1 DIABETIS AND PERITONEAL DIALYSIS: literature review

2

3 I. INTRODUCTION :

- Diabetic nephropathy (DNK) is a major health problem associated with an increased risk of morbidity
 and mortality. Treatment of MRD is challenging given changes in blood glucose homeostasis, unclear
- 6 accuracy of blood glucose measurements, and altered kinetics of hypoglycemic drugs.
- 7 There is uncertainty regarding the optimal glycemic target in this population, although recent
- 8 epidemiological data suggest that HbA1c ranges of 6–8%, as well as 7–9%, are associated with higher
- 9 survival rates in diabetic patients on dialysis. Furthermore, treatment of diabetes in patients
- 10 maintained on dialysis is challenging, and many hypoglycemic drugs are metabolized and excreted
- 11 renally, necessitating dose adjustment or avoidance in dialysis patients. [1]
- 12 Diabetes, along with vascular disease, is the most common cause of end-stage renal disease (ESRD).
- 13 Many authors have suggested that continuous ambulatory peritoneal dialysis should be the preferred
- 14 treatment for diabetics with chronic kidney failure. However, controversy persists regarding the
- 15 preferred treatment of dialysis in diabetic patients. Currently, the final choice of method will depend
- 16 on the patient's clinical conditions, preferences, socio-professional environment, the availability of
- 17 dialysis techniques, the personal beliefs of nephrologists, as well as local facilities and financial
- 18 considerations. [2]

19 II. METHODOLOGY:

- 20 PubMed, Google Scholar, and Medline were searched for all literature on the management of
- 21 diabetes in dialysis and peritoneal dialysis patients.

22 III. EPIDEMIOLOGY OF DIABETES

- 23 The incidence and prevalence of diabetes mellitus have increased significantly worldwide, particularly
- 24 with improvements in living standards and lifestyle changes. Diabetic patients now live longer than
- 25 when they were denied treatments such as dialysis. The number of adults with type 2 diabetes is
- expected to increase to approximately 642 million by 2040. This overall increase in the number of
- 27 diabetics has a major impact on the development of diabetic kidney disease (DKD) and is expected to
- have a significant social and economic impact on care and management in the future [3,4].
- 29 DKD affects approximately 20 to 40% of diabetic patients progressing to ESRD, a major cause of
- 30 significant morbidity and mortality. The WHO predicts that diabetes will be the seventh leading cause
- of death by 2030 [4,5].
- 32 The MAREMAR study conducted in 2016 in Morocco found a prevalence of diabetes reaching 16.8%
- in an adult population between 18 and 70 years old, with hypertension at 21.9%. It is therefore not
- 34 surprising that MRD is the leading cause of ESRD among the Moroccan dialysis population, affecting
- 35 more than 30% of all dialysis patients [6].

36 IV. EPIDEMIOLOGY OF DIABETES AND PD (HAS)

- 37 Studies based on national registries highlight differences in diabetic dialysis populations. Populations
- 38 from the USRDS and MEDICARE registries differ from those from Canadian, Italian, Danish, and Dutch
- registries in that they have a higher prevalence of diabetes and a poorer prognosis.
- 40 The literature has demonstrated an increased risk of mortality in diabetic women over 55 years of age
- 41 treated with PD compared to those treated with HD. This is a characteristic specific to US registries
- 42 that has not been described in other continents.
- The majority of the studies reviewed show that 2-year survival in diabetics under 55 years of age isbetter with PD than with HD.
- 45 However, in older diabetics, there is no evidence to suggest that 2-year survival is better or worse
- 46 with PD than with HD, with the exception of North American patients, for whom it appears to be
- 47 worse (Level II).
- 48 Across all ages, the possible benefit of PD on survival could fade over time and reverse, but these
- 49 data do not take into account new solutions used for PD.
- 50 The survival of diabetic chronic kidney disease patients is generally worse than that of non-diabetic
- 51 patients, regardless of the technique chosen: HD or PD (level II).

52 V. COMPLICATIONS OF DIABETES IN PERITONEAL DIALYSIS:

53 <u>a. Cardiovascular Morbimortality</u>

- 54 In addition to cardiovascular risks, diabetes is an independent risk factor for stroke in the
- 55 hemodialysis (HD) population [17]. Similarly, PD patients are at higher risk of cardiovascular death
- 56 due to the inflammatory process, calcifications, malnutrition, and possibly endothelial dysfunction
- 57 and oxidative stress associated with ESRD. The additional CV risks specific to PD are likely related to
- the glycemic load leading to insulin resistance and an increased atherogenic lipid profile. In addition,
- 59 loss of residual renal function, peritoneal membrane failure, and ultrafiltration failure can induce
- 60 overload, further increasing PD-related risk factors.

61 <u>b. Foot ulcers</u>

- 62 Diabetic patients on hemodialysis have a higher prevalence of ulceration (>4 times the risk of foot
- 63 ulceration), infection, osteomyelitis, and ischemia requiring either amputation or revascularization,
- 64 with a higher mortality rate [14,26,37,38]. Similarly, the presence of diabetic foot is a complication
- 65 strongly associated with mortality in diabetic patients on peritoneal dialysis (PD) [7].

66 <u>c. Health-related quality of life (HRQOL)</u>

- 67 Diabetic patients on HD or PD have lower perceived health-related quality of life and poorer
- 68 functional status than non-diabetic patients on dialysis, which is an independent predictor of
- 69 morbidity and mortality [8]. Martinez Castelao et al. reported a strong relationship between
- 70 perceived mental health during the first month of renal replacement therapy, particularly in diabetic
- patients on dialysis, and morbidity and mortality, regardless of comorbidity [8].

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73 VI. MEASUREMENT OF GLYCEMIC CONTROL IN DIALYSIS PATIENTS:

- 74 Uremic status is associated with various laboratory abnormalities that can influence the accuracy of
- various measures used to assess medium- and long-term glycemic control, including glycated
- 76 hemoglobin (HbA1c), fructosamine, and glycated albumin. Despite these limitations, the Kidney
- 77 Disease Quality Outcomes Initiative (KDOQI) and Kidney Disease Improving Global Outcomes
- 78 (KDIGO), as well as the clinical practice guidelines of the British Diabetes Societies, recommend
- routine measurement of long-term glycemic control using HbA1c in combination with home blood
- 80 glucose monitoring as the basis for diabetes management in patients with CKD and ESRD [9,10].

81 <u>1. Glycated hemoglobin (HbA1c)</u>

- 82 HbA1c is the current standard for glycemic monitoring in the general population because it measures
- the circulating blood glucose concentration over the previous 120 days, which is the average lifespan
- of red blood cells [11]. HbA1c is formed by a non-enzymatic reaction between glucose and the beta
- chain of hemoglobin. The rate of hemoglobin glycation is influenced by various factors, including 1)
- duration of glucose exposure, 2) blood glucose, 3) hemoglobin level, 4) pH, and 5) temperature.
- 87 Therefore, numerous confounding factors related to ESRD can lead to abnormal HbA1c levels and
- 88 make HbA1c testing less reproducible. Despite all the factors that influence HbA1c levels in dialysis,
- 89 HbA1c is still recommended in all current guidelines as the primary biomarker for assessing glycemic
- 90 control in dialysis patients. However, fructosamine and glycated albumin (GA) have been suggested as
- 91 better surrogate markers of glycemic control in patients with ESRD. Glycation of these proteins is not
- 92 affected by red blood cell lifespan or treatment with erythropoietin-stimulating agents.

93 <u>2.Fructosamine</u>

- Fructosamine is a medium-term (i.e., 7–14 days) measure of blood glucose, a measure of ketoamines formed by non-enzymatic glycation of serum proteins [66]. Fructosamine may be a more accurate measure of glycemic control in dialysis patients than HbA1c, but it can also be confounded by many disorders, including dysproteinemias; Therefore, falsely low fructosamine levels may be observed in patients undergoing peritoneal dialysis or due to protein losses in the peritoneal dialysate and in patients with hypoalbuminemia due to protein-energy wasting [10]. Fructosamine has been shown to be a powerful predictor of cardiovascular morbidity (hospitalizations and infections) and mortality
- 101 (hospitalization with sepsis) in diabetic patients on dialysis.

102 <u>3. Glycated Albumin</u>

- 103 Glycated albumin can assess glycemic control over a short period (7 to 14 days) and with greater 104 accuracy in diabetic patients on hemodialysis [9,12]. While fructosamine is a measure of all glycated 105 serum proteins, glycated albumin is a non-enzymatic reaction between blood glucose and albumin. 106 Fructosamine concentration is strongly influenced by serum protein concentrations and low-107 molecular-weight molecules such as urea and uric acid.
- However, glycated albumin (GA) is not affected by serum albumin or urea levels like fructosamine,
 nor by hemoglobin levels or erythropoietin injection like HbA1C; therefore, it may be superior to
 fructosamine as a measure of glycemic control in patients with advanced ESRD [9,12]. Furthermore,
 elevated glycated albumin levels have been associated with adverse cardiovascular outcomes such as

increased arterial stiffness and vascular calcification, which are associated with poor prognosis indialysis patients [12,13].

114 <u>4. Self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGMS)</u>

The use of self-monitoring of blood glucose (SMBG) using repeated finger-prick blood glucose (PPG) 115 116 remains the cornerstone for assessing glycemic control in diabetic patients on dialysis [9]. The 117 accuracy of CGMS may be limited by the precision of blood glucose meters, the age of the strips used, 118 the timing of measurement with medications and food, and the expertise of the person performing 119 the test [13]. CGMS results may also be affected by hemolysis, anticoagulation, hyperlipidemia, and 120 metabolic acidosis. Other potential interferences: Factors include environmental factors (strips should 121 not be exposed to air, humidity, temperature, and altitude), sample volume, use of generic test strips, 122 and strip reuse [9]. CGMS accuracy is instrument and user dependent, so it is important to evaluate 123 each patient's monitoring technique at regular intervals.

124 In contrast, continuous glucose monitoring (CGMS) can provide an accurate assessment of glycemic 125 control in diabetics on dialysis; however, its use is limited by technical issues related to device 126 calibration (less of an issue with 3rd generation devices), which must be considered for accurate data 127 interpretation [13,14]. Unlike HbA1c, CGMS can reveal short-term glycemic changes at the time of 128 dialysis with results that are unaffected by urea nitrogen level, red blood cell lifespan, and red blood 129 cell manufacturing [52]. Of particular importance for patients receiving peritoneal dialysis is the 130 finding that some glucometers (those using the enzyme glucose dehydrogenase pyrroloquinoline 131 quinone [GDH-PQQ]) will give falsely elevated readings in patients using icodextrin in peritoneal 132 dialysis fluids. This may overestimate blood glucose readings and may lead to a risk of "missing" 133 hypoglycemic episodes [15,16]. Therefore, blood glucose measurements in patients receiving 134 icodextrin should be performed with a glucose-specific method to avoid interference from maltose, 135 which is a metabolite of icodextrin. This effect can persist for two weeks after discontinuation of 136 icodextrin [17].

- 137 VII. ADVANTAGES OF PERITONEAL DIALYSIS IN DIABETICS
- 138 Better preservation of residual renal function
- 139 Fewer unnecessary subcutaneous punctures
- Better hemodynamic stability, leading to a reduction in cardiac and cerebrovascular
 complications
- 142 No need for vascular access
- 143 No need for anticoagulants
- The only out-of-center method free from technical complications involving immediate life threatening risks

146 VIII. DISADVANTAGES OF PERITONEAL DIALYSIS (PD) IN DIABETIC PATIENTS:

Potentially increased risk of peritoneal infection
Protein loss and increased malnutrition
Clinical and metabolic consequences of continuous absorption of glucose and the dialysate solution

The progressive loss over time of the peritoneal membrane's ability to remove water and salt
 can lead to the insidious development of subdialysis, requiring transfer to hemodialysis

153 IX. CHOICE OF DIALYSE IN DIABETIC PATIENTS

- 154 While glucose has been proven to be an effective osmotic agent for ultrafiltration during peritoneal
- dialysis, diabetic patients nevertheless absorb an average of 150 to 300 g of glucose per day when
- using conventional solutions.
- 157 1. Icodextrin Solution (Extraneal): Glucose Polymer:
- 158 This colloid-type osmotic agent advantageously replaces conventional glucose solutions to improve
- 159 UF volume during periods of long stasis. In addition, icodextrin helps reduce glucose absorption.
- 160 Mistry et al [18], in a randomized multicenter study comparing iso-osmolar icodextrin to plasma with
- 161 hyperosmolar glucose solutions in CAPD, observed a mean absorption of 29±5g when using
- 162 icodextrin versus a mean absorption of 62±5g of 3.86% glucose (p<0.01) after 8 hours of stasis when
- using conventional solutions in 18 patients. Carbohydrate-sparing PD regimens include: A) Icodextrin,
- 164 in which carbohydrate absorption is equivalent to a 2.5% dextrose bag, but is combined with
- ultrafiltration of a 4.25% dextrose bag; and B) amino acid (AA) dialysate solutions. As part of a
- 166 glucose-sparing policy, the use of 1 bag of icodextrin or amino acid (AA) dialysate solution daily can
- reduce glucose load by 15–30%. In addition, the AA-containing dialysate should serve as a source of
- 168 both protein and calories [15,16,17].
- 169 Other authors have reported a reduced rate of glucose breakdown products (GBPs) production
- 170 compared to conventional glucose solutions and a low potential for advanced glycation end products
- 171 (AGEs) formation when using this solution. Replacing a conventional glucose solution with icodextrin
- 172 may require adjustment of insulin doses. Blood glucose measurement must be performed using a
- 173 specific method to avoid interference with maltose.
- 174 2.<u>Amino acid solution:</u>
- 175 Completely glucose-free and therefore PDG-free, it helps reduce amino acid and protein loss and is
- 176 necessary to improve the nutritional status of malnourished patients. However, international
- 177 guidelines currently recommend amino acid-rich solutions as a glucose-sparing solution rather than a
- 178 nutrient solution.

179 3. Biocompatible solutions:

- 180 Several studies have shown that neutral pH solutions, bicarbonate/lactate buffer or pure bicarbonate,
- 181 with low PDG content and therefore low AGE formation, have improved biocompatibility indicators in
- 182 in vitro studies compared to lactate-buffered solutions. They preserve RRF longer than standard
- 183 solutions.

184 X. THERAPEUTIC OBJECTIVES

- 185 Target HbA1c levels for diabetic patients on dialysis have not yet been identified. A moderate HbA1c
- 186 range (less stringent than the levels suggested for diabetic patients without CKD) is probably
- 187 associated with greater survival in dialysis patients. It should be individualized for each patient.

- 188 Currently, the KDOQI and KDIGO clinical practice guidelines recommend a higher HbA1c target (e.g.,
- 189 <7.5% or <8.0%) in patients with multiple comorbidities, limited life expectancy, and those at risk of
- 190 hypoglycemia, which almost certainly includes dialysis patients [10,19]. The Joint British Diabetes
- 191 Societies guidelines recommended an HbA1c target for diabetic patients on dialysis of between 7.5
- and 8.5%. Hypoglycemic patients should have their doses reduced if HbA1c is <7.5% to avoid the risk
- 193 of hypoglycemia [9]. The National Institute for Health and Clinical Excellence (NICE) recommends
- 194 HbA1C targets between 6.5% and 7% in all diabetic patients, but has not specified a target for the
- dialysis population [20]. In contrast, Berns et al. recommend an HbA1C target of 7–8% for dialysis
 patients and the specific target should be individualized according to the risk of hypoglycemia and
- 197 comorbidities. For example, for younger patients (under 50 years) and without significant
- 198 comorbidities, the HbA1C target should be close to 7% (7–7.5%), while higher HbA1c (7.5–8%) should
- be aimed at in older dialysis patients with multiple comorbidities [15].

200 XI. MANAGEMENT OF HYPOGLYCEMIC THERAPY IN PD

- 201 A. Non-pharmacological Therapy
- 202 The management of diabetic patients on dialysis requires a multidisciplinary approach. Here, we
- 203 detail some general advice based on international recommendations.
- 204 a. Dietary Recommendations and Education

Dietary advice should include information on diabetes and the specific renal dietary requirements. Each dialysis unit should have appropriate dietary expertise ready to provide a tailored approach to each diabetic patient on dialysis. They provide professional and comprehensive support for patient adherence to their prescribed diet. The nutritional management of diabetic patients on dialysis should consider energy, protein, phosphate, potassium, salt, fluids, and vitamins.

210 Nutritional Status:

Regardless of the dialysis method used, patients are generally malnourished. Several factors 211 212 contribute to this: inadequate protein intake, gastroparesis, enteropathy, metabolic stress, to which 213 may be added intercurrent pathology, in particular peritoneal infection. Particular effort must be 214 made to limit sugar and unsaturated fat intake. It is therefore recommended that patients have an 215 intake of 140 to 160 g of carbohydrates and a protein intake of around 1.5 g/kg of body weight per 216 day. In these patients, nutrition can be improved by the use of an IP exchange per day of a 1.1% 217 amino acid-rich solution, preferably administered during the best meal. The dose of dialysis delivered 218 also plays an important role in nutritional status. Currently, the recommended dose of dialysis 219 delivered per week corresponds to a KT /V urea of 1.7 and a total creatinine clearance of 50 220 L/week/1.73 m². These targets do not differ from those of the non-diabetic population.

According to the NKF KDOQI guidelines, total energy should consist of 50–60% carbohydrates, <30% fat, and at least 15% protein. Fruits, vegetables, and low-potassium carbohydrates with a lowmoderate glycemic index should be encouraged to achieve the recommended "5 a day" servings of fruits and vegetables [21]. Salt intake <6 g/day is recommended and should be emphasized as part of fluid management. Nasogastric feeding or gastrostomy feeding may be necessary for some patients if oral nutrition is insufficient [9]

oral nutrition is insufficient [9].

PD may offer greater lifestyle benefits than hemodialysis, with fewer dietary restrictions and better preservation of residual renal function; however, one of the major problems of PD in diabetics is the increasing risk of peritoneal fibrosis. Diabetic patients have a thicker and poorly vascularized peritoneal membrane even before starting PD; this, in addition to recurrent peritonitis and the use of conventional high-glucose PD solutions, are all implicated in functional changes leading to peritoneal membrane failure [22, 23].

233 Recommendations:

- 234• Therapeutic education
- 235 Dietary advice
- 236 Oral nutritional supplementation
- 237 IP nutrition during long exchanges
- 238 Reduced carbohydrate intake
- 239 Glucose-sparing strategies
- 240 Regular exercise
- 241 Regular and meticulous glycemic control
- 242 b. Active exercise and weight control
- 243 A higher BMI should predict a lower mortality rate in dialysis patients because it determines a better
- status compared to malnutrition and reduced albumin levels, which are independent predictors of
- 245 mortality [24]. However, overweight and obese patients considering kidney transplantation should be
- encouraged to lose weight to reduce surgical complications and improve patient and allograft survival
- 247 post-transplant.

248 B. Pharmacologic Therapy

- 249 1. Insulin Therapy:
- 250 According to the KDOQI guidelines, insulin use should be encouraged in dialysis patients, particularly
- those whose properties are similar to human insulin physiology. Some oral agents should either be
- used with caution or not at all in dialysis patients [24]. Dialysis patients may require either basal
- insulin alone or basal insulin as part of multiple daily injections [25,26]. It is recommended that the
- initial insulin dose be reduced to approximately 50% of that of pre-dialysis patients, and the dose may
- be increased based on daily glycemic monitoring of CGMS and HbA1c levels [27,28,29].
- 256 Patients starting peritoneal dialysis may continue treatment if their blood glucose is controlled;
- 257 however, insulin may be introduced to maintain glycemic targets.
- 258 In PD, insulin can be administered either subcutaneously or intraperitoneally; the intraperitoneal (IP)
- route has a more favorable effect on glycemic control. Insulin is instilled directly into an empty
- 260 abdominal cavity before infusion of the dialysis solution into this cavity. It is physiologically delivered
- directly to the liver via the portal circulation. As a result, peripheral insulin action is minimized,
- resulting in better insulin sensitivity. The IP route requires higher doses of insulin because the
- 263 dialysate adsorbs and insulin comes into contact with the superficial plastic of the dialysate solution
- 264 [30]. Studies have shown that insulin dose requirements could be twice that of the subcutaneous
- route [31]. In addition, intraperitoneal insulin administration is associated with an increased risk of

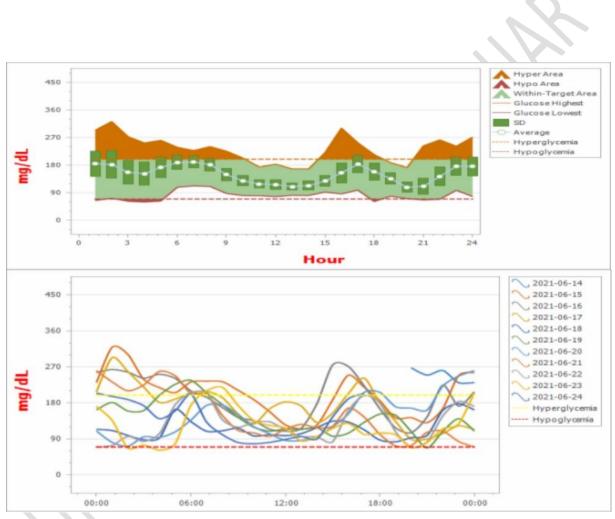
- bacterial infections, fibroblast proliferation, and hepatic subcapsular steatonecrosis [10, 32]. Another
- 267 disadvantage of intraperitoneal administration is dose fluctuation [33].
- 268 Determining the daily dose:
- 269 269 Add the total insulin dose administered pre-dialysis, then multiply by 2 to obtain the initial daily270 insulin dose.
- 271 I Gradually adjust the dose based on glycemic control.
- 272 I The final dose is usually 3 times the NPH dose + the usual dose.
- 273 2. Oral Hypoglycemic Drugs
- 274 The medications used to treat diabetes mellitus have expanded over the last decade. However, many
- 275 hypoglycemic drugs contain active metabolites that are metabolized and excreted by the kidneys;
- thus, they require dose adjustment or avoidance in dialysis patients . Oral agents can also be used in
- 277 dialysis patients.
- First-generation sulfonamides, including acetohexamide, tolbutamide, chlorpropamide, and
 tolazamide, are not recommended because they have a longer half-life and an increased risk of
 hypoglycemia. It is recommended to use a second-generation sulfonylurea such as gliclazide, which is
 metabolized by the liver and is associated with a reduced risk of hypoglycemia [34,35].
- 282 2. Glinides: Repaglinide is the preferred agent in this class because it is metabolized by the liver; the 283 inactive metabolites are excreted in the urine. It is therefore associated with a lower risk of 284 hypoglycemia. Nateglinide is less preferred because the metabolites are active, unlike repaglinide; 285 therefore, there is an increased risk of hypoglycemia [27,35].
- 3. Thiazolidinediones (TZDs). TZDs are metabolized by the liver, and neither the drug nor its metabolites are excreted by the kidneys. The main side effect of TZDs is fluid retention in dialysis patients, which is associated with a lower risk of hypoglycemia, improved lipid profiles, and reduced inflammation [36].
- 290 4. Dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors).
- 291 DPP4 inhibitors are generally safe in dialysis patients. Some doses of certain molecules may need to 292 be adjusted in patients with CKD and dialysis.
- 293 5. GLP-1 analogs:
- 294 Delay gastric emptying and promote early satiety and weight loss.[27] Exenatide and lixisenatide are 295 excreted by the kidneys and are not recommended for GFR <30/mL/min/1.73 m2. Liraglutide is not 296 metabolized or eliminated by the kidney; however, there are limited data on the use of liraglutide in 297 dialysis patients. Manufacturers caution against administration in moderate to severe renal 298 dysfunction; however, few authors suggest that no dose adjustment is necessary in patients with 299 ESRD [37,38]. Dulaglutide is a long-acting GLP1 analogue that is administered once weekly. In the 300 AWARD 7 trial, dulaglutide was compared with insulin, and it showed fewer hypoglycemic events and 301 renal benefits without compromising glycemic control. Manufacturers recommend use up to CKD 302 stage 4 and with caution in CKD stage 5 without dose adjustment [39]. The effect of dulaglutide on

- 303 renal function was evaluated in a study by Tuttle et al. who analyzed the effects of dulaglutide on 304 renal function in phase I and II trials. The authors concluded that dulaglutide did not affect eGFR and 305 slightly decreased albuminuria [40].
- 306 6. AGIs (alpha glucosidase inhibitors). Alpha-glucosidase inhibitors (acarbose, miglitol) are primarily307 renally excreted and should be avoided.
- 308 7. SGLT2 inhibitors. The use of SGLT2 inhibitors has been associated with significant cardiovascular
- 309 and renal benefits, however. The 2022 KDIGO guidelines for diabetes in CKD recommend the use of
- 310 SGLT2 inhibitors for patients with EGFR >20 mL/min per 1.73 m2 but not below, as there is a lack of
- 311 evidence of benefit and safety. The guidelines also recommended that patients already on SGLT2-i
- 312 may continue the drug until dialysis. These recommendations are likely to be revised pending the
- 313 results of ongoing clinical trials [41].

314 XII. CLINICAL CASE OF A DIABETIC PERSON ON PD

- 54-year-old patient on peritoneal dialysis, BMI 28 kg/m2, weight 87 kg, height 177 cm, BP 17/8 cmHg,
- Hb at 9.3 g/dL, HbA1c 9.5%, hypercholesterolemia 2.4 g/L, LDL 1.4 g/L, and TG 2.8 g/L with a UFT of
- 317 800 ml and urine output of 200 ml/day
- 318 Patient Concerns
- 319 Increased HbA1c and weight
- 320 Hypoglycemia +++
- OMI and dyspnea due to fluid and salt overload
- Chest X-ray reveals a sulcus with moderately abundant pleurisy
- Self-monitoring of blood glucose levels reveals the following values:

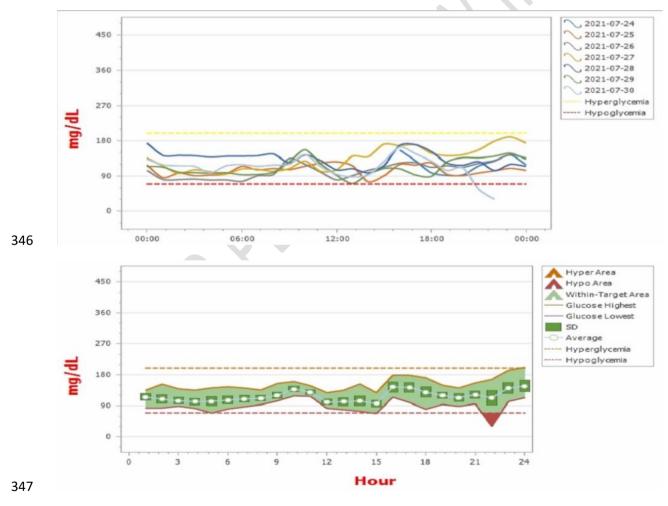
Finger-stick blood glucose (FBG)	D1	D2	D3	D4	D5
Fasting blood glucose (FBG) (mg/dl)	2.8	3	2.7	3.2	3.6
Pre-lunch blood glucose (mg/dl)	1.6	1.8	1,8	1.6	1.6
Pre-dinner blood glucose (mg/dl)	2.3	2	3	2	3.2



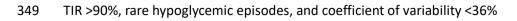
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- 326 CGMS Comment:
- A Time in Range < 70% with ART > 40% with several clinically asymptomatic hypoglycemic episodes
- 328 and a coefficient of variability > 36% (normal < 36%)
- The patient received 3 bags: two 1.36% glucose isotonic and one 2.5% glucose bag in the evening with :
- 331 Novomix 30: 28 IU in the morning and 16 IU in the evening

- Atorvastatin 10 mg/day, Lasilix 250 mg/day, Amlodipine 5 mg/day, Kardegic 75 mg/day, Calcium
- 333 Element 1.5 g/day, Darbapotine 50 μ g/week
- 334 Our management aims to reduce weight gain and episodes of excursion glycemic, asymptomatic
- hypoglycemia, for glucose saving and to improve ultrafiltration since the patient presented signs ofoverload with OMI, pleurisy and HBP. We opted for
- 337 3 PD exchanges: 2 iso 1.36% bags and one icodextrin bag in the evening on a full stomach
 338 With a basal-bolus regimen: based on GLARGINE U300 "TOUJEO": 30 IU in the evening
- 339 combined with rapid-acting insulin "Novorapid": 8 IU-8 IU-6 IU
- 340 Increased atorvastatin doses to 20 mg/day
- 341 Discontinued amlodipine due to an improvement in UF to 1500 ml and normalization of BP
 342 to 132/82 mmHg
- 343 The outcome was marked by improved glycemic figures (as shown below in the CGMS figures) with
- 344 less hyperglycemia and fewer hypoglycemic episodes, and especially glucose sparing with improved
- 345 ultrafiltrate.



348 CGMS Commentary:



350

351 XIII. CONCLUSION

- 352 The management of diabetic patients on dialysis is a real challenge and requires a multidisciplinary
- 353 approach. Ideally, treatment should be individualized for each diabetic patient on dialysis to reduce
- diabetes-related complications, minimize adverse events, and increase survival rates. This requires
- 355 continuous, effective glycemic assessment tailored to peritoneal dialysis patients, particularly
- 356 continuous interstitial glucose monitoring (CGMS), which, in our clinical case, demonstrated an ease
- 357 in achieving therapeutic targets with fewer complications and greater sensitivity to glycemic
- 358 variations. Above all, it enabled accurate interpretation of clinical and biological data, allowing for
- 359 profile-dependent therapeutic adaptation.
- 360 Kidney transplantation with or without simultaneous pancreas transplantation remains the primary
- 361 replacement therapy for diabetics with ESRD. It improves the patient's quality of life compared to
- 362 dialysis. However, this is often difficult with the presence of multiple comorbidities and reduced
- 363 availability of donor organs.
- 364

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