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An observational study on differential antidiabetic therapy in the management of chronic kidney disease

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ABSTRACT

BACKGROUND INFORMATION: Chronic Kidney Disease (CKD) is a serious complication of Diabetes Mellitus (DM) that leads to progressive loss of kidney function. Effective glycaemic control and appropriate treatment are essential to delay disease progression and improve patient outcomes.

AIM & OBJECTIVES: To compare the effectiveness of oral antidiabetic drugs, insulin therapy, and combination therapy in CKD patients with Diabetes Mellitus by assessing fasting blood sugar (FBS), serum creatinine levels, and clinical outcomes.

METHODOLOGY: A six-month concurrent observational study was conducted among 503 hospitalized CKD patients with diabetes. Data regarding CKD stage, FBS, serum creatinine, and treatment patterns were collected from patient records and analysed to evaluate treatment effectiveness.

RESULTS: Most patients were in Stage V CKD, followed by Stages IV and III. Significant reductions in FBS and serum creatinine levels were observed after treatment. Oral therapy was mainly used in early CKD stages, whereas insulin and combination therapy were more commonly prescribed in advanced stages, resulting in better glycaemic control and renal function.

CONCLUSION: Appropriate treatment and regular monitoring of blood glucose and renal function improve glycaemic control, slow CKD progression, and enhance clinical outcomes in patients with CKD and Diabetes Mellitus.

KEYWORDS: Chronic Kidney Disease, Diabetes Mellitus, Fasting Blood Sugar, Serum Creatinine, Oral Antidiabetic Drugs, Insulin Therapy, Combination Therapy, Glycaemic Control.

1. INTRODUCTION

Chronic kidney disease (CKD) is characterized by "the presence of kidney damage or an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m², persisting for 3 months or more, irrespective of the cause."[1]

Diabetes mellitus is a "metabolic disorder caused by either a lack of insulin secretion, impaired insulin action, or both. Notably, insulin plays an important role as an anabolic hormone, affecting the metabolism of carbohydrates, lipids, and proteins."[2]

In 2014, "the WHO announced that 8.5% of adults aged 18 and above were affected by diabetes. In 2019, diabetes was responsible for 1.5 million deaths, with 48% of these occurring before the age of 70. Additionally, diabetes led to another 460,000 deaths due to kidney disease, and roughly 20% of cardiovascular-related deaths" were attributed to elevated blood glucose levels. From 2000–2019, there was a 3% rise in standardized mortality rates related to diabetes. In lower-middle-income countries, the mortality rate associated with diabetes increased by 13%. In contrast, the likelihood of succumbing to any of the four primary non-communicable diseases (which include cardiovascular diseases, cancer, chronic respiratory diseases, or diabetes) between "the ages of 30 and 70 declined by 22% worldwide from 2000 to 2019."[3]

In clinical practice, identifying the precise origin of renal impairment in diabetic individuals remains highly challenging. The development of kidney disease is a multifactorial process heavily influenced by advanced age and concurrent illnesses, most notably high blood pressure. Furthermore, the overall frequency of renal dysfunction differs across various demographic groups, including sex, race, and ethnic background.

Compounding this diagnostic difficulty is a shifting clinical landscape the classic presentation of kidney disease among diabetic populations has evolved, showing a marked decline in detectable protein leakage alongside a rising incidence of isolated drops in the eGFR. Because of these changing patterns, isolating the exact impact of diabetes alone on modern renal disease remains elusive. This diagnostic ambiguity poses significant hurdles for establishing accurate clinical diagnoses and formulating targeted protocols for the prevention and management of kidney disease.

Over the last 30 years, the number of people with diabetes and CKD has grown in step with the rising prevalence of diabetes itself. "Approximately 8.4 million adults in the United States now have diabetes and CKD, and diabetes is now the presumed cause of End stage renal disease (ESRD) for approximately one half of patients with incident cases."[4,5]

According to the American diabetes association (ADA), the modern lifestyle has created a perfect storm for diabetes, pushing global patient numbers toward an estimated 380 million by 2025. This epidemic has triggered a secondary crisis: diabetic kidney disease (DKD), which develops in up to 40% of patients. DKD also referred to as diabetic nephropathy. The patients with diabetes and CKD presented a unique cohort of DKD population, which is identified by elevated urine albumin

excretion or reduced GFR or both.[6]

DKD is the leading cause of chronic and end-stage-renal disease worldwide (CKD and ESRD, respectively) and is the single strongest predictor of mortality in patients with diabetes. According to the national kidney foundation(NKF), in the united States about 200,000 patients receive ESRD care due to DKD, with 50,000 new patients starting dialysis each year.[7]

DKD does more than just drive progression toward total kidney failure (ESRD); it independently multiplies the risks of cardiovascular disease and premature death, creating an overwhelming financial crisis for global healthcare.

There is reduction in progression of CKD in Type 2 Diabetes (T2D) with angiotensin converting enzyme inhibitors (ACEi)/angiotensin II receptor blocker (ARB), sodium-glucose cotransporter-2 inhibitors (SGLT2i), and non steroidal mineralocorticoid receptor antagonists (MRA), as discussed in subsequent sections, as well as with endothelin receptor antagonists. Ongoing trials may offer additional new opportunities.[8]

CKD have shifted significantly over time. While glomerulonephritis (GN) was historically a leading cause of kidney failure worldwide, modern lifestyle shifts such as rising rates of obesity, diabetes, and high blood pressure combined with more effective, aggressive medical treatments for GN, have altered this dynamic. Consequently, diabetes and hypertension have firmly established themselves as the leading causes of CKD in developed nations.

Distinct disparity exists when comparing the root causes of ESRD between developed and developing countries. In wealthier nations like the United States, the underlying cause of kidney failure is usually clearly identified. Conversely, in developing regions, a remarkably high percentage of ESRD cases are classified as having an unknown origin. This gap is largely driven by healthcare access issues, as patients in developing countries often present with advanced disease and are referred to kidney specialists too late in the illness for a proper initial diagnosis to be made.

The stages of CKD:

Staging CKD is a way of quantifying its severity. CKD can be estimated by GFR (in mL/min/1.73 m^2) CKD has been classified into 5 stages.

- Stage 1: Normal GFR ($\geq$ 90 mL/min/1.73 m^2) plus either persistent albuminuria or known structural or hereditary renal disease
- Stage 2: GFR 60 to 89 mL/min/1.73 m^2
- Stage 3a: 45 to 59 mL/min/1.73 m^2
- Stage 3b: 30 to 44 mL/min/1.73 m^2
- Stage 4: GFR 15 to 29 mL/min/1.73 m^2
- Stage 5: GFR < 15 mL/min/1.73 m^2 [9]

Types of diabetes includes:

- **Type 1 diabetes** encompasses diabetes that is primarily a result of pancreatic beta cell destruction with consequent insulin deficiency, which is prone to ketoacidosis. This form includes cases due to an autoimmune process and those for which the etiology of beta cell destruction is unknown.
- **Type 2 diabetes** may range from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance. Ketosis is not as common.
- **Gestational diabetes mellitus** refers to glucose intolerance with onset or first recognition during pregnancy.

The diabetes connection with CKD

T2D is the leading cause of this damage. High blood sugar acts like sandpaper on the delicate filters of the kidney. Over years of irritation, these filters scar and lose their ability to function.

The standard rule for a formal diagnosis is that these abnormalities either a slow filtration speed or physical signs of damage must be present for at least three months. This ensures the issue is a permanent, chronic condition rather than a temporary spike caused by dehydration or a short-term illness.

- **Other specific types** include a wide variety of relatively uncommon conditions, primarily specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use.

Causes of CKD with diabetes mellitus:

Diabetic nephropathy is a condition where diabetes causes damage to the blood vessels and cellular structures within the kidneys. When diabetes impairs these delicate vessels, it triggers diabetic nephropathy. This progressive damage hinders normal kidney function and can ultimately culminate in kidney failure.

This condition frequently develops as a complication in individuals with poorly managed type 1 or type 2 diabetes.

- **Blood vessel damage:** Chronically high blood sugar levels gradually injure the renal blood vessels responsible for waste filtration.
- **The role of hypertension:** This initial kidney damage often triggers elevated blood pressure. In turn, high blood pressure increases strain on the kidneys filtering units, accelerating the cycle of organ damage.

Risk factors of CKD with diabetes mellitus:

- **Proteinuria:** High levels of albumin in the urine serve as a primary indicator of advancing renal damage.
- **Hyperglycemia:** Elevated and inconsistent blood sugar levels trigger oxidative stress and chemical changes that scar kidney tissue.
- **Hypertension:** High blood pressure strains the renal filtration system, significantly increasing the likelihood of organ failure.
- **Dyslipidemia:** Imbalanced cholesterol and fats can be toxic to kidney cells, leading to inflammation and cellular death.
- **Obesity:** Excessive body weight causes the kidney's filters to enlarge and malfunction, though weight loss can help delay progression.
- **Smoking:** Tobacco use accelerates kidney scarring and remains a major independent contributor to end-stage renal disease.

Signs and Symptoms of CKD with diabetes mellitus:

In the beginning, diabetic kidney disease often develops silently without obvious indicators. However, as renal function diminishes, several distinct warning signs and symptoms may emerge:

- **Proteinuria (Albumin in the Urine):** An early, vital marker of renal decline is the excretion of albumin in urine. Medical screenings can identify this protein buildup long before physical changes are noticeable.
- **Fluid retention (Edema):** Inefficient removal of surplus sodium and fluids by the kidneys can cause visible puffiness or swelling, particularly in the lower legs, ankles, hands, and facial area.
- **Persistent lethargy:** When compromised kidneys fail to filter waste effectively, toxins accumulate in the circulation, resulting in ongoing exhaustion and general malaise.
- **Increased nighttime urination:** Alterations in renal capability frequently manifest as a frequent need to void the bladder during sleeping hours.
- **Frothy urine:** High concentrations of protein can alter the appearance of urine, making it seem distinctly bubbly or foamy**.**
- **Elevated blood pressure:** Hypertension shares a cyclical relationship with renal damage. Impaired kidneys lose the capacity to stabilize blood pressure, which can accelerate organ strain.
- **Nausea and reduced appetite:** The accumulation of metabolic waste products often triggers a loss of appetite, feelings of sickness, or a distinct metallic taste.
- **Cognitive difficulties:** Advanced toxin accumulation can impact neurological clarity, culminating in confusion, brain fog, or an inability to maintain focus.

Pathophysiology of CKD with diabetes mellitus

1. The trigger: Hyperglycemia to chemical damage

Diabetes mellitus/rightarrow persistent hyperglycemia: Chronic high blood glucose levels overwhelm the body's metabolic pathways.

Formation of advanced glycation end products (AGEs): Excess glucose binds non-enzymatically to proteins and lipids in the blood vessel walls, forming harmful molecules called AGEs.

Oxidative stress and inflammation: AGEs bind to specific receptors, triggering a cascade of free radical production (oxidative stress) and inflammatory cytokines that damage local tissue.

2. Structural and hemodynamic changes in the kidney

Activation of RAAS: The renin-angiotensin-aldosterone system (a hormone system that regulates blood pressure) becomes hyperactive. Angiotensin II constricts the efferent arterioles (the exit ramp of the kidney's filtering units).

Increased glomerular pressure (Hyperfiltration): Constricting the exit ramp creates a backup of pressure inside the glomerulus (the kidney's filtering capillary bed).

Basement membrane thickening, podocyte injury, & mesangial expansion: The high pressure and inflammation stretch and damage the podocytes (specialized cells that act as a colander to keep proteins in the blood). The basement membrane thickens in a flawed attempt to repair itself. Mesangial cells expand, compressing the capillaries and reducing the actual filtering surface area.

3. The clinical hallmark: proteinuria

Albuminuria/Proteinuria: Because the structural "colander" (podocytes and basement membrane) is physically damaged and has lost its negative electrical charge, proteins (like albumin) leak from the blood into the urine. This is the definitive clinical sign of diabetic kidney disease.

4. The vicious cycle of chronic kidney disease (CKD)

The diagram features a feedback loop representing the progressive, self-perpetuating nature of kidney disease:

Reduced number of functioning nephrons: As individual filters (nephrons) are destroyed by inflammation and scarring (glomerulosclerosis), they cannot be replaced.

Decreased GFR: With fewer working filters, the kidney's overall capacity to clean the blood drops.

Accumulation of urea and creatinine: Waste products normally cleared by the kidneys begin to build up in the bloodstream (known as azotemia).

Fluid and electrolyte imbalance: The kidneys fail to properly balance water, sodium, potassium, and acid-base levels in the body.

Systemic hypertension and renal structural damage: Fluid retention and vascular stiffness cause overall

high blood pressure. This systemic high pressure forces the remaining healthy nephrons to work even harder under higher pressure, which accelerates their destruction.

The loop: This damage circles back, reducing the number of functioning nephrons even further, creating a downward spiral.

5. Final Stage: kidney failure

Progressive decline/rightarrow severe reduction in GFR/rightarrow worsening CKD: The vicious cycle causes a relentless drop in kidney function over years or decades.

ESRD: This is the final stage of CKD (Stage 5), where the kidneys can no longer sustain life on their own (typically when GFR drops below 15 mL/min). At this point, the patient requires renal replacement therapy either dialysis or a kidney transplant to survive.[10]

Diabetes mellitus

↓

Hyperglycemia (High blood sugar)

↓

Insulin resistance

↓

Formation of advanced glycation end products (AGEs)

↓

Oxidative stress + inflammation

↓

Damage to glomerular blood vessels

↓

Glomerular hypertension

(Increased pressure inside glomeruli)

↓

Glomerular damage

Mesangial expansion

Thickening of glomerular basement membrane

↓

Proteinuria

(Protein leakage into urine)

↓

Tubulointerstitial inflammation & fibrosis

↓

Nephron loss

(Decrease in functional nephrons)

↓

Decline in GFR

↓

Progressive renal dysfunction

↓

CKD

↓

ESRD

The two pillars of diagnosis

1. **Filter quality (Albuminuria):** The checks for a protein called albumin in the urine. For example the kidney is like a coffee filter; if grounds (protein) are getting into the cup (the urine), it means there's a hole in the filter.
2. **Filter speed (eGFR):** It is a calculated number based on creatinine levels in the blood. It acts like a speedometer for the kidneys, showing how many milliliters of blood are being cleaned every minute.

The two essential biomarkers used to screen for and diagnose CKD in patients with T2D are:

- The blood test measures the filtering capacity of kidneys (filtering waste). A persistent decline in eGFR (specifically below 60 mL/min/1.73 m^2) indicates reduced kidney function.

- UACR (Urine Albumin-to-Creatinine Ratio): The test identifies kidney damage by measuring the amount of albumin (a protein) leaking into the urine. A value greater than 30 mg/g indicates abnormal albumin excretion.[11]

Treatment/management of CKD with diabetes mellitus

The management of CKD in diabetes mellitus mainly focuses on controlling blood glucose levels, maintaining blood pressure, reducing proteinuria, and preventing cardiovascular complications. Glycemic control is one of the most important components in the management of DKD. Elevated blood glucose levels increase glomerular pressure and damage renal tissues over time. Studies have shown that maintaining hemoglobin A1c around 7% can significantly reduce the risk of microvascular complications, including nephropathy. However, treatment targets should be individualized according to the patient's age, stage of kidney disease, and associated comorbidities.

Blood pressure management is another essential aspect in the treatment of CKD with diabetes mellitus. Hypertension accelerates kidney damage and increases the risk of cardiovascular disease. Angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs) are commonly recommended because they not only reduce blood pressure but also decrease albuminuria and protect kidney function. Proper blood pressure control slows the progression of chronic kidney disease and decreases the chances of heart failure, stroke, and myocardial infarction.

Cardiovascular disease is highly prevalent among patients with CKD and diabetes mellitus. Patients with diabetic kidney disease are at increased risk for coronary artery disease, heart failure, and stroke. Therefore, management strategies should also focus on reducing cardiovascular risk factors. Lipid-lowering therapy, blood pressure control, glycemic management, and lifestyle modifications are essential components of comprehensive patient care. Multidisciplinary management involving nephrologists, endocrinologists, dieticians, and nurses is often necessary to achieve optimal outcomes.

Anemia, electrolyte imbalance, metabolic acidosis, and bone mineral disorders are common complications seen in advanced chronic kidney disease. These complications can worsen patient outcomes and decrease quality of life if not managed appropriately. Early recognition and treatment of CKD-related complications are important to prevent hospitalization and mortality. Nutritional support, erythropoietin therapy, phosphate binders, and electrolyte correction may be required depending on the patient's condition.

Lifestyle modification plays a significant role in the management of CKD associated with diabetes mellitus. Patients are advised to follow a healthy diet low in sodium, sugar, and saturated fats. Dietary protein intake may also need adjustment depending on the stage of kidney disease. Regular physical activity, smoking cessation, weight management, and avoidance of alcohol consumption are important interventions that help improve glycemic control and overall renal health. Lifestyle changes can reduce insulin resistance, improve cardiovascular function, and

delay complications.

Monitoring kidney function regularly is important in diabetic patients to identify kidney damage at an early stage. Healthcare professionals commonly assess serum creatinine levels, eGFR, and urinary albumin excretion to evaluate kidney function. Microalbuminuria is considered an early marker of diabetic nephropathy. Early detection allows timely intervention and helps prevent irreversible kidney damage. Regular screening is therefore strongly recommended in all diabetic patients, especially those with long-standing diabetes.

Medication management is particularly important in CKD patients with diabetes because impaired kidney function alters drug metabolism and excretion. Some oral antidiabetic medications may accumulate in the body and increase the risk of adverse effects such as hypoglycemia. Therefore, dosage adjustments are often necessary in CKD patients. Insulin therapy may also require careful monitoring because insulin clearance decreases as kidney function declines. Healthcare providers must select medications carefully to ensure safety and effectiveness.
Newer antidiabetic medications such as SGLT2 inhibitors and GLP-1 receptor agonists have shown promising benefits in patients with diabetic kidney disease. Clinical studies demonstrate that these medications not only improve glycemic control but also provide renal and cardiovascular protection. SGLT2 inhibitors help reduce intraglomerular pressure and slow the progression of kidney disease. These advances have significantly improved the management of diabetic kidney disease in recent years.

Patient education and self-management are also essential in the management of CKD with diabetes mellitus. Patients should understand the importance of medication adherence, dietary restrictions, blood glucose monitoring, and routine follow-up visits. Education improves patient participation in treatment and promotes early reporting of symptoms and complications. Family support and counseling further enhance adherence to treatment plans & improve psychological well-being.

Non-pharmacological management:

Nutrition:
Non–dialysis-dependent CKD, daily protein should be 0.8 g/kg of body weight to slow kidney decline. Eating more than 1.3 g/kg/day (or >20% of daily calories) harms kidney function and increases heart disease risks, while eating less than 0.8 g/kg/day provides no benefit. Additionally, limiting sodium to <2,300 mg/day helps manage blood pressure, and potassium should be customized, as lower kidney function makes it harder to filter these minerals. In contrast, patients on dialysis need more protein to prevent malnutrition, and their sodium and potassium limits must be personalized based on labs, medications, and blood pressure.

Glycemic:
Intensive glucose lowering delays albuminuria and slows kidney function loss in both type 1 and type 2 diabetes, proving that reducing blood sugar itself helps prevent CKD progression. However, for patients with existing CKD, intensive management increases the risks of dangerous hypoglycemia and

mortality. Because the kidney benefits of strict control take years to manifest (2+ years for type 2 and 10+ years for type 1 diabetes) and A1C metrics become less reliable in advanced CKD stages, a less intensive approach with higher A1C goals is often recommended for patients with kidney disease and major comorbidities to prevent severe low blood sugar.

Management of proteins:

ACE inhibitors and ARBs effectively treat diabetic kidney disease regardless of protein levels, but for nondiabetic kidney disease, they only slow progression if proteinuria exceeds 500 mg/day. Regarding diet, the Modification of Diet in Renal Disease (MDRD) study found that restricting protein (0.58 vs. 1.3 g/kg/day) did not significantly impact average kidney function decline over three years, though secondary analysis and a meta-analysis suggest it may mildly slow progression and reduce protein loss in rapidly worsening cases. Because low

pre-dialysis albumin levels predict poor survival outcomes, the National Kidney Foundation advises strict nutritional monitoring for adults on low-protein diets and completely discourages protein restriction in children with chronic kidney disease.

Fluid balance:

CKD impairs the kidneys' ability to manage sodium and fluid balance. When the GFR drops below 10–15 mL/min/1.73 m^2, compensatory processes fail. This failure prevents the excretion of sodium and free water, causing fluid accumulation and extracellular volume expansion. As the disease advances, this fluid retention routinely triggers peripheral edema, high blood pressure, and potentially life-threatening pulmonary edema. Notably, these same complications can emerge even at higher GFR levels if a patient's dietary intake of salt and water surpasses the kidneys' remaining capacity to eliminate them.

Pharmacological management:

Glucose lowering medication:

Certain glucose-lowering medications protect the kidneys through direct mechanisms that do not depend on blood sugar control. For instance, SGLT2 inhibitors help slow the loss of kidney function (GFR) by lowering blood pressure, weight, fluid pressure within the kidneys, and protein leakage in the urine. They also significantly reduce kidney inflammation and oxidative stress. Similarly, GLP-1 receptor agonists show promising direct benefits for kidney health, though their exact protective effects are still being fully evaluated. Because of these distinct advantages, a medication's specific impact on the kidneys should be a key factor when choosing a diabetes treatment.

SGLT2 inhibitors:

SGLT2 inhibits (canagliflozin, dapagliflozin, and empagliflozin) significantly improve renal outcomes when added to RAAS blockade in patients with proteinuric kidney disease, with or without diabetes. Key clinical trials underscore these benefits:

- **CREDENCE (Canagliflozin):** Stopped early due to efficacy; it demonstrated a 30% reduction in the relative risk of ESKD, doubled creatinine levels, or renal death in patients

with type 2 diabetes

- **DAPA-CKD (Dapagliflozin):** Lowered the risk of a combined primary event (≥50% eGFR decline, ESKD, or renal/Cadiovascular death) to 9.2% compared to 14.5% for the placebo group, showing consistent efficacy regardless of diabetes status.
- **EMPA-KIDNEY(Empagliflozin):** Reduced kidney disease progression or cardiovascular death to 13.1% (vs. 16.9% for placebo) across a wide range of baseline kidney functions, benefiting patients with eGFR levels as low as 20 mL/min/1.73 m².

Glucagon-like peptide-1 agonist (GLP-1) therapy:

In January 2025 the FDA approved the GLP-1 agonist semaglutide (Ozempic) to reduce the risk of sustained eGFR decline, end-stage kidney disease and cardiovascular death in adults with type 2 diabetes mellitus and CKD. Approval for this indication was based on results from the phase 3b flow trial, in which the addition of semaglutide to standard of care resulted in a 24% relative risk reduction of CKD worsening, ESKD, and death due to cardiovascular disease compared with placebo. Semaglutide had previous approval for use in adults with T2D to improve glycemic control and reduce the risk of major cardiovascular events in those with known heart disease. [12]

Renin angiotensin aldosterone system blockade (RAAS):

RAAS blockade using ACEis or ARBs is crucial for slowing CKD progression, significantly lowering long-term dialysis and mortality risks in patients with advanced disease. A large cohort study of advanced CKD patients showed that these medications reduced the composite risk of dialysis or death by 6%, despite a slight increase in hyperkalemia-associated hospitalizations. However, benefits vary greatly by age; a simulation study revealed that ACEis/ARBs provide only marginal benefit in preventing end-stage kidney disease (ESKD) in patients aged 70 and older. While the number needed to treat (NNT) to prevent one ESKD case ranges from 9 to 25 in younger patients, it exceeds 100 for older adults, likely due to differences in baseline risk and life expectancy.

Mineralocorticoid receptor antagonist (MRA):

In the finerenone in reducing kidney failure and disease progression in diabetic kidney disease (FIDELIO-DKD) trial of finerenone (Kerendia), a first-in-class selective nonsteroidal mineralocorticoid receptor antagonist, significant reductions in adverse renal and cardiovascular outcomes were seen in patients with type 2 diabetes and CKD.

Antidiabetics drugs used in renal impairment

S.NO	Category	Drug	T1/2	Duration of Action	Dialysis
1	Sulfonylureas	Glibenclamide	6–10 h	18–24 h	No
		Glimepiride	5–7 h	>24 h	No
		Gliclazide	6–15 h	18–24 h	No
2	Glinides	Repaglinide	0.6–1.8 h	4–6 h	Yes
		Nateglinide	1.2–1.8 h	4 h	No

3	Biguanide	Metformin	4–9 h	—	No
4	Glitazone	Pioglitazone	3–7 h; metabolites:	—	Limited experience;
			16–24 h		caution
5	Alpha-glucosidase inhibitors	Acarbose	—	—	No
6	GLP-1 receptor agonists	Exenatide	2.4 h	—	No
		Liraglutide	13 h	—	No
7	DPP-4 inhibitors	Sitagliptin	8–24 h	—	Limited experience with caution
		Linagliptin	10–40 h	—	No experience with caution
8	SGLT2	Dapagliflozin	12.5-13h	18-24h	No
		Empagliflozin	11-13h	24h	No
9 9	MRA	Finerenone	2-3h	-	Rapid clearance
1 0	ERAs	Macitentan	16h	-	No

Prevention for CKD

- Keep the blood sugar under control every day can help protect the kidneys from further damage and reduce future complications.
- Take medicines regularly and following the doctor's advice can slow the worsening of kidney disease in diabetic patients.
- Eat healthy foods with less salt, sugar, and oily items may help maintain both kidney health and diabetes control.

- Regular exercise and maintaining a healthy body weight can improve overall health and decrease stress on the kidneys.
- Avoid smoking and alcohol can reduce additional damage to the kidneys and improve blood circulation in the body.

2. REVIEW LITERATURE

- The authors Toshiki et.al, Iwai in the study titled "Diabetes mellitus as a cause or comorbidity of chronic kidney disease and its outcomes: the Gonryo study" demonstrated that during a median follow-up of 4.44 years, 281 patients (11.3%) developed End Stage Kidney Disease(ESKD).At Chronic Kidney disease(CKD) stage glomerular filtration rate(G3b) in Diabetic Nephropathy(DN) patients had a higher ESKD risk with Hazard Ratio(HR) 7.10 (95% CI: 2.46–20.49), while Diabetes Mellitus(DM) with Non-Diabetic Renal Disease(NDRD) had HR 0.89 (95% CI: 0.19–4.24). DN patients also showed a faster eGFR decline of −9.7% per year.

  This study concludes that DN patients had a higher risk of (ESKD) and a rapid GFR decline at CKD stage G3b compared to DM with NDRD and non-DM patients. DM with NDRD showed renal outcomes similar to non-DM CKD. Proper risk stratification is important to determine whether DM is the cause or a comorbidity of CKD.

- The authors Johannes Ruhe et.al, in the study titled "Cardiovascular risk due to diabetes mellitus in patients with chronic kidney disease-prospective data from the German Chronic Kidney Disease cohort" demonstrated that over 6.5 years, DM increased the risk of non-cardiovascular death (HR 1.92; 95% CI 1.59–2.32), cardiovascular death (HR 2.25; 95% CI 1.62–3.12), 4-point Major Adverse Cardiovascular Events(MACE) (HR 1.93; 95% CI 1.62–2.31), and Hospitalization for Heart Failure(HHF) (HR 1.87; 95% CI 1.48–2.36). HHF risk was highest in CKD cardiovascular metabolic disease patients (HR 2.07; 95% CI 1.55–2.77).

  This study concludes that DM contributes to cardiovascular and mortality excess risk in patients with moderate to severe CKD in both, CKD cardio vascular metabolic disease and CKDgenetics. Patients with DM and CKDcardiovascular and metabolic causes are particularly susceptible to heart failure hospitalization.

- The authors Olivera Stojceva-Taneva et.al, in the study titled "Prevalence of diabetes mellitus in patients with chronic kidney disease" demonstrated that mean age was 45.97 ± 16.55 years; 17.97% were >60 years and 44.14% were males. Diabetes Mellitus prevalence was 13.9%, and Chronic Kidney Disease prevalence was 7.53%. Subjects aged ≥60 years had a 20-times higher CKD risk. Diabetics had a 3.13-times higher risk of CKD stage 3–5. Diabetes was more strongly associated with low eGFR in younger subjects (<60 years) than older subjects (OR 3.29 vs 1.21).

  This study concludes that our study showed that chronic kidney disease is frequent in the republic of macedonia and is associated with older age and diabetes. Diabetes had a

significantly stronger association with CKD at younger age.

- The authors Jesse D Schold et.al, in the study titled "Diabetes control and the risks of ESRD and mortality in patients with CKD" demonstrated that during 2.3 years of follow-up, 957 patients died and 205 reached ESRD. HbA1c <6% increased mortality risk (HR 1.23; 95% CI 1.01–1.50), while HbA1c ≥9% also increased all-cause mortality (HR 1.34; 95% CI 1.06–1.69) compared with HbA1c 6–6.9%. Diabetes accounted for >12% of deaths overall and >19% in patients with HbA1c >9%.

  This study concludes that in this cohort of patients with CKD with diabetes, HbA1c levels < 6% and ≥9% were associated with higher risk for death. HbA1c levels were not associated with ESRD in this specific CKD population. Diabetes-related deaths increased with higher HbA1c levels.

- The authors You-Bin Lee et.al, in the study titled "Risk of end-stage renal disease from chronic kidney disease defined by decreased glomerular filtration rate in type 1 diabetes: a comparison with type 2 diabetes and the effect of metabolic syndrome" demonstrated that during 10,701,375.84 person-years of follow-up, 43,693 ESRD cases developed. In Type 1 Diabetes Mellitus(T1D) patients with CKD, ESRD risk was higher compared with Type 2 Diabetes Mellitus(T2D) (HR 2.580; 95% CI 2.336–2.849) and non-diabetics (HR 9.267; 95% CI 8.378–10.251). Presence of Metabolic Syndrome(MS) further increased ESRD risk in T1D patients (HR 2.023; 95% CI 1.501–2.727).

  This study concludes that the presence of diabetes increases the risk for ESRD development from CKD. Furthermore, patients with Type 1 Diabetes have a higher risk for ESRD incidence from CKD than do patients with Type 2 Diabetes in a korean population. Metabolic syndrome may be a useful predictor for ESRD in CKD patients with T1D.

- The authors Xue Wang et.al in the study titled "Diabetes and chronic kidney disease in Chinese adults: a population-based cohort study" demonstrated that during 11.8 years of follow-up, 5,417 adults developed CKD. Diabetes mellitus increased the risk of CKD (HR 4.52; 95% CI 4.23–4.83), Diabetic Kidney Disease(DKD). (HR 33.85; 95% CI 29.56–38.76), and glomerulonephritis (HR 1.66; 95% CI 1.40–1.97). Uncontrolled diabetes showed higher risks, and DKD risk also increased in pre-diabetes and with elevated Random Plasma Glucose(RPG) levels.

  This study concludes that among chinese adults, diabetes was positively associated with CKD, DKD, and glomerulonephritis. Screen-detected and uncontrolled DM had a high risk of CKD, and pre-diabetes was associated with a greater risk of DKD, highlighting the significance of lifelong glycemic management.

- The authors Charuhas V Thakar et.al, in the study titled "Acute kidney injury episodes and chronic kidney disease risk in diabetes mellitus" among 3,679 patients (mean age 61.7 ± 11.2 years; creatinine 1.10 ± 0.3 mg/dL), 530 developed Acute Kidney Injury(AKI). Any AKI increased the risk of stage 4 CKD (HR 3.56; 95% CI 2.76–4.61), and each AKI episode doubled

the risk (HR 2.02; 95% CI 1.78–2.30).

This study concludes that AKI episodes are associated with a cumulative risk for developing advanced CKD in diabetes mellitus, independent of other major risk factors of progression.

- The authors Dr.Leila R.Zelnick et.al, in the study titled "Diabetes and CKD in the united states population,2009-2014"demonstrated that diabetic participants, 25% had CKD, whereas only 5.3% of non-diabetic participants had CKD. Albumin-to-creatinine ratio ≥30 mg/g was found in 16% of diabetics compared to 3% of non-diabetics, while severe albuminuria (≥300 mg/g) was seen in 4.6% versus 0.3%, respectively. Reduced kidney function with eGFR <60 ml/min/1.73 m² occurred in 12% of diabetics and 2.5% of non-diabetes. Approximately 24% of CKD cases in U.S adults were attributed to diabetes.

  This study concludes that diabetes is closely linked with albuminuria and decreased kidney function, regardless of age, gender, or hypertension, and plays a major role in increasing the burden of chronic kidney disease (CKD) in the United States.

- The authors DN Koye et.al, in the study titled "Incidence of chronic kidney disease among people with diabetes: a systematic review of observational studies" demonstrated that 71 studies type-1 range from 1.3-3.8% patients and type-2 range from 3.8-12.7% patients are participants. The incidence of reduced kidney function, as eGFR <60 mL/min/1.73 m², generally ranged from 1.9% to 4.3% per year, although one study reported a higher rate of 8.9%. In addition, the annual incidence of end-stage renal disease ranged from 0.04% to 1.8%. The study concluded that people with diabetes, especially Type 2 diabetes, have a higher risk of developing kidney disease. Around 2–3% of Type 1 diabetic patients and about 8% of Type 2 diabetic patients develop microalbuminuria or albuminuria every year. The risk of reduced kidney function was about 2–4% per year, showing that kidney disease commonly progresses in diabetic patients over time.

- The authors Sabin Shurraw et.al, in the study titled " Association between glycemic control and adverse outcomes in people with diabetes mellites and chronic kidney disease" demonstrated that among 23,296 patients these study found that both in very low HbA1c levels (<6.0%) and high HbA1c levels (>8.0%) increased the risk of death with sever CKD (eGFR 15–29.9 mL/min/1.73 m²), the ESRD risk increased by 3% for HbA1c levels of 7–9% and by 13% for HbA1c levels above 9%.

  This study concludes that, people with diabetes and kidney who have very high sugar levels may get more health problems and kidney failure. Very low sugar levels may also be dangerous. so, blood sugar should be controlled properly, but not too much.

3. AIM AND OBJECTIVE

Aim: To do observational study on the management of chronic kidney disease with diabetes mellitus who is on oral, insulin and combination treatment.

Objectives:

- To assess and compare the treatment in oral, insulin and both therapies in the management of chronic kidney disease (CKD) with diabetes mellitus patients.
- To identify the changes in serum creatinine levels during treatment in the CKD stages.
- To identify and compare the blood sugar levels among patients receiving oral, insulin and both treatments.
- To compare the overall clinical outcomes and disease progression among the three treatment groups.

4. METHODOLOGY

Study designs:
This research utilizes a concurrent observational study design.

Study duration:
The study was conducted over a period of 6 months, encompassing data collection, patient observation, and subsequent analysis.

Study criteria:
Inclusion criteria:

- The people who have confirmed diagnosis of CKD in any clinical stage with concomitant diagnosis of diabetes mellitus.
- In patients who are receiving a regimen of antidiabetic and nephroprotective therapy.

Exclusion criteria:

- Severe comorbid illnesses or emergency conditions in which patients/patients caretakers are unable to cooperate.
- Patient case sheet which doesn't consist of both diabetes mellitus and chronic kidney diseases management/treatment.

Sources of data:

- Data was collected from multiple professional sources to ensure accuracy, form inpatient medical reports, which includes treatment charts, laboratory test/diagnostic reports, nurse's records, doctor's prescriptions which reveal CKD management and diabetes mellitus condition.

Procedure:

- **Data collection:**

The study followed a standardized procedure by using a data collection form which includes details about patient's demographics such as name, age, gender, educational background, occupation, residential status along with their differential diagnosis/current disease progression state, biological

data details regarding the laboratory report(FBS, Serum creatinine, eGFR) the values specifically related to CKD and diabetes and information regarding the type of therapy received by the patient were collected like oral therapy, insulin therapy and both/combination therapy. The management of CKD in diabetes mellitus was assessed based on laboratory reports. The inpatients were observed on daily basis until they discharge over a period of hospital stay that is 4-5 days, constantly for over a periods of 3-4 months to monitor changes in blood glucose levels and serum creatinine levels & the type of therapy they received any adverse effects like hypoglycemia were recorded during this cause a part of management of diabetes and CKD.

✓ **Analysis and interpretation of data:**

The data was analyzed manually and by using the range of FBS & serum creatinine values the no.of cases in which both FBS & serum creatinine values were decreased are identified which indicates the management of CKD of diabetes mellitus form which the type of therapy(oral, insulin and both/combination therapy) there are receiving are also identified form that which drugs/it's combination were prescribed(oral anti diabetics, insulin types & combination of oral anti diabetic, insulin types) to control diabetes managing CKD were identified. Results were interpreted to evaluate the effectiveness of each therapy in managing CKD with diabetes mellitus.

The results obtained was represented using tables, graphs, and pie charts along with statistical analyses using chi-square test method.

5. RESULTS AND DISCUSSION

RESULTS

Stages of CKD	No. of cases
Stages-1	15(2.98%)
Stages-2	70(13.92%)
Stages-3	124(24.65%)
Stages-4	146(29.03%)
Stages-5	148(29.42%)

Table 1: The table shows no. of cases in different stages of CKD

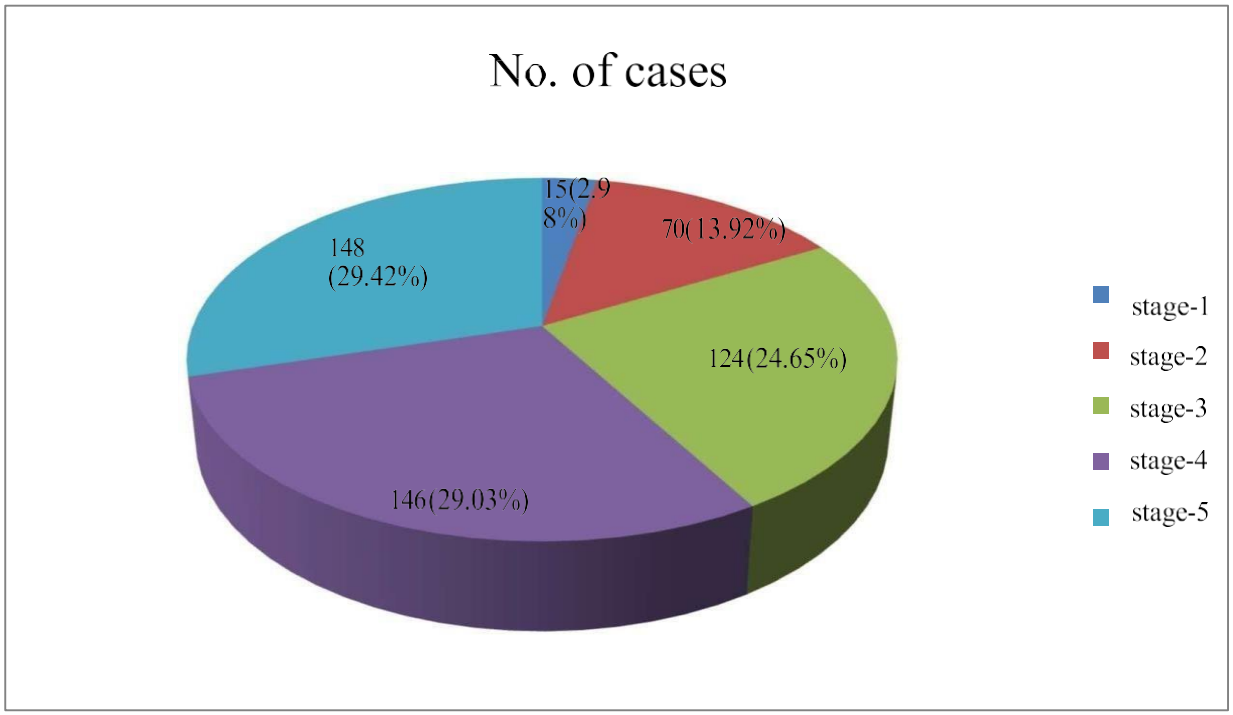

Fig 1: The above pie chart shows no. of cases in different stages of CKD

Based on the data, we identified that among 503 cases studied across different stages, 15 cases (3.0%) were in stage-1, 70 cases (13.9%) were in stage-2, 124 cases (24.7%) were in stage-3, 146 cases (29.0%) were in stage-4 and 148 cases (29.4%) were in stage-5.

We found that, in 503 cases, no. of cases was high in stage-5 when compared with stage-1.

Stages of CKD	Increased (sr. creatinine)	Decreased (sr. creatinine)	Fluctuated (sr. creatinine)
Stage-1	4(26.67%)	9(60.0%)	2(13.33%)
Stage-2	8(11.43%)	47(67.14%)	15(21.43%)
Stage-3	5(4.07%)	100(81.30%)	18(14.63%)
Stage-4	11(7.53%)	99(67.81%)	36(24.66%)
Stage-5	11(7.43%)	112(75.68%)	25(16.89%)

Table 2: Table shows serum creatinine levels in different stages of CKD

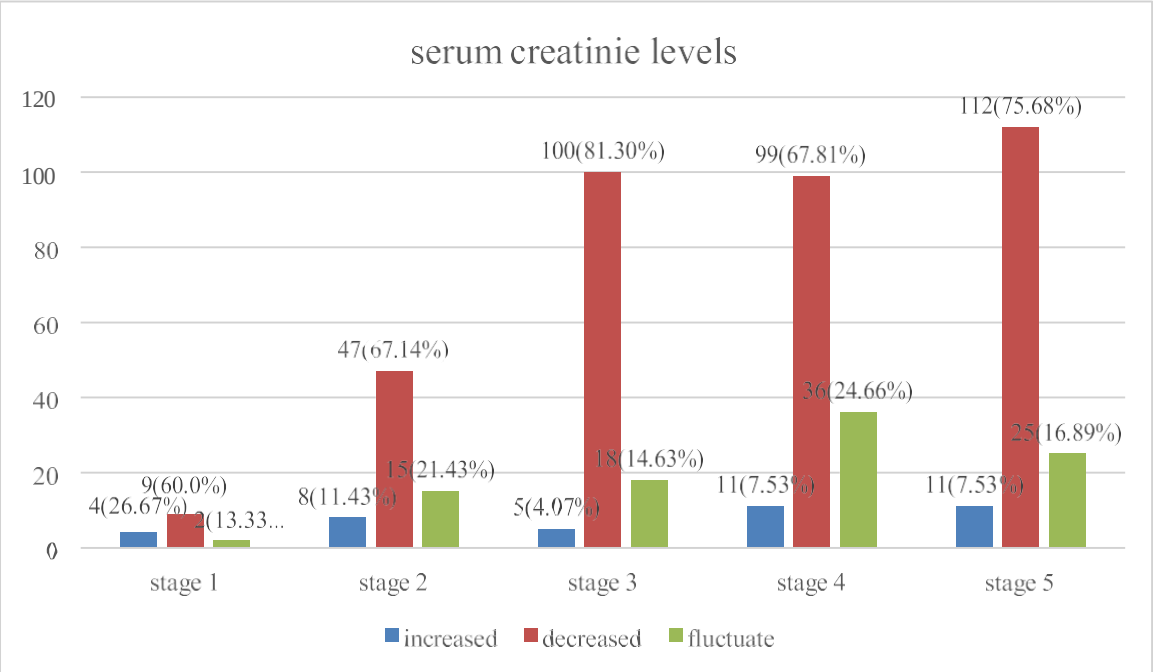

Fig 2: Graphs shows serum creatinine level in different stages of CKD

Based on the above data, the increased levels of serum creatinine was found highest in stage 4 and 5 cases (11) and lowest is stage 1 (4), the decreased serum creatinine levels were highest in stage 5 cases (112) and lowest is in stage -1 cases (9), the fluctuated serum creatinine levels were highest in stage 4 cases (36) and lowest is stage 1 cases (2).

Test	Value
Chi-square(x^2)	17.30
Degrees of freedom	8
p-value	0.027

Table 2.1: table shows chi-square test for the serum creatinine levels.

We found that, in overall cases decreased levels of serum creatinine are highest and increased levels of serum creatinine are lowest. A Chi-square test demonstrated a significant association between CKD stage and serum creatinine response pattern ($\chi^2 = 17.30$, df = 8, p = 0.027), indicating that changes in serum creatinine varied significantly across CKD stages.

Stages of CKD	Increased (FBS)	Decreased (FBS)	Fluctuated (FBS)
Stage-1	1(6.67%)	13(86.67%)	1(6.67%)
Stage-2	4(5.71%)	56(80.0%)	10(14.29%)
Stage-3	3(2.42%)	112(90.32%)	9(7.26%)
Stage-4	3(2.05%)	125(85.62%)	18(12.33%)
Stage-5	5(3.38%)	131(88.51%)	12(8.11%)

Table 3: Table shows FBS level in different stages of CKD

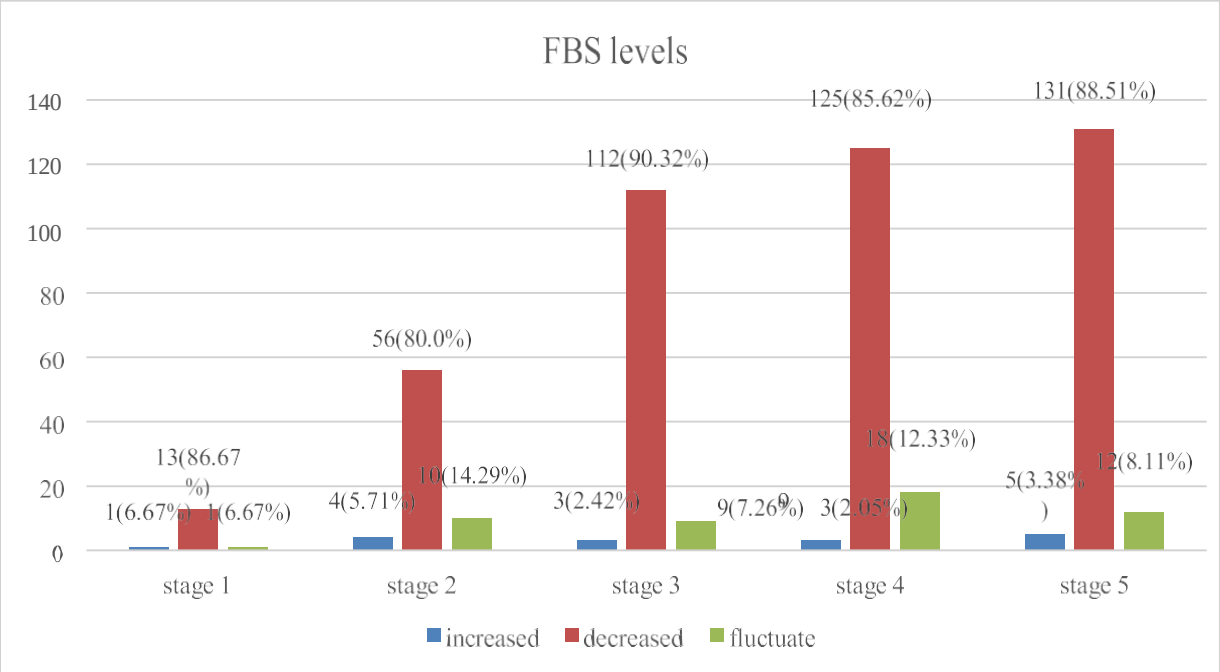

Fig 3: Graphs shows FBS level pattern across different stages

Based on the above data, the increased FBS levels were highest in stage 5 cases (5) and lowest in stage 1 (1), the decreased FBS levels were highest in stage 5 cases (131) and the lowest found in stage 1 cases (13), and the fluctuated FBS levels were highest in stage 4 cases (18) and lowest is in stage 1 cases (1).

Test	Value
Chi-square(x^2)	7.16
Degrees of freedom	8
p-value	0.519

Table 3.1: table shows chi-square test for the FBS levels.

We found that, in overall cases the FBS levels were highly decreased. The chi-square test no significant association was observed between CKD stage and FBS response pattern ($\chi^2 = 7.16$, df = 8, p = 0.519).

stages of CKD	FBS levels(decreased)	Sr. creatinine(decreased)
Stage-1	13(2.9%)	9(2.5%)
Stage-2	56(12.7%)	43(12.3%)
Stage-3	113(25.8%)	100(28.8%)
Stage-4	125(28.9%)	94(27.0%)

Stage-5	131(29.9%)	101(29.1%)

Table 4: Table shows no. of serum creatinine decreased cases from FBS decreased cases

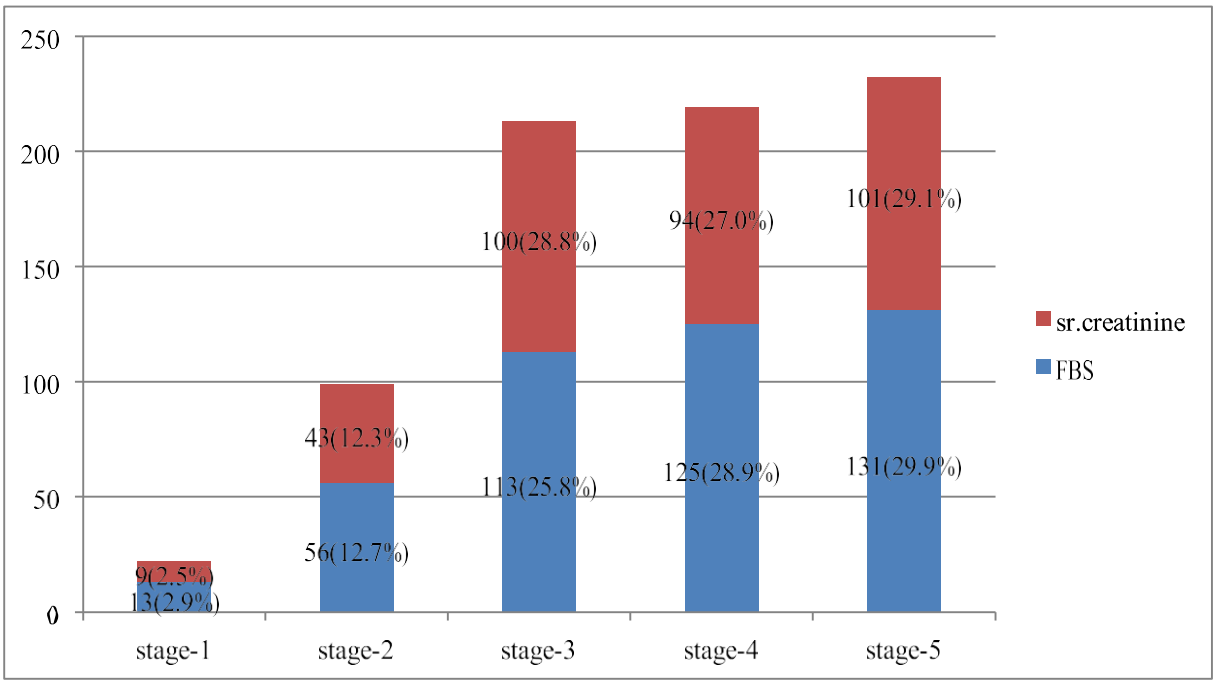

Fig 4: Graph shows no. of serum creatinine decreased cases from FBS decreased cases

Based on the above data, we identified that in stage-1 cases 13(2.9%) as low FBS levels from 9(2.5%) consist of serum creatinine levels decreased which are found to the lowest in the all stages and highest was found in stage-5 where 131(29.9%) cases have seen FBS levels decreased form that 101(29.1%) cases has serum creatinine levels low.

We found that,in different stages of CKD FBS levels decreased along with serum creatinine levels which indicates management of CKD along with diabetes mellitus.

Stage of CKD	No. of cases on Oral therapy	No. of cases on Insulin therapy	No. of cases on Both therapy
stage 1	9(100%)	0(0%)	0(0%)
stage 2	41(95.35%)	1(2.33%)	1(2.33%)
stage 3	75(75.76%)	5(5.05%)	19(19.19%)
stage 4	24(25.53%)	15(15.96%)	55(58.51%)
stage 5	14(13.86%)	42(41.58%)	45(44.55%)

Table 5: Table shows the type of therapy for DM controlled cases along with CKD management cases.

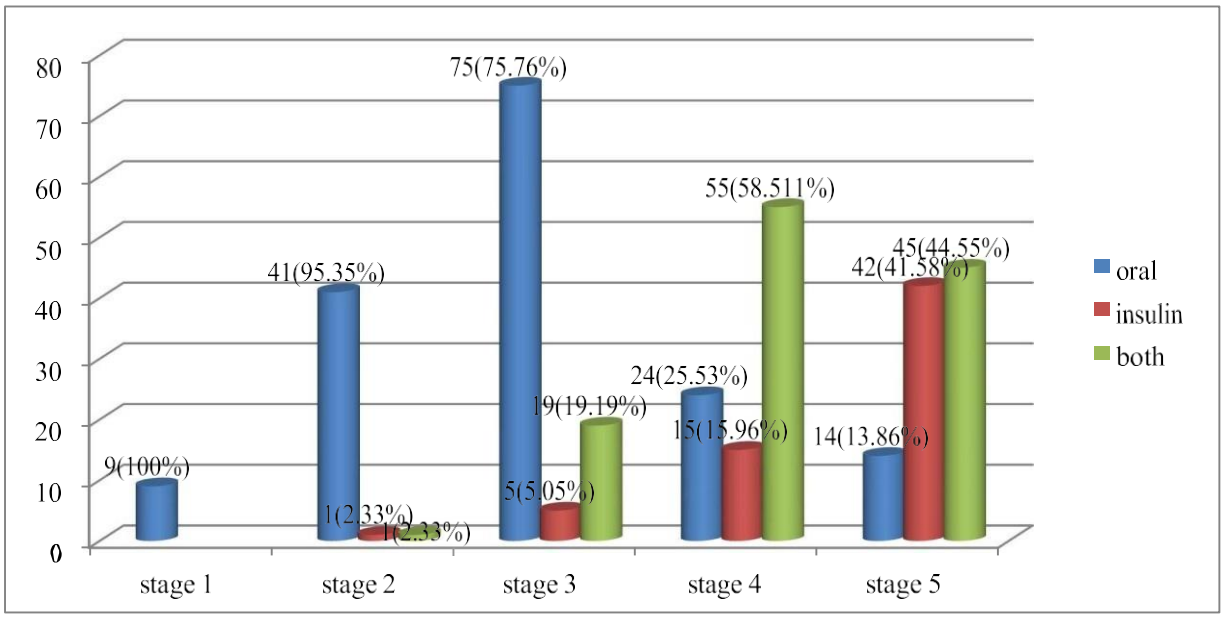

Fig 5: Graph shows the type of therapy for DM controlled cases along with CKD management cases.

Based on the above data, we identified that oral therapy was given highest in the stage-3 cases75(75.76%) and lowest in the stage-1 cases 9(100%) when we compare it with insulin therapy highest cases 42(41.58%) were found in stage-5 and the combination therapy (oral & insulin) were found highest in stage-4 with no. of cases 55(58.51%) and the nil cases found in stage-1.

Test	Value
Chi-square(x^2)	214.90
Degrees of freedom	8
p-value	0.001

Table 5.1: table shows chi-square test for the different types of therapy.

We found that, in most of the cases oral therapy was given to control DM in case of CKD when we compare with insulin and combination therapy.

The chi-square test shows treatment modality differed significantly across CKD stages ($\chi^2 = 214.90$, df = 8, $p < 0.001$). Oral therapy predominated in the early stages, whereas combination therapy and insulin use increased significantly in advanced CKD stages.

S.No	Oral therapy	No. of cases
1	Metformin	1(11.1%)
2	Empagliflozin	1(11.1%)
3	Metformin+sitagliptin	3(33.3%)
4	Metformin+empagliflozin	1(11.1%)
5	Dapagliflozin+Sitagliptin	1(11.1%)

6	Metformin+Glimepirede	2(11.1%)

Table 6.1: Table shows type of drugs given in the oral therapy in stage-1

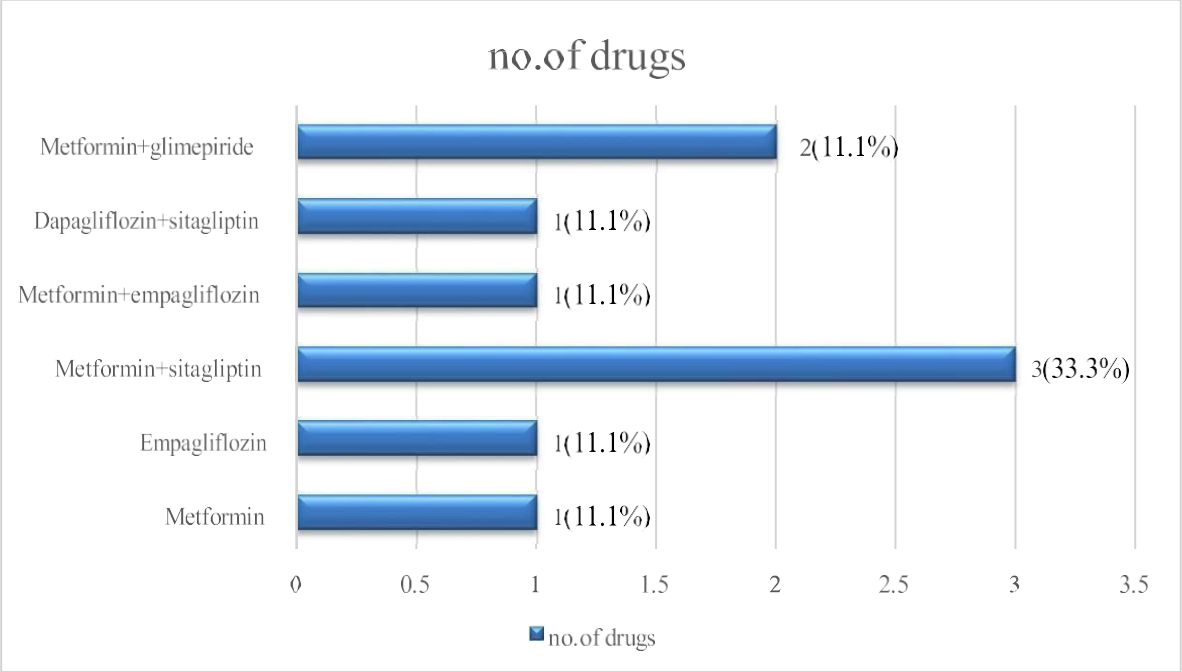

Fig 6.1: Graph shows type of drugs given in the oral therapy in stage-1

Based on the above data, we found that in stage-1 metformin+sitagliptin combination was given in majority of cases 3(33.3%) and other drugs like Metformin1(11.1%), Empagliflozin 1(11.1%), Metformin+empagliflozin 1(11.1%), Dapagliflozin+Sitagliptin 1(11.1%) were given minorly.

We found that, in the stage-1 metformin+sitagliptin combination were given more.

s.no	Oral therapy drugs	No. of cases
1	Linagliptin+metformin	4(9.30%)
2	Metformin	2(4.65%)
3	Vidagliptin+metformin	3(6.98%)
4	Dapagliflozin+metformin	7(16.28%)
5	Dapagliflozin+linagliptin	5(11.63%)
6	Metformin+empagliflozin	8(18.60%)
7	Metformin+glimepiride	2(4.65%)
8	Metformin+sitagliflozin	4(9.30%)
9	Repaglinide+empagliflozin	1(2.33%)
10	Glimepiride+empagliflozin	1(2.33%)

11	Empagliflozin+teneligliptin	1(2.33%)
12	Dapagliflozin+teneligliptin	1(2.33%)
13	Teneligliptin+metformin	1(2.33%)
14	Glimepiride+dapagliflozin	1(2.33%)

Table 7.1: Table shows type of drugs given in the oral therapy in stage-2

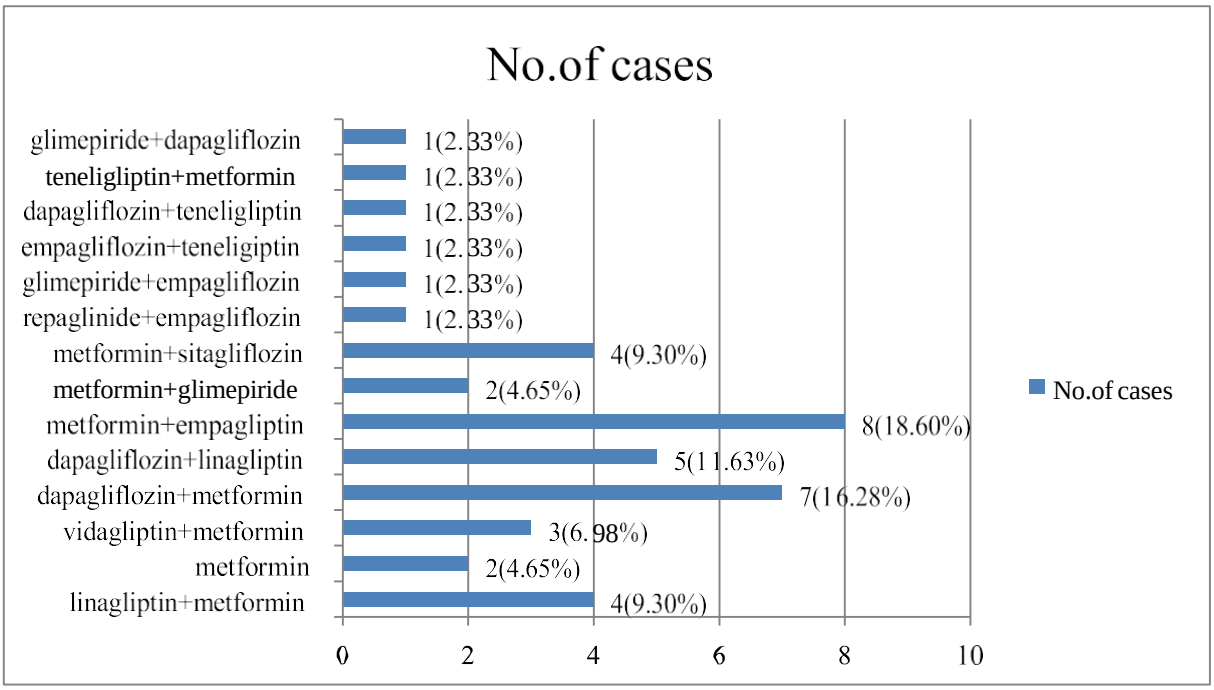

Fig 7.1: Graph shows type of drugs given in the oral therapy in stage-2

Based on the above data, we found that in stage-2 metformin+empagliflozin combination was given in majority of cases 8(18.60%) and other drug combinations like Repaglinide+empagliflozin 1(2.33%), Glimepiride+empagliflozin 1(2.33%), Empagliflozin+teneligliptin 1(2.33%), Dapagliflozin+teneligliptin 1(2.33%), Teneligliptin+metformin 1(2.33%), Glimepiride+dapagliflozin 1(2.33%) were given minorly.

We found that, in the stage-2 metformin+ empagliflozin combination were given more.

S.no	Insulin therapy	No.of cases
1	Insulin gargline+insulin lispro	1(100%)

Table 7.2: Table shows type of insulin therapy given in stage-2

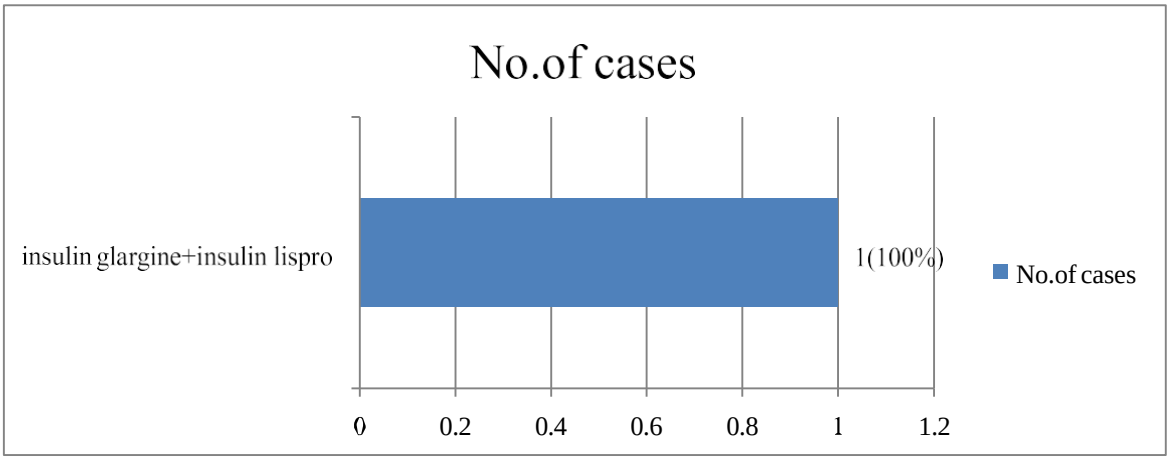

Fig 7.2: Graph shows type of insulin therapy given in stage-2

Based on the above data, we found that in one and only case (1) of stage-2 was given insulin glargine+ insulin lispro.

We found that, in the stage-2the one and only case was given insulin glargine+ insulin lispro combination.

s.no	Combination therapy	No.of cases
1	Empaglifozin+insulin glargine	1(100%)

Table 7.3: Table shows type of drugs given in the combination therapy in stage-2

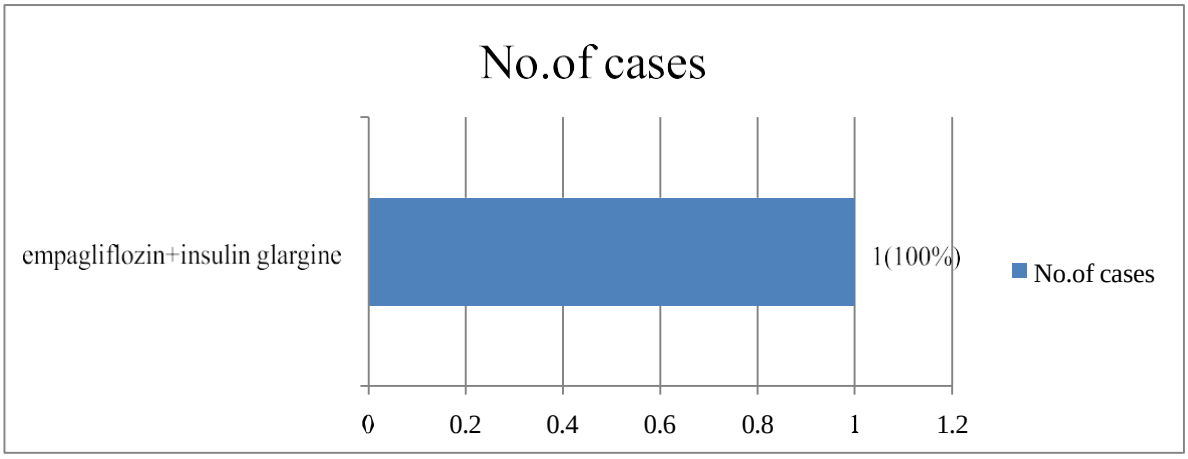

Fig 7.3: Graph shows type of drugs given in the combination therapy in stage-2

Based on the above data, we found that in one and only case (1) of stage-2 was given empagliflozin+insulin glargine combination.

We found that, in the stage-2 empagliflozin+insulin glargine combination was given.

s.no	Oral therapy drugs	No.of cases
1	Metformin	9(12.0%)

2	Glipizide	3(4.0%)
3	Empagliflozin	6(8.0%)
4	Metformin+empagliflozin	12(16.0%)
5	Metformin+glipizide	9(12.0%)
6	Metformin+dapadliflozin	8(10.67%)
7	Metformin+glimepiride+empagliflozin	1(1.33%)
8	Metformin+glimepiride+glicazide	1(1.33%)
9	Metformin+sitagliptin	3(4.0%)
10	Sitagliptin+glimepiride	1(1.33%)
11	Metform+linagliptin	6(8.0%)
12	Vildagliptin+glimepiride	1(1.33%)
13	Empagliflozin+linagliptin	1(1.33%)
14	Dapagliflozin+glimepiride	1(1.33%)
15	Linagliptin+glimepiride	2(2.67%)
16	Metformin+glimepiride	2(2.67%)
17	Teneligliptin+metformin	1(1.33%)
18	Teneligliptin+pioglitazone	1(1.33%)
19	Metformin+vildagliptin	1(1.33%)
20	Empagliflozin+glimepiride	2(2.67%)
21	Empagliflozin+sitagliptin	1(1.33%)
22	Teneligliptin+glimepiride	2(2.67%)
23	Metformin+empagliflozin+dapagliflozin	1(1.33%)

Table 8.1: Table shows type of drugs given in the oral therapy in stage-3

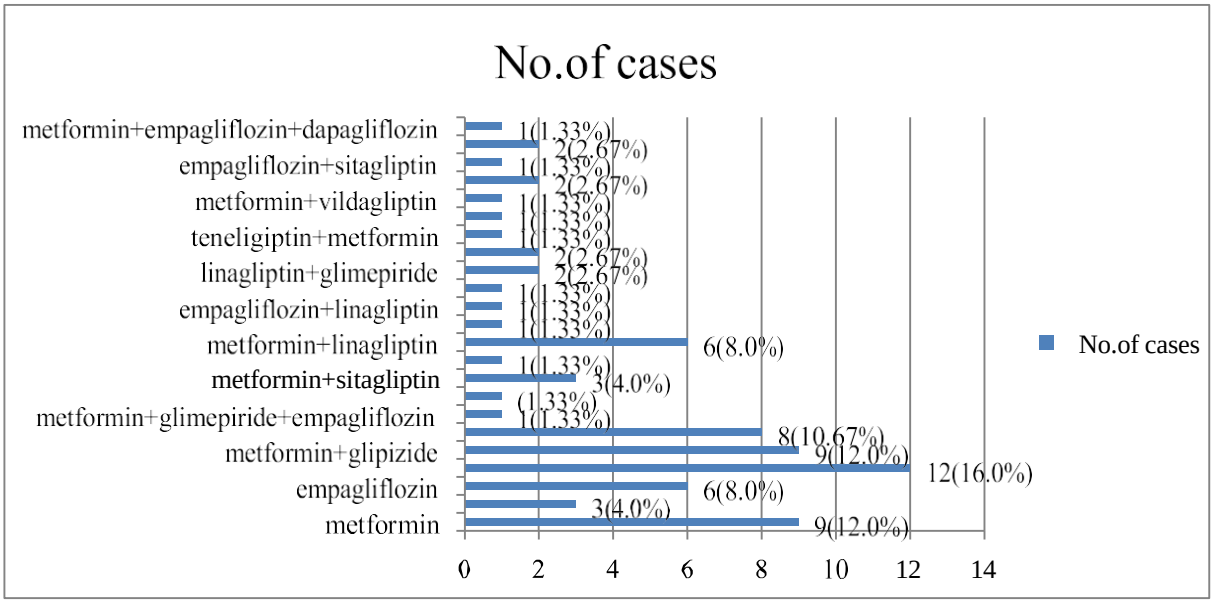

Fig 8.1: Graph shows type of drugs given in the oral therapy in stage-3

Based on the above data, we found that in stage-3 metformin+empagliflozin combination was given in majority of cases 12(16.0%) and other drugs like

Metformin+glimepiride+empagliflozin 1(1.33%), Metformin+glimepiride+glicazide 1(1.33%), Sitagliptin+glimepiride 1(1.33%), Vildagliptin+glimepiride 1(1.33%), Empagliflozin+linagliptin 1(1.33%), Dapagliflozin+glimepiride 1(1.33%), Teneligliptin+metformin 1(1.33%), Teneligliptin+pioglitazone 1(1.33%), Metformin+vildagliptin 1(1.33%), Empagliflozin+sitagliptin 1(1.33%), Metformin+empagliflozin+dapagliflozin 1(1.33%) were given minority of cases.

We found that, in the stage-3 metformin+ empagliflozin combination were given to more cases

s.no	Insulin therapy	No.of cases
1	Insulin glargine	2(40.0%)
2	Insulin lispro	3(60.0%)

Table 8.2: Table shows the type of insulin therapy given in stage-3

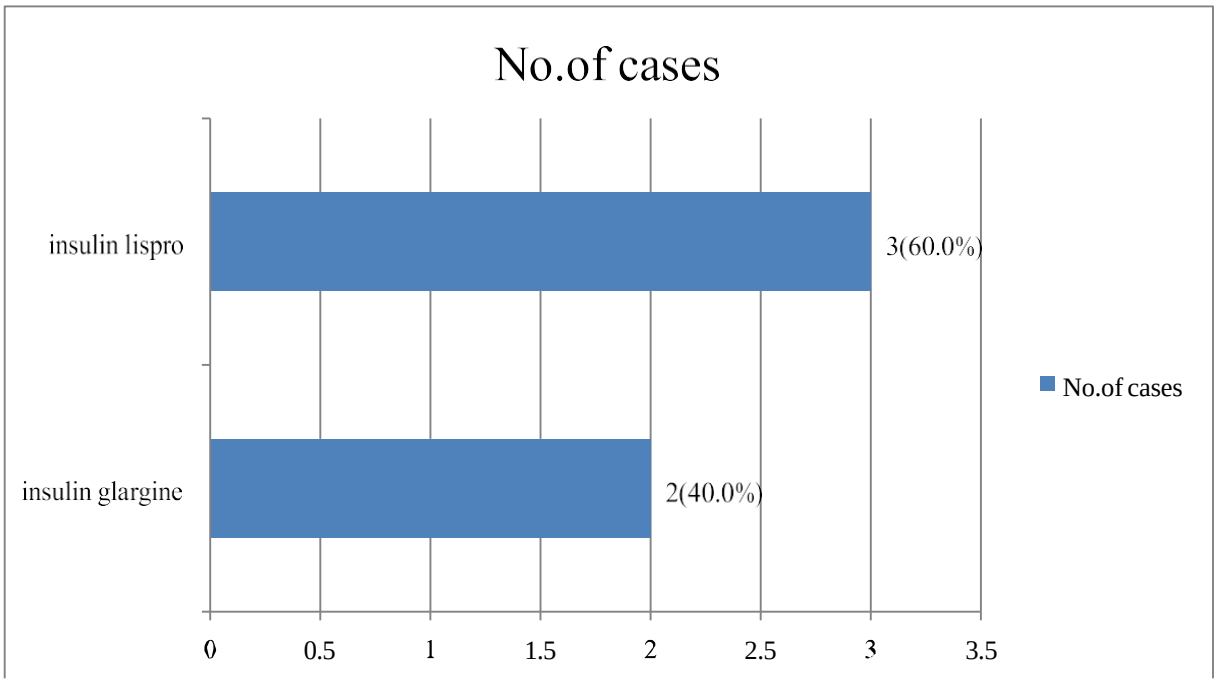

Fig 8.2: Graph shows the type of insulin therapy given in stage-3.

Based on the above data, we found that in stage-3 insulin lispro was given in majority of cases 3(60.0%) and other drugs like insulin glargine 2(40.0%) were given minorly.

We found that, in the stage-3 insulin lispro was given more.

S.no	Combination therapy	No.of cases
1	Empagliflozin+insulin glargine	2(10.53%)
2	Glipizide+insulin glargine	1(5.26%)
3	Metformin+glimepiride+insulin+glargine	1(5.26%)

4	Metformin+glimeoiride+insulinregular	1(5.26%)
5	Metformin+dapagliflozin+insulin regular	1(5.26%)
6	Metformin+linagliptin+insulin regular+insulin glargine	1(5.26%)
7	Metformin+sitagliptin+insulin glargine	1(5.26%)
8	Repagliptin+insulin glargine	1(5.26%)
9	Linagliptin+insulin glargine	1(5.26%)
10	Sitagliptin+insulin glargine	4(21.05%)
11	Empagloflozin+insulin lispro	1(5.26%)
12	Metformin+linagliptin+insulin regular	2(10.53%)
13	Metformin+insulin glargine	2(10.53%)

Table 8.3: Table shows type of drugs given in the combination therapy in stage-3

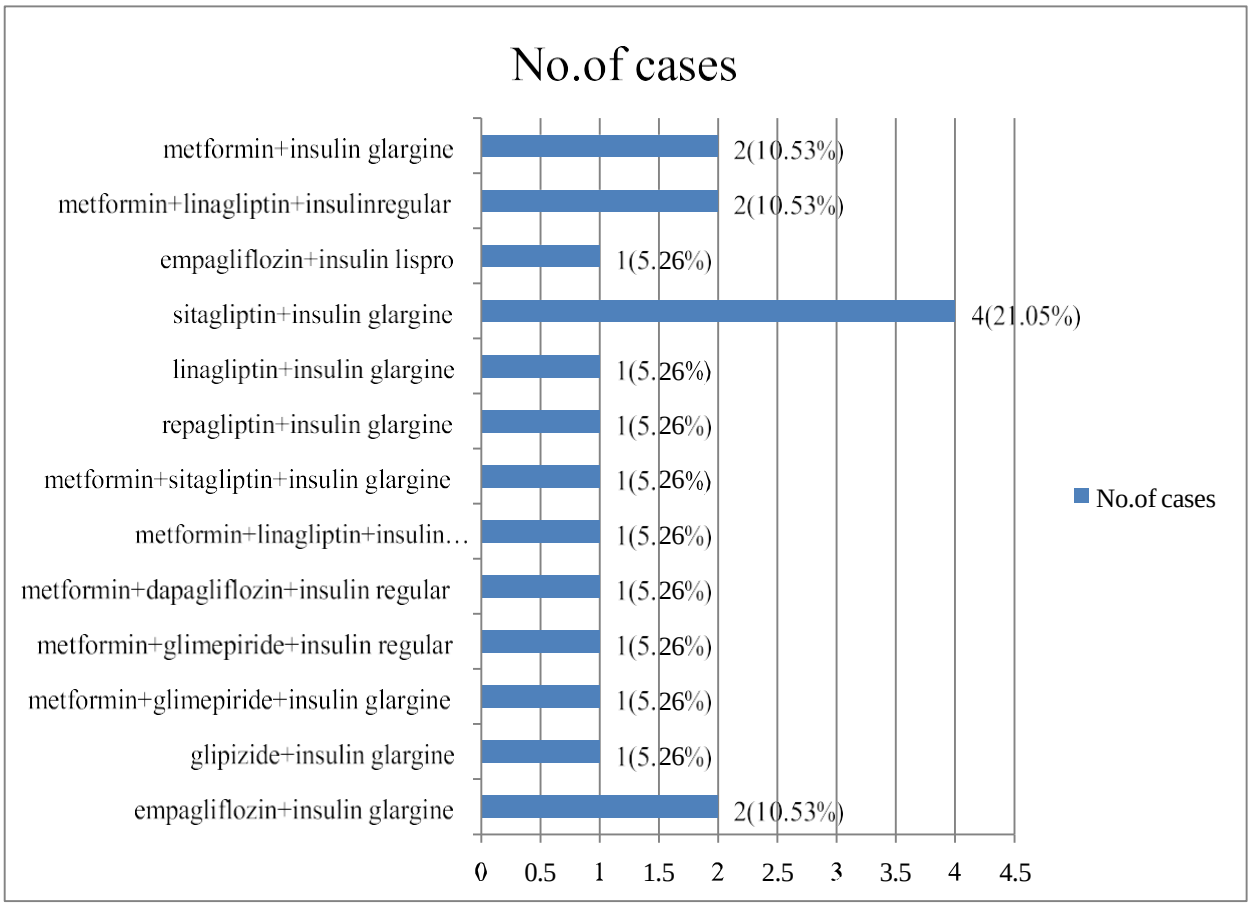

Fig 8.3: Graph shows type of drugs given in the combination therapy in stage3

Based on the above data, we found that in stage-3 sitagliptin+insulin glargine combination was given in majority of cases 4(21.05%) and other drugs like Glipizide+insulin glargine 1(5.26%), Metformin+glimepiride+insulin+glargine 1(5.26%), Metformin+glimeoiride+insulin regular 1(5.26%), Metformin+dapagliflozin+insulin 1(5.26%), regular Metformin+linagliptin+insulin 1(5.26%), regular+insulin glargine 1(5.26%),

Metformin+sitagliptin+insulin glargine 1(5.26%), Repagliptin+insulin glargine 1(5.26%), Linagliptin+insulin glargine 1(5.26%), Empagloflozin+insulin lispro 1(5.26%) were given minorly.

We found that, in the stage-3 sitagliptin+insulin glargine combination was given more.

s.no	Oral therapy	No.of cases
1	Metformin+empagliflozin	3(12.50%)
2	Glimepiride+repaglinide	2(8.33%)
3	Metformin+glipizide	3(12.50%)
4	Metformin	8(33.33%)
5	Metformin+linagliptin	5(20.83%)
6	Glimepiride+empagliflozin	1(4.17%)
7	Lingliptin+glipizide	1(4.17%)
8	Lingliptin+glipizide	1(4.17%)

Table 9.1: Table shows type of drugs given in the oral therapy in stage-4

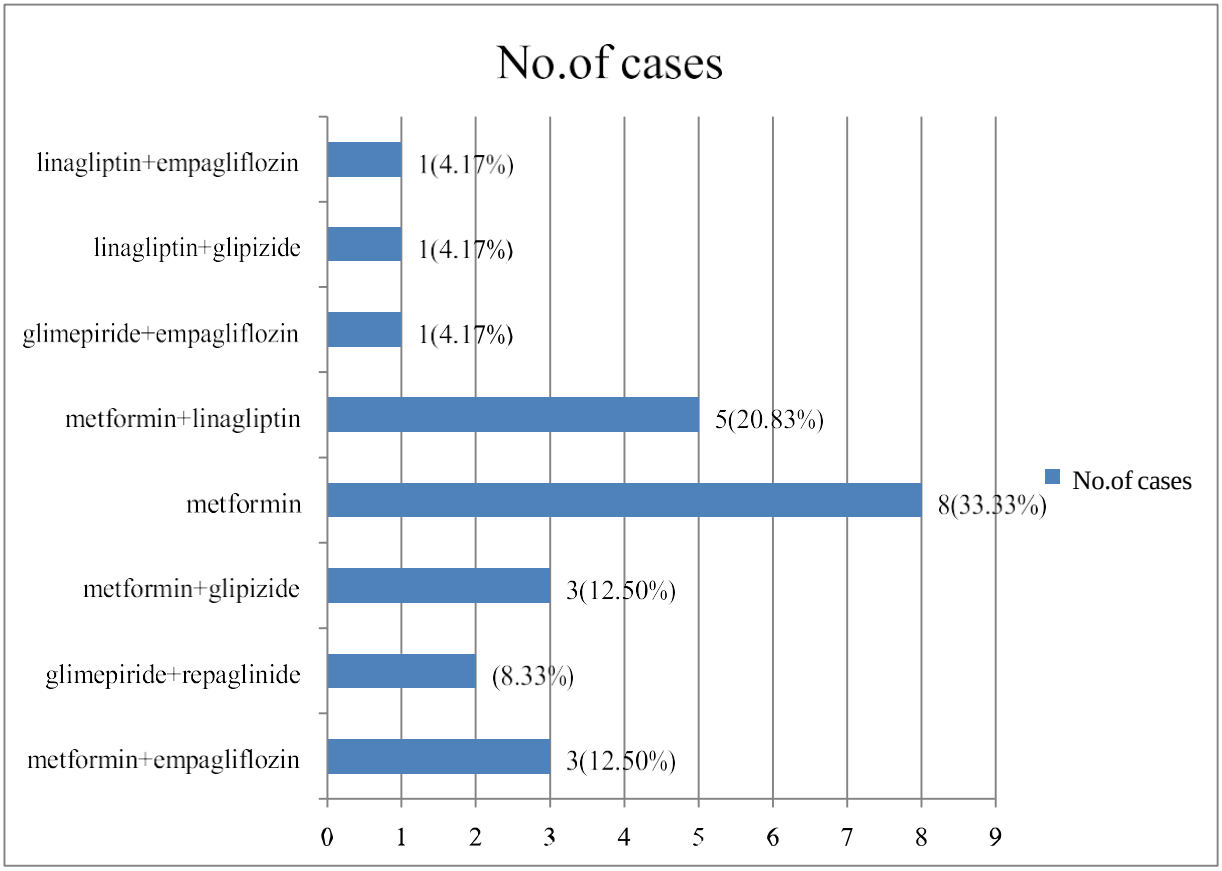

Fig 9.1: Graph shows type of drugs given in the oral therapy in stage-4

Based on the above data, we found that in stage-4 metformin was given in majority of cases

8(33.33%) and other drug combinations like Glimepiride+empagliflozin 1(4.17%), Lingliptin+glipizide 1(4.17%), Lingliptin+glipizide 1(4.17%) were given minorly.

We found that, in the stage-4 metformin was given more.

s.no	Insulin therapy	No.of cases
1	Insulin glargine+insulin lispro	2(13.33%)
2	Insulin degludec+insulin lispro	2(13.33%)
3	Insulin lispro	2(13.33%)
4	Insulin glargine	5(33.33%)
5	Human insulin	1(6.67%)
6	Insulin regular+insulin glargine	3((20.0%)

Table 9.2: Table shows insulin therapy given in stage-4

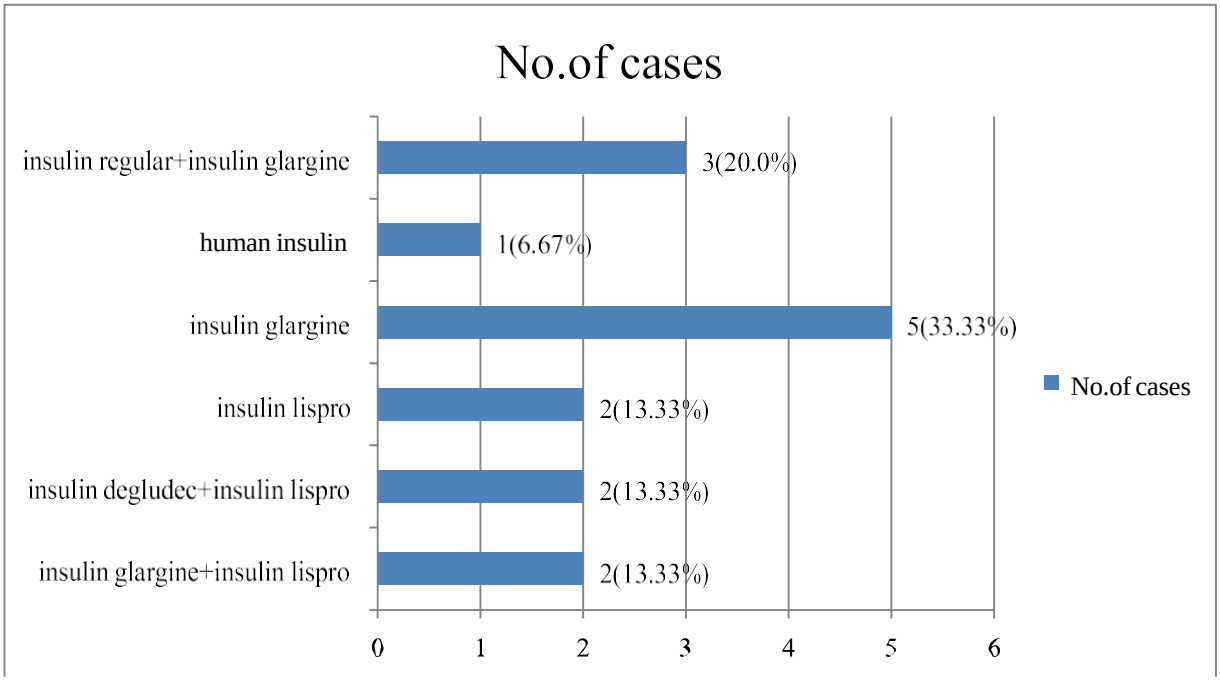

Fig 9.2: Graph shows insulin therapy given in stage-4

Based on the above data, we found that in stage-4 insulin glargine combination was given in majority of cases 5(33.33%) and other drug like human insulin 1(6.67%) was given minorly.

We found that, in the stage-4 insulin glargine combination was given more.

s.no	Combination therapy	No.of cases
1	Metformin+insulin regular	9(16.98%)
2	Linagliptin+insulin regular	2(3.77%)
3	Sitaglipitin+glimepiride+insulin regular	1(1.89%)

4	Metformin+glimepiride+insulin regular	2(3.77%)
5	Metformin+sitagliptin+insulin glargine	2(3.77%)
6	Metformin+insulin lispro	59.43%)
7	Metformin+actrapid insulin	1(1.89%)
8	Metformin+insulin glargine	5(9.43%)
9	Glipizide+regular insulin	2(3.77%)
10	Empagloflozin+ insulin regular	6(11.32%)
11	Sitagliptin+insulin regular	3(5.66%)
12	Teneligiptin+insulin regular	4(7.55%)
13	Linagliptin+insulin regular	4(7.55%)
14	Empagliflozin+metformin+insulin lispro+insulin regular	1(1.89%)
15	Metformin+canagliflozin+insulin glargine	1(1.89%)
16	Repaglipinde+insulin regular	1(1.89%)
17	Glimepiride+human insulin	1(1.89%)
18	Linagliptin+insulin lispro	1(1.89%)
19	Glimepiride+insulin glargine	1(1.89%)
20	Metformin+linagliptin+insulin regular+insulin glargine	1(1.89%)

Table 9.3: Table shows type of drugs given in the combination therapy in stage-4

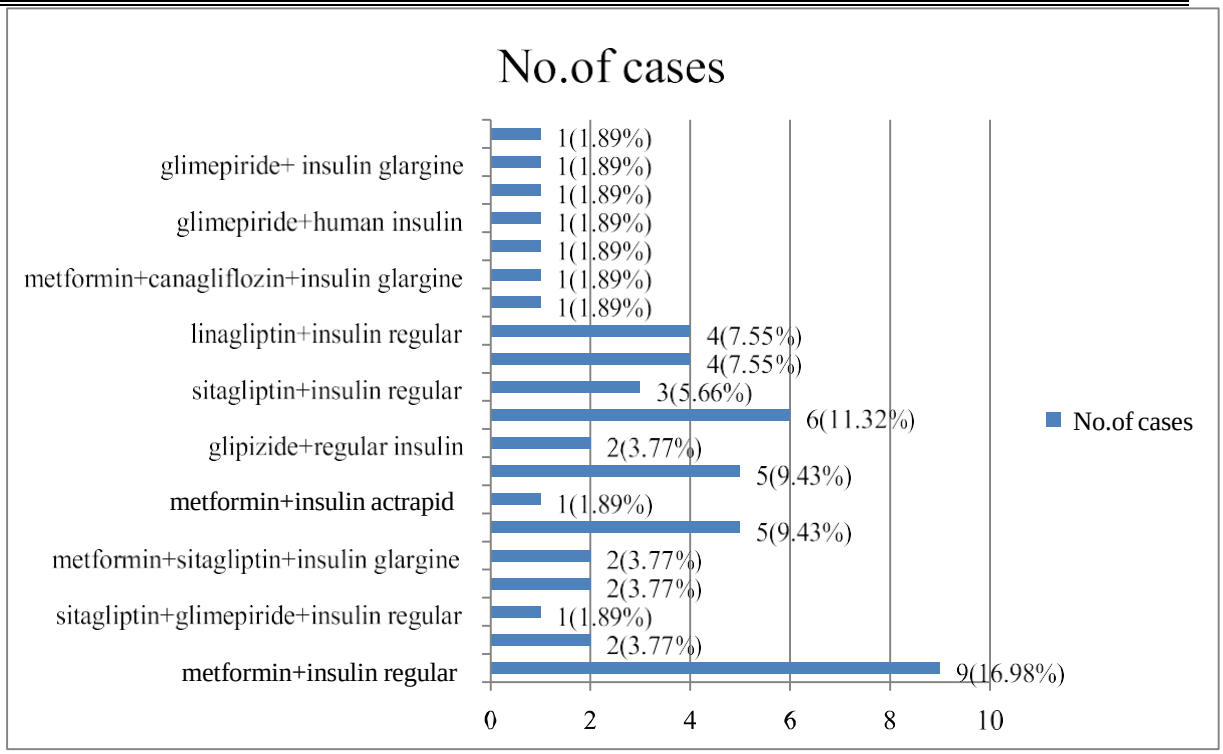

Fig 9.3: Graph shows type of drugs given in the combination therapy in stage-4

Based on the above data, we found that in stage-4 metformin+insulin regular combination was given in majority of cases 9(16.98%) and other drugs like Sitaglipitin+ glimepiride +insulin regular 1(1.89%), Metformin+actrapid insulin1(1.89%), Empagliflozin+ metformin+insulin lispro+insulin regular 1(1.89%), Metformin+canagliflozin+insulin glargine 1(1.89%), Repaglipinde+insulin regular 1(1.89%), Glimepiride+human insulin 1(1.89%), Linagliptin+insulin lispro 1(1.89%), Glimepiride+insulin glargine 1(1.89%), Metformin+linagliptin+insulin regular+insulin glargine 1(1.89%) was given minorly.

We found that, in the stage-4 metformin+insulin regular glargine combination was given more.

s.no	Oral therapy	No.of cases
1	Metformin+sitagliptin	2(14.29%)
2	Metformin	1(7.14%)
3	Glimepiride+lingaliptin	3(21.43%)
4	Empagliflozin+glimepiride	2(14.29%)
5	Sitagliptin+dapagliflozin	2(14.29%)
6	Sitagliptin+glimepiride	2(14.29%)
7	Metformin+glimepiride	1(7.14%)
8	Empagliflozin+dapagliflozin	1(7.14%)

Table 10.1: Table shows type of drugs given in the oral therapy in stage-5

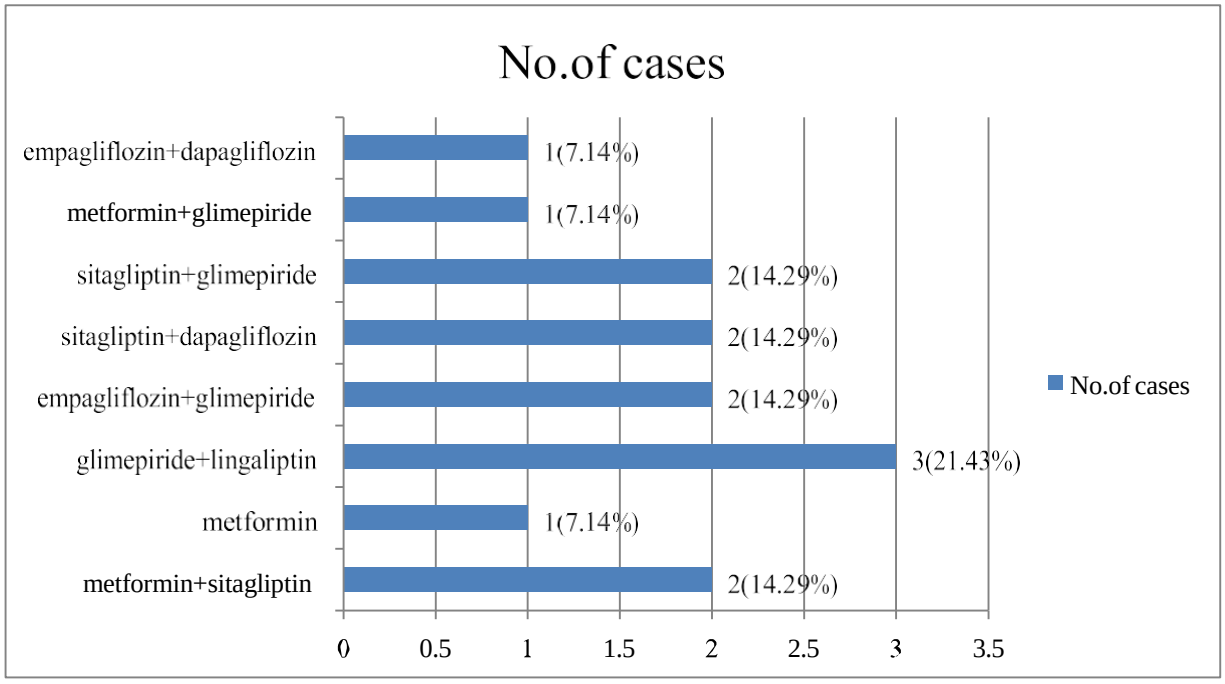

Fig 10.1: Graph shows type of drugs given in the oral therapy in stage-5

Based on the above data, we found that in stage-5 glimepiride+lingaliptin combination was given in majority of cases 3(21.43%) and other drugs empagliflozin+dapagliflozin 1(7.14%), metformin+ glimepiride 1(7.14%), metformin 1(7.14%) was given minorly.

We found that, in the stage-5 glimepiride+lingaliptin combination was given more.

s.no	Insulin therapy	No.of cases
1	Insulin regular+insulin glargine	23(56.10%)
2	Insulin glargine	6(14.63%)
3	Insulin glargine+insulin actrapid	4(9.76%)
4	Insulin glargine+insulin aspart	2(4.88%)
5	Insulin regular+insulin (NPH)	2(4.88%)
6	Insulin lispro+insulin glargine	2(4.88%)
7	Insulin glargine+ insulin(NPH)	1(2.44%)
8	Insulin regular+insulin lispro	1(2.44%)

Table 10.2: Table shows type of insulin therapy given in stage-5

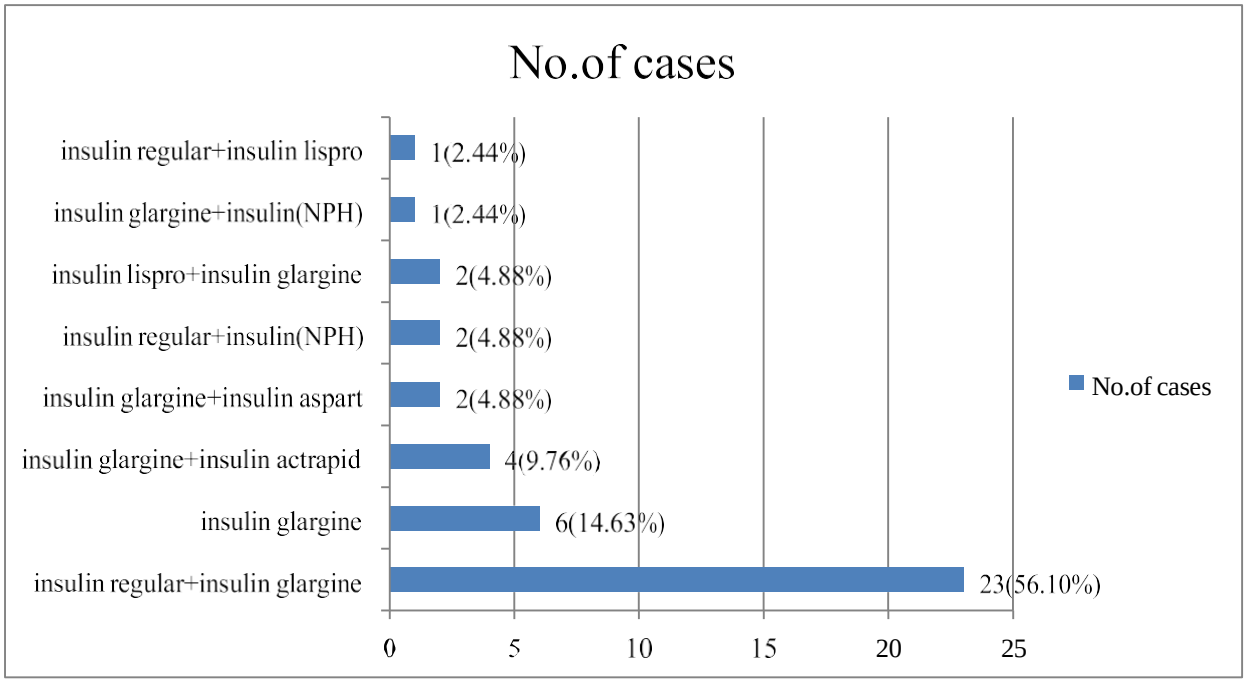

Fig 10.2: Graph shows type of insulin therapy given in stage-5

Based on the above data, we found that in stage-5 insulin regular+insulin glargine combination was given in majority of cases 23(56.10%) and other drug combinations like insuin regular+insulin lispro1(2..44%), insulin glargine+insulin (NPH) 1(2.44%)was given minorly.

We found that, in the stage-5 insulin regular+insulin glargine combination was given more.

s.no	Combination therapy	No.of cases
1	Lingaliptin+insulin glargine	3(6.82%)
2	Lingaliptin+insulin lispro	2(4.55%)
3	Sitagliptin+insulin regular	4(9.09%)
4	Metformin+dapagliflozin+insuli n glargine	1(2.27%)
5	Metformin+insulin regular	9(20.45%)
6	Glimepiride+insulin glargine	5(11.36%)
7	Metformin+insulin glargine	8(18.18%)
8	Glipizide+insulin lispro	3(6.82%)
9	Sitagliptin+insulin glargine	5(11.36%)
10	Metformin+insulin lispro	3(6.82%)
11	Metformin+insulin regular+insulin glargine	1(2.27%)

12	Glimepiride+insulin regular	1(2.27%)

Table 10.3: Table shows type of drugs given in the combination therapy in stage-5

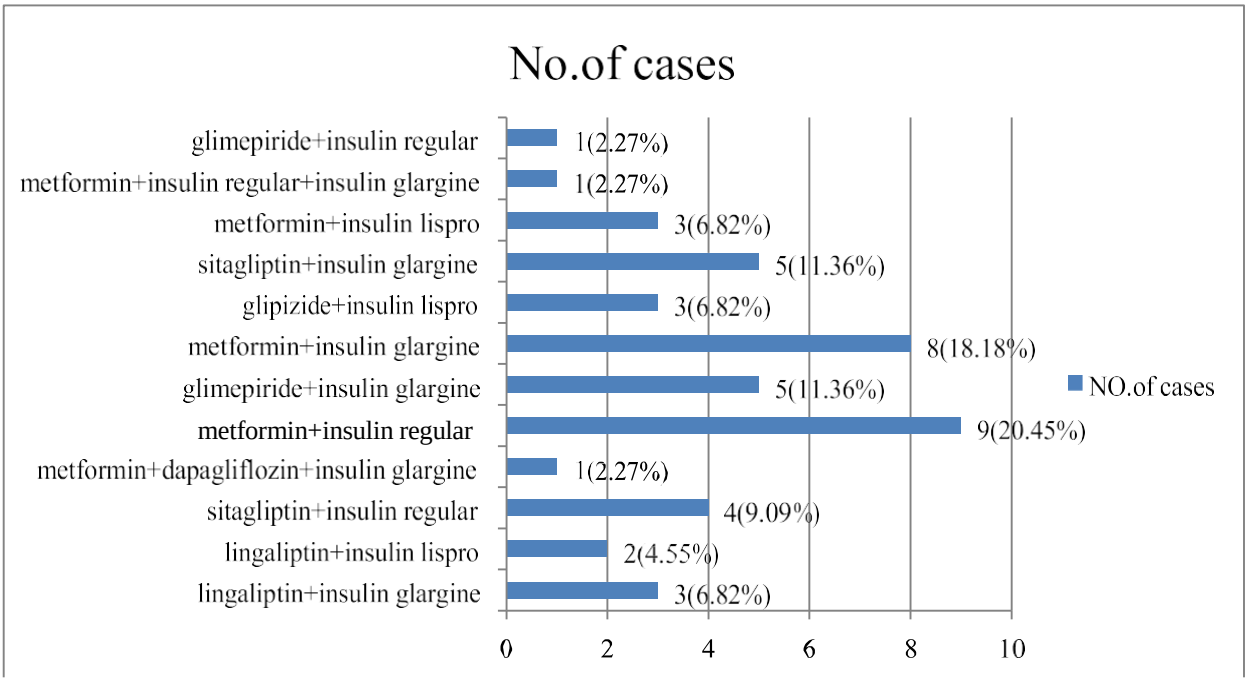

Fig 10.3: Graph shows type of drugs given in the combination therapy in stage-5

Based on the above data, we found that in stage-5 metformin+insulin regular combination was given in majority of cases 4(21.05%) and other drugs like glimepiride+insulin regular 1(2.27%), metformin+insulin regular+insulin glargine 1(2.27%), metformin+dapagliflozin+insulin glargine was given minorly.

We found that, in the stage-5 metformin+insulin regular combination was given more.

Stages of CKD	No. of cases in oral therapy	No. of cases in insulin therapy
Stage-1	-	-
Stage-2	03	-
Stage-3	04	-
Stage-4	-	02
Stage-5	-	-

Table 11: Table shows hypoglycemic levels of across different stages of CKD

Table shows the distribution of hypoglycemic cases across different stages of CKD based on the type of antidiabetic therapy. Hypoglycemia was observed in 3 cases receiving oral therapy in Stage-2, 4 cases receiving oral therapy in Stage-3, and 2 cases receiving insulin therapy in Stage-4. No hypoglycemic cases were reported in the remaining stages.

Overall, hypoglycemic episodes were more commonly observed with oral antidiabetic therapy in Stage-2 and Stage-3, while insulin-related hypoglycemia was reported only in Stage-4.

DISCUSSION

Chronic Kidney Disease (CKD) is a long-term condition in which the kidneys gradually lose their ability to filter waste products and excess fluids from the blood. It is a major public health problem affecting millions of people worldwide and can lead to serious complications if not managed properly.

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose levels due to insufficient insulin production or impaired insulin action. Long-term uncontrolled diabetes can damage various organs, including the kidneys, eyes, heart, and nervous system.

Diabetes is one of the leading causes of CKD. Persistent high blood sugar levels damage the small blood vessels in the kidneys, reducing their filtering capacity. This condition is known as diabetic kidney disease or diabetic nephropathy.

Patients with both CKD and diabetes are at a higher risk of complications such as hypertension, cardiovascular diseases, anaemia, and ESRD. As kidney function declines, patients may eventually require dialysis or kidney transplantation.

Early diagnosis, proper blood glucose control, blood pressure management, and lifestyle modifications are essential to slow the progression of CKD in diabetic patients. Therefore, studying CKD management with DM is important for improving patient outcomes, reducing complications, and enhancing quality of life.

The main purpose of this study is to evaluate and compare the management of patients suffering from CKD associated with DM who are receiving oral antidiabetic therapy, insulin therapy, or a combination of both treatments. CKD and diabetes are major public health problems, with diabetes being one of the leading causes of kidney damage and end-stage renal disease. This study aims to understand how different treatment approaches influence glycaemic control and renal function and optimize patient health outcomes.

This study is an concert observational study design, in which collection of information from individual patients who have both CKD with diabetes mellitus through their response to therapy (oral, insulin and both) by observing the laboratory results.

One of main reasons for picking this project as diabetes is the leading cause of CKD, and the prevalence of both diseases is increasing. Comparing oral therapy, insulin therapy, and combination therapy helps determine the most effective and safe treatment approach to improve glycaemic control, slow CKD progression, and enhance patient outcomes.

In our study we have collected 503 cases through data collection forms from participants suffering with CKD and diabetes mellitus by comparing different types of therapies given to them we found out of the 503 patients receiving oral treatment (233), insulin treatment (83),combination of both treatment (187).

We assessed the patients in regarding to the CKD with diabetes mellitus treatment in different stages. It is observed that out of the 503 cases, we found that CKD stage-1 as15 cases (2.98%), followed by Stage-2 as 70 cases (13.92%), Stage-3 as124 cases (24.65%), stage-4 as accounted for 146 cases (29.03%), while Stage-5 as 148 cases (29.42%).

We assessed the patients regarding serum creatinine levels across the different CKD stages. The decreased serum creatinine levels was more frequently observed in all the stages, indicating improvement of kidney function with treatment. The highest percentage of decreased creatinine levels was observed in stage-1 with 9 cases (60.0%), followed by stage-2 with 47 cases (67.14%), stage-3 with 100 cases (81.30%), stage-4 with 99 cases (67.81%), and stage-5 with 112 cases (78.68%) when we compare it with fluctuating and increasing creatinine levels. Next to the decreased levels of serum creatinine fluctuating levels were observed, the stage-1 consist of 2 cases (13.33%),stage-2 consist of 15 cases (21.43%), stage-3 consist of 18 cases (14.63%), stage-4 consist of 36 cases (24.66%)stage-5 consist of 25 cases (16.89%). While increased creatinine levels were observed in a small proportion of patients across all stages. Stage-1 had 4 cases (26.67%), stage-2 had 8 cases (11.43%), stage-3 had 5 cases (4.07%), stage-4 had 1 case (7.53%) and stage-5 had 11 cases (7.43%) with average duration of hospital stay among the patients was 4 to 5 days. A Chi-square test demonstrated a significant association between CKD stage and serum creatinine response pattern ($\chi^2 = 17.30$, df = 8, p = 0.027), indicating that changes in serum creatinine varied significantly across CKD stages.

We assessed the patients regarding blood sugar levels especially Fasting Blood Sugar (FBS) levels across the different CKD stages were found in more number of cases across in all stages. A decrease in FBS was a greater number of cases were found to have decreased FBS levels in all stages. The highest percentage of decreased FBS levels was observed in stage-1

with 13 cases (86.67%), stage-2 with 56 cases (80.0%), stage-3 with 121 cases(90.32%), stage-4 with 125 cases (85.62%) and stage-5 with 131 cases (88.51%). When we are comparing with fluctuating FBS levels were main outcome observed in stage-1 consist of 1case (6.67%) stage-2 consist of 10 cases (14.29%), stage-3 consist of 9 cases (7.26%), stage-4 consist of 18 cases (12.33%), stage-5 consist of 12 cases (8.11%). While increased FBS levels were observed in small proportion patients in all stages in stage-1 had 1case (6.7%), stage-2 had 4 cases (5.71%), stage-3 had 3cases (2.42%), stage-4 had 3 cases (2.05%) stage-5 had 5 cases (3.38%). The chi-square test shows no significant

association was observed between CKD stage and FBS response pattern ($\chi^2 = 7.16$, df = 8, p = 0.519).

We have assessed the patients regarding management of CKD cases with DM based on the levels of FBS and serum creatinine and we found that decreasing FBS also decreasing the serum creatinine levels we identify that in overall 503 cases both FBS and serum creatinine levels cases are 347 cases are decreased. When we divided according to stages in stage-1 out of 13 cases(2.9%) of reduced FBS levels with stage-1 9 cases (2.5%) had reduced serum creatinine levels, in the stage-2 out of 56 cases (12.7%) of reduced FBS levels with stage-2 43 cases (12.3%) had reduced serum creatinine levels, in the stage-3 out of 113 cases (25.8%) reduced of FBS levels with stage-3 100 cases (28.8%) had reduced serum creatinine levels, in the stage-4 out of 125 cases (28.9%) reduced of FBS levels, with stage-4 94 cases (27.0%) had reduced serum creatinine levels, in the stage-5 out of 131 cases (29.9%) reduced of FBS levels with stage-5 101 cases (29.1%) had reduced serum creatinine. Decreasing serum creatinine levels was more in all stages of CKD with DM. Which is an indicating improvement of kidney function with diabetes.

We assessed the patients regarding out of 503 cases, 346 cases were identified to control FBS levels and serum creatinine levels with oral, insulin and combination therapies. Among 163 cases oral therapy was mostly used in the control of DM and in turn CKD in stage-1 with 9 cases(100%), stage-2 with 4 cases (95.35%),stage-3 with 75cases (75.76%),stage-4 with 24 cases(25.53%), stage-5 with 14cases (13.86%). Among 63 cases insulin therapy in stage-1 consist of 0 cases (0%), stage-2 consist of 1cases (2.33%), stage-3 consist of 5 cases (5.05%),stage-4 consist of 15 cases (15.96%), stage-5 consist of 42 cases (41.58%). Among 120 cases combination therapy was mainly used in advanced stages, particularly in stage-1 as 0 cases (0%), stage-2 as 1 case (2.33%), stage-3 as 19cases (19.19%),stage-4 as 55 cases (58.51%), stage-5 as 45 cases (44.55%). From this oral therapy was the preferred treatment in the initial FBS stages, whereas insulin and combination therapies became more common as the

disease progressed used in advanced stages. The chi-square test shows Treatment modality differed significantly across CKD stages ($\chi^2 = 214.90$, df = 8, $p < 0.001$). Oral therapy predominated in the early stages, whereas combination therapy and insulin use increased significantly in advanced CKD stages.
In this study we found out the patients regarding oral drugs in stage-1, metformin + sitagliptin 3 cases (33.3%) combination was the most commonly prescribed oral therapy in these stage.

In this study we found out the patients regarding oral therapy in stage-2, metformin + empagliflozin 8 cases (18.60%) combination was the most frequently prescribed oral therapy. Among those receiving insulin therapy, insulin glargine + insulin lispro was the most commonly prescribed regimen, observed in 1 case (100%). For combination therapy, empagliflozin + insulin glargine (oral + insulin) was the most frequently prescribed combination, accounting for 1 case (100%) of the patients receiving combination treatment.

In this study we found out the patients regarding oral therapy in stage-3, metformin

+ empagliflozin 12 cases (16.0%) combination was the most frequently prescribed oral therapy. Among insulin therapy, insulin lispro was the most commonly prescribed, accounting for 3 cases (60.0%). For combination therapy, sitagliptin + insulin glargine (oral + insulin) was the most frequently

prescribed regimen, accounting for 4 cases (21.05%).

In this study we found out the patients regarding oral therapy in stage-4, metformin 8 cases (33.33%) were the most frequently prescribed oral therapy. Among insulin therapies, the combination of insulin glargine + insulin lispro was the most commonly prescribed regimen, accounting for 2 cases (13.33%). For combination therapy, metformin + insulin regular (oral + insulin) was the most frequently prescribed regimen, accounting for 9 cases (16.98%).

In this study we found out the patients regarding oral therapy in stage-5, glimepiride+ linagliptin 3 cases (21.43%)combination was the most frequently prescribed oral therapy. Among insulin therapy, the combination of insulin regular + insulin glargine (insulin + insulin) was the most commonly prescribed regimen, accounting for 23 cases (56.10%). For combination therapy, metformin + insulin regular was the most frequently prescribed regimen, accounting for 9 cases (20.45%).

In this study from the graph no. 6.1, 7.1, 7.2, 7.3, 8.1, 8.2, 8.3, 9.1, 9.2, 9.3, 10.1 & 10.2 we have finally analysed the therapy which is mostly used in all the stages of CKD. In stage-1 3 cases of metformin+ sitagliptin were mainly observed only in oral combination therapy. In stage -2 out of 10 cases which were associated in oral, insulin and combination therapy 8 were metformin + empagliflozin and in stage-3 out of total 19 cases of oral, insulin and combination therapies 12 were metformin+ empagliflozin which gives total of 20 cases in both stages (2 and 3) . In stage-4 the total no. of cases 22 prescribed in oral, insulin and combination therapies among them metformin+ insulin regular is prescribed in 9 cases which is highest. In stage-5 the total no. of cases was 35 prescribed in oral, insulin and combination therapies among them insulin regular + insulin glargine is prescribed in 23 cases.

In overall 90 cases of highly preferred drugs in all the stages of CKD, the metformin is the most commonly prescribed drug in 49 cases either as a single drug or in combination (with oral or insulin) and insulin glargine in combination with oral or insulin drugs is given in 34 cases in four stages except the stage-1.

In this study 9 hypoglycaemic cases were also identified which were found in stage-2,3,4 in which combination drugs were prescribed (oral+oral, oral+insulin).

6. CONCLUSION

The study concludes that, early diagnosis, regular monitoring and appropriate treatment selection plays a crucial role in the management of CKD with diabetes mellitus receiving differential antidiabetic therapy. The poor glycemic control was associated with kidney function deterioration and in turn disease progression, the management through combination therapy of diabetes mellitus has given the better outcomes in controlling blood glucose level (FBS) & in turn managing CKD (serum creatinine) compared to monotherapy (oral/insulin therapy) and was more commonly used in advanced CKD stages due to its effectiveness. Metformin being one of the oldest drug in treating the diabetes mellitus condition is also effective in the reduced progression of CKD with diabetes, which

has been used as a single or combination drug in many cases and also managed all the stages of CKD effectively, in the same way insulin glargine which has given in combination and also as a single drug has been managed many stages of CKD but the only disadvantage of combination therapy in managing CKD with diabetes mellitus is it's hypoglycemic effect with some of the drug combinations that reduces the kidney function further creating oxidative stress, sympathetic stimulation increases the risk of cardiovascular events, dangerous arrhythmia, neurocological symptoms & near-term morality. In future there is a need to study which drug combinations are commonly causing such hypoglycemic effects for the safe & effective treatment of diabetes mellitus in turn managing the CKD.

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