Prevalence, management and control of diabetes mellitus among Syrian refugees in Duhok governorate, Kurdistan Region of Iraq – a cross sectional study in the camp of Domiz 1

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SUMMARY

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Title: Prevalence, management and control of diabetes mellitus among Syrian refugees in Duhok governorate, Kurdistan Region of Iraq – a cross sectional study in the camp of Domiz 1.

Background: We are today facing our era's worst humanitarian crisis. The Syrian Civil War has left more than 13.5 million in need with 6.5 million people internally displaced and more than 4.8 million refugees. Priority has been focused on acute injuries and communicable diseases while chronic diseases have been left in the shadows to slowly become silent killers – with diabetes as one of the diseases taking the lead. Duhok governorate in Kurdistan/Northern Iraq hosts a large number of refugees and IDPs. Limited resources in the area have affected the local population as well as the refugees.

Aim: The aim of the study was to assess management of diabetes mellitus and its complications among Syrian refugees in the area's largest refugee camp Domiz 1.

Objectives: 1. To evaluate risk factors for development of disease complications. 2. To describe diabetes control parameters; the means through which it is assessed and how often. Treatment options and availability. 3. To evaluate prevalence of diabetic complications. 4. To analyze potential areas of improvement regarding management of diabetes.

Method: There were 204 participants in the study. There were no age restrictions. The study was composed of three parts: I – short interview, II - clinical examination and III – blood analysis.

Results and Conclusion: The prevalence of diabetes mellitus within camp Domiz 1 was 0.80%. Results showed that risk factors for development of disease complications were: long duration of residency within the camp; high BMI, decreased physical activity and bad glycemic control. The diabetic control parameters were assessed by Hemoglobin A1c (HbA1c) for the study. Results showed that both T1DM and T2DM had bad glycemic control. Pharmacological therapy for glycemic control was insulin for T1DM and mainly dual therapy with biguanides and sulfonylureas for T2DM patients. Diabetic complications presented as nephropathies, peripheral polyneuropathies, hypertension, dyslipidemia and PAD. The complications were not sufficiently controlled despite pharmacological therapies with statins and anti-hypertensive agents. Prevalence of complications were less among those who had left Syria during later years - suggesting significant lifestyle modifications associated with life within the camp. Among the refugees that participated in the study 45.45% and 61.66% with T1DM and T2DM respectively got their diagnosis after the year of 2011 – the year the Syrian war started.

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My forever-beloved Grandfather,
I dedicate this work to you.
I wish you had been here to share this with me.
You may be gone, but you will never be forgotten.

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CONFLICTS OF INTEREST

The author declares no conflict of interest.

ETHICS COMMITTEE CLEARANCE

The study was performed in accordance with the World Medical Association (WMA) developed Declaration of Helsinki. The interview, clinical examination and blood sampling was approved by the Department of Planning, Scientific Research Division - Duhok Directorate General of Health; Approval of Research Ethics Committee. Reference number: 09102016-7. Date of issue: October 9th 2016.

Oral consent was obtained from the participants before entry into the examination room.

Kurdistan Regional Government
Ministry of Health
Duhok Directorate General of Health
Department of Planning
Scientific Research Division

Form B: Approval of Research Ethics Committee

Date: 09th October, 2016

Reference number: 09102016-7

Research title: Prevalence, management and control of acute and chronic complications in diabetes mellitus among Syrian refugees in Duhok governorate, Kurdistan Region of Iraq – a cross sectional study in the camp of Domiz 1.

Researcher name(s): Gaziza Shamsi

Type of approval: Conditional, taking into consideration the following mandates:

1) Obtaining the approval of Directorate of Domiz 1 Camp.
2) Filling the Consent Form (Form C) for all the participants in the study and returning them to Research Ethics Committee at Duhok Directorate General of Health after completion of the study.
3) Grantee of this letter is not given the right to publish the results of the study until returning Form C (Consent Form). Upon returning these forms, the researcher(s) will be provided by unconditional letter from Research Ethics Committee to publish the results.
4) The participants don't bear the responsibility for paying for any procedure.
5) The participants have the right to withdraw from the study.
6) Confidentiality of the data should be secured.
7) Notifying the participant about the results of the procedure performed if applicable.
8) Any change in the methods of the study needs prior approval of Research Ethics Committee.

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LIST OF ABBREVIATIONS

ABI	Ankle-Brachial-Index
ACE	Angiotensin Converting Enzyme
ADA	American Diabetes Association
ARB	Angiotensin II Receptor Blocker
BB	Beta blocker
BMI	Body Mass Index
CABG	Coronary Artery Bypass Grafting
CCB	Calcium Channel Blocker
CKD	Chronic Kidney Disease
EDTA	Ethylenediaminetetraacetic Acid
FFA	Free Fatty Acids
GFR	Glomerular Filtration Rate
GIP	Gastric Inhibitory Polypeptide
GLP1	Glucagon Like Peptide 1
GLUT-4	Glucose Transporter Type 4
HbA1c	Hemoglobin A1c
HCT	Hydrochlorothiazide
HDL	High Density Lipoprotein
HPA	Hypothalamic-pituitary-adrenal
IDF	International Diabetes Federation
IDP	Internally Displaced Persons
IGT	Impaired Glucose Tolerance
IHD	Ischemic Heart Disease
IP	Interphalangeal
KRG	Kurdistan Regional Government
LDL	Low Density Lipoprotein
MENA	Middle East and North Africa
NGO	Non-Governmental Organizations
NPH	Neutral Protamine Hagedorn

PAD	Peripheral Arterial Disease
PIC	Pro-inflammatory cytokines
PPBG	Post-Prandial Blood Glucose
PTCA	Percutaneous Transluminal Coronary Angioplasty
PTSD	Post-Traumatic Stress Disorder
RAS	Renin-Angiotensin System
SES	Socioeconomic status
SD	Standard Deviation
SNS	Sympathetic Nervous System
T1DM	Type 1 Diabetes mellitus
T2DM	Type 2 Diabetes mellitus
TG	Triglycerides
UKPDS	UK Prospective Diabetes Study
UNHCR	United Nations High Commissioner for Refugees
UNRWA	United Nations Relief and Work Agency
USA	United States of America
WHO	World Health Organisation
WMA	World Medical Association

INTRODUCTION

The Syrian Civil War has lead to the worst humanitarian crisis of the 21st century leaving more than 13.5 million in need with 6.5 million people internally displaced and more than 4.8 million refugees. The war has resulted in the death of more than 300 000 people and left more than one million injured[1]. People have sought refuge in neighboring countries such as Iraq, Lebanon, Turkey and Jordan each hosting 200 000, 1.1 million, 2.5 million and 600 000 respectively. With the simultaneously ongoing Iraq crisis the total Internally Displaced Persons (IDP) together with the refugees made up a total number of 2 927 920 within Iraq in May 2015, with Duhok governorate hosting the biggest population of 500 274[2]. Looking at a report published just months later, the total number of IDPs in Iraq had increased to 3.2 million[3] and today with the ongoing Mosul Crisis another 161 886 have been registered by the United Nations High Commissioner for Refugees (UNHCR)[4]. Syrian refugees began arriving to Duhok governorate in 2012, leading to opening of the camp Domiz 1 the same year. This camp was hosting about 60 000 people in 2014[5] and does today remain the largest permanent camp in Northern Iraq even though the population has decreased by fifty percent[6].

The war in Syria has resulted in severe destruction of health care systems. At the end of 2013 78% of Syria's existing ambulances and about 57% of public hospitals had been destroyed, making health care access one of the biggest concerns for people. Acute injuries and communicable diseases have been prioritized in different health care settings while treatment of chronic diseases have been considered a luxury treatment that with limited access to medications have been unavailable and hence a silent killer not included in war-related statistics[7,8]. According to an estimation made by The Syrian American Medical Society in 2013, chronic illness with lack or shortage of treatment had been the cause of 200 000 deaths since the beginning of the Syrian Civil War[9]. Diabetes mellitus, a condition that without proper treatment can be life-threatening, is one of the main non-communicable diseases that have been difficult to manage[10,11].

Type 1 Diabetes mellitus (T1DM) mainly has its etiopathogenesis in a T-cell mediated autoimmune response against pancreatic beta cells. Studies on identical twins show that T1DM has a genetic component that needs to be triggered by the environment. The *Accelerator Hypothesis* suggests that this environmental trigger is needed for the disease to be expressed, that individuals can be more susceptible to diabetes mellitus by genome but that other factors such as lifestyle cause an increased insulin demand, accelerating the already existing destructive process, hence compromising insulin production. Type 2 Diabetes mellitus (T2DM) is a chronic hyperglycemic condition caused by decreased insulin secretion and increased insulin resistance. It accounts for about 90% of Diabetes mellitus worldwide. The disease is of multifactorial etiology including genetics – a strong component, age, physical inactivity and overweight (Body Mass Index (BMI) 25-30 kg/m^2), with the latter increasing the risk by 10-30 times[12]. Insulin secretion is in normal conditions stimulated by the incretins Glucagon Like Peptide 1 (GLP 1) and Gastric Inhibitory Polypeptide (GIP). In T2DM

incretins are believed to have decreased effect on pancreatic cells hence disturbing insulin secretion. Insulin resistance is yet being studied; it is however believed that Glucose Transporter Type 4 (GLUT-4) that is sensitive to insulin stimulation is decreased on the cell surface of adipose cells in patients with T2DM. Decreased glucose uptake in peripheral tissues and decreased inhibition of glycogen synthesis and gluconeogenesis in the liver, further increases insulin resistance. Chronic hyperglycemia results in glucotoxicity and lipotoxicity leading to further increase in weight and decrease in insulin production. Chronic hyperglycemia eventually leads to changes in the vascular beds causing both macro and microangiopathies. Among the latter nephropathy is the most serious diabetic complications and is strongly correlated with mortality. Macroangiopathies do usually take the form of atherosclerosis and the development occurs faster in diabetic patients. The cause of this rapid development is not clear but is believed to partially occur because of increased oxidative stress in endothelial cells. Macroangiopathies are responsible for 80% of mortality in diabetic patients with consequent stroke, peripheral arterial disease (PAD) and ischemic heart disease (IHD) that takes the lead. Dyslipidemia increases the risk for development of macroangiopathies and is present in about 60% of diabetic patients compared to less than 25% in those without the disease[13]. The UK Prospective Diabetes Study (UKPDS), one of the largest and longest studies on diabetes mellitus, including 5 102 participants, demonstrated that glycemic and blood pressure control reduce diabetic complications[14]. Hyperglycemia if left untreated, especially in T1DM, due to lack of medication or for other reasons, can progress to the life-threatening state of diabetic ketoacidosis causing dehydration, coma and if still untreated resulting in death.

In times of war it is common for non-communicable diseases to be of less priority. It is also understandable that victims of war focus less on healthy lifestyle-issues while trying to survive the day. They do often not have the necessary means for implementing diet restrictions or increased physical activity while living on food support and in a refugee camp. In light of our era's biggest humanitarian crisis and the consequences that the health sector has suffered, it is important to look closer at how people affected by this war have been managing diabetes and its complications. We previously mentioned that Kurdistan/Northern Iraq currently hosts a large number of refugees as well as IDPs. Non-Governmental Organizations (NGO) are working in the area together with the Kurdistan Regional Government (KRG) providing shelter, nutrition, education and health care among other things. The pressure on the region is however increasing with the rising number of IDPs coming into Kurdistan. Local doctors report that health care provision to the local population has lately been compromised.

As Duhok governorate hosts a large number of refugees and IDPs, a cross-sectional study was conducted with the aim of assessing management of diabetes mellitus and its complications among Syrian refugees in the areas largest refugee camp Domiz 1.

AIM AND OBJECTIVES OF THE THESIS

Aim

The aim of the study was to assess management of diabetes mellitus and its complications among Syrian refugees in the areas largest refugee camp Domiz 1.

Objectives

Objectives of the study:

1. Evaluate risk factors for development of disease complications
2. Describe diabetes control parameters; the means through which it is assessed and how often. Treatment options and availability.
3. Evaluate prevalence of diabetic complications
4. Analyze potential areas of improvement regarding management of diabetes

LITERATURE REVIEW

Studies on refugee and immigrant groups in the United States of America (USA) and Scandinavia show that they suffer increased risk for development of diabetes mellitus. An observational, longitudinal cohort study from the USA reports disproportionality in the burden of diabetes mellitus affecting socioeconomically vulnerable and ethnic minorities among whom incidence rate is increasing. Increased risk for development of the disease among refugees compared to immigrants does however not show any significant difference, but when compared to English speaking US-born controls of similar socioeconomic background, the refugee and immigrant groups suffer a significantly higher risk[15]. In the paper previously mentioned, the authors mention different factors to consider when looking at this increased risk. Resettlement in new environments, cultural differences, potentially fewer resources and social support, as well as different levels of education are all factors that may expose immigrants and refugees to health risks other than those in their homelands. This can probably be the case for many immigrants and possibly refugees as well. However when we talk about new environments and cultural differences we need to specify what exactly we are referring to. Yes, the new environment can be a risk factor, but it is important to not confuse the new environment with an already present cultural risk factor. The new environment can be a source of continuous stress with adaptation difficulties, previous psychological trauma, fear of the future etc., which in turn is believed to activate the hypothalamic-pituitary-adrenal (HPA) axis and the Sympathetic Nervous System (SNS) that via norepinephrine and cortisol lead to insulin resistance (see section below - PTSD). But there is also the new environment that many argue involves new dietary habits, more consumption of processed food, and a more sedentary lifestyle, in other words what we refer to as the Western lifestyle. When studying people from different origins in today's globalized world it is important to understand the culture in matter with regards to lifestyle there within diet, physical activity and also the general perception of the individual's role in society. The Western lifestyle might be a significant risk factor for certain populations but when studying people from Middle Eastern countries, this so-called Western lifestyle may be an already well-established risk factor within their societies. Cultural difference – a well-discussed subject in many countries comprehend a wide spectrum of issues. Cultures can be individual within the same population and it can in some cases restrict possibilities of adapting a healthy lifestyle by interfering with the freedom of a large part of the population. How can we approach cultural differences that restrict the choice of healthy lifestyle and decreased exposure to risk factors? We know that fundamentals like physical inactivity and high BMI are risk factors for development of T2DM as well as for worsening management and outcomes for those with an already existing diagnosis. How much are we as the international community actually doing to tackle this issue? Are we settling with pharmacological treatment because a change of lifestyle in those countries is too difficult to achieve? Another study done on immigrants in the USA reveal that the longer immigrants stay in the USA the more their cardiovascular risk profile approaches that of US-born

individuals[16]. Yet once again we can ask, is this because of the new environment and the Western lifestyle or is it inevitable due to an already existing cultural risk factor? Fewer resources and decreased social support could possibly be argued a weak risk factor since when looking at immigrants in Sweden, that have good resources and social support while seeking asylum and throughout their integration process, they are still more prone to have impaired glucose tolerance (IGT), to get diabetes or to be less likely of meeting optimal glycemic control criteria and diabetes care[17,18]. This was found in a cross-sectional total population study done on Turkish immigrants in Sweden in which the immigrants were compared to data from the TURDEP study of their area of origin in Turkey. They found that Turkish women in Sweden had a higher prevalence of diabetes (12.8%) when compared to women in Turkey (7.6%) and that there was a higher prevalence of Turkish men in Sweden suffering from IGT (17.8%) compared to men in Turkey (4.9%)[19]. A vulnerable socioeconomic background can however certainly be associated with diabetes mellitus. Lower education levels can compromise understanding of the concept of a healthy lifestyle. We go back to the problem with cultural differences; education is intertwined there within. Will people understand the actual importance of a healthy lifestyle despite lower education levels? Will adherence to treatment and therapies prescribed be optimal without full understanding of the disease itself? We need to raise the question; even if the person in matter did understand the concept of lifestyle changes, would they be able to introduce them in their current life as it is right now? Avoiding fast food, mass production products, switching to a more green diet and becoming more physically active requires money and time. Is that a resources that refugees are considered to have – recently having fled war and living in suboptimal living conditions, a non-planned life-event that is filled with uncertainty and fear of the future? To what extent are they in charge of their lives? Does that mean that the international community needs to reorganize diabetes care in order to adapt it to these groups?

Studies conducted in the Middle East and North Africa (MENA) region shown an increased prevalence of diabetes mellitus. The International Diabetes Federation (IDF) estimated that about 35.4 million people had diabetes in 2015 and their prospective estimation is double the number i.e. 72.1 million by the year of 2040[20]. In 2015 it was estimated that around 40.6% of the population had not been diagnosed, 342 000 deaths that year were caused by diabetes and that 51.3% of those deaths were before the age of 60[21]. A systematic review in the region showed that obesity is a clear and leading risk factor for development of T2DM. Macrovascular and microvascular complications were present in around 9-12% and 15-54% respectively in the population of the MENA region. More than 50% of those with diabetes showed signs of insufficient diabetes control as glucose, lipid and/or blood pressure treatment targets were not met[22]. This review did however exclude studies focusing on T1DM, available studies used different age-sex distributions and research methods and the number of

studies conducted by each of the MENA countries varied widely. Diabetes mellitus was previously considered "rich people's" disease, but according to data from the World Health Organization (WHO), low-income countries are today facing an increased incidence of the disease. It is estimated that the coming years will result in a 40-50% increase in industrial countries while that of low-income countries will more than double[23].

A study performed in a Palestinian refugee camp in Syria investigated the level of care, the patient's general understanding of the disease and its management and possible areas for improvement. In this study with 154 participants it was reported that health care professionals almost always neglected foot examinations, eye examinations were not provided by the United Nations Relief and Work Agency (UNRWA) clinics, 67% of patients had to at least once buy their medications at their own expenses due to lack in the UNRWA clinics. Drugs were prescribed but they were not always available due to delays from the central depot. In those times, patients were advised to buy their medications on their own, if they could not afford it the initiation of treatment was delayed, even if the drug in matter was insulin. Many patients (48%) had poor knowledge regarding exacerbating factors of diabetes, with as much as 88% being overweight or obese and 74.2% having a blood glucose level higher than the target for control (< 7mmol/L). In outpatient follow-up each patient had less than 5min with the doctor and only 8% were physically examined. Up to 62% tended to associate their disease with sadness or stress. About 44% of the diabetics did not know how long they would have to take their oral hypoglycemic agents, some thought it was temporary "until they got better" [24]. A retrospective cohort study, done monitoring persons with diabetes mellitus in a primary healthcare clinic for Palestinian refugees in Jordan, reports that among a total of 1 981 diabetic patients remaining in care 79% had hypertension, 18% had one or more late complications, 9% had suffered a myocardial infarction, 2% were blind and less than 1% had end-stage renal disease. 42% of the diabetic population had post-prandial blood glucose (PPBG) checked; the results showed that 50% of those patients had PPBG ≤180 mg/dl[25]. The perception of one's illness is an important aspect in diabetes management in order to optimize understanding and adherence to treatment. Adherence and compliance to medications poses a challenge to caregivers globally and it is crucial in managing diabetes. By improving and altering patients' illness and treatment perceptions studies show that adherence and compliance increases [26].

Wars and the subsequent refuge that people have been forced to seek has left many with poor psychiatric health. Many people suffer from Posttraumatic Stress Disorder (PTSD), depression or severe emotional disorders after what they have gone through. We have discussed that lifestyle and dietary changes are the key to manage the growing problem of diabetes in the world. What many

forget in discussions like these is how poor psychiatric health can be one of the major risk factors for development of T2DM. It has two aspects; one is that poor psychiatric health leaves the individual less motivated and less likely to adhere to prescribed health care plans. A sedentary lifestyle with bad dietary habits, consumption of alcohol and smoking becomes more likely and further increases the risk. Another aspect is that conditions such as PTSD, depression, and stress among others, cause acute or chronic psychological stress. Mediators in psychological stress are mainly norepinephrine and cortisol that together with Renin-Angiotensin System (RAS), Pro-inflammatory Cytokines (PIC) and Free Fatty Acids (FFA) are believed to cause an inflammatory response leading to insulin resistance[27]. The exact mechanism remains unclear but studies suggest that the activation of the HPA axis and the SNS are the main underlying factors[28]. A study done on 105 180 asylum seekers in the Netherlands reported that prevalence of T2DM was higher among individuals with PTSD compared to those without[29].

Refugees living in camps setup in neighboring countries surrounding Syria have difficult living conditions, in crowded, unsanitary climates with limited access to medications and health care. Many of them have suffered psychological and/or physical trauma, there among victims of gender-based violence and child abuse [30,31]. Mental health and its effect on diseases need to be integrated into the management of somatic conditions. As our oath as medical/health care professionals reaches beyond only disease management, we need to work just as hard on disease prophylaxis in these areas. If we address the need for mental health care among traumatized populations that live under continuous stress and fear for their lives and future, we might be able to decrease the incidence of T2DM.

MATERIAL AND METHODS

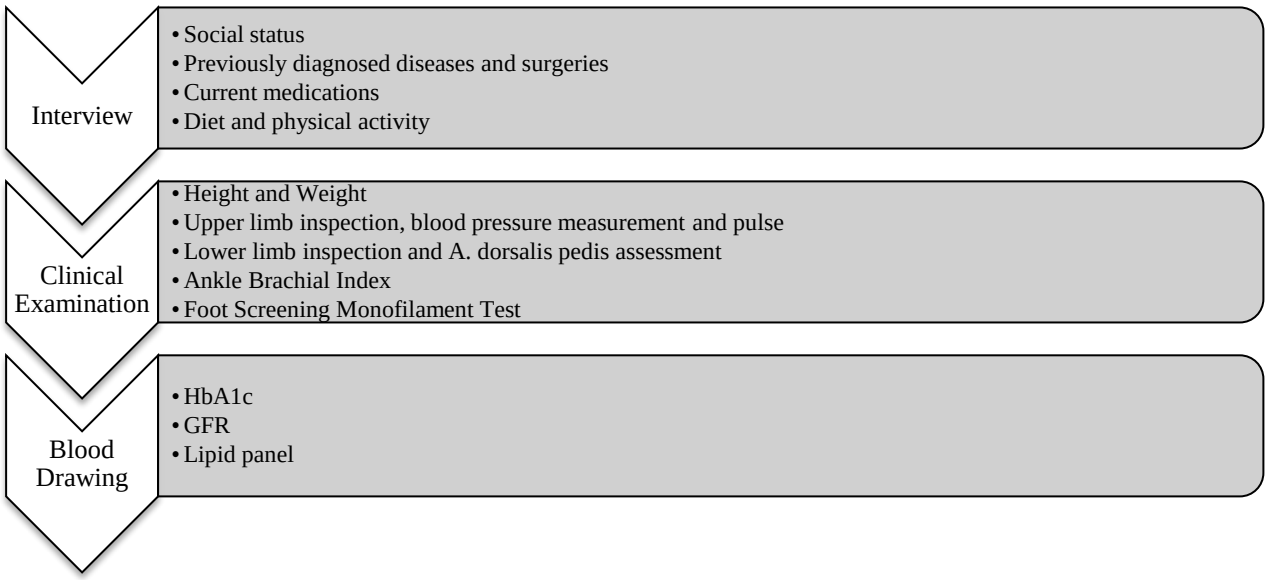
This study was conducted in camp Domiz 1 in Kurdistan/Northern Iraq where the majority of the refugees were from Kurdish inhabited cities in Syria. The sample selection was initially planned to be a simple random sample; however this was not possible since there were no established communication methods to contact the individuals within the camp. According to the official documents the total diabetic population within the camp were 328 which was 0.80% of the total population of 40 400 people in 2016[32]. After discussions with the camp director and the Directorate of Health in the region it was decided to do a *waiting-room-study*. This meant that the sample selection consisted of patients that during October 2016 were coming for regular check-ups to the Primary Health Care Center - section for Non-Communicable Diseases. They would be informed about the ongoing study and the possibility to participate. They would also be asked to spread the word among other refugees with the diagnosis of diabetes. The prevalence of T1DM and T2DM was estimated using official camp records and we could hence keep track of how many of the total amount that we had been able to meet.

The total number of registered cases was 328, and the aim was to have a sample selection of at least 50%. We managed to include 204 participants in our study without any age restrictions applied.

STUDY DESIGN

The study was composed of three parts with the first one being a short interview, second a clinical examination and last blood sampling.

Figure 1. Overview of the Study Design



INTERVIEW (Part I)

The interview was conducted following a questionnaire that we had developed (Annex). The aim of the interview was to collect anamnestic data with regards to social status, previously diagnosed diseases and performed surgeries, current medications, dietary and physical activity habits. We considered this information to be of importance with regards to possible variable patterns that could emerge in the results. While developing the questionnaire we focused on including questions that would reveal possible risk factors for development of diabetes complications. The first part of the questionnaire focused on social status related factors such as age, civil status, current living situation, number of children, their city of origin, the year they had to leave Syria and whether they ever had received medical care elsewhere than within the refugee camp. The second part regarded collecting medical anamnestic data regarding current treatment and with yes/no answers to questions about complaints of numbness and decreased visual acuity, previous episodes of stroke; myocardial infarction, hyperosmolar hyperglycemic state, diabetic ketoacidosis and hypoglycemia. The last part dealt with life-style including dietary habits, physical activity and cigarette smoking. Dietary habits were evaluated by questions regarding the main constituents of their meals before life in refuge and the current situation. The patients got to evaluate how they considered their physical activity to have changed when comparing life before they sought refuge to life as it is now. Cigarette smoking was evaluated for further assessment of peripheral arterial disease.

CLINICAL EXAMINATION (Part II)

The clinical examination was started by measurement of height to the nearest centimeter, using a wall mounted metric band, and weight to the nearest kilogram with indoor clothes on but no shoes using a calibrated electronic scale. We used the WHO's Global Database on Body Mass Index[33] for BMI classification: *Underweight* (< 18.50), *Normal range* (18.50 – 24.99), *Overweight* (≥ 25), *Obese class I* (30.00 – 34.99), *Obese class II* (35.00 – 39.99) and *Obese class III* (≥ 40). The patients were asked to lie down on the bunk and roll up their sleeves to allow measurement of blood pressure. The blood pressure was then taken on both arms with the patient in supine position to allow later calculation of Ankle-Brachial-Index (ABI). The blood pressure measurement was repeated three times on the left arm to enable later calculation of the blood pressure mean. The measurement was done using a manual sphygmomanometer (Riester precisa N Aluminium) together with 3M™ Littmann® Classic II S.E. Stethoscope. Blood pressure was classified according to degree of control with regards to the 2017 guidelines for diabetes care from the American Diabetes Association (ADA)[34]: *Well Controlled* (< 129/80 mmHg), *Moderately Controlled* (130 – 139/80-85 mmHg), *Insufficiently Controlled* (< 160/100 mmHg) and *Dangerously High* (> 160/100 mmHg). Upper limb palpation with manual temperature assessment was documented as decreased, normal or increased. Radial pulse

assessment included beats per minute, strength described as strong/weak and regularity as regular/irregular. Lower limb inspection was performed by asking the patients to roll up their trouser-legs. We checked for signs of PAD by inspecting the lower limbs for amputations, erythema, cyanosis, pallor, hair loss and ulcers. The ulcers were described according to location and morphology with maceration, hyperkeratosis, dry skin, cracked skin and/or necrosis. PAD was also assessed by lower limb palpation using manual temperature assessment as for the upper limb and assessment of arteria dorsalis pedis bilaterally as absent/present and weak/strong. Bilateral blood pressure was manually measured at the lower limbs by the use of manual sphygmomanometer (Riester precisa N Aluminium) together with 3M™ Littmann® Classic II S.E. Stethoscope. We did not have access to a handheld Doppler device. However according to a study done on the effectiveness of auscultating arteria dorsalis pedis and arteria tibialis posterior compared to using a Doppler device in primary health care settings, this method is still useful[35]. The cuff was applied just above the tibial malleoli and auscultation was done bilaterally first at arteria dorsalis pedis and then at arteria tibialis posterior to enable later calculation of ABI. The method of measurement and later classification was according to Stanford Medicine 25[36].

Neuropathies were assessed by asking the patient a set of yes or no questions regarding: sensations of numbness/tingling in lower extremities and decreased visual acuity. We used a foot screening monofilament 10g to assess pressure touch sensation bilaterally. The results were based on the patient's assessment of touch on the plantar surface of the first digit, and along the foot pad (see Annex for scheme). If there was any abnormality in the test, we proceeded with checking bilateral lower extremity proprioception at the interphalangeal joint of hallux, and the Achilles and patellar reflex. These were then documented as normal/abnormal proprioception and normal, hyporeflexia or hyperreflexia respectively. [37]

BLOOD DRAWING (Part III)

Blood samples were taken by a nurse in accordance to the WHO guidelines on drawing blood; section for venipuncture[38]. The equipment provided for blood drawing was non-sterile single use gloves, alcohol swabs, needle and syringe system, ethylenediaminetetraacetic acid (EDTA) and serum separator tubes, tourniquet and dry cotton-wool balls. The samples taken were for assessment of HbA1c, lipid levels, hemoglobin and albumin. Glycemic control was assessed by HbA1c using COBAS HbA1c analyzing device. Glycemic control was then classified according to the 2017 guidelines for diabetes care from the ADA[39]. For T1DM patients *Good Control* was < 7.5%, *Inadequate Control* was > 7.5% and *Bad Control* was > 8%. For T2DM patients *Good Control* was < 6.5%, *Inadequate Control* was < 8% and *Bad Control* was > 8%. Lipid levels were analyzed by COBAS and BIOLAS devices and were also classified according to the 2017 guidelines for diabetes

care from the ADA[40]. Total Cholesterol was classified as high if > 200 mg/dL, Low Density Lipoprotein (LDL) was classified as high if > 100 mg/dL, triglycerides (TG) if the value was ≥ 150 mg/dL, and high density lipoprotein (HDL) as low if < 40 mg/dL. Hemoglobin analyzed by SWELAB and MEDONIC equipment. Serum albumin and creatinine were assessed by COBAS and BIOLAS analyzing devices and creatinine levels were then further used to assess glomerular filtration rate (GFR). Using the Cockcroft-Gault equation: (140-age) × (weight in kg) × (0.85 if female) ÷ (72 × Cr)[41] we classified stages of chronic kidney disease[42] (CKD) (Table 1). Serum albumin was classified as hypoalbuminemia if < 3.0 g/dL[43].

By 11 AM the samples were transported in refrigerated containers to the Azadi University Hospital in Duhok city for further processing and analysis. Patients who were seen after 11 AM were therefore asked to come back the next day to complete their participation by leaving blood samples.

Table 1: Stages of chronic kidney disease

CKD stage	**GFR level (mL/min/1.73 m^2)**	**Description**
Stage 1	≥ 90	Normal kidney function but urine findings, structural abnormalities or genetic trait point to kidney disease.
Stage 2	60 – 89	Mildly reduced kidney function, and other findings (as for stage 1) point to kidney disease.
Stage 3	30 – 59	Moderately reduced kidney function.
Stage 4	15 – 29	Severely reduced kidney function.
Stage 5	< 15	Very severe, or end-stage kidney failure.

ANALYSIS AND STATISTICAL METHODS

IBM SPSS Statistics program was used for analysis of data.

Non-parametrical continuous variables were presented as median. Parametrical continuous variables were presented as mean.

Social and living conditions were analyzed checking frequency of variable with median and quartiles selected for analysis. Analysis of physical activity comparing life before seeking refuge and life as a refugee was done by assessing frequency of variable and significance of decrease in physical activity was analyzed using McNemars test. Assessment of correlations between changes in physical activity and living and social conditions was done using Pearson Correlation. Changes in physical activity in correlation to risk factors for disease control were done using linear regression analysis. Diet before and after taking refuge was analyzed for any significant differences using the Marginal Homogenity test. BMI was analyzed by assessment of variable frequency with estimation of mean. Analysis of correlations between BMI and living and social conditions was done using Pearson Correlation. Correlation to risk factors for disease control was done using linear regression analysis. HbA1c was analyzed by assessment of variable frequency with estimation of mean. Assessment of correlations between HbA1c and living and social conditions was done using Pearson Correlation. HbA1c correlation to risk factors for disease control was done using linear regression analysis.

Hypoglycemic agents were analyzed by variable frequency assessment. Mono- and bi-therapy were analyzed by crosstabs. Statins were assessed by variable frequency analysis. Significant effect on lipid levels was evaluated using linear regression analysis. Furosemide and CKD stage relationship was analyzed to assess whether treatment with Furosemide was related to decreased kidney function.

Correlation between age to GFR and serum albumin levels was assessed by linear regression analysis. The relationship between CKD stages and risk factors for disease control and development, and social and living conditions was assessed using linear regression analysis. Peripheral neuropathies were analyzed in relation to risk factors for disease control and social and living conditions using linear regression analysis. Blood pressure parameters were assessed in link to risk factors for disease control and social and living conditions using linear regression analysis. Assessment of blood pressure control with anti-hypertensive treatment was analyzed using linear regression analysis. Dyslipidemia was analyzed by variable frequency assessment with estimation of median and percentiles. Control of lipid levels with statin treatment was assessed using linear regression analysis. PAD was evaluated by variable frequency assessment with estimation of mean and standard deviation. Correlation between ABI and clinical signs of PAD, living and social situation and role of treatment with statins was analyzed using linear regression analysis. Hypoglycemia and diabetic ketoacidosis was analyzed using variable frequency assessment. The correlation to glycemic control was assessed by using linear regression analysis.

RESULTS

PREVALENCE OF DIABETES MELLITUS

There were a total of 328 people with diabetes mellitus within Domiz 1, 16 (5.18%) individuals with T1DM and 312 (94.82%) with T2DM. Within the studied population of 204 patients; 11 (5.39%) had T1DM and 193 (94.61%) had T2DM.

T1DM

The median age was 23 (17; 41) years. There was a male gender predominance with 63.64% males and 36.36% females.

T2DM

The median age was 52 (46; 57) years. There was a female predominance with 77.20% females and 22.80% males.

LIVING AND SOCIAL CONDITIONS

T1DM

There were 36.36 % of the patients who were living in tents provided by the UNHCR while 63.64% had managed to replace the tent with a brick house that they had built by themselves. Amongst the patients with T1DM 72.73% were married and 27.27% were single. The median number of people in each household was 5 (4; 8). The median number of children per person was 1 (0; 4). The majority of the patients (54.55%) were from the city Derik.

T2DM

There were 42.49% living in tents provided by the UNHCR while 57.51% had built brick houses by themselves. Among the T2DM patients there were 2.38% whom were married, 3.63% divorced and 13.99% widowed. The median number of people in each household was 5 (4; 7). The median number of children per person was 7 (5; 8). The majority of the patients were from Qamilshli (45.10%), Derik (23.83%), Damascus (13.47%) and Hasseke (9.84%).

YEAR OF ONSET OF DISEASE AND LEAVING SYRIA

T1DM

There were 9.09% that did not know the year of onset of their diabetes. The percentage of patients that had gotten their diagnosis before or during the year of 2010 were 54.55%, while 9.09% got their diagnosis during 2011 and 27.27% during 2012 (Figure 2). Among the participants 9.09% left Syria in 2011, 72.73% in 2012, 0% in 2013 and 2014, 9.09% in 2015 and 9.09% in 2016.

T2DM

There were 4.66% that did not know the year of onset of their diabetes. There were 38.34% that got diagnosed before or during the year of 2010, while 21.24% were diagnosed during 2011 – 2013 and 35.75 % during 2014 – 2016 (Figure 3). Among the participants 20.73% left Syria in 2011, 45.60% in 2012, 27.46% in 2013, 3.11% in 2014, 1.55% in 2015 and 1.55% in 2016.

Figure 2: Percentage of T1DM patients that were diagnosed prior and post to relocation.

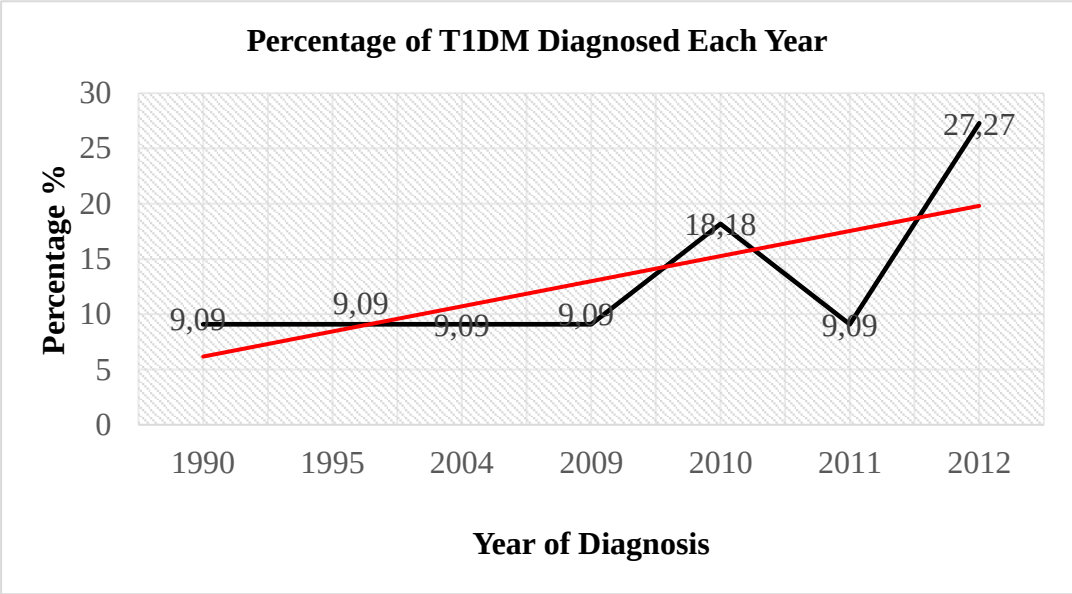
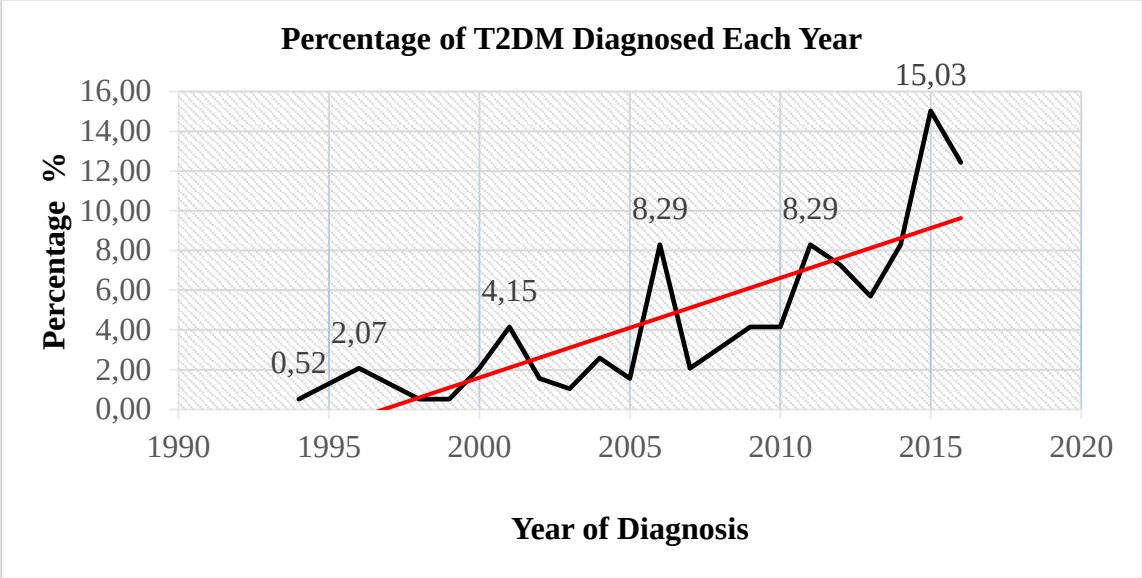


Figure 3: Percentage of T2DM patients that were diagnosed prior and post to relocation.



PHYSICAL ACTIVITY

T1DM

All patients reported being physically active before seeking refuge. Regarding their situation today 27.27% reported no change in physical activity while 72.73% reported a decrease. There was a significant decrease in physical activity (p = < 0.05) when comparing life before seeking refuge to life as a refugee.

T2DM

There were 69.95% who reported being physically active before seeking refuge, while 30.05% reported a sedentary lifestyle. Regarding their current situation 34.72% reported no change in physical activity while 58.55% reported a decrease and 6.74% reported an increase in physical activity compared to life before seeking refuge. There was a significant decrease in physical activity (p = < 0.05) when comparing life before seeking refuge to life as a refugee. Decreased physical activity was associated with hypoglycemia ($p < 0.05$). Married people reported significantly less on decreased physical activity compared to divorced, widowed or single people ($p < 0.05$). The later patients had left Syria, the less they reported decreased physical activity ($p < 0.05$). Women were currently significantly less active than men which was not the case before seeking refuge ($p < 0.05$). Among individuals with many people within the same household there was less reports of decreased physical activity ($p < 0.05$).

DIETARY HABITS

T1DM

There were 9.09% whom reported that they had to change breakfast to mainly carbohydrates since they became refugees since they could not afford having more variation in the meal (Figure 4). Another 9.09% reported that they did not eat lunch anymore since they were diagnosed with T1DM, believing that it was better for disease management (Figure 5). There were 18.18% stating that they did not eat dinner since they took refuge (Figure 6). There was no significant difference in breakfast, lunch or dinner comparing diet before taking refuge to diet now ($p > 0.05$).

T2DM

There were 1.55% that reported not eating breakfast before seeking refuge or now (Figure 4 and 5). Another 1.55% reported that they did not eat lunch anymore, one among those stated that the reason was that she was trying to eat healthy since she got diabetes (Figure 6 and 7). There was an increase in reports of not eating dinner anymore with a total of 7.25% compared to 2.59% before (Figure 8 and 9). One patient among the 7.25% stated financial reasons for this. There was no significant change in main breakfast and lunch constituents comparing diet before being a refugee compared to now ($p > 0.05$). There was however a significant difference in dinner habits when comparing current diet to the one before seeking refuge ($p < 0.05$).

Figure 4: Main breakfast constituent before and taking refuge.

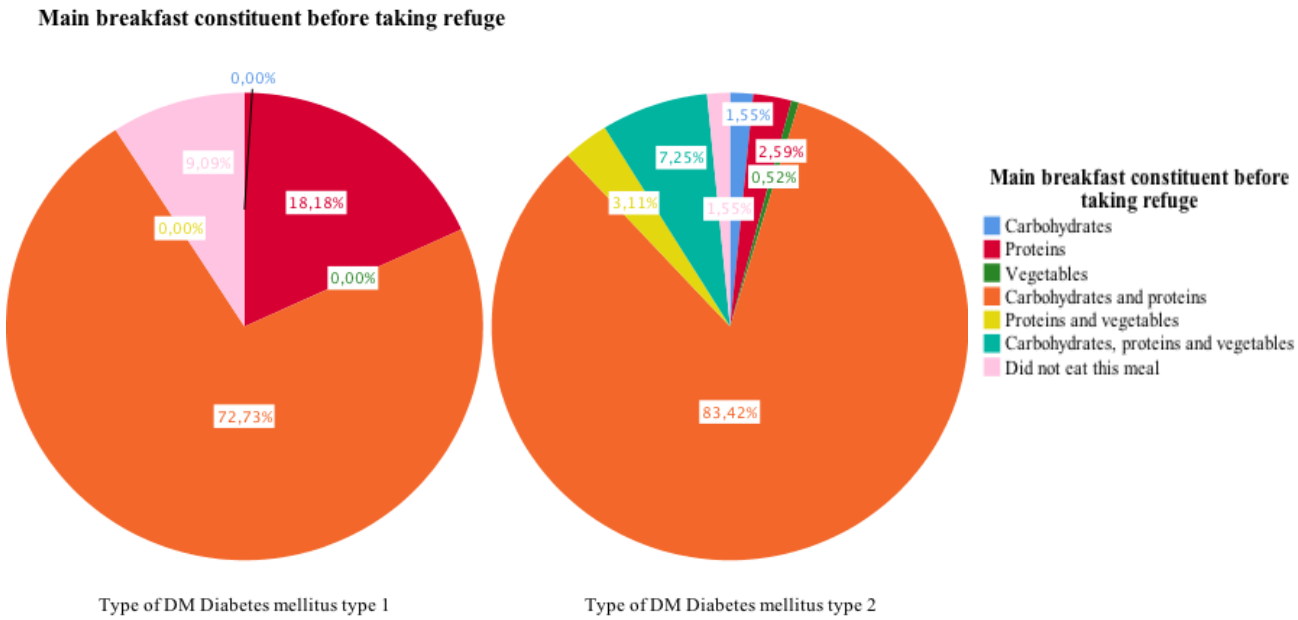


Figure 5: Main breakfast constituent now.

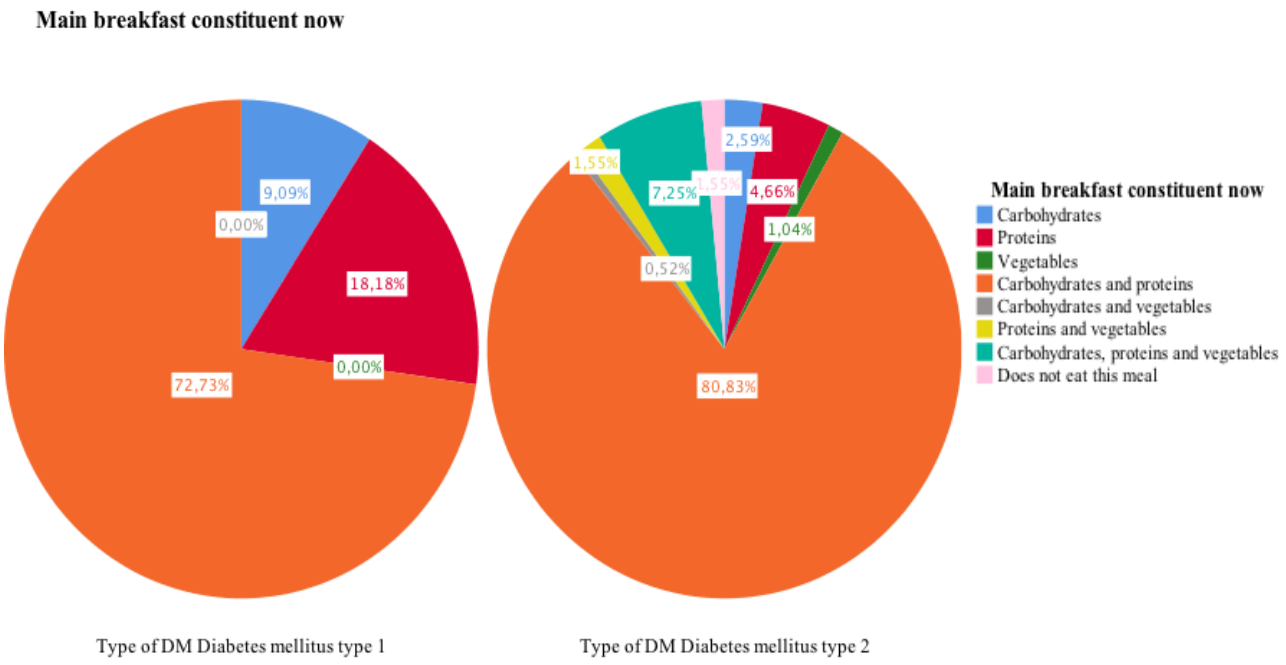


Figure 6: Main lunch constituent before taking refuge.

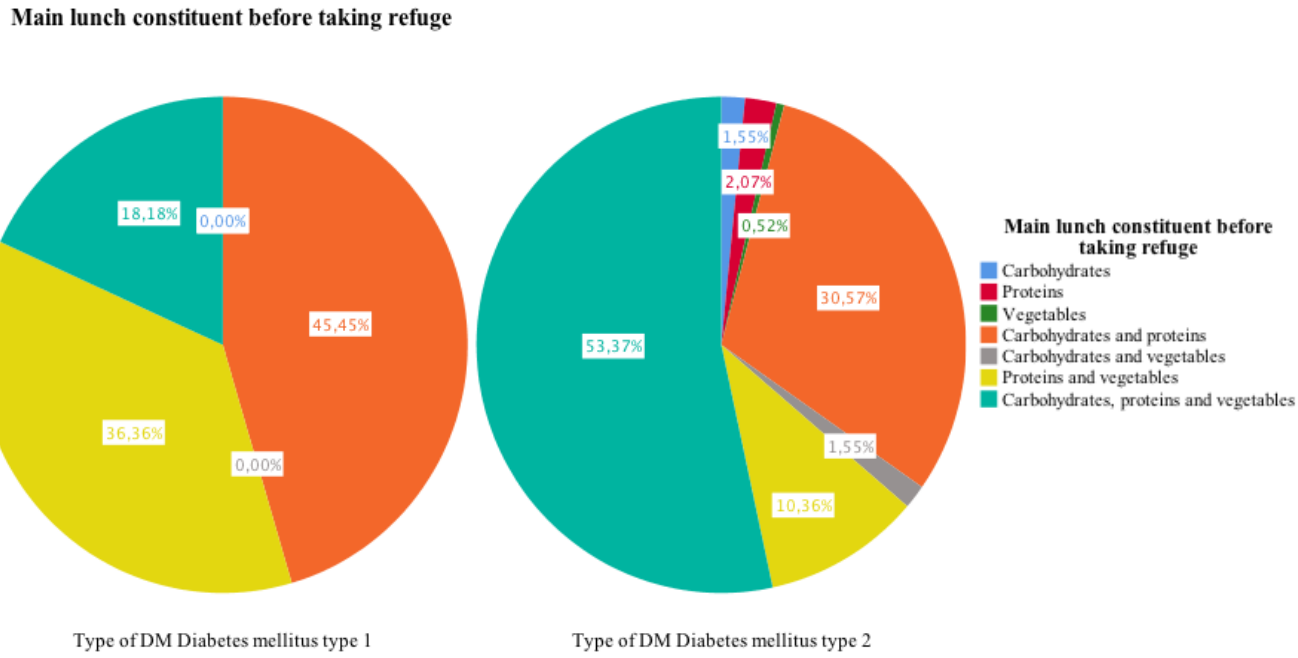


Figure 7: Main lunch constituent now.

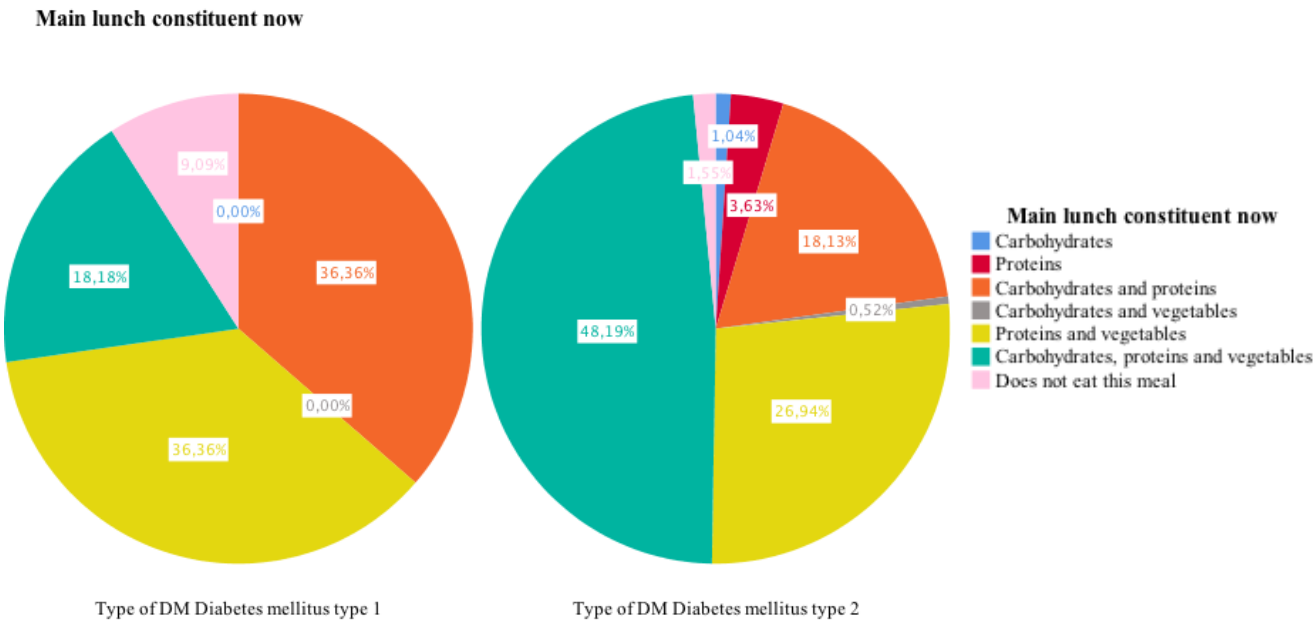


Figure 8: Main constituent of dinner before taking refuge.

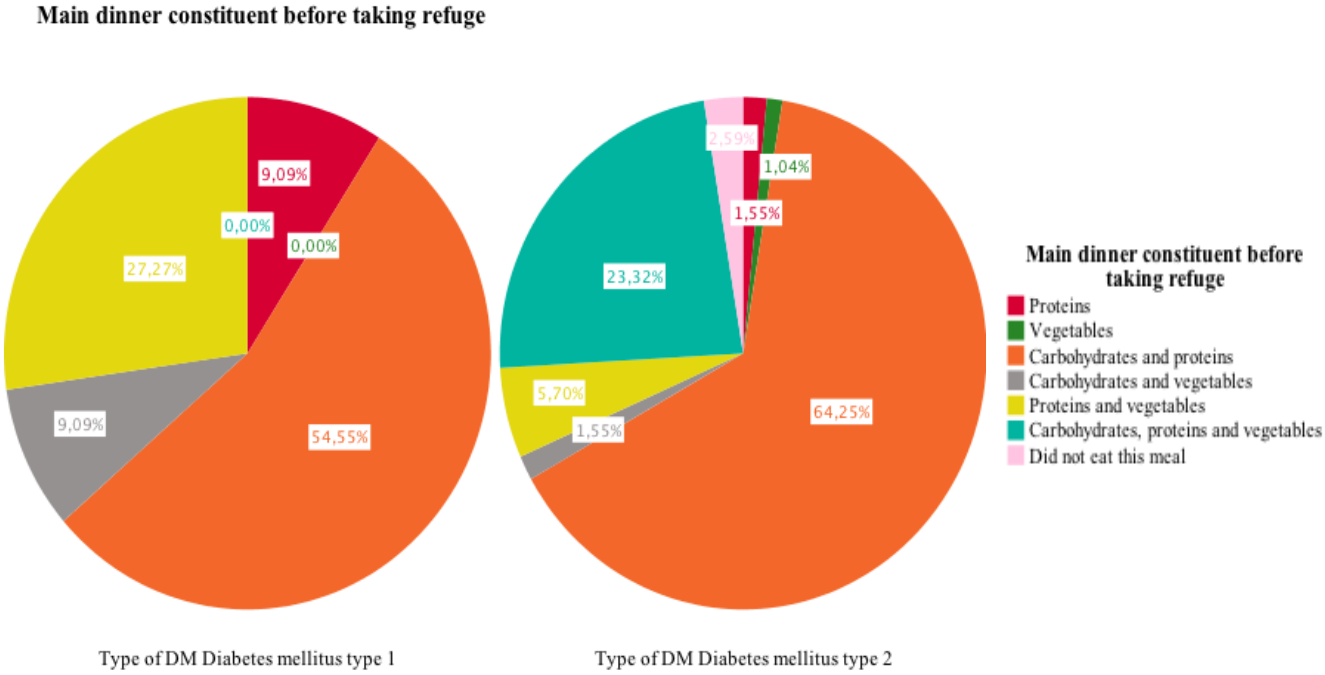
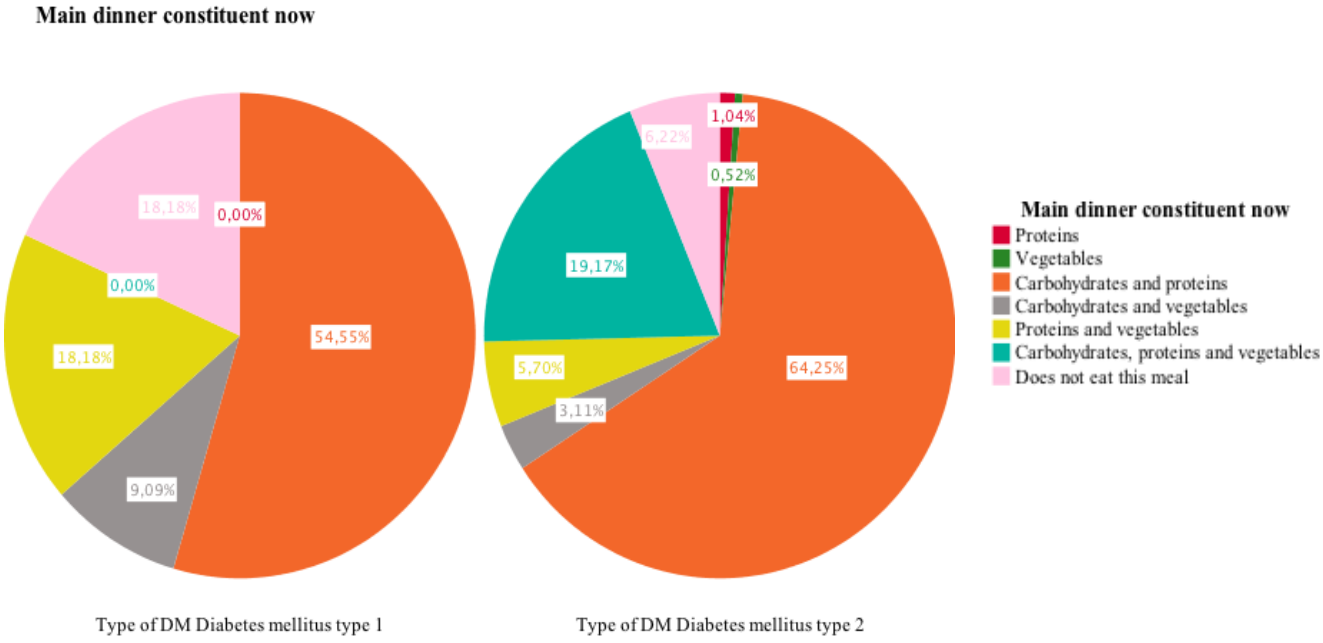


Figure 9: Main constituent of dinner now.



BODY MASS INDEX

T1DM

The mean BMI among the patients was 22.87 ± 2.82 kg/m^2. There were 9.09% who were underweight, 72.73% within normal range and 18.18% were overweight. Lower BMI was associated with marital civil status ($p < 0.05$). Higher BMI, was associated with increased HDL levels and increased systolic blood pressure ($p < 0.05$).

T2DM

The mean BMI was 31.41 ± 5.53 kg/m^2. There were 8.81% within normal range, 47.67% were overweight, 27.46% had obesity class I, 10.88% had obesity class II and 2.59% had obesity class III. There were 2.59% among whom BMI was not assessed. Two of those were wheel-chair bound, two were on chronic use of crutches and could hence not stand properly on the scale and one patient's BMI – data was lost. Female gender was associated with higher BMI ($p < 0.05$). Higher BMI was associated with cracked skin on the soles ($p < 0.05$). The later patients had been diagnosed with T2DM, the higher were their BMI levels ($p < 0.05$). Having more children was associated with higher BMI levels ($p < 0.05$). BMI was significantly higher the younger the patients were ($p < 0.05$).

SMOKING

T1DM

There were 27.27% current smokers within this group and 9.09% whom were previous smokers. The median pack-year was 32 (24.38; 38.50).

T2DM

There were 24.35% current smokers with T2DM and 21.24% who were previous smokers. The median pack-year was 15 (4.13; 30).

DIABETIC CONTROL PARAMETERS

There were 6.9% among patients with T2DM that did not come back to leave blood samples.

GLYCEMIC CONTROL

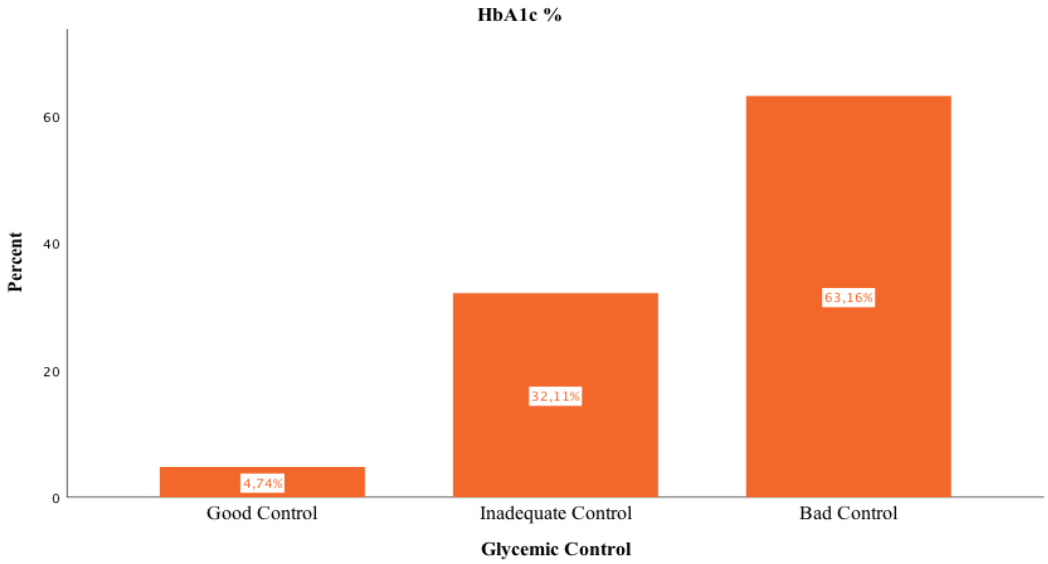
T1DM

The mean HbA1c was 9.35 ± 1.92 % indicating bad glycemic control. There were 9.09% with good control, 9.09% with inadequate control and 81.82% had bad glycemic control. There was no correlation between HbA1c and BMI or physical activity ($p > 0.05$). Bad glycemic control was associated with higher total cholesterol levels and higher HDL levels ($p < 0.05$). It was also associated with dry skin, maceration and hyperkeratosis on the feet as well as absent arteria dorsalis pedis ($p < 0.05$).

T2DM

The mean HbA1c was 8.80 ± 1.75 % indicating bad glycemic control. There were 4.66% with good control, 31.60% with inadequate control and 62.18% with bad glycemic control (Figure 8). There was no correlation between HbA1c and BMI or physical activity ($p > 0.05$). Bad glycemic control was associated with lower HDL levels ($p < 0.05$). Married civil status was linked to better glycemic control ($p < 0.05$).

Figure 8: Glycemic control among T2DM patients.



HYPOGLYCEMIC AGENTS

T1DM

All patients were treated with Insulin. Basal-bolus regimen with Neutral Protamine Hagedorn (NPH) and regular insulin was used by 36.36%, morning and night time and 63.64% were using Insulin Mix morning and night.

T2DM

There were 192 patients on treatment with Metformin with 21.88% on 500mg and 78.13% on 850mg. Among those 192 patients, 42.71% were on monotherapy with Metformin treatment. There were 55.21% on bi-therapy with Metformin and Glibenclamide, 0.52% with Metformin and Sitagliptin, 1.04% with Metformin and Gliclazide and 0.52% with Metformin and Glimepride. There were 2.08% on bi-therapy with Metformin and Insulin Mix morning and night.

STATINS

T1DM

There were 9.09% treated with Atorvastatin 20mg. There was no significant difference in lipid levels among those on Atorvastatin treatment compared to those without.

T2DM

Among patients with T2DM 49.74% were treated with Statins. Pravastatin was used by 56.25% of the patients, among those 40.74% were on 10mg and 59.26% were on 20mg. Atorvastatin was used by 41.67% among whom 50% were on 10mg, 45% on 20mg and 5% on 40mg. There were 2.08% of the patients that used Rosuvastatin, 50% on 10mg and 50% on 20mg. Total cholesterol, LDL and HDL were not significantly decreased/increased in patients on statins compared to those without. Triglycerides were however lower in patients treated with Atorvastatin ($p < 0.05$).

ANTIHYPERTENSIVE AGENTS

T1DM

Among the patients with T1DM there were 9.09% treated with Calcium channel blockers (CCB).

T2DM

There were 55.44% of the patients who were on antihypertensive treatment. Angiotensin-converting enzyme inhibitors (ACE-inhibitors) were the most commonly used substance (67.29%). Second most used substance was β - blockers (58.88%), then CCB's (26.17%), Hydrochlorothiazide (HCT) (25.23%), Angiotensin II Receptor blockers (ARB) (3.74%) and last Spironolactone (2.80%). Hypertensive management was by monotherapy among 37.38% of the patients. Among those on monotherapy treatment 42.50% were on β – blockers (BB), 30% on ACE-inhibitors, 15% on CCB, 7.50% on ARB, 2.50% on HCT and 2.50% on Spironolactone. Bi – therapy was the choice of management among 43.93%. Among those, there were 51.06% on ACE and BB therapy, 14.89% with ACE and CCB, 14.89% with ACE and HCT, 4.26% on CCB and HCT, 2.13% on BB and ARB, 2.13% on double BB, 2.13% on CCB and BB, 2.13% on BB and HCT, 2.13% on ACE and spironolactone and 2.13% on BB and spironolactone. There were 17.76% on tri – therapy management, among them 47.37% were on ACE-inhibitors, BB and HCT, 26.32% on ACE – inhibitors, BB and CCB, 10.53% on ACE-inhibitors, CCB and HCT, 10.53% on BB, CCB and HCT, and 5.26% on double ACE-inhibitors and HCT. There were 1.87% on quadri-therapy with anti-hypertensives, among those 50% with ACE – inhibitors, double CCB, and HCT and 50% on ACE-inhibitors, BB, CCB and HCT.

OTHER MEDICATIONS

T1DM

There were 9.09% of the T1DM patients who were on treatment with Tricyclic Antidepressants.

T2DM

There were 4.15% on treatment with Tricyclic Antidepressants. Among the patients with T2DM 10.36% were treated with Isosorbid mononitrate and 30% among those also had Nitroglycerine spray for usage when needed. Anti-platelet agents was in used in 41.45% of the patients. There were 37.82% of those who had Aspirin only while 3.63% were on concomitant Clopidogrel treatment. Within the group of T2DM there were 4.66% treated with Furosemide.

DIABETIC COMPLICATIONS

NEPHROPATHIES

T1DM

There were 18.18% patients who had a GFR corresponding to CKD stage 2. All patients had normal serum albumin levels. There was no correlation between CKD stages and serum albumin levels ($p > 0.05$). There was no correlation between risk factors for disease control and CKD stages ($p > 0.05$). Females were more prone to having GFR levels corresponding to higher CKD stages ($p < 0.05$). Individuals who had left Syria in later years and those living in tents had GFR levels in accordance with higher CKD stages ($p < 0.05$).

T2DM

Among patients with T2DM 12.44% had a GFR corresponding to CKD stage 3 and 48.70% had a GFR corresponding to CKD stage 2. There were 8.81% patients with serum albumin levels reflecting hypoalbuminemia. There was no correlation between CKD stages and serum albumin levels ($p > 0.05$). There was an inverse relationship between GFR and age among the T2DM group, the higher the age, the lower GFR ($p < 0.05$). There was no correlation between risk factors for disease control and CKD stages ($p > 0.05$). Single, divorced or widowed patients as well as patients with many children and females, had a higher likelihood of having a GFR corresponding to higher CKD stages ($p < 0.05$).

PERIPHERAL POLYNEUROPATHIES

T1DM

There were 45.45% among the patients that complained of numbness/tingling feeling in the lower extremities. The monofilament test was abnormal in 18.18%, among those 50% had abnormal proprioception at their interphalangeal (IP) joint of hallux but the Achilles tendon and patellar reflex was normal in all. There was an inverse relation between age and monofilament test and also between age and proprioception results ($p < 0.05$). The higher the age, the worse the monofilament test/proprioception results. There was also an inverse relation between number of children each person had and monofilament test and proprioception results ($p < 0.05$). The more children, the more prone were the patients to abnormal monofilament test and proprioception results.

T2DM

Among the T2DM group 55.44% complained of numbness/tingling in the lower extremities. The monofilament test was abnormal in 13.99% of the patients. There were 40.74% of them who had abnormal proprioception at their IP-joint of hallux and 11.11% had abnormal reflex tests. There was an inverse relation between age and monofilament test results ($p < 0.05$). The higher the age, the worse the monofilament test results. The later the onset of disease, the better were the outcomes of the monofilament test and for complaints of numbness/tingling in the lower extremities ($p < 0.05$). Individuals with more children were more prone to have abnormal reflex results ($p < 0.05$). The higher the ABI index the better were the outcomes of the monofilament test ($p < 0.05$). Marital status was associated the less were the complaints of numbness/tingling in the lower extremities ($p < 0.05$). Females were more prone to have complaints of numbness/tingling in the lower extremities ($p < 0.05$).

CARDIOVASCULAR PATHOLOGY

BLOOD PRESSURE

T1DM

Systolic blood pressure was well controlled in 81.82% while 9.09% presented with insufficiently controlled systolic blood pressure but was on antihypertensive treatment and 9.09% had a dangerously high blood pressure, without any antihypertensive treatment (Figure 9). Diastolic blood pressure was well controlled in 72.73% of the patients while 18.18% had insufficiently controlled diastolic blood pressure and 9.09% had a dangerously high blood pressure.

T2DM

Systolic blood pressure was well controlled in 54.92% of the T2DM population. There were 17.62% who had moderately controlled blood pressure, 13.99% had insufficiently controlled and 13.47% had dangerously high blood pressure (Figure 10). Diastolic blood pressure was well controlled in 36.27% of the patients, 27.46% had moderately controlled, 29.02% had insufficiently controlled and 7.25% had a dangerously high blood pressure. Age was related to higher systolic blood pressure ($p < 0.05$). Usage of the ACE-inhibitors Captopril and Enalapril showed a direct relationship with systolic blood pressure, but only with Captopril for diastolic blood pressure ($p < 0.05$). High systolic blood pressure was directly related to increased cerebrovascular events ($p < 0.05$).

Figure 9: Systolic blood pressure control in T1DM patients.

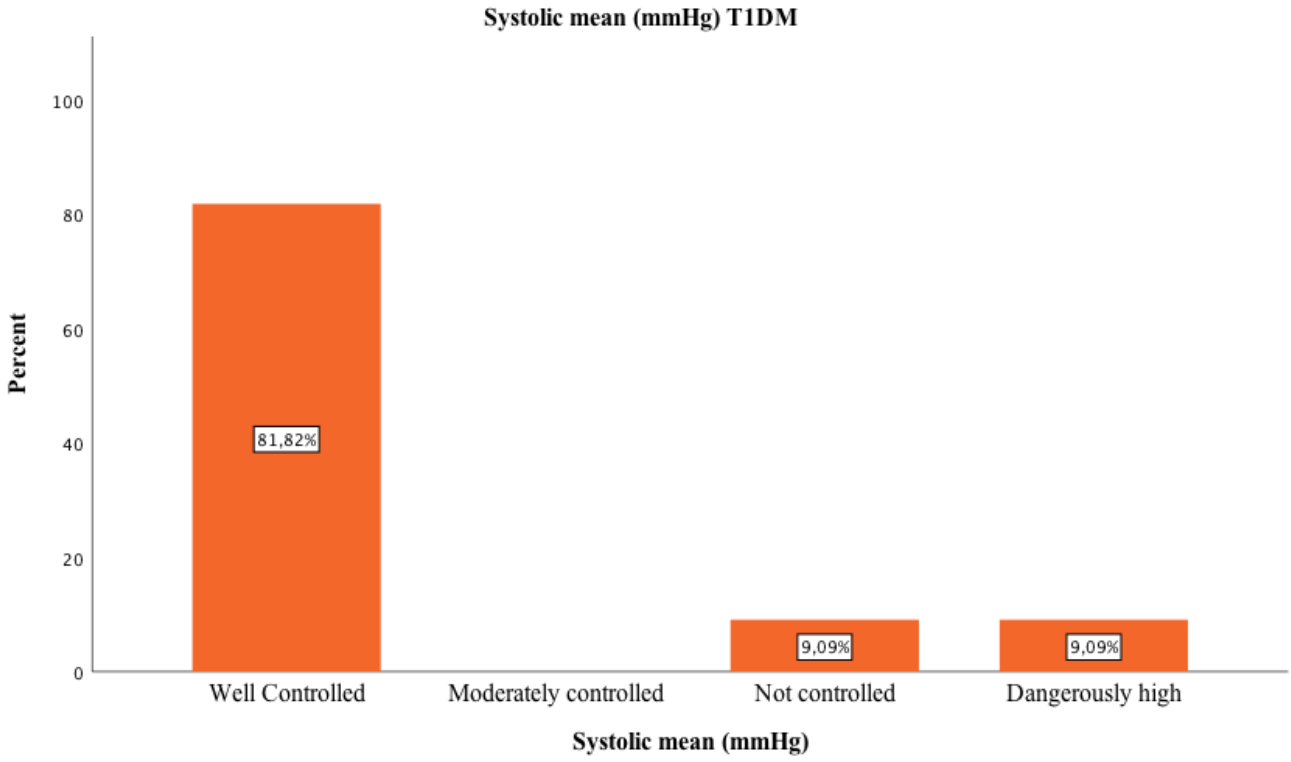
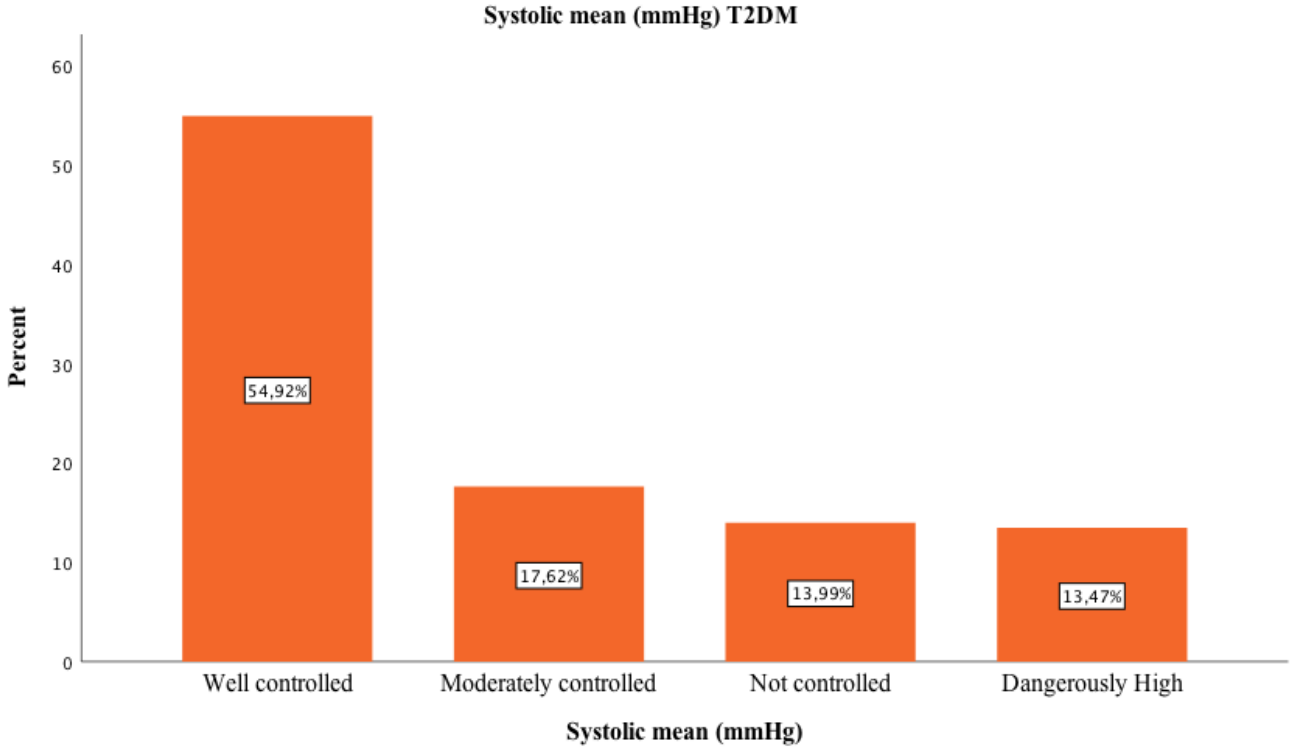


Figure 10: Systolic blood pressure control in T2DM patients.



DYSLIPIDEMIA

T1DM

There were 54.55% among the T1DM patients with high total cholesterol levels, 81.82% with high TG levels, 63.64% had high LDL levels and 81.82% had low HDL levels (Table 2).

T2DM

Among patients with T2DM 33.68% presented with high total cholesterol levels, 71.50% had high TG and 54.92% had high LDL levels and 65.80% had low LDL levels (Table 3). Triglycerides were significantly lower in patients treated with Atorvastatin ($p < 0.05$).

Table 2: Lipid levels of patients with T1DM.

		Total Cholesterol mg/dL	Triglycerides mg/dL	LDL mg/dL	HDL mg/dL
Median		200	167	122	37
Percentiles	25	180	153	68	31
	50	200	167	122	37
	75	252	209	153	39

Table 3: Lipid levels of patients with T2DM.

		Total Cholesterol mg/dL	Triglycerides mg/dL	LDL mg/dL	HDL mg/dL
Median		186	169	103	37
Percentiles	25	165	145	91	33
	50	186	169	103	37
	75	211	193	124	41

PERIPHERAL ARTERIAL DISEASE (PAD)

T1DM

There were 18.18% of the patients that presented with macerations, 9.09% with lower limb pallor, 9.09% had hyperkeratosis, 9.09% had dry skin and 9.09% had cracked soles. There were 9.09% that presented with absent arteria dorsalis pedis on palpation, 9.09% had decreased lower limb temperature and 1.55% had weak arteria dorsalis pedis. The mean left ABI was 1.06 ± 0.14 and the right ABI was 1.05 ± 0.21. There were 27.27% with some arterial disease, 63.64% with acceptable ABI and 9.09% with normal ABI. There was no correlation between lower limb temperature or pallor and ABI ($p > 0.05$). Higher ABI was associated with less dry skin and less hyperkeratosis ($p < 0.05$). People with higher ABI were less prone to have absent arteria dorsalis pedis pulses ($p < 0.05$).

T2DM

The results showed that 70.47% of the patients had hair loss on their lower limbs, 50.26% had dry skin, 48.19% had cracked soles, 15.03% had hyperkeratosis and 11.40% had macerations on their lower limbs. There were 34.20% whom presented with weak arteria dorsalis pedis on pulse palpation,

18.13% with pallor on the lower limbs, 15.03% had decreased lower limb temperature, 1.04% had cyanosis. There were 1.04% with absent arteria dorsalis pedis and 1.04% had some form of previous lower limb amputation. The mean left ABI was 1.06 ± 0.16 and the right ABI was 1.08 ± 0.14. There were 0.52% with severe arterial disease, 1.04% had moderate arterial disease, 26.94% had some arterial disease, 55.44 had acceptable ABI and 15.03% had normal ABI. There was an inverse relationship between age and ABI, the higher age the lower ABI ($p < 0.05$). Patients who had left Syria later were less prone to have low ABI ($p < 0.05$). Those with higher ABI were less prone to present with absent or weak arteria dorsalis pedis, decreased lower limb temperature or pallor ($p < 0.05$).There was no correlation between hair loss and ABI and no correlation between treatment with statins and ABI ($p > 0.05$).

DIABETIC KETOACIDOSIS AND HYPOGLYCEMIA

T1DM

There were 63.64% who reported having had episodes of hypoglycemia. There were 36.36% who reported having had at least one episode of diabetic ketoacidosis. There was no significant correlation between glycemic control and reported episodes of hypoglycemia or diabetic ketoacidosis ($p > 0.05$).

T2DM

There were 24.35% that reported having had at least one episode of hypoglycemia and 0.52% among the T2DM patients reported having had at least one episode of diabetic ketoacidosis. There was no significant correlation between glycemic control and reported episodes of hypoglycemia, hyperosmolar hyperglycemic state or diabetic ketoacidosis ($p > 0.05$).

DISCUSSION

Findings from this study suggest that prevalence of diabetes mellitus within camp Domiz 1 was lower than expected. Data from the World Bank shows that the estimated prevalence of disease within the population of Syrian Arab Republic was 8.10% in 2015. This means that 3 232 of the 40 400 Syrian refugees living in Domiz 1 would be expected to have diabetes mellitus. Our study did however only find 328 registered cases. Among the 328, 5.18% had T1DM, while T1DM usually stands for about 10% of diabetes mellitus in a population. The question is where the reasons for this difference in epidemiological estimation lies. Is it due to a part of the population being undiagnosed, or because of significant epidemiological changes – with rising death tolls due to lack of medications, proper treatment or because of war related traumas? Could it be that those with T1DM have relocated elsewhere or have not been able to relocate at all? Lack of medications have been a known problem for the victims of this war, especially lack of insulin. Could fear of compromised disease management have forced people to stay behind despite the risk of facing an even more uncertain future? Many different ethnical and religious groups live within the borders of today's Syria, there among the Kurds. The refugees in Domiz 1 were mainly Kurdish Syrian refugees. Could possibly a different culture with regards to factors such as life in rural or urbanized areas, dietary habits and lifestyle in general, impact epidemiological estimations?

The analysis of onset of the disease and the year the patients left Syria among T1DM patients, showed that more patients were diagnosed during the year of 2012. Among patients with T2DM there was a linear increase in disease onset as we got further away from the start of the war. One of the reasons could be that those 73.06% that arrived during 2012 – 2013 already had the disease but did not know about it before, due to the slow onset of T2DM. People received a medical evaluation upon registering in the camp and the onset of disease can possibly be associated with that. As mentioned before, studies have argued that stress and poor psychological health can be a risk factor for onset of T2DM through increased insulin resistance with activation of the HPA – axis. Could this be what we have seen amongst the population in camp Domiz 1? Is this increase in diabetes mellitus a consequence of the war? Another aspect to consider is lifestyle as a refugee and its impact on health. As much as 72.73% of the patients with T1DM and 58.55% with T2DM reported decreased physical activity comparing life before and after seeking refuge. The longer they had lived in the camp, the more they reported on being less physically active. Being married, being a male and living many people within the same household seemed to reduce reports on decreased physical activity. Physical activity is a concept that is restricted to some sense in parts of the MENA region. Depending on culture and religion women are commonly among those affected. We did therefore evaluate how the patients considered their lifestyle before taking refuge and how they considered it being now. Our results showed that women were significantly less physically active today compared to male patients

but this had not been the situation before they took refuge. The question is what contributed to this change? If these people were from rural areas, with agricultural work and chores requiring more daily physical activity before they fled, their current living situation in tents and small brick houses could be a substantial alteration.

We gathered information about dietary habits but the concept of macronutrients was not clear to the subjects and many did not know what they were answering to. We did therefore not consider this data reliable. The problem with unreliability of data could have been avoided if posing the questions with more specificity, possibly detailed descriptions and more concrete alternatives. The patients could have been given an Eat Well Plate to evaluate compared to their own diet habits. The collection of dietary information did however reveal other problematic conditions like patients believing it was better for their diabetes to skip some meal per day or that some did not eat certain meals because they could not afford it or for other unspecified reasons. As the patients did not understand the concept of main constituents of a meal, as some thought not eating would help their disease and many seemed surprised or irritated over the question of dietary habits – seeming to not understand why it was asked, we came to the conclusion that diet was an area that needed more focus and implementation in the treatment strategy of diabetes mellitus. Diabetes education could most probably improve understanding of disease. The refugees had Food Aid Programs from different organizations that gave them a certain amount of money per person with which they could buy groceries from the camp supermarket. They were in charge of what they were buying in that store so with improved disease education there could be room for patient inducted lifestyle changes. The supplies in the supermarket were not assessed. Consequently a patient that has a more profound understanding for her/his disease could feel more in charge of their own life and take more responsibility in regards to disease management.

Given the general idea of war and refuge one could believe that BMI at levels of underweight would be the main problem within a population like this. The results obtained raised questions. The patients with T1DM were in majority within normal range BMI. Among the T2DM population there were only 8.81% within normal range and as much as 47.67% were overweight and 40.93% were obese. What factors in this war and among these people's consequent environment were contributing to this unhealthy lifestyle? Had they been overweight and obese before the war? Comparing our data to the World Health Organization's Global Data Base on Body Mass Index[44] we found that 25.90% of the females in Aleppo had normal range BMI in 2004, however 27.70% were overweight and 46.40% were obese. The BMI ranges among the males in Syria during 2004 was 34.40% within normal range, 36.90% overweight and 28.80% obese. Our results showed that high BMI was associated to female gender and was inversely related to age, with younger patients having higher BMI. When comparing to

the data from Syria in 2004 it appears that the problem was prevalent even before the war, however there were distinctly less people with normal BMI among our studied population in 2016. The issue of BMI in the MENA region complex with many factors intertwined. Cultural and religious backgrounds may be playing an important role with regards to lifestyle restrictions with women commonly be the main victims of these circumscriptions. Education could be one of the main influencing factors as the data from Syria in 2004 showed; students, people with higher socioeconomic status (SES) scores and employed individuals had among the highest percentage of normal BMI. This is an interesting topic that should be considered more often when discussing chronic diseases in the MENA region. Many argue that we need to respect other cultures and religious lifestyles, but that should not stop us from focusing more on disease prophylaxis in this region with long-term benefits in sight. Resources will be scarce every now and then, access to medications will be restricted depending on the political situation in the region - which is one that cannot be guaranteed anytime soon - and people will, as they have done during this war, die because of lack of medications and education. Decreased physical activity, insufficient understanding of the role of diet in disease management, continuous stress and poor psychological health might be the factors aggravating or even initiating insulin resistance, creating a negative loop leading to increases in BMI which further leads to insulin resistance and so on.

Glycemic control was not managed well among either of the diabetes types. The mean HbA1c was 9.35% and 8.80% in the T1DM and T2DM groups respectively. There were 81.82% with T1DM and 62.18% with T2DM that had bad glycemic control. Bad control among patients with T1DM was positively correlated to absent arteria dorsalis pedis, dry skin, macerations and hyperkeratosis on the lower extremities. These patients were also more prone to have higher total cholesterol levels. T2DM patients with bad glycemic control had lower HDL levels. All patients in the study were on treatment with hypoglycemic agents, T1DM with insulin and T2DM with 59.37% on dual therapy with Metformin and either a sulfonylurea, dipeptidyl peptidase – 4 or insulin. Yet this was not sufficient. The camp doctor at the primary health care center for non – communicable diseases explained that those 4 patients with T1DM who were treated with NPH + regular insulin initially had Insulin Mix but their insulin was changed due to lack of sufficient stocks of Insulin Mix.

Pharmacological management of micro and macrovascular complications was attempted. There were 9.09% and 49.74% on treatment with statins among patients with T1DM and T2DM respectively, yet the majority had not obtained normal lipid levels. Atorvastatin treatment in T2DM did however appear to be significantly correlated to lower levels of TG. The patients with T2DM and hypertension were on antihypertensive treatment. There were 43.93% on dual therapy, 17.76% were on triple therapy and 1.87% were on quadra therapy, yet the blood pressure among this population was well controlled in only 54.92% - putting the population at a significantly increased risk of

cerebrovascular events. The White Coat Syndrome or other stressing factors on individual level were not further evaluated in this study, but 2 patients among the 204 evaluated mentioned that they had a well-known White Coat Syndrome.

Nephropathies in CKD stages 1 and 2 were not evaluable due to lack of urine tests in the patients. We tried to include urine tests in our study but did not manage due to limited resources available. The results on analysis of nephropathies did however show that T1DM patients were prone to have increased CKD stages if they were living in tents or if they had left Syria during later years. Patients with T2DM who were single, divorced, widowed, had many children or were females had a higher likelihood of having higher CKD stages. We could see that 12.44% of patients with T2DM had CKD stage 3, indicating moderately reduced kidney function. Serum albumin levels could not be of clear value due to lack of urine tests as low serum albumin can be caused by other conditions, there among malnutrition. Having had the possibility to conduct urine test analysis the results on nephropathy analysis as a diabetic complication could have been more profound.

Many patients in both groups complained of numbness/tingling in the lower extremities. Age was a risk factor for abnormal proprioception and monofilament test results in patients with T1DM and having more children made the patients more prone to have worse outcomes on peripheral polyneuropathy testing both among patients with T1DM and in those with T2DM. The test results from patients with T2DM showed that the later the onset of disease and the higher the ABI, the better were the results of monofilament testing and less were the complaints of numbness/tingling in the lower extremities. Higher ABI leaves us with better extremity circulation possibly meaning less deterioration of vasa nervorum and hence later onset of complications involving peripheral polyneuropathies. Having more children being a risk factor we could argue that its correlation to higher BMI and hence further insulin resistance causes worse diabetic control which in turn increases the risks of peripheral polyneuropathies.

Assessing peripheral arterial disease the results showed that individuals with T2DM whom had left Syria in later years had higher ABI suggesting that the living conditions in the camp were inferior to the individual's previous settings. Patients with T1DM had a significant correlation between lower ABI and dry skin, while those with T2DM showed no such correlation. The reason for the dry skin and cracked soles in patients with T2DM could be caused by other conditions as they were walking around in slippers, with no socks on, in sand and gravel streets. Patients with lower ABI were more prone to present with absent or weak arteria dorsalis pedis, decreased temperature or pallor on the lower extremities, suggesting that the clinical findings of PAD were indeed related to lower ABI. The results of reported decreased visual acuity was in retrospective considered too subjective to imply a diabetic complication and could be related to other age-related degenerative ophthalmological conditions. The

results were hence considered not reliable. The question about decreased visual acuity was initially included because we were hoping to be able to check for retinopathies. This was however not possible due to limited resources and time.

Assessment of hypoglycemia and diabetic ketoacidosis was assessed by only asking the patients if they ever had episodes of either of the previously mentioned. These results were not reliable as we had not defined either of the two for the patients, meaning that many of them could have answered without knowing what the question actually was implying. The patients with T1DM did describe their episodes of diabetic ketoacidosis as those times when they had been emergently transported to the hospitals due to their high blood sugar levels. All stated that it was the way they got their diagnosis in the first place.

Complications were not studied as independent diseases, not being secondary to diabetes. With that done it would have been more clear whether these conditions were secondary to bad diabetes management and hence a complication versus if the diseases were primary. This was however not investigated further as such an analysis would be beyond the scope of this paper.

We are facing the biggest humanitarian crisis of our times and its consequent effects on health. It is understandable that victims of war focus less on healthy lifestyle-issues while trying to survive. They do most often not have the necessary means, not materialistically nor knowledge wise, for implementing necessary measures. Stress and poor psychological health is, as many have argued before, a large contributing factor to many chronic diseases. With our study we would like to bring forward how the onset of disease could be related to the debut of the Syrian war. We would like to argue that helping these people getting back to their routines and their lives should be the main focus of the international community. Seeking refuge starts as a temporary action that in many cases results in permanent relocation. The relocation brings with it enormous amounts of stress with adaptation difficulties, cultural differences, language barriers and other problems that in the long run, as the cross-sectional total population study done on Turkish immigrants in Sweden[45] shows. Those factors can in turn be a possible cause of increased insulin resistance and less healthy lifestyles. The international community should focus on helping the refugees to help themselves. We should work hard to enable these people a return to the place that they call home. A return to the land that they long after, the comfort and security that no other place could offer them.

CONCLUSION

This is the first study of its kind that has looked specifically at displaced diabetic victims of the Syrian war. The prevalence of diabetes mellitus within camp Domiz 1 was 0.80%. Results showed that risk factors for development of disease complications were: long duration of residency within the camp; high BMI, decreased physical activity and bad glycemic control. The diabetic control parameters were assessed by HbA1c for the study. Results showed that both T1DM and T2DM had bad glycemic control. Pharmacological therapy for glycemic control was insulin for T1DM and mainly dual therapy with biguanides and sulfonylureas for T2DM patients. Diabetic complications presented as nephropathies, peripheral polyneuropathies, hypertension, dyslipidemia and PAD. The complications were insufficiently controlled despite pharmacological therapies with statins and anti-hypertensive agents. Prevalence of complications were less among those who had left Syria during later years - suggesting significant lifestyle modifications and severe mental distress associated with life within the camp. Among the refugees that participated in the study 45.45% and 61.66% with T1DM and T2DM respectively got their diagnosis after the year of 2011 – the year the Syrian war started.

PRACTICAL RECOMMENDATIONS

Diabetes is a well-pronounced problem in the MENA region, as in the rest of the world. With the area being a conflict zone inducing more stress and poor psychological health in the population, we may expect to see an even faster rise in the incidence of diabetes. Challenges posed by diabetes require a patient-education treatment approach. As we have seen in the results, glycemic and lipid control as well as control of complications have not been achieved by pharmacological therapy, once again underlining the importance of patient-education to involve, encourage and enable patients to take responsibility in regards to lifestyle modification and prophylaxis. Assessment of patient-knowledge regarding disease and exacerbating factors could be an interesting topic for future research.

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ANNEX

Scheme of the plantar surface of feet with locations for monofilament screening.