

# A Real-World Consensus on Management of Type 2 Diabetes Mellitus by Experts in Iraq

Abbass Almousawy<sup>1</sup>, Atheer Alyass<sup>1</sup>, Mahmoud Shakeer<sup>1</sup>, Gelal Altaiee<sup>1</sup>, Abdul Munem Dabagh<sup>1</sup>, Baker Alhajami<sup>1</sup>, Muqdad Alkuzaie<sup>1</sup>, Ammar W. Ashor<sup>1</sup>, Ali Alsaiedy<sup>2</sup>, Raed Sabri<sup>1</sup>, Anwar Tuama<sup>1</sup>, Haider Aladresi<sup>1</sup>, Sherwan Bahaa<sup>2</sup>, Uday Almaliky<sup>2</sup>, Mohammed Qasim Alwash<sup>2</sup>, Hasan Mortada<sup>1</sup>, Ayad Khazal<sup>1</sup>, Salim Marzoki<sup>1</sup>, Sabah Alhelw<sup>2</sup>, Majeed Al Rufaieey<sup>2</sup>, Ali Hussain<sup>3</sup>, Abbas Ali Mansoor<sup>2</sup>, Shirley Dsouza<sup>4†</sup>

## ABSTRACT

**Background:** Diabetes has reached epidemic status in Iraq over the last decade.

**Methodology:** The modified Delphi method was used to develop the best practice recommendations for the management of type 2 diabetes for adults in a real-world setting in Iraq. Diabetologists, Cardiologists, Nephrologists, Dieticians, and Physicians with clinical expertise in the management of T2DM were invited to participate in this consensus program.

**Results:** Obesity in the T2DM population in Iraq must be addressed concomitantly with diabetes by the initiation of measures to reduce abdominal obesity by lifestyle modification. Patients with established ASCVD or indicators of high ASCVD risk must be given optimum tailored therapy. SGLT2 inhibitors were recommended by clinical experts as the first choice in diabetic kidney disease patients in accordance with the ADA guidelines. Initiate treatment with Dapagliflozin /SGLT2i with proven CV benefits to reduce recurrent CV events/ hospitalizations due to heart failure.

**Conclusion:** There is a discrepancy in the diagnosis and management of diabetes in Iraq, though it has a bulk of the world's diabetic population. In light of the recent ADA and ESC guidelines, there was a need to revisit the existing Iraqi consensus.

**Keywords:** Type 2 Diabetes, Consensus, Iraq.

## Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The huge majority of cases of diabetes fall into two broad etiopathogenetic categories, such as type 1 diabetes (T1DM), the cause is an absolute deficiency of insulin secretion and the much more prevalent category, type 2 diabetes (T2DM), the cause is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response.

Diabetes is broadly recognized as an evolving epidemic that has an increasing impact on almost every age group, country, and economy across the world. The chronic complications of diabetes are generally divided into microvascular (which is more prevalent, comprising of neuropathy, nephropathy, and retinopathy) and macro vascular comprising of cardiovascular disease (CVD), stroke, and peripheral artery

disease (PAD). Another complicated outcome of diabetes is the diabetic foot syndrome which has been defined as the presence of foot ulcer associated with neuropathy, PAD, and infection, and it is a major cause of lower limb amputation [1-2].

As per the ADA 2022 guidelines, the HbA1c (glycated hemoglobin) goal for many nonpregnant adults of <7% (53 mmol/mol) without significant hypoglycemia is appropriate. According to a study, it was observed that more than 70% of patients were not meeting the recommended HbA1c goal of less than 7%. In the UKPDS 35 prospective observational study by Stratton IM and colleagues, it was shown that each 1% reduction in updated mean HbA1c was associated with reductions in risk of 21% for any endpoint related to diabetes, 21% for deaths related to diabetes, 14% for myocardial infarction, and 37% for microvascular complications.

**Received:** 24-April-2023, Manuscript No. IJOCS-23-96883;  
**Editor assigned:** 27-April-2023, PreQC No. IJOCS-23-96883(PQ);  
**Reviewed:** 29-April-2023, QC No. IJOCS-23-96883(Q); **Revised:** 30-April-2023, Manuscript No. IJOCS-23-96883(R);  
**Published:** 30-April-2023;  
DOI: 10.37532/1753-0431.2022.17(4).291

<sup>1</sup>Department of Internal Medicine, National Diabetes Center, Mustansyriah University, Iraq

<sup>2</sup>Department of Medicine, University Of Baghdad, Iraq

<sup>3</sup>Department of Internal Medicine, Babylon University, Iraq

<sup>4</sup>Senior Manager, Medical Services, Ajanta Pharma, India

\*Author for correspondence: Shirley Dsouza, Senior Manager, Medical Services, Ajanta Pharma, Mumbai, India E-mail: drdsouza2023@rediffmail.com

As per IDF (International Diabetes Federation) 2021 data, diabetes is spiralling out of control with 537 million people between the ages of 20 and 79 years being affected with diabetes worldwide. This means that 1 in 10 adults are living with diabetes. As per the IDF MENA (Middle East and North Africa) region data of 2021, about 73 million adults (20-79 years) have been estimated to be living with diabetes.<sup>6</sup> The MENA region is expected to have the second highest expected increase of 86% in the number of people with diabetes reaching 136 million by 2045.

Consistent with worldwide trends for the prevalence of diabetes mellitus, it was reported that diabetes has reached an epidemic status in Iraq over the last decade, with a dramatic (115%) increase from 19.58/1000 in the year 2000 to 42.27/1000 in 2015. Therefore, diabetes is a main public health concern in Iraq given its high prevalence rate, increasing incidence rate, and overall economic burden. DM is considered as a principal cause of death in most developing countries, especially in Iraq and this may be accredited to uncontrolled hyperglycemia, which is related with many serious complications such as renal failure and cardiovascular disorders.

Looking at the tertiary care database analysis over a 9-year period from the largest cohort of T2DM patients from Iraq by Mansour AA and colleagues, showed that poor glycemic control in Iraqi patients with an HbA1c target (<7%) was achieved by only 13.8% of patients who were followed up for an average of 3.2 years and were under oral antidiabetic (OAD) treatment alone or in combination with insulin therapy. The findings of this cohort study, emphasized the need for improved diabetes care practices in Iraq, with considerations for tailored treatment strategies and continuous education programs as well as the development of healthcare strategies and national system-based approaches to update and prioritize diabetes screening and management across the country to overcome the barriers of inadequate glycemic control [3-8]

The present consensus report aims to address issues in the management approach of diabetes in the adult population in Iraq in order to reach the set glycemic target along with the issues of reduction of both the microvascular and macrovascular complications associated with diabetes. The focus is on comprehensive and patient-centred management of type 2 diabetes. These recommendations are not applicable to

patients with monogenic diabetes, secondary diabetes, type 1 diabetes, children or pregnant and lactating women.

#### ■ Scope and purpose of the consensus

There is a discrepancy in the management of patients with type 2 diabetes in Iraq, with it being not optimal and not uniform.<sup>8</sup>, the objective of this consensus is to provide evidence-based and practical recommendations for the management of type 2 diabetes in Iraq based on clinical expert recommendations. This consensus is developed for the real-world setting to enable healthcare professionals to optimize the management of type 2 diabetes in the Iraqi adult population.

#### ■ Identifying the evidence

The clinical experts (Diabetologists, Cardiologists, Nephrologists, Dietician, Physicians) conducted a systematic search using Ovid MEDLINE based on the predefined scope of the consensus. The search keywords included type 2 diabetes, management, Iraq, guidelines.

---

### Methodology

The modified Delphi method was used to develop the best practice recommendations for the management of type 2 diabetes for the adults in the real-world setting in Iraq. Diabetologists, Cardiologists, Nephrologists, Dieticians, and Physicians with clinical expertise in the management of T2DM were invited to participate in this consensus program. The modified Delphi method was adopted for arriving at the consensus statements. The statements were developed over a span of 2 rounds of discussions and reviews. In round 1, the expert guidance of a core group of clinical experts from Iraq was taken to prepare the questionnaire for the survey. Round 2 consisted of dissemination of the questionnaire to the clinical experts who were asked to answer the questions by polling during a meeting. Along with the questionnaire, references from literature were disseminated for the clinical experts to study. Their answers to the questions were analysed. More than 70% concurrence for an answer by voting was taken as a positive indicator for inclusion in framing of the consensus statements. The statements were disseminated via an email to the clinical experts to seek their final comments and suggestions. The consensus document was finalized after incorporating the review comments from the clinical experts.

The modified Delphi method has defined the methodology to develop consensus recommendations by enlisting the participation of experts as shown in **Figure 1**.

The consensus statements were framed under the 4 sections namely:

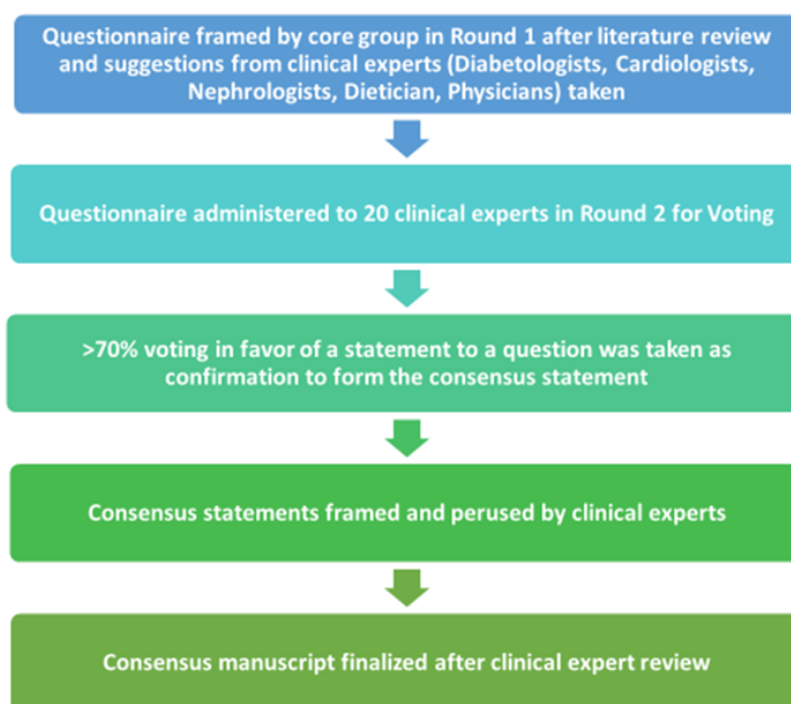
1. A Diabetologist's Perspective: Regarding the Management of Diabetes in Iraq.
2. The Cardiologist's perspective: Regarding the Management of Diabetes and CVD.
3. The Nephrologist's Perspective: Regarding Diabetes and CKD (Chronic Kidney Disease).
4. The Dietician's Perspective: Regarding Diet, Lifestyle modification and Weight management in type 2 diabetes.

#### ■ A Diabetologist's Perspective: Regarding the Management of Diabetes in Iraq

There is an increased prevalence of diabetes in Middle Eastern countries including Iraq. During the consensus meeting, the clinical experts agreed that the prevalence of diabetes is high in the Middle East and in Iraq with no gender disparity. In Iraq, the treatment of diabetes is glucocentric. The American Diabetes Association's (ADA) Standards of Medical Care

in Diabetes 2022 and ESC (European Society of Cardiology) 2019 guidelines have laid emphasis on comorbidities, prevention of cardiovascular, renal and cerebrovascular complications. The recommendation by guidelines regarding the use of SGLT2i (Sodium/glucose cotransporter-2 inhibitors) based on the observations from the CVOTs (Cardiovascular Outcome Trials), has been the turning point in the management of diabetes-related complications [9-13]

During the consensus meeting, the clinical experts agreed that issues faced by diabetologists in Iraq encompass the spectrum from diagnostic tests to the treatment of diabetes. Variations in HbA1c test values between different laboratories are attributed to different methodologies followed as mentioned in previous publication as well. Reaching the ADA defined HbA1c targets in the elderly population is an issue due to the increase in the prevalence of early morning headache which signifies hypoglycemia. The dilemmas faced by clinicians treating diabetes include weight gain, dyslipidemia, cardiac and renal complications. Anxiety and depression are also observed in the patients with diabetes in Iraq. The clinical experts agreed that a multidisciplinary approach is warranted to treat diabetes and the comorbid disorders including mood disorders and gastrointestinal disorders as well.



**Figure 1:** The modified Delphi method followed for framing the consensus statements.

■ **How do we address drivers of insulin resistance in Iraqi population?**

**The evidence**

Insulin resistance (IR) is caused by an excess of metabolic changes in lipid, glucose and hormone status as well as chronic oxidative stress and a chronic inflammatory state. The main outcomes comprise, but are not limited to, increased risk of CVD, alterations in lipid and glucose metabolism, and lower quality of life in general. The metabolic impact of IR includes resulting hyperglycemia, elevated blood pressure, dyslipidemia, visceral adiposity, innate and chronic inflammatory responses, endothelial layer function impairment, and dysregulation of the homeostasis balance. In the DPP (Diabetes Prevention Program), it was demonstrated that the lifestyle intervention reduced the incidence by 58% and metformin by 31%, as compared with placebo; the lifestyle intervention was significantly more effective than metformin.

Data from a 2015 nationally representative cross-sectional survey of 3916 persons 18 years or older in Iraq, indicated that about 31.8% of the adult population were overweight while 33.9% of the population were obese with a higher proportion of women being obese as compared to men. The incidence of type 2 DM is increasing and this has been attributed in part to a Western style diet, increasing obesity and sedentary lifestyle. Excess central adiposity can lead to insulin resistance, which when combined with hyperinsulinemia can lead to metabolic syndrome. Metabolic syndrome among Iraqi obese is relatively common with female gender, old age, and multiparity as risk factors.

**The expert opinion**

The response generated on the questionnaire on “how do we address drivers of insulin resistance in Iraqi population?” is shown in the **Table 1** below.

The initiation of measures to reduce abdominal obesity by lifestyle modification was recommended by 92% of the clinical experts followed by an early initiation of insulin

sensitizer drugs by 42%. The early recognition of non-alcoholic fatty liver disease (NAFLD) was recommended by 33% of the clinical experts.

**Expert Consensus statement:** Obesity in the T2DM population in Iraq must be addressed concomitantly with diabetes by the initiation of measures to reduce abdominal obesity by li

■ **Optimum therapy of type 2 diabetes patients in Iraq: Why, Who, How?**

**The evidence**

The primary goals of optimum therapy are to achieve/maintain near normoglycemia concomitant with preservation of beta cell function and improvement in insulin resistance. Majority of patients with T2DM have a probability to experience some form of cardiac or renal complication late in the course of disease, treatment with drugs that decelerate processes of ASCVD (atherosclerotic cardiovascular disease), CHF (congestive heart failure) and CKD are clearly indicate early on to reduce clinical events and mortality.

The ADA 2022 guidelines have recommended that an early combination therapy can be considered in some patients at treatment initiation to extend the time to treatment failure. When HbA1c is  $\geq 1.5\%$  (12.5 mmol/mol) above the glycemic target, many patients will require dual combination therapy to achieve their target HbA1c level. In individuals with T2DM and established ASCVD or with high cardiovascular (CV) risk, established kidney disease, or heart failure, a SGLT2i and/or glucagon-like peptide 1 receptor agonist (GLP1-RA) with demonstrated cardiovascular disease benefit is recommended in the glucose lowering treatment regimen. Emerging data suggest that use of both classes of drugs will offer additional cardiovascular and kidney outcomes benefit; thus, combination therapy with an SGLT2 inhibitor and a GLP1-RA may be considered to provide the complementary outcomes benefits associated with these classes of medication [12].

**The expert opinion**

The response generated on the questionnaire on

**Table 1. Poll response of “How do we address drivers of insulin resistance in Iraqi population?”**

Q. No.	Questions	Options	Poll (% response)
1.	How do we address drivers of insulin resistance in Iraqi population?	a. Initiate measures to reduce abdominal obesity by lifestyle modification.	92%
		b. Reduce ectopic fats stores and increase lean muscle mass.	17%
		c. Early initiation of insulin sensitizer drugs.	42%
		d. Address dyslipidaemia with statins, fibrates.	8%
		e. Early recognition of Non-alcoholic fatty liver disease (NAFLD).	33%

“optimum tailored therapy of type 2 diabetes patients in Iraq: Why? In Whom? How?” are shown in the **Tables 2** below.

During the poll, 71% of the clinical experts agreed that patients with established ASCVD or indicators of high ASCVD risk must be given optimum tailored therapy whereas 64% recommended optimum tailored therapy in patients with HbA1c levels 1.5–2.0% above target. Fifty three percent of the clinical experts opined that dual/ combination therapies either oral or injectable are largely superior to monotherapy. Every 1% decrease in HbA1c results in reduced risk of morbidity/mortality was agreed upon by 40% of the clinical experts. 33% experts opined that initial combination therapy is superior to sequential addition of medications for extending primary and secondary failure.

#### Expert Consensus statements:

- Patients with established ASCVD or indicators of high ASCVD risk must be

given optimum tailored therapy.

- For patients with CKD or clinical heart failure and atherosclerotic CVD, an SGLT2 inhibitor with proven benefit should be considered.

#### ■ The Cardiologist's perspective: Regarding the Management of Diabetes and CVD

Cardiovascular disease ranks as the leading a cause of death in Iraq. In a cross-sectional study conducted in Iraq, it was shown that the most prevalent risk factor was hypertension (55.3%), followed by dyslipidemia (42.7%), type 2 diabetes mellitus (29%), smoking (11%) and ex-smoking (9.3%) in 300 adult patients with coronary artery disease.

Diabetes has long been considered a “cardiovascular risk equivalent”. The relative risk of CVD mortality for patients with diabetes ranges from 2.83 to 4.46 according to the level

**Table 2. Poll response of “optimum therapy of type 2 diabetes patients in Iraq: Why?”**

Q. No.	Questions	Options	Poll (% response)
2.a.	Early optimum therapy of type 2 diabetes patients in Iraq: Why?	a. Due to lack of infrastructure, social and religious constraints, strict lifestyle changes may be not achievable for most patients in Iraq.	53%
		b. Medical Nutrition Therapy (MNT) is only sporadically implemented in Iraq due to the limited number of dieticians.	27%
		c. Every 1% decrease in HbA1c results in reduced risk of morbidity/mortality.	40%
		d. Initial combination therapy is superior to sequential addition of medications for extending primary and secondary failure.	33%
		e. Risk of long-term complications reduced significantly by modulating metabolic memory.	33%
		f. Initial combination therapy is associated with slower decline of glycaemic control compared with sequential therapy.	20%
		g. Dual/ combination therapies either oral or injectable are largely superior to monotherapy.	53%

**Table 3. Poll response of “optimum therapy of type 2 diabetes patients in Iraq: In Whom?”**

Q. No.	Questions	Options	Poll (% response)
2.b.	Optimum tailored therapy of type 2 Diabetes patient in Iraq: In Whom?	a. HbA1c levels 1.5-2.0% above target	64%
		b. Presence of established ASCVD or indicators of high ASCVD risk.	71%
		c. Patients with HF.	14%
		d. Patients with LVH.	21%
		e. Patients with CKD.	29%

HF: Heart failure; LVH: Left ventricular hypertrophy.

**Table 4. Poll response of “optimum therapy of type 2 diabetes patients in Iraq: How?”**

Q. No.	Questions	Options	Poll (% response)
2.c.	Optimum therapy of type 2 diabetes patients in Iraq: How?	a. Assess CV risk in the patient.	57%
		b. Combination with SGLT2i in high CV risk, HF patient.	43%
		c. Combination with GLP-1 receptor agonist with proven CV benefit.	29%
		d. Combination with SGLT2i/ DPP4i to increase HbA1c reduction.	7%
		e. For patients with CKD or clinical heart failure and atherosclerotic CVD, an SGLT2 inhibitor with proven benefit should be considered.	79%

DPP4i: Dipeptidyl peptidase 4 inhibitors.

of cholesterol. Thus, cholesterol is a strong and independent risk factor for CVD mortality, which is potentiated by diabetes. Hypertension and diabetes mellitus demonstrate rapidly rising trends which may, in turn, augment the occurrence of ischemic heart diseases and cerebrovascular accidents.

**■ Do you recommend a resting ECG to be taken in all type 2 diabetes patients?**

**The evidence**

The ESC 2019 guidelines recommend resting ECG in patients with diabetes with hypertension or suspected CVD. A resting ECG may detect silent MI in 4% of individuals with DM, which has been associated with increased risk of CVD and all-cause mortality in men but not women. The ESC 2019 guidelines also recommend that routine assessment of microalbuminuria is indicated to identify patients at risk of developing renal dysfunction or at high risk of future CVD.

**The expert opinion**

The response generated on the questionnaire on “do you recommend a resting ECG to be taken in all type 2 diabetes patients?” is shown in the **Table 5** below.

The opinion was equally divided among the clinical experts for recommending a baseline ECG in all T2DM patients.

**■ How can recurrent CV events / hospitalization for heart failure be reduced?**

**The evidence**

Tighter glucose control initiated early in the course of DM in younger individuals leads to a reduction in CV outcomes over a 20-year timescale. It was mentioned in the ESC 2019 guidelines that it is recommended to apply tight glucose control targeting a near-normal HbA1c (<7.0% or <53 mmol/mol), to decrease microvascular complications in individuals with DM. Also, SGLT2 inhibitors (dapagliflozin, empagliflozin, canagliflozin) are recommended to lower risk of HF hospitalization. Metformin should be considered in patients with DM and HF if eGFR (estimated glomerular filtration

rate) >30 mL/min/1.73 m<sup>2</sup>. GLP1-RAs and DPP4 inhibitors (sitagliptin and linagliptin) have a neutral effect on risk of HF and may be considered. Insulin treatment in HF may be considered and DPP4 inhibitor saxagliptin in HF is not recommended. Thiazolidinediones (pioglitazone and rosiglitazone) in HF are not recommended.

The SGLT2 inhibitors canagliflozin, dapagliflozin, empagliflozin, ertugliflozin and sotagliflozin were studied in patients with established CV disease in the EMPA-REG OUTCOME and VERTIS-CV trials, with established CV disease or CV risk factors in the CANVAS and DECLARE-TIMI 58 trials, and with CKD and CV risk in the SCORED trial, respectively. In a meta-analysis of these trials and one further trial in patients with CKD (CREDENCE), overall SGLT2 inhibitors reduced HF and CV hospitalization by 22%. As per the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, sotagliflozin) recommended in patients with diabetes at high risk of CV disease or with CV disease in order to prevent HF hospitalizations (Class I recommendation). SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin and sotagliflozin) are also recommended in patients with T2DM at risk of CV events, end-stage renal dysfunction, and CV death (Class I recommendation). SGLT2 inhibitors (dapagliflozin, empagliflozin, and sotagliflozin) are recommended in patients with T2DM and HFrEF to reduce hospitalizations for HF and CV death (Class I recommendation) [13-28]

**The expert opinion**

The response generated on the questionnaire on “how can recurrent CV events / hospitalization for heart failure be reduced?” is shown in the **Table 6** below.

Additionally, the Experts opined that CKD could be a marker for recurrent CVD risk

**Expert Consensus statements:**

Mapping of patients at risk of recurrent CV events

Q. No.	Questions	Options	Poll (% response)
3.	Do you recommend a resting ECG to be taken in all type 2 diabetes patients?	A. Yes.	50%
		B. No.	50%

ECG: Electrocardiogram.

by using clinical markers: T2DM duration, History of retinopathy and/or neuropathy.

Initiate treatment with Dapagliflozin /SGLT2i with proven CV benefits to reduce recurrent CV events/ hospitalizations due to heart failure.

### The Nephrologist's Perspective: Regarding Diabetes and CKD

Chronic kidney disease is defined as persistently elevated urine albumin excretion ( $\geq 30$  mg/g [3mg/mmol] creatinine), persistently reduced estimated glomerular filtration rate (eGFR  $< 60$  ml/min per 1.73 m<sup>2</sup>), or both, for  $> 3$  months. Worldwide, chronic kidney disease is a progressive condition that affects more than 10% of the general population amounting to  $> 800$  million individuals. CKD is more prevalent in older individuals, women, racial minorities, and in people experiencing DM and hypertension. Diabetic kidney disease (DKD) develops in  $\approx 40\%$  of patients who are diabetic and is leading cause of CKD worldwide. The natural history of DKD includes glomerular hyperfiltration, progressive albuminuria, declining GFR, and ultimately, end-stage renal disease (ESRD). The prevalence of ESRD is up to 10 times higher in people with diabetes.

From the findings of Global Burden of Disease 2015 study, it was observed that Disability-adjusted life years (DALYs) rates in Iraq of CKD due to DM was 25 in male and 28 in female. A study conducted in Iraq showed that diabetes mellitus (33%) and hypertension (22.6%) were the most common causes of chronic renal failure. A case-control study conducted in 300 persons (150 cases and 150 controls) in a tertiary care hospital in Iraq, indicated that patients with diabetes mellitus had 12.9-fold risk for developing of CKD and both type 1 and type

2 DM had significant role for developing CKD.

### ■ What percentage of your diabetes patients with reduced kidney function have normoalbuminuria (which could lead to misdiagnosis of DKD)?

#### The evidence

Renal insufficiency is associated with a considerably increased risk of mortality in T2DM patients. Almost 23.3%-56.6% of patients with T2DM and kidney function decline have normal albuminuria. Normoalbuminuric renal insufficiency is a strong predictor of mortality in individuals with T2DM.

#### The expert opinion

The response generated on the questionnaire on “what percentage of your diabetes patients with reduced kidney function have normoalbuminuria (which could lead to misdiagnosis of DKD)?” is shown in the **Table 7** below.

### ■ Which class of OHAs do you prefer as 1st choice in DKD patients?

#### The evidence

All types of diabetes are associated with increased risk of impaired kidney function (referred to as diabetic nephropathy or DKD). SGLT2 inhibitors exert a variety of effects on the kidney, directly and indirectly linked to reduced glucose reabsorption, providing acute and chronic nephro-protective effects that reduce progression and may partially reverse the characteristic markers of DKD. Several meta-analyses of clinical trial data have concluded that use of an SGLT2 inhibitor in T2DM reduces risk of acute kidney injury (AKI) by 30–40%, and analyses of data from ‘real world’ observational studies have showed reductions in risk of AKI by  $> 40\%$ .

**Table 6. Poll response of “How can recurrent CV events / hospitalization for heart failure be reduced?”**

Q. No.	Questions	Options	Poll (% response)
4.	How can recurrent CV events / hospitalization for heart failure be reduced?	a. Mapping of patients at risk of recurrent CV events by using clinical markers: T2DM duration, History of retinopathy and/or neuropathy.	0%
		b. Initiate treatment with Dapagliflozin /SGLT2i with proven CV benefits.	15%
		c. Both of the above.	85%

CV: Cardiovascular.

**Table 7. Poll response of “What percentage of your diabetes patients with reduced kidney function have normoalbuminuria (which could lead to misdiagnosis of DKD)?”**

Q. No.	Questions	Options	Poll (% response)
5.	What percentage of your diabetes patients with reduced kidney function have normoalbuminuria (which could lead to misdiagnosis of DKD)?	a. $< 10\%$ .	14%
		b. 11-20%.	43%
		c. 21-30%.	21%
		d. $> 30\%$ .	21%

In the EMPA-REG OUTCOME trial, the renal composite (doubling of serum creatinine,  $eGFR \leq 45$  ml/min/1.73 m<sup>2</sup>, initiation of renal replacement therapy or death from kidney disease) was reduced by 46% in the groups receiving empagliflozin. The DECLARE-TIMI 58 trial found that use of dapagliflozin was associated with a 47% reduction in a renal composite of a sustained decrease of  $eGFR$  by  $\geq 40\%$  to  $< 60$  ml/min/1.73 m<sup>2</sup>, new ESRD or death from a renal cause. Combined analysis of the CANVAS and CANVAS-R trials (CANVAS program) noted that use of canagliflozin reduced by 40% a renal composite of sustained ( $\geq 2$  consecutive measures) reduction (by  $\geq 40\%$ ) in  $eGFR$ , need for renal replacement therapy or death from renal causes. In the VERTIS CV trial, the renal composite, which did not include a measure of  $eGFR$  (doubling of the serum creatinine, starting renal replacement therapy or death from a renal cause), was numerically reduced by 19% (not statistically significantly) with use of ertugliflozin. A separate analysis of a renal composite comprising a sustained  $\geq 40\%$  reduction in  $eGFR$ , renal dialysis/transplant or renal death noted a 34% reduction with ertugliflozin, and by 5 years, the decline in  $eGFR$  was significantly less (by 2.6 ml/min/1.73 m<sup>2</sup>) than with placebo.[29-37]

The ADA 2022 guidelines recommend that optimal glucose control is required to reduce risk or slow progression of CKD. The ADA 2022 guidelines have mentioned that for patients with type 2 diabetes and DKD, use of a SGLT2 inhibitor in patients with an  $eGFR \geq 20$  mL/min/1.73 m<sup>2</sup> and urinary albumin  $\geq 200$  mg/g creatinine is recommended to reduce chronic kidney disease progression and cardiovascular events.

**The expert opinion**

The response generated on the questionnaire

on “which class of OHAs do you prefer as 1st choice in DKD patients?” is shown in the **Table 8** below.

**Expert Consensus statement:** SGLT2 inhibitors were recommended by the clinical experts as first choice in diabetic kidney disease patients in accordance with the ADA guidelines.

■ **How much is the reduction in albuminuria with SGLT2i?**

**The evidence**

Randomised clinical trials and ‘real world’ observational studies, mostly involving type 2 diabetes patients, have observed that use of an SGLT2 inhibitor can slow the decline in glomerular filtration rate (GFR), reduce onset of microalbuminuria and slow or reverse progression of proteinuria.<sup>37</sup> In patients with chronic kidney disease who have  $\geq 300$  mg/g urinary albumin, a reduction of 30% or greater in mg/g urinary albumin is recommended to slow chronic kidney disease progression as per ADA 2022 recommendations .[38]

**The expert opinion**

The response generated on the questionnaire on “how much is the reduction in albuminuria with SGLT2i?” is shown in the **Table 9** below.

A total of 83% clinical experts opined that SGLT2i reduced albuminuria by 30-50% in their patients.

**Expert Consensus statement:** SGLT2i can cause a significant reduction in microalbuminuria and reduce the decline in renal function in DKD patients.

■ **What is your approach to elderly patients with DKD?**

**The evidence**

Age-related metabolic and renal changes

**Table 8.** Poll response of “Which class of OHAs do you prefer as 1st choice in DKD patients?”

Q. No.	Questions	Options	Poll (% response)
6.	Which class of OHAs do you prefer as 1 <sup>st</sup> choice in DKD patients?	SGLT2i.	92%
		DPP4i.	0%
		GLP1RA.	8%
		Metformin.	0%

OHAs: Oral hypoglycaemic agents.

**Table 9.** Poll response of “How much is the reduction in albuminuria with SGLT2i?”

Q. No.	Questions	Options	Poll (% response)
7.	How much is the reduction in albuminuria with SGLT2i?	A. 30% to 50%.	83%
		B. <30%.	8%
		C. >50%.	8%



predispose older people to an augmented risk of DM and diabetic kidney disease, respectively. As the prevalence of the ageing population is increasing, because of increased life expectancy, the prevalence of older people with DKD is likely to increase. Diabetic kidney disease is associated with an increased risk of adverse outcomes. The management comprises of promotion of a healthy lifestyle and control of CV risk factors such as hyperglycaemia, hypertension and dyslipidaemia. Management in this age group should be individualized, based on a patient's functional level adopting tight metabolic control in the fit individual and relaxed targets in the frail person.

### The expert opinion

The response generated on the questionnaire on “what is your approach to elderly patients with DKD?” is shown in the **Table 10** below.

#### Expert Consensus statements:

- In elderly patients with DKD, recommendation comprised of promotion of a healthy lifestyle and control of CV risk factors such as hyperglycemia, hypertension and dyslipidemia.
- Management in elderly patients with DKD, should be based on a patient's functional level.
- Glycemic control can be tight in non-frail patients but, in frail patients, follow relaxed targets to avoid hypoglycemia.

**The Dietician's Perspective:** Regarding Diet, Lifestyle modification and Weight management in type 2 diabetes

There is strong and reliable evidence that obesity management is highly beneficial in the treatment of type 2 diabetes. In patients with type 2 diabetes and overweight or obesity, modest weight loss improves glycemic control and reduces need for glucose-lowering medications. Nutrient distribution should be based on an individualized evaluation of current eating patterns, preferences, and metabolic goals.[39-42]

As per ADA 2022 guidelines, diet, physical activity, and behavioral therapy to achieve and maintain  $\geq 5\%$  weight loss is recommended for most people with type 2 diabetes and overweight or obesity.<sup>40</sup> Vegetables, legumes, fruits, and wholegrain cereals should be part of a healthy diet. A Mediterranean diet supplemented with olive oil and/or nuts reduces the incidence of major CV events.

In a 2-year trial done by Shai I, et al., it was concluded that Mediterranean and low-carbohydrate diets may be effective alternatives to low-fat diets. The more favorable effects on lipids (with the low-carbohydrate diet) and on glycemic control (with the Mediterranean diet) suggest that personal preferences and metabolic considerations might inform personalized tailoring of dietary interventions.

### ■ What kind of meal for breakfast and dinner would be helpful in improving glycemic control?

#### The evidence

For individuals who are overweight or obese, weight loss is effective in preventing and improving the management of type 2 diabetes. Together with other lifestyle factors like exercise and behavior modification, diet plays a central role in achieving weight loss. Diets vary based on the type and amount of carbohydrate, fat, and protein consumed to meet daily caloric intake goals. A number of popular diets are reviewed as well as studies evaluating the effect of various diets on weight loss, diabetes, and cardiovascular risk factors. Current trends favor the low-carbohydrate, low-glycemic index, Mediterranean, and very-low-calorie diets.

According to the results of a meta-analysis, the low-carbohydrate, the low glycemic index, the high-protein and the Mediterranean diets all led to a greater improvement in glycemic control [HbA1c reductions of  $-0.12\%$  ( $p = 0.04$ ),  $-0.14\%$  ( $p = 0.008$ ),  $-0.28\%$  ( $p < 0.001$ ) and  $-0.41\%$  ( $p < 0.001$ ) respectively, compared with their respective control diets.

**Table 10. Poll response of “What is your approach to elderly patients with DKD?”**

Q. No.	Questions	Options	Poll (% response)
8.	What is your approach to elderly patients with DKD?	Promotion of a healthy lifestyle and control of CV risk factors such as hyperglycemia, hypertension and dyslipidemia.	0%
		Management in this age group should be based on a patient's functional level.	0%
		Adopt tight metabolic control in the fit individual.	0%
		Adopt relaxed targets in the frail person.	0%
		All of the above.	100%

**Table 11. Poll response of “What kind of meal for breakfast and dinner would be helpful in improving glycemic control?”**

Q. No.	Questions	Options	Poll (% response)
9.	What kind of meal for breakfast and dinner would be helpful in improving glycemic control?	Low carbohydrate, high fibre.	50%
		High protein.	0%
		Balanced diet.	50%

**Table 12. Poll response of “How can adherence to diet be improved?”**

Q. No.	Questions	Options	Poll (% response)
10.	How can adherence to diet be improved?	Tailor the diet as per the patient’s preferences with healthy substitution.	33%
		Increase patient awareness of importance of diet in diabetes control.	33%
		Explain the concept of glycaemic index to the patient / family members.	33%

**The expert opinion**

The response generated on the questionnaire on “what kind of meal for breakfast and dinner would be helpful in improving glycemic control?” is shown in the **Table 11** below.

About 50% of the clinical experts recommended a low carbohydrate, high fibre diet and the other 50% were in favour of a balanced diet.

**■ How can adherence to diet be improved?**

**The evidence**

The factors that drive type 2 diabetes occurrence and severity are unhealthy behaviours, including diet and physical activity, coupled with genetic predisposition. Guidelines constantly propose reducing energy intake to counteract the obesity epidemic, often resulting in sarcopenic obesity, a condition associated with poorer metabolic control and CVD. Various dietary approaches have been proposed with largely similar results, with a preference for the Mediterranean diet. The best practice being the diet that patients feel confident of maintaining in the long term based on individual preferences. Patient adherence is indeed the crucial factor for weight loss and long-term maintenance, requiring intensive lifestyle intervention.

The treatment of T2DM must be individualized, based on the patient's age, glycemic control, body weight, comorbidities, work situation, adherence, and personal priorities. Dietary interventions must be accompanied by 150 minutes or more of moderate- to vigorous-intensity aerobic activity per week spread at least 3 days/week with no more than 2 consecutive days without activity. It is preferable to offer the patient a diet plan that is individualized, practical, and acceptable rather than to focus on individual nutrients.

**The expert opinion**

The response generated on the questionnaire on “how can adherence to diet be improved?” is shown in the **Table 12** below.

**Discussion**

During this consensus programs, the Iraqi clinical experts agreed that since there is an increased burden of diabetes in the Middle East countries including Iraq, there is a necessity of conducting step-wise surveys in diabetes in order to manage the condition more optimally and appropriately. The treatment of diabetes is like an investment to prevent the future associated complications such as cardiovascular-related complications, nephropathy, neuropathy, and any others. A multi-disciplinary approach with collaboration of clinical experts from different specialities (such as Diabetologist, Cardiologist, Nephrologist, Dietician, Neurologist, Psychiatrist, Gastroenterologist, Podiatrist) is warranted for the optimal management of diabetes and its related complications and associated disorders. The Iraqi clinical experts agreed that steps need to be taken to recognise population in the prediabetic range and ensure they are managed appropriately, as diabetes occurs earlier in their population compared to other ethnic populations. The Iraqi clinical experts agreed that there is a lot of discrepancy in the HbA1c testing, which needs to be addressed.

During this consensus programs, the Iraqi clinical experts agreed that diet, lifestyle modification and weight management in type 2 diabetes play crucial roles in the overall management. Nutrition plays an essential role in diabetes as in the case of cardiovascular conditions. A generalized diet advice is not effective but the approach needs to be patient-centric keeping in mind available options in the local market, in addition to the patients likes/dislikes. The use of sweeteners is controversial with opposing evidences of its benefits. Foods with a low

glycemic index are considered beneficial as is the supplementation of vitamins in patients with diagnosed deficiencies. While providing dietary advice to a patient or their care giver, one must bear in mind that “no one shoe fits all” and only if a personalized nutrition is provided than a patient will be more compliant. Patients should be offered a variety of food options so that they can be consistent to the given dietary advice. Patient need to adopt a more active lifestyle and need to reduce a sedentary lifestyle by including some form of exercise per day or in a week. [43–48].

During this consensus programs, the Iraqi clinical experts agreed that smoking cessation is essential for the optimal management of diabetes. As reported in a study by Nilsson PM and colleagues, patients with type 1 and type 2 diabetes and smokers had a higher mean HbA1c compared to nonsmokers. In addition, smoking was associated with both poor glycaemic control and microalbuminuria, independently of other study characteristics.

Due to the cardio- and renal benefits of the newer anti-diabetic class of drugs such as SGLT2 inhibitors, DPP4 inhibitors, and GLP1-RA, there is a change in the management of diabetes as reflected in the current ADA 2022 and ESC 2019 guidelines. With the recent ADA 2022 and ESC 2019 guidelines emphasizing the need to recognise patients with different risk factors (ASCVD, HF, CKD), to better manage them, the clinical experts felt that it is essential to incorporate these guideline recommendations to treat diabetic patients in Iraq. In addition, it also essential to ensure that while treating the patients, side effects such as hypoglycemic events which hamper the proper management needs to be evaded. Keeping this in mind, the newer class of anti-diabetic agents such as DPP4 inhibitors, GLP1-RA and SGLT2 inhibitors which have a lower risk of hypoglycaemia along with their cardio-and renal benefits are considered valuable treatment options.

The clinical experts considered this is a fertile period for change in the outlook towards diabetes management focusing in a more patient-centric approach as advocated in the ADA 2022 guidelines. The following statements had a ≥50% agreement from the clinical experts who participated in the polling during the consensus program:

1. Due to lack of infrastructure, social and religious constraints, strict lifestyle changes may be not achievable for most patients in

Iraq.

2. Dual/ combination therapies either oral or injectable are largely superior to monotherapy.
3. HbA1c levels 1.5–2.0% above target needs to be considered for an optimum tailored therapy.
4. Assess CV risk in the patient
5. A resting ECG needs to be taken in all type 2 diabetes patients.
6. There was an equal consensus on the type of meal that would be helpful in improving glycemic control:
  - Low carbohydrate, high fibre.
  - Balanced diet.

### Conclusion

There is a discrepancy in the diagnosis and management of diabetes in Iraq, though it has a bulk of the world diabetic population. In light of the recent ADA 2022 and ESC 2019 guidelines, there was a need to re-visit the existing Iraqi consensus. The following statements had a more than 70% agreement from the clinical experts who participated in the polling during the consensus program:

1. Obesity in the T2DM population in Iraq must be addressed concomitantly with diabetes by the initiation of measures to reduce abdominal obesity by lifestyle modification.
2. Patients with established ASCVD or indicators of high ASCVD risk must be given optimum tailored therapy.
3. For patients with CKD or clinical heart failure and atherosclerotic CVD, an SGLT2 inhibitor with proven benefit should be considered.
4. Mapping of patients at risk of recurrent CV events by using clinical markers: T2DM duration, History of retinopathy and/or neuropathy.
5. Initiate treatment with Dapagliflozin / SGLT2i with proven CV benefits to reduce recurrent CV events/ hospitalizations due to heart failure.
6. SGLT2 inhibitors were recommended by the clinical experts as first choice in diabetic kidney disease patients in accordance with

the ADA guidelines.

7. SGLT2i can cause a significant reduction in microalbuminuria and reduce the decline in renal function in DKD patients.
8. In elderly patients with DKD, recommendation comprised of:
  - Promotion of a healthy lifestyle and control of CV risk factors such as hyperglycemia, hypertension and dyslipidemia.
  - Management in elderly patients with DKD, should be based on a patient's functional level.
  - Glycemic control can be tight in non-frail patients but, in frail patients, follow relaxed targets to avoid hypoglycemia.

## References

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes care.* 32,562(2009)
2. Papatheodorou K, Banach M, Bekiari E, et al. Complications of diabetes 2017. *J. diabetes res.*2018. [Crossref]
3. Chous A. 2022 updates to ADA standards of care for patients with diabetes.
4. Dietz CJ, Sherrill WW, Stancil M, Rennert L, Parisi M, McFall D. Health Extension for Diabetes: Impact of a Community-Based Diabetes Self-Management Support Program on Older Adults' Activation. *J. diabetes res.*36,59-68(2023).
5. Stratton IM, Adler AI, Neil HA, Matthews DR, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Bmj.*321,405-412(2000)
6. IDF Diabetes.
7. Al-Sebaei MO, Bamashmous M, Bassyoni L, Alsubaie R, Alnahdi DO. Pre-Procedure Blood Sugar Levels in Diabetic and High-Risk Patients Visiting King Abdulaziz University Dental Hospital: The Role of the Dentist in Diabetes Screening. *Diabetes Metab. Syndr. Obes.*1021-1027(2023).
8. Mansour AA, Alibrahim NT, Alidrisi HA, Alhamza AH, Almomin AM, et al. Prevalence and correlation of glycemic control achievement in patients with type 2 diabetes in Iraq: A retrospective analysis of a tertiary care database over a 9-year period. *Diabetes Metab. Syndr.: Clin. Res. Rev.*14,265-272(2020)
9. Mikhael EM, Hassali MA, Hussain SA, Shawky N. Self-management knowledge and practice of type 2 diabetes mellitus patients in Baghdad, Iraq: a qualitative study. *Diabetes metab. syndr.* 17,1-7(2018)
10. Abusaib M, Ahmed M, Nwayyir HA, Alidrisi HA, Al-Abbood M, et al. Iraqi experts consensus on the management of type 2 diabetes/prediabetes in adults. *Clin. Med. Insights: Endocrinol. Diabetes.* 1179551420942232(2020).
11. Alsairafi ZK, Taylor KM, Smith FJ, Alattar AT. Patients' management of type 2 diabetes in Middle Eastern countries: review of studies. *Patient prefer. adherence.* 10,1051-1062(2016).
12. Draznin B, Aroda VR, Bakris G, Benson G, Brown FM, et al. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2022. *Diabetes care.* 45,125-143(2021).
13. Cosentino F, et al; ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J.*41, 255-323(2020).
14. Wolosowicz M, Prokopiuk S, Kaminski TW. Recent advances in the treatment of insulin resistance targeting molecular and metabolic pathways: Fighting a losing battle?. *Medicina.*58, 472(2022).
15. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.
16. Pengpid S, Peltzer K. Overweight and obesity among adults in Iraq: prevalence and correlates from a national survey in 2015. *Int. j. environ. res. public health.*18,4198 (2021).
17. Ali NS, Allela OQ, Salih HM, Ahmed IH. Prevalence of Type 2 Diabetes Associated Complications in Kurdistan Region Iraq. *J. Basic Clin. Pharm.*10,(2023)
18. Saleh AA, Hayawi AH, Al-Samarrai AY, Lafta RK. Metabolic syndrome among obese adults in Baghdad, Iraq. *Saudi J. Obes.*5,1-8(2017).
19. Cersosimo E, et al. The evidence behind early aggressive multi-drug treatment in type 2 diabetes. *Trends Diabetes Metab.* 1-11(2021).
20. Mohammad AM, Rashad HH, Habeeb QS, Rashad BH, Saeed SY. Demographic, clinical and angiographic profile of coronary artery disease in kurdistan region of Iraq. *Am. J. Cardiovasc. Dis.*11,1-39(2021).
21. Bertoluci MC, Rocha VZ. Cardiovascular risk assessment in patients with diabetes. *Diabetol. metab. Syndr.*9,1-3(2017).
22. Hussain AM, Lafta RK. Burden of non-communicable diseases in Iraq after the 2003 war. *Saudi med. j.*40,1-72(2019).
23. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N. engl. j. med.*26,2117-2128(2015).
24. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med.* 1834-1844(2016).
25. Neal B, Perkovic V, Mahaffey KW, De Zeeuw D, Fulcher G, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N. Engl. J.*

- Med.377,644-657(2017).
26. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N. Engl. J. Med.*380,347-357(2019).
  27. Bhatt DL, et al; SCORED Investigators. Sotagliflozin in patients with diabetes and chronic kidney disease. *N Engl J Med.*384,129-139(2021).
  28. Cannon CP, Pratley R, Dagogo-Jack S, Mancuso J, Huyck S, et al. Cardiovascular outcomes with ertugliflozin in type 2 diabetes. *N. Engl. J. Med.*383,1425-1435(2020).
  29. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur. heart j.*42,3599-3726(2021).
  30. de Boer IH, Caramori ML, Chan JC, Heerspink HJ, Hurst C, et al. Executive summary of the 2020 KDIGO Diabetes Management in CKD Guideline: evidence-based advances in monitoring and treatment. *Kidney int.*98,839-848 (2020).
  31. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. *Kidney Int Suppl.* 12,7–11(2022).
  32. Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease: challenges, progress, and possibilities. *Clin. j. Am. Soc. Nephrol.* 12,2032-2045 (2017).
  33. International Diabetes Foundations.
  34. GBD 2015 Eastern Mediterranean Region Diabetes and Chronic Kidney Disease Collaborators. Diabetes mellitus and chronic kidney disease in the Eastern Mediterranean Region: findings from the Global Burden of Disease 2015 study. *Int J Public Health.* 63 ,S177–S186 (2018).
  35. Awad SM. Chronic renal failure in Al-Anbar of Iraq. *Saudi J. Kidney Dis. Transplant.*22,1280 (2011).
  36. Khaleel FF, Hussain SS, Hmood AH. Risk Factors of Chronic Kidney Disease among Patients Attending Ibn Sina Teaching Hospital in Mosul City. *Iraqi J. Med. Sci.*17, (2021).
  37. Li A, et al. Urinary NGAL and RBP are biomarkers of normoalbuminuric renal insufficiency in Type 2 Diabetes Mellitus. *J. Immunol.* 11,(2019)
  38. Bailey CJ, Day C, Bellary S. Renal protection with SGLT2 inhibitors: effects in acute and chronic kidney disease. *Curr. Diabetes Rep.* 22, 39-52 (2022).
  39. American Diabetes Association Professional Practice Committee; Draznin B, et al. 11. Chronic Kidney Disease and Risk Management: Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 45, S175-S184 (2022).
  40. Abdelhafiz AH. Diabetic kidney disease in older people with type 2 diabetes mellitus: improving prevention and treatment options. *Drugs Aging.* 37,567-584(2020).
  41. American Diabetes Association Professional Practice Committee; Draznin B, et al. 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care.*45,S113-S124 (2022).
  42. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, et al. Bolotin A, Vardi H, Tangi-Rozental O. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N. Engl. J. Med.*359,229-241(2008).
  43. Sandouk Z, Lansang MC. Diabetes with obesity--Is there an ideal diet. *Cleve Clin J Med.* 84,S4-14(2017).
  44. Georgoulis M, Kontogianni MD, Yiannakouris N. Mediterranean diet and diabetes: prevention and treatment. *Nutrients.* 6,1406-1423 (2014).
  45. Petroni ML, Brodosi L, Marchignoli F, Sasdelli AS, Caraceni P, et al. Nutrition in patients with type 2 diabetes: Present knowledge and remaining challenges. *Nutrients.*13,2748 (2021).
  46. Pfeiffer AF, Klein HH. The treatment of type 2 diabetes. *Deutsches Ärzteblatt International.* 111,69(2014).
  47. American Diabetes Association. Standards of Medical Care in Diabetes-2022 Abridged for Primary Care Providers. *Clin Diabetes.* 40,10-38 (2022).
  48. Cederholm J, Eliasson B, Nilsson PM, Weiss L, Gudbjörnsdóttir S, Steering Committee of the Swedish National Diabetes Register. Microalbuminuria and risk factors in type 1 and type 2 diabetic patients. *Diabetes res. clin. pract.*67,258-266 (2005).