strong risk factor for cardiovascular events and mortality among persons with diabetes. Quitting smoking was associated with lower risk of such events [42]. The current study found that ex-smokers were still at higher risk of having macrovascular complications compared to non-smokers. As this is a cross-sectional study, it is hard to know if they quit smoking before or after the onset of the complications or the duration since they quit; there is some evidence suggesting that the risk remains high after smoking cessation for a short term, which eventually decreases with time [43]. One peculiar finding was that the association with complications was with ex-smokers but not current smokers. In addition to the sample size and study design issues raised previously, this may be partially explained by the duration of smoking years before quitting, and that some participants may have quit smoking because of diabetes complications and comorbidities.

Poor glycemic control is a main modifiable risk factor for diabetes complications that should be targeted to reduce complications. A treatment goal for HbA1c (below 7%) was set by the ADA to prevent developing glycemic related complications [23,44]. Overwhelming evidence shows that good glycemic control can reduce the risk of developing complications, in particular microvascular [28,45–47]. In the PDCCS, 4 out of 5 persons with diabetes had HbA1c above 7% (53 mmol/mol); persons with diabetes with HbA1c 10% (86 mmol/mol)or more were 4 times more likely to have microvascular complications compared to those with controlled HbA1c (below 7%). The study showed a very high rate of dyslipidemia (86.7%), which was not associated with complications' levels in any of the regression models. Furthermore, no variation was observed in the level of dyslipidemia among the controlled and uncontrolled persons with diabetes, where it was higher than 80% for both groups. This might be an indication of poor lipid control among these persons with diabetes and reflects the need for more tight control for lipids. It is worth noting here that in the current study the lipid profile was obtained by direct measurement rather than depending on patients' reports, and this might shed some light on the high level of early-stage undiagnosed dyslipidemia that may contribute to complications. Macrovascular complications in the PDCCS study were more related to blood pressure and hypertension status rather than glycemic control level, this finding was supported by the UKPDS which indicated that the association between HbA1c and macrovascular complications was of lower strength and that the latter was more related to hypertension [45].

Looking at specific complications, diabetic nephropathy was present in almost half of the PDCCS study participants. These persons with T2DM if not managed or controlled may progress to proteinuria and develop kidney failure [5]. On the other hand, microalbuminuria among persons with T2DM is a major risk factor for CAD [24] where many persons with diabetic nephropathy die from CVDs even before developing ESRD [48]. Both poor glycemic control and high blood pressure contribute to diabetic nephropathy [48]. Having such a high rate of diabetic nephropathy is alarming and calls for urgent action. Targeting these persons with better glycemic control strategies and other risk factors including blood pressure and lipids can help in preventing major endpoints including ESRD or CVD events.

Peripheral neuropathy is the main cause of foot complications among persons with diabetes including ulceration and foot amputation [49]. Foot complications are a major cause of hospitalization among persons with diabetes. 15% of persons with diabetes develop foot ulcers during their lives [50]. In the PDCCS study, around 10% of the persons with diabetes had foot ulcers and around 2% had lower limb amputations; these were mainly toe amputations. This percentage may be an underestimation of the real prevalence of amputations due to a selection bias; since some of the amputees maybe bedridden and do not attend primary health care clinics regularly. Diabetic foot complications have a negative impact on the persons with diabetes quality of life, in addition to the economic burden imposed on the health systems through hospitalization and rehabilitation services [38]. Early detection is important for the prevention of serious health conditions [51]. However, persons with diabetes rarely observe or detect the ulcers and lesions themselves; pathogenesis of neuropathy is poorly linked to the development of symptoms [50,51]. On the other hand, early detection and management of high-risk individuals with neuropathy was associated with decreasing prevalence of foot ulcers by 60% and amputations by 85%. Basically, this can be done by improving glycemic control [51]. To optimize this intervention, screening is recommended to detect early stage neuropathy and to prevent further complications. Simple low-cost screening methods can be effective in detecting these conditions such as those used in the current study including the vibration test using tuning forks and sensation test using monofilament. This was suggested by Perkins et al. in a study conducted to assess different methods for detecting peripheral neuropathy [51].

CADs, PVDs, and stroke among persons with diabetes were mediated by several factors with different pathological mechanisms. In general, diabetes increases the risk of developing CVD events. People with diabetes are at higher risk of developing stroke and CADs with 2 to 4 folds higher than those without diabetes as well as higher fatality rates from CAD [5,52,53]. Almost one-third of persons with diabetes in this study had at least one macrovascular disease. Intensive treatment and control, and primary and secondary prevention are needed [5].

A major strength of this research project is that it is the first study in the central West Bank that looked at diabetes control and complications systematically using both measured and reported estimates. It provided a comprehensive picture of the

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situation of chronic complications among persons with T2DM in Ramallah and al Bireh governorate seeking health care at the primary health care level. Secondly, this study was was conducted in primary health care clinics targeting the patients at the point of care. Although this can be looked at as an advantage because it facilitates access to persons with diabetes, but it may have introduced a limitation since some complications such as amputations and ESRD were expected to be underestimated due to the nature of the design specifically targeting patients at the primary health care clinics. Furthermore, this study covered the public sector health providers only, excluding the private sector. However, this should not be a major problem as more than 70% of people living in the West Bank have health insurance with even higher levels having access to public sector chronic disease health services where the MoH, UNRWA, and NGOs have extended programs.

Although a higher prevalence of diabetes among men compared to women was estimated in Palestine [54], two-thirds of the PDCCS sample were women. This was a clinic-based study on persons with diabetes consulting their clinics for regular care, where the number of men seeking health care for diabetes was lower than women. This was also reported in the diabetes complications study conducted recently in the southern part of the West Bank where 65% of the study sample attending diabetes clinics were women [10]. Furthermore, based on the Palestinian annual health report 2016, 42% of the reported visits for the primary health care diabetes clinics were men and 58% were women [8]. One of the reasons behind the lower fraction of men among study participants is that men usually work during the daytime while the clinics are opened, and there are fewer services in the afternoon. Also, this might be related to gender-based health care seeking behaviors were women tend to seek primary care services more than men do [55]. Addressing this major barrier for seeking health care among men with diabetes is crucial.

At the level of clinical practice, persons with diabetes should be targeted with effective interventions to reduce complications mainly through glycemic, hypertension, and dyslipidemia control. Optimal secondary prevention for diabetes requires lifestyle modification in addition to the management of biological risk factors. Since the Palestinians suffer from difficulties in mobility in terms of having military checkpoints between cities, and some important services such as dialysis and foot care services are located in major cities, the referral system should be improved, and capacity building for the diabetes care teams on issues such as foot care should be implemented to ensure that persons with diabetes receive the needed care at the primary health care clinics. Primary health care clinics should be supplied with equipment and materials needed for such interventions.

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Conflict of interest

The authors state that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.pcd.2018.07.002.

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