

A REVIEW ON ADVERSE DRUG REACTIONS AND PATIENT COUNSELLING OF ANTI-DIABETIC MEDICATIONS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CHRONIC KIDNEY DISEASE

Sona Manzoor M.*¹, Dr. Nithin Manohar R.², Anjana U. J.³, Dr. Prasobh G. R.⁴, Asheena A.¹, Nahid Nazimuddin¹, D. Ajin Raj¹

¹Fifth Year Doctor of Pharmacy Student, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

²Professor & HOD, Department of Pharmacy Practice, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

³Associate Professor, Department of Pharmacy Practice, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

⁴Principal, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

Article Received: 15 April 2026

Article Review: 05 May 2026

Article Accepted: 26 May 2026

*Corresponding Author: Sona Manzoor M.

Fifth Year Doctor of Pharmacy Student, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

DOI: <https://doi.org/10.5281/zenodo.20702457>

How to cite this Article: Sona Manzoor M., Dr. Nithin Manohar R., Anjana U. J., Dr. Prasobh G. R., Asheena A., Nahid Nazimuddin, D. Ajin Raj (2026). A REVIEW ON ADVERSE DRUG REACTIONS AND PATIENT COUNSELLING OF ANTI-DIABETIC MEDICATIONS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CHRONIC KIDNEY DISEASE. World Journal of Pharmacy and Medical Science, 2(6): 142-153.



Copyright © 2026 Sona Manzoor M. | World Journal of Pharmacy and Medical Science

This is an open-access article distributed under creative Commons Attribution-NonCommercial 4.0 International license (CC BY-NC 4.0)

ABSTRACT

Type 2 diabetes mellitus (T2DM) is one of the leading causes of chronic kidney disease (CKD) worldwide and is associated with significant morbidity and mortality. Management of T2DM in CKD patients is highly challenging due to altered pharmacokinetics, multiple comorbidities, polypharmacy, and increased susceptibility to adverse drug reactions (ADRs). Anti-diabetic medications such as metformin, sulfonylureas, insulin, sodium-glucose co-transporter-2 (SGLT-2) inhibitors, dipeptidyl peptidase-4 (DPP-4) inhibitors, thiazolidinediones, and glucagon-like peptide-1 (GLP-1) receptor agonists may produce various adverse effects ranging from mild gastrointestinal disturbances to severe hypoglycemia, lactic acidosis, dehydration, and cardiovascular complications. Early identification and appropriate therapy modification are essential to improve therapeutic safety and prevent disease progression in CKD patients. Therapy modifications including dose adjustment according to renal function, discontinuation of offending agents, switching to safer alternatives, and continuous monitoring of renal and glycemic parameters play an important role in minimizing ADR-related complications. Individualized treatment strategies are necessary to optimize glycemic control while reducing medication-related risks in patients with impaired renal function. Patient counselling is another crucial component in the management of diabetic CKD patients. Effective counselling improves medication adherence, disease awareness, self-monitoring practices, lifestyle modifications, and early recognition of complications. Clinical pharmacists play a significant role in educating patients regarding medication use, dietary modifications, insulin administration, and preventive healthcare measures. In addition, Patient Information Leaflets (PILs) serve as valuable educational tools that reinforce verbal counselling and improve patient understanding and compliance. This review focuses on the adverse drug reactions associated with anti-diabetic medications in T2DM patients with CKD, therapy modifications following ADR occurrence, and the importance of patient counselling and educational interventions in improving therapeutic outcomes and quality of life.

KEYWORDS: Type 2 Diabetes Mellitus, Chronic Kidney Disease, Adverse Drug Reactions, Patient Counselling.

INTRODUCTION

Renal architecture and function are both impacted by the diverse range of illnesses that make up chronic kidney disease (CKD). CKD is defined by the National renal Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) as renal disease and/or a reduced glomerular filtration rate of less than 60 mL/min/1.73 m² for three months or longer.^[1]

Uncontrolled blood concentrations of phosphorus, calcium, potassium, sodium, urea, and creatinine are shown by a dialysis outcome study. These patients are at a significant risk of experiencing adverse drug events due to drug-drug interactions because of the frequent medication modifications made during dialysis days, the unstable nature of the disease, their restricted lifestyles, and the large number of prescriptions prescribed.^[1]

A drug is a single active chemical entity found in medications used for disease diagnosis, prevention, and treatment.

Person-to-person variability in drug response is a significant issue in clinical practice and drug development. It can result in therapeutic failure or adverse drug reactions (ADRs) in individuals or patient subpopulations. Adverse drug reactions are unexpected effects of drugs on humans and animals and are thought to be a contributing factor in hospitalized patients' morbidity and mortality.^[2]

Adverse drug reactions will likely continue to rise as more medications are sold and more people use several medications. Adverse drug reactions are still seen as an issue with medication therapy since they are linked to high direct and indirect medical costs, significant morbidity, mortality, decreased compliance, and therapeutic success.^[2]

Patients with chronic kidney disease (CKD) frequently experience changes in pharmacokinetic parameters, including drug absorption, distribution, protein binding, metabolism, and renal excretion. Since the kidneys eliminate many medications and their metabolites, adequate renal function is crucial to prevent toxicity.

Patients with severe renal insufficiency may accumulate metabolites, which may contribute to pharmacological activity or toxicity. Patients may also have altered pharmacodynamic response to a particular drug because of physiological and biochemical changes linked to progressive renal insufficiency.^[3]

ADEs that could have been prevented with proper medication selection or management were known as preventable ADEs.^[3]

If there was inadequate information available at the time of pharmaceutical prescription that could influence the treatment choice, ADE was not preventable.^[3]

The aim of the study is to perform a review on assessing the Adverse Drug Reaction (ADR) in type 2 diabetes mellitus patients with chronic kidney disease.

DEFINITION OF ADVERSE DRUG REACTION

The World Health Organization (WHO) defines adverse drug reactions (ADRs) as "a noxious, unintended effect of a drug that occurs in doses normally used in humans for the diagnosis, prophylaxis, and treatment of disease."^[4]

Examples:

- Mild: Nausea
- Moderate: Skin rash
- Severe: Hypoglycemia, lactic acidosis

CLASSIFICATION OF ADVERSE DRUG REACTIONS

CLASSIFICATION OF ADVERSE DRUG REACTIONS (ADR)				
Type	Other Name	Description	Key Features	Example
Type A	Augmented	Related to known pharmacological action of the drug	• Predictable • Dose dependent • Common • Usually mild	Hypoglycemia due to insulin
Type B	Bizarre	Not related to known action of the drug	• Unpredictable • Not dose dependent • Uncommon • Often severe	Penicillin allergy
Type C	Chronic	Occurs due to long term or prolonged use	• Related to duration • Appears after months/years	Adrenal suppression with corticosteroids
Type D	Delayed	Occurs after a delay following drug exposure	• Not immediate • May appear after weeks, months or years	Carcinogenic effects of some drugs
Type E	End of use	Withdrawal reaction that occurs after stopping the drug suddenly	• Due to abrupt discontinuation • Opposite of the pharmacological effect	Opioid withdrawal syndrome
Type F	Failure	Drug fails to produce the intended effect	• Therapeutic failure • May lead to treatment failure	Antibiotic resistance

IMMUNOLOGICAL ADR			NON-IMMUNOLOGICAL ADR		
Subtype	Mechanism	Example	Subtype	Description	Example
Type I	IgE mediated (Immediate hypersensitivity)	Anaphylaxis, Urticaria	Side effects	Expected secondary effects related to the pharmacological action	Drowsiness with antihistamines
Type II	Cytotoxic (antibody mediated)	Hemolytic anemia	Toxic effects	Excessive pharmacological effect due to high dose or accumulation	Liver toxicity with paracetamol overdose
Type III	Immune complex mediated	Serum sickness	Drug interaction	Reaction due to interaction between two or more drugs	Increased bleeding risk with warfarin + aspirin
Type IV	Cell mediated (Delayed hypersensitivity)	Contact dermatitis	Idiosyncratic reaction	Abnormal response in predisposed individuals; not dose related	Hemolysis in G6PD deficiency after primaquine

Note: ADR – Any response to a drug which is noxious, unintended and occurs at doses normally used in humans for prophylaxis, diagnosis or therapy.

Figure 1: Classification of Adverse Drug Reaction.

WHY CKD INCREASES ADR RISK?

Nephrotoxicity from drugs is common and well-researched. However, when kidney function deteriorates, the kidney also plays a significant role in the removal of numerous medications and toxic compounds that can lead to adverse drug reactions (ADRs). Patients with chronic kidney disease (CKD) utilize a variety of medications and are frequently exposed to some that are given improperly, despite compromised pharmacokinetics and pharmacodynamics. Patients with chronic kidney disease have relied on self-reported ADRs have been limited to ADRs during hospitalization or to certain types of ADRs, or they have involved particular medications during clinical trials.^[5]

ADVERSE DRUG REACTION OF ANTI-DIABETIC MEDICATIONS**SGLT-2 inhibitors**

Sodium-glucose co-transporter-2 (SGLT-2) inhibitors such as dapagliflozin, empagliflozin, and canagliflozin are increasingly prescribed in patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) because of their renoprotective and cardioprotective effects. These agents act by inhibiting glucose reabsorption in the proximal renal tubules, thereby promoting urinary glucose excretion and lowering blood glucose levels. Despite their therapeutic benefits, SGLT-2 inhibitors are associated with several adverse drug reactions, particularly in patients with impaired renal function.^[11]

The most commonly reported adverse drug reactions include genital mycotic infections, urinary tract infections, polyuria, dehydration, dizziness, and hypotension. Increased urinary glucose concentration creates a favorable environment for fungal growth, thereby increasing the incidence of genital infections.

CKD patients are especially susceptible to volume depletion and hypotension because of altered renal handling of fluids and electrolytes.^[11,12]

One of the serious but uncommon adverse effects associated with SGLT-2 inhibitors is euglycemic diabetic ketoacidosis (DKA). In this condition, patients may develop ketoacidosis despite having near-normal blood glucose levels, making diagnosis challenging. Additional serious reactions include acute kidney injury and Fournier's gangrene, a rare but life-threatening necrotizing infection of the perineal region.^[12]

Therapy modification is often necessary in CKD patients receiving SGLT-2 inhibitors. Dose adjustments are recommended based on estimated glomerular filtration rate (eGFR), and some agents may need to be avoided in advanced renal impairment. Temporary discontinuation is advised during acute illness, dehydration, prolonged fasting, or surgical procedures to minimize the risk of ketoacidosis and renal injury.^[11]

Patients should receive counselling regarding adequate hydration, maintenance of genital hygiene, recognition of symptoms of urinary infections, and early identification of ketoacidosis symptoms such as nausea, vomiting, abdominal pain, and fatigue. Proper patient education can significantly reduce preventable adverse drug reactions and improve medication adherence.^[8,9]

Biguanides (Metformin)

Metformin is considered the first-line pharmacological therapy for type 2 diabetes mellitus because of its efficacy, safety profile, affordability, and cardiovascular benefits. It acts primarily by reducing hepatic gluconeogenesis and improving peripheral insulin sensitivity. However, metformin use in CKD patients requires careful monitoring because impaired renal function may lead to drug accumulation and increased toxicity.^[13]

The most common adverse drug reactions associated with metformin are gastrointestinal disturbances such as nausea, vomiting, diarrhea, abdominal discomfort, anorexia, and metallic taste. These adverse effects are

usually mild and transient but may negatively affect medication adherence in some patients.^[13]

A rare but potentially fatal adverse drug reaction associated with metformin is lactic acidosis. Metformin-associated lactic acidosis occurs due to accumulation of lactate secondary to impaired metabolism and reduced renal clearance. CKD patients are at particularly high risk because declining kidney function decreases drug elimination. Conditions such as dehydration, sepsis, hepatic impairment, hypoxia, and alcohol abuse further increase the risk.^[14]

Therapy modification is essential in CKD patients receiving metformin. Current guidelines recommend dose reduction when eGFR declines below specific thresholds and discontinuation in severe renal impairment. Metformin should also be temporarily withheld before contrast imaging procedures to reduce the risk of acute kidney injury and lactic acidosis.^[14]

Patient counselling should emphasize taking metformin with meals to minimize gastrointestinal side effects, maintaining hydration, avoiding excessive alcohol consumption, and immediately reporting symptoms such as muscle pain, respiratory distress, unusual fatigue, or persistent vomiting. Regular monitoring of renal function is also important for safe therapy.^[8]

Sulfonylureas

Sulfonylureas such as glimepiride, gliclazide, and glibenclamide stimulate insulin secretion from pancreatic beta cells and are widely used in the management of type 2 diabetes mellitus. Although effective in reducing blood glucose levels, these drugs are commonly associated with hypoglycemia, especially in elderly patients and those with chronic kidney disease.^[15]

Hypoglycemia is the most significant adverse drug reaction associated with sulfonylureas. Symptoms may include sweating, tremors, dizziness, palpitations, confusion, blurred vision, and loss of consciousness in severe cases. CKD increases the risk of hypoglycemia because reduced renal clearance prolongs the half-life and pharmacological action of these medications.^[15]

Other adverse effects include weight gain, nausea, skin rash, and gastrointestinal disturbances. Long-acting sulfonylureas such as glibenclamide are particularly associated with prolonged hypoglycemia in CKD patients and are generally avoided in moderate to severe renal impairment.^[16]

Therapy modification includes selecting shorter-acting agents, initiating therapy at low doses, and frequent blood glucose monitoring. Dose adjustments based on renal function are necessary to prevent severe hypoglycemia.^[16]

Patients should be educated about recognizing early symptoms of hypoglycemia, carrying glucose sources

such as sugar or glucose tablets, avoiding skipped meals, and maintaining regular meal timings. Counselling regarding self-monitoring of blood glucose is also essential for preventing adverse outcomes.^[9]

DPP-4 Inhibitors

Dipeptidyl peptidase-4 (DPP-4) inhibitors such as sitagliptin, vildagliptin, saxagliptin, and linagliptin are commonly prescribed in patients with type 2 diabetes mellitus because they improve glycemic control with a relatively lower risk of hypoglycemia. These agents act by inhibiting the DPP-4 enzyme, thereby prolonging the activity of incretin hormones, which stimulate insulin secretion and suppress glucagon release. In CKD patients, DPP-4 inhibitors are generally considered safer than sulfonylureas; however, several adverse drug reactions have been reported.^[17]

Common adverse drug reactions associated with DPP-4 inhibitors include headache, nasopharyngitis, upper respiratory tract infections, dizziness, nausea, and gastrointestinal disturbances. Although these reactions are usually mild, prolonged use may contribute to reduced treatment adherence in some patients.^[17]

Serious adverse drug reactions such as acute pancreatitis, severe joint pain, hypersensitivity reactions, angioedema, and skin reactions including Stevens-Johnson syndrome have also been reported. Saxagliptin has additionally been associated with an increased risk of hospitalization due to heart failure, especially in patients with underlying cardiovascular and renal disease.^[18]

Renal impairment significantly affects the elimination of several DPP-4 inhibitors. Sitagliptin, saxagliptin, and vildagliptin require dose adjustment in CKD patients to prevent drug accumulation and toxicity. Linagliptin is primarily excreted through the hepatobiliary route and usually does not require dose adjustment in renal impairment.^[19]

Therapy modifications in CKD patients include renal dose adjustment, periodic monitoring of renal function, and discontinuation of therapy if severe hypersensitivity or pancreatitis occurs. Clinicians should carefully evaluate cardiovascular status before prescribing saxagliptin in high-risk patients.^[18]

Patient counselling should focus on recognizing symptoms of pancreatitis such as severe abdominal pain radiating to the back, monitoring blood glucose regularly, maintaining adherence to dietary recommendations, and immediately reporting hypersensitivity reactions including rash, swelling, or breathing difficulty. Proper counselling improves early detection of adverse drug reactions and enhances medication safety.^[8,9]

Insulin

Insulin therapy remains one of the most effective treatment modalities for type 2 diabetes mellitus, particularly in patients with advanced chronic kidney disease. Progressive renal impairment decreases endogenous insulin clearance and alters glucose metabolism, making insulin therapy both essential and potentially hazardous in CKD patients.^[20]

Hypoglycemia is the most common and clinically significant adverse drug reaction associated with insulin therapy. Symptoms include sweating, tremors, palpitations, confusion, blurred vision, seizures, and loss of consciousness. CKD patients are highly vulnerable because the kidneys play a major role in insulin degradation and gluconeogenesis. Reduced renal clearance prolongs insulin action and increases hypoglycemia risk.^[20]

Other adverse effects of insulin therapy include weight gain, lipodystrophy at injection sites, peripheral edema, allergic reactions, and local injection-site reactions such as pain and erythema. Recurrent hypoglycemia may also contribute to cardiovascular complications, cognitive impairment, and poor quality of life in CKD patients.^[21]

Therapy modification is necessary in patients with declining renal function. Insulin doses often require gradual reduction as eGFR decreases. Frequent blood glucose monitoring and individualized insulin regimens are important to minimize fluctuations in glycemic control. Short-acting insulin preparations may be preferred in some CKD patients to reduce prolonged hypoglycemic episodes.^[21]

Patient counselling should include education regarding proper insulin injection techniques, rotation of injection sites, safe storage of insulin, recognition and management of hypoglycemia, meal timing, and adherence to prescribed dosing schedules. Patients should also be advised to carry glucose sources at all times for emergency management of hypoglycemia.^[8]

Thiazolidinediones (TZDs)

Thiazolidinediones such as pioglitazone improve insulin sensitivity by activating peroxisome proliferator-activated receptor gamma (PPAR- γ). These agents are effective in improving glycemic control without significantly increasing hypoglycemia risk when used as monotherapy. However, their adverse effect profile limits their use in many CKD patients.^[22]

Common adverse drug reactions associated with thiazolidinediones include weight gain, fluid retention, peripheral edema, headache, and fatigue. Fluid retention is particularly concerning in CKD patients because it may worsen hypertension and precipitate congestive heart failure.^[22]

Serious adverse effects include worsening heart failure, increased risk of fractures, hepatotoxicity, and possible association with bladder cancer after long-term pioglitazone use. CKD patients often have coexisting cardiovascular disease, making them more vulnerable to these complications.^[23]

Although thiazolidinediones generally do not require dose adjustment in renal impairment, careful patient selection and monitoring are necessary. Therapy modification may involve avoiding these drugs in patients with symptomatic heart failure or severe edema.

Monitoring liver function and fluid status is also important during treatment.^[23]

Patient counselling should emphasize monitoring for swelling of the legs, sudden weight gain, shortness of breath, and fatigue. Patients should also be advised regarding lifestyle modifications including dietary sodium restriction and regular physical activity to minimize cardiovascular complications.^[9]

GLP-1 Receptor Agonists

Glucagon-like peptide-1 (GLP-1) receptor agonists such as liraglutide, semaglutide, and dulaglutide are increasingly used in type 2 diabetes mellitus patients because of their glucose-lowering efficacy, weight reduction benefits, and cardiovascular protection. These agents enhance glucose-dependent insulin secretion, suppress glucagon secretion, delay gastric emptying, and promote satiety. Recent studies have also demonstrated renoprotective benefits in CKD patients.^[24]

The most common adverse drug reactions associated with GLP-1 receptor agonists are gastrointestinal in nature, including nausea, vomiting, diarrhea, abdominal pain, constipation, and reduced appetite. These adverse effects are usually dose-dependent and more common during treatment initiation. Persistent gastrointestinal symptoms may contribute to dehydration and worsening renal function in CKD patients.^[24]

Serious adverse drug reactions include acute pancreatitis, gallbladder disease, acute kidney injury secondary to dehydration, and rarely medullary thyroid carcinoma risk in susceptible individuals. CKD patients are particularly vulnerable to volume depletion because vomiting and diarrhea can further impair renal perfusion.^[25]

Therapy modification may involve gradual dose titration to improve tolerability and temporary discontinuation during severe gastrointestinal illness or dehydration. Renal function monitoring is recommended in patients experiencing prolonged vomiting or fluid loss.^[25]

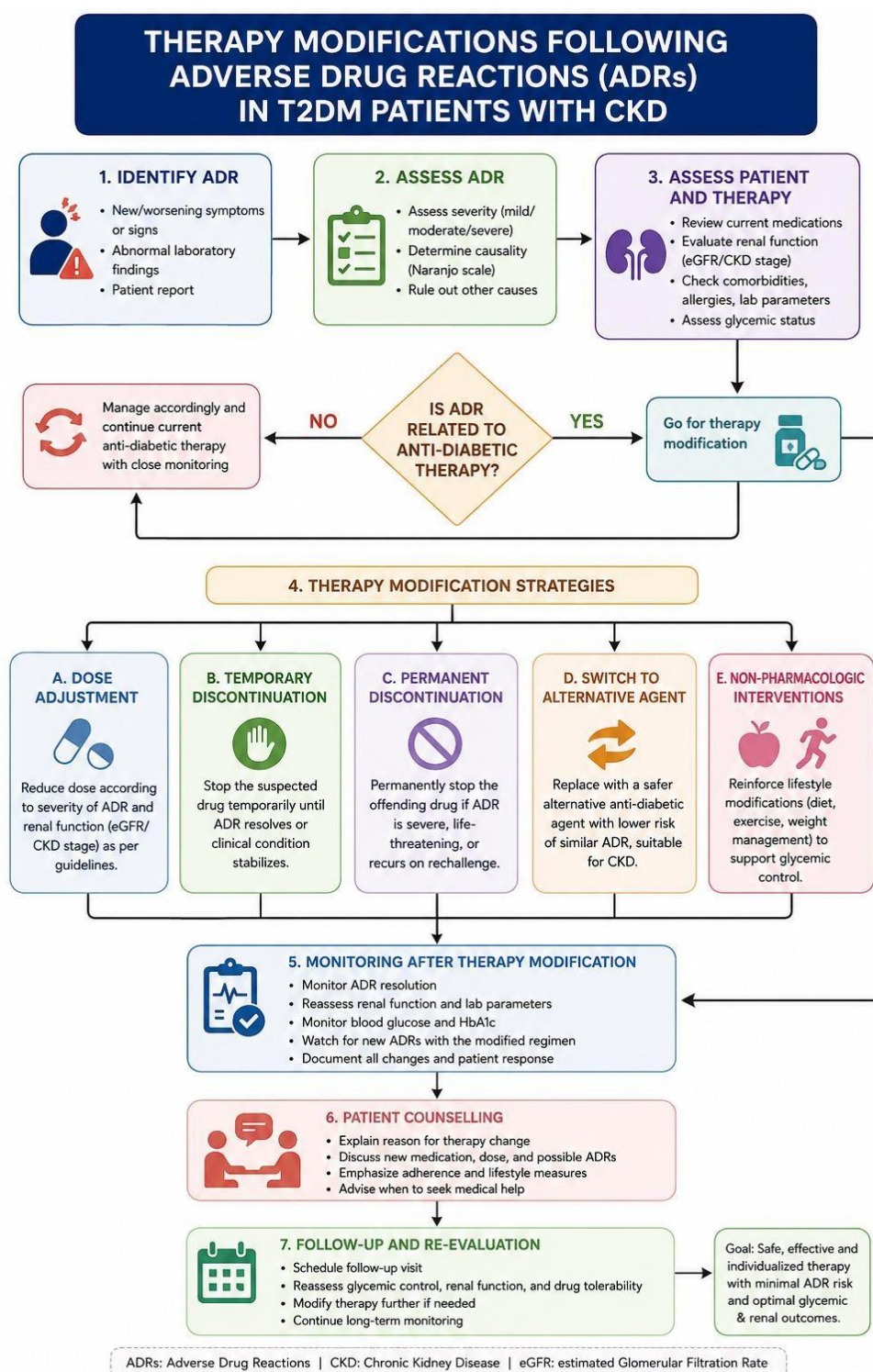
Patient counselling should focus on dietary modifications, maintaining adequate hydration, recognizing symptoms of pancreatitis such as severe abdominal pain, and understanding the importance of

adherence despite mild transient gastrointestinal effects. Patients should also be educated regarding proper injection techniques for injectable formulations.^[8,9]

THERAPY MODIFICATIONS FOLLOWING ADVERSE DRUG REACTIONS

Patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) are highly susceptible to adverse drug reactions because of altered pharmacokinetics, impaired renal drug clearance,

polypharmacy, and multiple comorbidities. Early identification and appropriate therapy modification are essential to minimize toxicity, prevent disease progression, improve therapeutic outcomes, and enhance patient safety. Management strategies may include dose adjustment, temporary discontinuation, switching to safer alternatives, individualized therapy selection, and close monitoring of renal function and blood glucose levels.^[28]



Dose Adjustment According to Renal Function

Dose adjustment is one of the most important strategies for preventing and managing adverse drug reactions in CKD patients. Declining glomerular filtration rate (GFR) reduces renal elimination of many anti-diabetic medications and their metabolites, increasing the risk of drug accumulation and toxicity. Therefore, anti-diabetic drug dosing should be individualized according to estimated glomerular filtration rate (eGFR).^[29]

Metformin dosage should be reduced in patients with moderate renal impairment and discontinued in severe CKD to reduce the risk of lactic acidosis. Sulfonylureas require cautious dosing because impaired renal clearance significantly increases the risk of prolonged hypoglycemia. DPP-4 inhibitors such as sitagliptin and saxagliptin also require renal dose adjustment, whereas linagliptin usually does not require modification due to its non-renal elimination pathway.^[14,19]

Frequent monitoring of renal function helps clinicians identify patients requiring therapy modification and prevents avoidable adverse drug reactions.^[29]

Drug Discontinuation and Switching Therapy

Severe or persistent adverse drug reactions may require temporary or permanent discontinuation of therapy. In patients who develop recurrent hypoglycemia with sulfonylureas, switching to agents with lower hypoglycemic risk such as DPP-4 inhibitors or GLP-1 receptor agonists may improve safety. Similarly, metformin should be discontinued in patients developing lactic acidosis, severe dehydration, sepsis, or acute kidney injury.^[14]

SGLT-2 inhibitors may need temporary discontinuation during acute illness, surgery, prolonged fasting, or severe dehydration to prevent euglycemic diabetic ketoacidosis and worsening renal injury. Therapy may be restarted once the patient becomes clinically stable and hydration status improves.^[12]

Switching therapy should always consider renal status, cardiovascular risk, glycemic control, patient tolerance, and comorbid conditions to ensure individualized and safe treatment.^[30]

Monitoring Strategies During Therapy Modification

Continuous monitoring plays a critical role in minimizing adverse outcomes in CKD patients receiving anti-diabetic medications. Monitoring parameters include blood glucose levels, glycated hemoglobin (HbA1c), renal function tests, serum electrolytes, body weight, hydration status, and symptoms suggestive of toxicity or hypoglycemia.^[31]

Patients receiving insulin therapy require frequent glucose monitoring because reduced renal insulin clearance may predispose them to recurrent hypoglycemia. Similarly, patients on SGLT-2 inhibitors should be monitored for signs of dehydration, hypotension, urinary tract infections, and ketoacidosis.^[20]

Laboratory monitoring also assists in evaluating treatment response and determining whether dose reduction or therapy discontinuation is necessary. Early detection of ADRs through regular follow-up significantly reduces hospitalization and morbidity associated with anti-diabetic therapy in CKD patients.^[31]

Individualized Therapy Selection in CKD Patients

Individualization of anti-diabetic therapy is essential in CKD patients because treatment goals and drug tolerance vary among individuals. Selection of therapy should consider renal function, age, cardiovascular status, hypoglycemia risk, body weight, concomitant medications, and patient adherence.^[32]

Agents with lower hypoglycemia risk such as DPP-4 inhibitors, SGLT-2 inhibitors, and GLP-1 receptor agonists are often preferred in appropriate CKD patients. Insulin therapy should be carefully individualized with gradual dose titration to avoid severe glucose fluctuations. Elderly patients and those with multiple comorbidities may require less stringent glycemic targets to minimize adverse drug reactions.^[32]

Patient-specific therapy modification improves medication safety, treatment adherence, and overall quality of life while reducing preventable hospital admissions related to adverse drug events.^[5]

Multidisciplinary Approach in ADR Management

Effective management of adverse drug reactions in CKD patients requires collaboration between physicians, clinical pharmacists, nurses, and patients. Clinical pharmacists play an important role in identifying drug-related problems, recommending dose adjustments, detecting drug interactions, and providing medication counselling.^[33]

Pharmacist-led medication review and monitoring programs have shown significant benefits in reducing medication errors, improving adherence, and preventing preventable adverse drug reactions in diabetic CKD patients. Interprofessional collaboration ensures safer prescribing practices and promotes rational drug utilization.^[33]

MULTIDISCIPLINARY APPROACH IN ADR MANAGEMENT



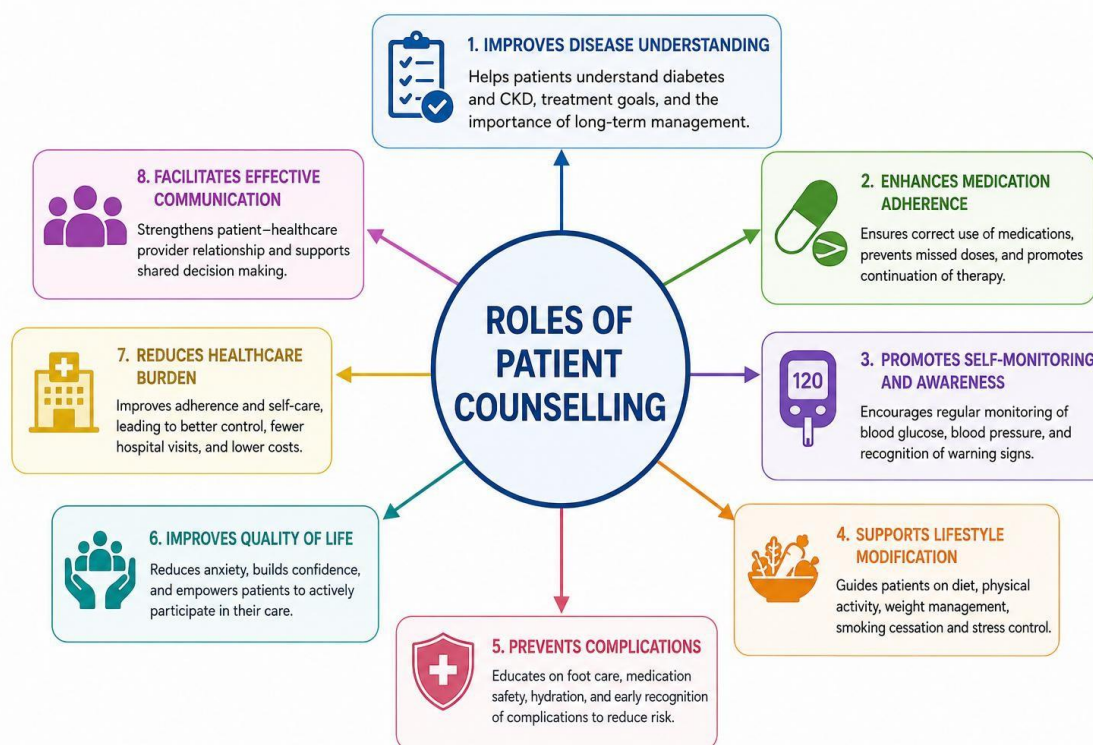
ROLE OF PATIENT COUNSELLING IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CHRONIC KIDNEY DISEASE

Patient counselling is an essential component in the management of type 2 diabetes mellitus (T2DM) patients with chronic kidney disease (CKD). These patients frequently require long-term pharmacotherapy, multiple medications, dietary restrictions, lifestyle modifications, and continuous monitoring, making disease management highly complex. The coexistence of diabetes and CKD significantly increases the risk of medication-related problems, poor therapeutic adherence, adverse drug reactions (ADRs), recurrent hospitalization, and disease progression. Therefore, effective patient counselling plays a major role in improving therapeutic outcomes, enhancing quality of life, and reducing healthcare burden.^[34]

Chronic kidney disease alters the pharmacokinetics and pharmacodynamics of several anti-diabetic medications, increasing the risk of toxicity and treatment-related complications. In addition, diabetic CKD patients often

suffer from hypertension, cardiovascular disease, dyslipidemia, anemia, and electrolyte abnormalities, resulting in polypharmacy and increased treatment complexity. Lack of adequate understanding regarding disease progression, medication use, dietary restrictions, and self-care practices may negatively affect treatment outcomes. Structured counselling by healthcare professionals helps patients better understand their disease condition and encourages active participation in treatment planning and self-management.^[35]

Patient counselling is not limited to medication instructions alone but also includes education regarding lifestyle modifications, self-monitoring of blood glucose, dietary control, prevention of complications, adherence strategies, psychological support, and early identification of warning signs requiring medical attention. Proper counselling has been shown to improve glycemic control, reduce hospitalization rates, delay progression of nephropathy, and improve patient satisfaction and medication adherence.^[36]



IMPORTANCE OF PATIENT COUNSELLING

Patient counselling helps patients understand the chronic and progressive nature of diabetes mellitus and chronic kidney disease. Since both conditions require lifelong management, patients often experience anxiety, emotional stress, treatment fatigue, and fear regarding complications such as dialysis, vision loss, cardiovascular disease, and hypoglycemia.

Counselling provides psychological reassurance and improves patients' confidence in managing their disease effectively.^[35]

Education regarding disease progression and therapeutic goals enables patients to understand the importance of maintaining blood glucose levels, blood pressure control, renal function monitoring, and adherence to prescribed medications. Patients who receive proper counselling are more likely to comply with treatment plans and adopt healthy lifestyle practices. Studies have demonstrated that diabetes self-management education significantly improves glycemic control, self-care behavior, and overall clinical outcomes in diabetic patients.^[36]

Another important benefit of counselling is the early recognition of warning signs associated with disease progression and medication-related complications.

Patients should be educated to identify symptoms such as hypoglycemia, hyperglycemia, edema, reduced urine output, fatigue, dehydration, breathlessness, blurred vision, and foot ulcers. Early identification of these symptoms can prevent severe complications and reduce

emergency hospital admissions.^[35]

Patient counselling also strengthens communication between healthcare professionals and patients, allowing better understanding of patient concerns, cultural beliefs, treatment barriers, and socioeconomic challenges.

Effective communication improves patient trust, promotes shared decision-making, and enhances long-term therapeutic adherence.^[38]

MEDICATION ADHERENCE COUNSELLING

Medication adherence is one of the most important determinants of successful diabetes and CKD management. Poor adherence to anti-diabetic medications can result in uncontrolled hyperglycemia, accelerated renal damage, cardiovascular complications, increased hospitalization, and mortality. Non-adherence is highly prevalent among CKD patients because of polypharmacy, frequent dosing schedules, financial burden, fear of adverse drug reactions, forgetfulness, and inadequate understanding of disease conditions.^[37]

Patients should be educated regarding the importance of taking medications at the prescribed dose and time and avoiding abrupt discontinuation without medical supervision. Counselling should emphasize that even when symptoms improve, discontinuation of therapy may worsen disease progression and increase the risk of complications. Healthcare professionals should also assess individual barriers affecting adherence and provide personalized strategies to improve compliance.^[38]

Patients receiving insulin therapy require detailed counselling regarding insulin administration techniques, injection site rotation, storage conditions, disposal of needles, and management of hypoglycemia. Improper injection techniques may lead to lipodystrophy, inconsistent absorption, and poor glycemic control. Similarly, patients taking oral anti-diabetic agents should understand the mechanism and purpose of each medication and the importance of regular monitoring.^[37]

Medication adherence counselling should also include education regarding missed doses, drug interactions, timing of medications with meals, and avoidance of self-medication with over-the-counter drugs without professional advice. Continuous reinforcement during follow-up visits significantly improves long-term adherence and therapeutic success.^[36]

LIFESTYLE MODIFICATION COUNSELLING

Lifestyle modification is considered the cornerstone of diabetes and CKD management. Counselling regarding healthy lifestyle practices helps reduce disease progression, improve glycemic control, and minimize cardiovascular and renal complications. Patients should receive individualized counselling regarding dietary management, physical activity, smoking cessation, alcohol restriction, stress reduction, and weight management.^[39]

Dietary counselling is particularly important in CKD patients because improper intake of sodium, potassium, phosphorus, protein, and fluids may worsen renal function and contribute to cardiovascular complications.

Patients should be advised to reduce excessive salt intake, avoid processed foods, limit sugary beverages, and follow physician-recommended fluid restrictions when necessary. Individualized meal planning according to renal status and diabetic requirements can significantly improve disease management.^[39]

Regular physical activity improves insulin sensitivity, glycemic control, cardiovascular health, and body weight management. However, exercise recommendations should be individualized according to the patient's age, renal function, cardiovascular condition, and overall physical status. Excessive physical exertion may not be suitable for advanced CKD patients, especially those with cardiovascular complications or anemia.^[40]

Smoking cessation counselling is extremely important because smoking accelerates progression of diabetic nephropathy and significantly increases cardiovascular morbidity and mortality. Alcohol restriction should also be emphasized because alcohol may precipitate hypoglycemia, worsen dehydration, and negatively affect renal function. Psychological counselling and stress management techniques may further improve patient motivation and treatment adherence.^[40]

SELF-MONITORING AND DISEASE AWARENESS

Self-monitoring of blood glucose is an essential component of diabetes self-management and should be strongly reinforced during counselling sessions. Patients should be educated regarding the proper use of glucometers, interpretation of glucose values, frequency of monitoring, maintenance of glucose records, and identification of abnormal readings requiring medical attention.^[41]

Patients should also be educated regarding symptoms and management of hypoglycemia and hyperglycemia. Hypoglycemia symptoms such as sweating, dizziness, tremors, palpitations, and confusion should be explained clearly, along with immediate corrective measures including oral glucose administration. Similarly, patients should understand symptoms of hyperglycemia such as excessive thirst, frequent urination, fatigue, and blurred vision.^[41]

Disease awareness counselling should include information regarding the importance of regular follow-up visits, renal function tests, HbA1c monitoring, blood pressure control, foot care, and ophthalmic examinations. Foot care counselling is especially important because diabetic neuropathy and poor circulation increase the risk of foot ulcers, infections, and amputations. Patients should be instructed to inspect their feet daily, maintain foot hygiene, avoid walking barefoot, and seek medical attention for wounds or infections.^[42]

Educational interventions empower patients to actively participate in disease management and improve self-care behavior, resulting in improved quality of life and reduced disease burden. Better disease awareness also improves patient confidence and reduces dependence on emergency healthcare services.^[42]

ROLE OF CLINICAL PHARMACISTS IN PATIENT COUNSELLING

Clinical pharmacists play a vital role in the multidisciplinary management of diabetic CKD patients. Pharmacists contribute significantly to medication therapy management, identification of drug-related problems, patient education, medication adherence counselling, and prevention of adverse drug reactions. Pharmacist-led interventions have demonstrated substantial improvements in glycemic control, patient knowledge, therapeutic adherence, and rational medication use.^[33]

Pharmacists are uniquely positioned to educate patients regarding appropriate medication use, renal dose adjustments, adverse effect monitoring, insulin administration techniques, and lifestyle modifications. They can simplify complex medication regimens and provide individualized counselling according to patient literacy level and clinical status.^[43]

In addition to patient education, pharmacists also help identify drug-drug interactions, inappropriate prescribing, therapeutic duplication, and nephrotoxic medications. Continuous pharmacist involvement improves treatment safety and promotes early detection of medication-related problems in CKD patients.^[33]

Pharmacist-led counselling programs have also been associated with reduced hospitalization rates, improved medication adherence, and enhanced patient satisfaction. Collaborative healthcare approaches involving physicians, pharmacists, nurses, and dieticians provide more effective and comprehensive patient care.^[43]

USE OF PATIENT INFORMATION LEAFLETS (PILs)

Patient Information Leaflets (PILs) are written educational materials designed to supplement verbal counselling and improve patient understanding regarding disease conditions and medication therapy. PILs are particularly useful in diabetic CKD patients because they provide easily accessible information regarding medication schedules, dosage instructions, precautions, dietary recommendations, lifestyle modifications, and warning signs requiring medical attention.^[44]

PATIENT INFORMATION LEAFLET (PIL)
 For Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease

Take Charge Today
 For a Healthier
 Tomorrow



GOOD CONTROL OF DIABETES PROTECTS YOUR KIDNEYS AND YOUR HEALTH.

Follow your medicines, eat healthy, stay active and keep regular check-ups.

Name: _____

Age/Sex: _____

Date: _____

Doctor: _____

Hospital/Clinic: _____

1. ABOUT YOUR CONDITION

- Diabetes can damage the kidneys over time.
- Chronic Kidney Disease (CKD) means your kidneys are not working as well as they should.
- Good sugar, blood pressure and kidney control can slow down kidney damage and prevent complications.

5. SELF-MONITORING

Check your blood sugar regularly as advised. Keep a record.

Check your blood pressure regularly. Target < 130/80 mmHg (as advised).

Do regular tests: kidney function (serum creatinine, eGFR), urine test, HbA1c, electrolytes, etc.

Check your weight regularly. Sudden weight gain may mean fluid retention.

6. WARNING SIGNS

Seek medical help immediately if you have:

- Very low or very high blood sugar
- Swelling of feet, face or around eyes
- Less urine or dark coloured urine
- Shortness of breath
- Nausea, vomiting, loss of appetite
- Dizziness, confusion
- Chest pain

3. DIETARY GUIDELINES

- Limit salt intake (< 5 g/day). Avoid pickles, papad, processed and packed foods.
- Depending on kidney function, you may need to limit potassium (banana, orange, coconut water, potatoes, tomato, spinach) and phosphorus (milk, cheese, nuts, cola drinks).
- Eat balanced diet: more vegetables, whole grains, less oil and sugar.
- Follow the protein intake advised by your doctor.
- Drink adequate water as advised. Do not restrict fluids unless advised.
- Avoid alcohol.

7. FOOT CARE

- Check your feet daily for cuts, blisters, redness or swelling.
- Wash with lukewarm water and dry properly.
- Moisturize dry skin.
- Wear comfortable footwear.
- Do not walk barefoot.
- Consult doctor for any wound or infection.

8. PREVENT INFECTIONS

- Wash your hands regularly.
- Keep your skin, mouth and nails clean.
- Get recommended vaccines (Flu, Hepatitis B, Pneumococcal, COVID-19) as advised.

4. PHYSICAL ACTIVITY

- Be physically active every day.
- 30 minutes of brisk walking or any activity you enjoy.
- Avoid heavy exercise if you have heart problems or severe kidney disease.
- Always consult your doctor.

9. LIFESTYLE TIPS

- Do not smoke or use tobacco.
- Limit alcohol consumption.
- Manage stress and get enough sleep.
- Maintain healthy weight.
- Take rest, but avoid being sedentary for long hours.

10. KEEP FOLLOW-UP

- Keep all your appointments.
- Do not miss follow-up visits and tests.
- Carry your medicines list and reports during visits.

IMPORTANT REMINDERS

Take medicines on time, every time.

Follow diet and activity plans.

Monitor regularly and maintain records.

Work with your healthcare team for better health.

Protect your kidneys, protect your life.

This leaflet is for your information only. It does not replace medical advice. Always consult your doctor or pharmacist for any concerns.

IN CASE OF EMERGENCY, CONTACT YOUR DOCTOR OR NEAREST HOSPITAL IMMEDIATELY.

Many patients may forget verbal instructions provided during hospital visits due to stress, anxiety, or information overload. PILs reinforce important counselling points and improve retention of medical information. Studies have shown that well-designed PILs improve medication adherence, patient knowledge, self-care practices, and treatment satisfaction.^[44]

An effective PIL should contain simple and understandable language, short sentences, adequate spacing, culturally appropriate content, and visual aids whenever possible.

Information regarding insulin administration, blood glucose monitoring, dietary restrictions, foot care, hydration, medication storage, and emergency management of hypoglycemia should be clearly explained.^[45]

Multilingual PILs may improve accessibility among diverse populations and help overcome communication barriers. PILs should also be periodically updated according to current treatment guidelines and patient needs. Combining verbal counselling with written educational materials significantly improves patient comprehension and promotes long-term disease management.^[45]

REFERENCES

1. Abhisek PA, Panda R, Samal R, Mohapatra N, Mohanty S. Drug utilisation pattern and adverse events in patients with chronic kidney disease undergoing maintenance haemodialysis at a tertiary care hospital of Odisha. *J Clin Diagn Res*, 2017; 11(10): FC11-FC16.
2. Shibbiru T, Tadesse F. Adverse drug reactions: an overview. *J Med Physiol Biophys*, 2016; 23: 7-14.
3. Hassan Y, Al-Ramahi RJ, Aziz NA, Ghazali R. Adverse drug events in hospitalized patients with chronic kidney disease. *Int J Clin Pharmacol Ther*, 2010; 48(9): 571–576.
4. Gurmesa LT, Dedefo MG. Factors affecting adverse drug reaction reporting of healthcare professionals and their knowledge, attitude, and practice towards ADR reporting in Nekemte Town, West Ethiopia. *BioMed Research International*, 2016; 2016: 5728462.
5. Laville SM, Gras-Champel V, Moragny J, Metzger M, Jacquelinet C, Combe C, Fouque D, Laville M, Frimat L, Robinson BM, Stengel B, Massy ZA, Liabeuf S, on behalf of the Chronic Kidney Disease-Renal Epidemiology and Information Network (CKD-REIN) Study Group. Adverse drug reactions in patients with CKD. *Clin J Am Soc Nephrol*, 2020 Aug; 15(8): 1090–1102.
6. Nazzal Z, Hamdan Z, Masri D, Abu-Kaf O, Hamad M. Prevalence and risk factors of chronic kidney disease among Palestinian type 2 diabetic patients: a cross-sectional study. *BMC Nephrol*, 2020; 21: 484.
7. Tariq M, Fareed M, Salam S, Ghaffar K, Malik L. Development and validation of Chronic kidney disease knowledge, attitude and practice (CKD-KAP) questionnaire. *Front Med (Lausanne)*, 2022; 9: 956449.
8. Koochi F, Amiri P, Mehrabi Y, Karimi M, Khalili D. Development and validation of a knowledge, attitude, and practice questionnaire regarding cardiovascular diseases in an Iranian general population. *BMC Public Health*, 2021; 21: 2050.
9. Andrade C, Menon V, Ameen S, Praharaj SK. Designing and conducting knowledge, attitude, and practice surveys in psychiatry: practical guidance. *Indian Psychiatric Society Indian J Psychol Med*, 2020; 42(5): 478–481.
10. Puckrin R, Saltiel MP, Reynier P, Azoulay L, Yu OHY, Filion KB. SGLT-2 inhibitors and the risk of infections: a systematic review and meta-analysis of randomized controlled trials. *Acta Diabetol*, 2018; 55(5): 503–514.
11. U.S. Food and Drug Administration. FDA Drug Safety Communication: FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes. Silver Spring, MD: U.S. Food and Drug Administration, 2018.
12. Flory J, Lipska K. Metformin in 2019. *JAMA*, 2019; 321(19): 1926–1927.
13. Inzucchi SE, Lipska KJ, Mayo H, Bailey CJ, McGuire DK. Metformin in patients with type 2 diabetes and kidney disease: a systematic review. *JAMA*, 2014; 312(24): 2668–2675.
14. Moen MF, Zhan M, Hsu VD, Walker LD, Einhorn LM, Seliger SL, et al. Frequency of hypoglycemia and its significance in chronic kidney disease. *Clin J Am Soc Nephrol*, 2009; 4(6): 1121–1127.
15. Kalra S, Gupta Y. Sulfonylureas and renal impairment. *Indian J Endocrinol Metab*, 2015; 19(1): 9–13.
16. Gallwitz B. Clinical use of DPP-4 inhibitors. *Front Endocrinol (Lausanne)*, 2019; 10: 389.
17. Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, et al. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N Engl J Med*, 2013; 369(14): 1317–1326.
18. Scheen AJ. Pharmacokinetics of dipeptidylpeptidase-4 inhibitors. *Diabetes Obes Metab*, 2010; 12(8): 648–658.
19. Abe M, Kalantar-Zadeh K. Haemodialysis-induced hypoglycaemia and glycaemic disarrays. *Nat Rev Nephrol*, 2015; 11(5): 302–313.
20. Alsahli M, Gerich JE. Hypoglycemia in patients with diabetes and renal disease. *J Clin Med*, 2015; 4(5): 948–964.
21. Yki-Järvinen H. Thiazolidinediones. *N Engl J Med*, 2004; 351(11): 1106–1118.
22. Soccio RE, Chen ER, Lazar MA. Thiazolidinediones and the promise of insulin sensitization in type 2 diabetes. *Cell Metab*, 2014; 20(4): 573–591.
23. Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1

- receptor agonists in the treatment of type 2 diabetes. *Lancet*, 2021; 398(10295): 2180–2198.
24. Muskiet MHA, Tonneijck L, Smits MM, Kramer MHH, Diamant M, Joles JA, et al. GLP-1 and renoprotection: from physiology to clinical outcomes. *Lancet Diabetes Endocrinol*, 2017; 5(10): 801–810.
 25. Marbury T, Huang WC, Strange P, Lebovitz H. Repaglinide versus glyburide: a one-year comparison trial. *Diabetes Res Clin Pract*, 1999; 43(3): 155–166.
 26. Holstein A, Stumvoll M. Contraindications can damage your health—is metformin a case in point? *Diabetologia*, 2005; 48(12): 2454–2459.
 27. Tuttle KR, Bakris GL, Bilous RW, Chiang JL, de Boer IH, Goldstein-Fuchs J, et al. Diabetic kidney disease: a report from an ADA Consensus Conference. *Diabetes Care*, 2014; 37(10): 2864–2883.
 28. Aronoff GR, Bennett WM, Berns JS, Brier ME, Kasbekar N, Mueller BA, et al. *Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children*. 5th ed. Philadelphia: American College of Physicians, 2007.
 29. American Diabetes Association. Standards of medical care in diabetes—2024. *Diabetes Care*, 2024; 47(Suppl 1): S1–S350.
 30. KDIGO Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int*, 2020; 98(4 Suppl): S1–S115.
 31. Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease: challenges, progress, and possibilities. *Clin J Am Soc Nephrol*, 2017; 12(12): 2032–2045.
 32. Chisholm-Burns MA, Kim Lee J, Spivey CA, Slack M, Herrier RN, Hall-Lipsy E, et al. US pharmacists' effect as team members on patient care: systematic review and meta-analyses. *Med Care*, 2010; 48(10): 923–933.
 33. Powers MA, Bardsley J, Cypress M, Duker P, Funnell MM, Fischl AH, et al. Diabetes self-management education and support in type 2 diabetes. *Diabetes Care*, 2015; 38(7): 1372–1382.
 34. Shrivastava SR, Shrivastava PS, Ramasamy J. Role of self-care in management of diabetes mellitus. *J Diabetes Metab Disord*, 2013; 12(1): 14.
 35. Chrvala CA, Sherr D, Lipman RD. Diabetes self-management education for adults with type 2 diabetes mellitus: a systematic review of the effect on glycemic control. *Patient Educ Couns*, 2016; 99(6): 926–943.
 36. Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. *Patient Prefer Adherence*, 2016; 10: 1299–1307.
 37. Jimmy B, Jose J. Patient medication adherence: measures in daily practice. *Oman Med J*, 2011; 26(3): 155–159.
 38. American Diabetes Association. Lifestyle management: standards of medical care in diabetes. *Diabetes Care*, 2018; 41(Suppl 1): S38–S50.
 39. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives. *Lancet*, 2013; 382(9888): 260–272.
 40. American Diabetes Association. Glycemic targets: standards of medical care in diabetes. *Diabetes Care*, 2021; 44(Suppl 1): S73–S84.
 41. Funnell MM, Anderson RM. Empowerment and self-management of diabetes. *Clin Diabetes*, 2004; 22(3): 123–127.
 42. Pousinho S, Morgado M, Falcão A, Alves G. Pharmacist interventions in the management of type 2 diabetes mellitus: a systematic review of randomized controlled trials. *J Manag Care Spec Pharm*, 2016; 22(5): 493–515.
 43. Koo MM, Krass I, Aslani P. Evaluation of written medicine information: validation of the Consumer Information Rating Form. *Ann Pharmacother*, 2007; 41(6): 951–956.
 44. Raynor DK, Dickinson D. Key principles to guide development of consumer medicine information. *Patient Educ Couns*, 2009; 75(1): 93–97.