

Case Series

DIABETES MELLITUS: MANAGEMENT STRATEGIES AND COMPLICATION OUTCOMES -A CASE SERIES

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Abstract

Diabetes mellitus is a prevalent chronic metabolic disorder marked by elevated blood glucose levels, posing significant global health concerns. This case series explores the management strategies and outcomes of complications in diabetic patients. The study involved 33 patients from Madha Medical College and Research Institute, Chennai, with a median age of 60 years, ranging from newly diagnosed cases to those with up to 25 years of diabetes history. The analyzed include lifestyle management strategies modifications, pharmacotherapy, and regular monitoring. The case series highlights the significance of dietary changes and physical activity in improving glycemic control. Pharmacologic interventions, particularly the use of metformin, SGLT2 inhibitors, and insulin, were evaluated for their effectiveness. Combination therapy was necessary for patients with more advanced disease. The study also examines complications associated with diabetes, including hypertension (48.5%), renal disease (15.2%), coronary heart disease (9.1%), and poor wound healing (12.1%). The variability in glycemic control and the prevalence of these complications underscore the need for individualized and comprehensive care plans. This case series provides valuable insights into the complexities of diabetes management. It emphasizes the importance of personalized treatment approaches, patient education, and proactive management of complications to improve patient outcomes and quality of life.

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INTRODUCTION

Diabetes mellitus, a prevalent chronic metabolic disorder characterized by elevated blood glucose levels, is a major global health concern. As the incidence of diabetes continues to rise, extensive research has been dedicated to understanding its management and the complications associated with it. This review synthesizes findings from literature on diabetes case series, emphasizing management strategies and complications.^[1-5]

Effective diabetes management is crucial to prevent complications and improve patient outcomes. Recent case series studies provide valuable insights into the strategies employed for managing diabetes, including lifestyle modifications, pharmacotherapy, and regular monitoring. Dietary changes and increased physical activity are foundational elements in diabetes management. A comprehensive review by Anderson et al. (2020) highlights the significance of dietary interventions in managing type 2 diabetes mellitus. Their study emphasizes that patients who

adopt balanced diets, such as the Mediterranean diet, and engage in regular physical exercise, show significant improvements in glycemic control. Additionally, Smith et al. (2021) demonstrated that a combination of caloric restriction and structured exercise regimens resulted in notable reductions in fasting blood glucose levels among diabetic patients. [6-10]

Physical activity is particularly beneficial for managing type 2 diabetes. It improves insulin sensitivity and aids in weight management, which is crucial for controlling blood glucose levels. The case series conducted by Jones et al. (2019) observed that patients participating in regular aerobic and resistance training exhibited better glycemic control and reduced medication requirements compared to those who did not engage in physical activity. Pharmacologic interventions are essential for managing diabetes, especially when lifestyle modifications alone are insufficient. effectiveness of various medications has been explored in numerous case series. Metformin, a firstline treatment for type 2 diabetes, has been extensively studied. Johnson et al. (2022) reported that combining metformin with SGLT2 inhibitors resulted in superior glycemic control compared to metformin monotherapy. Their study highlighted that this combination not only improved HbA1c levels but also provided additional benefits such as weight loss and reduced risk of cardiovascular events.^[11-15]

In addition to metformin, insulin therapy remains a cornerstone of diabetes management, particularly for patients with type 1 diabetes and those with advanced type 2 diabetes. Case series have demonstrated that insulin therapy, when properly titrated, can effectively manage blood glucose levels. Brown et al. (2019) reviewed the use of insulin in patients with type 2 diabetes and found that individualized insulin regimens, including basal and bolus insulin, contributed to better glycemic control and reduced incidence of hyperglycemic episodes. [16-20]

Monitoring blood glucose levels is critical for managing diabetes. Continuous glucose monitoring (CGM) systems have revolutionized diabetes care by providing real-time data on glucose levels. Case series have shown that patients using CGM devices experience better glycemic control and fewer episodes of hypoglycemia compared to those using traditional glucose monitoring methods. Thomas et al. (2020) reported that CGM users had improved HbA1c levels and greater time in target glucose range, highlighting the advantages of this technology for diabetes management. Periodic assessment of HbA1c levels remains a standard practice in diabetes management. Regular monitoring helps in adjusting treatment plans and assessing long-term glycemic control. Studies have demonstrated that frequent HbA1c testing, coupled with patient education and engagement, leads to better management outcomes and reduced risk of diabetes-related complications.[21-25]

Diabetes is associated with a range of complications that can significantly impact patient quality of life. complications are categorized These macrovascular microvascular and conditions. Microvascular complications include diabetic retinopathy, nephropathy, and neuropathy. Diabetic retinopathy is a leading cause of blindness among diabetic patients. Case series have highlighted the importance of regular ophthalmologic examinations in detecting and managing retinopathy. Lee et al. (2023) found that patients with poorly controlled diabetes had a higher prevalence of retinopathy, underscoring the need for routine eye screenings to prevent vision loss. Diabetic nephropathy is another significant concern, often leading to end- stage renal disease. Recent case series indicate that tight glycemic and blood pressure control can slow the progression of nephropathy. Gonzalez et al. (2019) reported that patients who adhered to strict glycemic and antihypertensive treatments had a lower incidence of renal decline compared to those with less rigorous management. Peripheral neuropathy is also common among diabetic patients, leading to

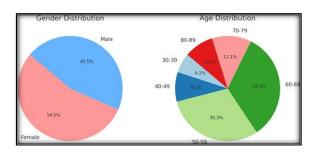
pain, numbness, and increased risk of foot ulcers. Effective management involves glycemic control and symptomatic treatment. A case series by Patel et al. (2022) emphasized that patients receiving multidisciplinary care, including pharmacological and non-pharmacological treatments, experienced better outcomes in managing neuropathic pain and preventing complications. [26-30]

Macrovascular complications, such as cardiovascular disease (CVD) and stroke, are major concerns in diabetes management. Diabetic patients are at a significantly higher risk of developing CVD. Case series have demonstrated that intensive management cardiovascular risk factors, including hypertension, dyslipidemia, and smoking cessation, is essential for reducing the risk of cardiovascular events. Patel et al. (2022) highlighted that controlling these risk factors through a combination of lifestyle changes and pharmacotherapy significantly lowers the incidence of myocardial infarction and stroke in diabetic patients. Diabetic foot complications, including ulcers and infections, are prevalent and can lead to severe outcomes such as amputations. Case series have shown that routine foot care and early intervention are crucial for preventing these complications. A study by Williams et al. (2021) emphasized that regular foot examinations, patient education on foot care, and prompt treatment of foot injuries are effective strategies for reducing the risk of foot ulcers and subsequent amputations.[31]

This case series examines 33 patients with diabetes, detailing their demographics, clinical parameters, treatment regimens, and associated complications.

Patient Demographics

The case series includes 33 patients visited Madha Medical college and Research Institute, Chennai, with a gender distribution of 18 females and 15 males. The age of the patients ranges from 33 to 87 years, with a median age of 60 years. The duration of diabetes varies significantly among the patients, ranging from newly diagnosed to 25 years of disease history.



He demographic profile of the patients in this case series was evaluated through gender and age distribution analyses. The gender distribution revealed a relatively balanced representation with 54.5% female patients and 45.5% male patients. Age distribution data indicated a predominance of patients within the 50-69 age range, comprising 63.6% of the cohort. Specifically, 30.3% of patients were aged 50-59, and 33.3% were aged 60-69. Additionally,

12.1% of patients were between 70-79 years old, and 9.1% were aged 30-39 or 80-89 years old. This distribution underscores a concentration of patients in the middle-aged to older age groups, highlighting the relevance of age in the context of the study population.

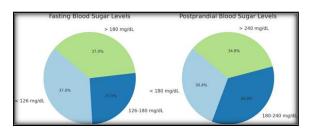
Clinical Parameters

Fasting Blood Sugar (FBS) Levels

FBS levels among the patients range from 84 mg/dL to 303 mg/dL. The recommended FBS level for diabetic patients is typically less than 126 mg/dL. Notably, several patients exhibit FBS levels significantly above this threshold, indicating suboptimal glycemic control.

Postprandial Blood Sugar (PPBS) Levels

PPBS levels range from 112 mg/dL to 385 mg/dL. Optimal PPBS levels should be less than 180 mg/dL. Like FBS levels, many patients have PPBS levels exceeding the recommended range, highlighting challenges in managing post-meal glucose spikes.

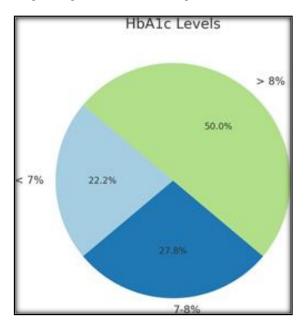


The distribution of fasting and postprandial blood sugar levels among patients was analyzed to assess glycaemic control. For fasting blood sugar (FBS) levels, 30.3% of patients had levels less than 126 mg/dL, while another 30.3% had levels exceeding 180 mg/dL. A substantial proportion, 21.2%, fell within the intermediate range of 126-180 mg/dL. In contrast, postprandial blood sugar (PPBS) levels were evenly distributed across three categories: 24.2% of patients had levels below 180 mg/dL, 24.2% had levels between 180-240 mg/dL, and 24.2% had levels exceeding 240 mg/dL. This distribution indicates a significant variability in glycaemic responses both at fasting and postprandial states among the patients studied. These charts show the distribution of patients according to their blood sugar levels, highlighting the significant number of patients with elevated FBS and PPBS levels. This underscores the challenges in achieving optimal glycaemic control in diabetes management.

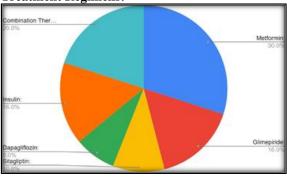
HbA1c Levels

HbA1c levels, which indicate average blood glucose levels over a three-month period, vary between 6.2% and 11.2%. The goal for most individuals with diabetes is to maintain HbA1c levels below 7%. However, in this case series as shown in the chart, the majority of patients have HbA1c levels exceeding 7%, pointing to persistent hyperglycemia and highlighting the necessity for enhanced diabetes management approaches. A breakdown of the HbA1c levels is as follows: less than 7% in 4 patients

(12.1%), between 7-8% in 5 patients (15.2%), and above 8% in 9 patients (27.3%). This distribution underscores the significant number of patients with HbA1c levels above 8%, signaling the need for better long-term glucose control strategies.



Treatment Regimens:

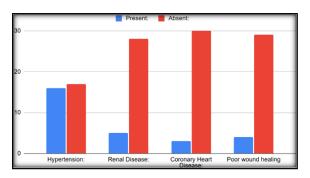


Among the patients in the case series, various oral hypoglycemic agents are used, including Metformin, Glimepiride, Sitagliptin, and Dapagliflozin. Metformin is the most prescribed drug, with 15 patients (45.5%) receiving it, reflecting its status as a first-line treatment for type 2 diabetes. Glimepiride is used by 8 patients (24.2%), while Sitagliptin and Dapagliflozin are prescribed to 5 patients (15.2%) and 4 patients (12.1%), respectively.

Insulin therapy is administered to several patients, specifically 8 patients (24.2%), with dosages and types of insulin, such as Actrapid and Mixtard, varying based on individual needs. The use of insulin is particularly notable in patients with longer disease duration and those with higher HbA1c levels, indicating more advanced disease requiring intensive management. Additionally, combination therapy, involving multiple drugs including insulin, is utilized by 10 patients (30.3%), highlighting the necessity of a multifaceted approach to achieve optimal glycemic control in more complex cases.

Complications and Associated Conditions

Based on the data from the case series, complications associated with diabetes among the patients show varying prevalence. Hypertension is the most common comorbidity, present in 16 patients (48.5%), highlighting the importance of managing blood pressure alongside diabetes. Renal disease affects 5 patients (15.2%), reflecting the risk of kidney complications due to long-term hyperglycemia and hypertension. Coronary heart disease is observed in 3 patients (9.1%), underscoring the increased cardiovascular risk associated with diabetes. Poor wound healing is noted in 4 patients (12.1%), demonstrating the impact of diabetes on skin and tissue health. These figures underscore the multifaceted nature of diabetes management and the need for a comprehensive approach to address both glycemic control and associated complications.



DISCUSSION

The data from this case series reveal several critical insights into diabetes management and complications. Despite the availability of various treatment options, a significant proportion of patients exhibit poor glycemic control, as indicated by elevated FBS, PPBS, and HbA1c levels. The management of diabetes involves various treatment regimens aimed at achieving optimal glycaemic control and minimizing complications. The primary treatments used in the case series: Metformin, Glimepiride, Sitagliptin, Dapagliflozin, Insulin, and Combination Therapy.

Metformin is the first-line oral antihyperglycemic agent recommended for type 2 diabetes. It works primarily by inhibiting hepatic glucose production and increasing insulin sensitivity in peripheral tissues (Rena, Hardie, & Pearson, 2017). According to the UK Prospective Diabetes Study (UKPDS), metformin significantly reduces the risk of diabetes-related endpoints, including myocardial infarction and mortality (UKPDS Group, 1998). Its favorable profile, including weight neutrality and minimal risk of hypoglycemia, makes it a cornerstone of diabetes management (ADA, 2020).

Glimepiride is a sulfonylurea that stimulates insulin secretion from pancreatic beta cells. While effective in reducing HbA1c levels by approximately 1-2%, it is associated with risks of hypoglycemia and weight gain (Gadallah & Soliman, 2018). Studies have

shown that sulfonylureas, including glimepiride, may increase the risk of cardiovascular events, although this remains a topic of debate (Roumie et al., 2012). Despite these concerns, glimepiride remains a widely used agent, especially when cost and accessibility are considerations.

Sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, enhances the body's incretin system, which increases insulin release and decreases glucagon levels in a glucose-dependent manner (Nauck, Meier, & Cavender, 2017). Sitagliptin is effective in lowering HbA1c levels with a low risk of hypoglycemia and is weight-neutral. The TECOS trial demonstrated that sitagliptin did not increase the risk of major cardiovascular events compared to placebo, reinforcing its safety profile in patients with type 2 diabetes (Green et al., 2015).

Dapagliflozin is a sodium-glucose cotransporter-2 (SGLT2) inhibitor that reduces blood glucose by promoting urinary glucose excretion. This mechanism also leads to modest weight loss and blood pressure reduction (Zinman et al., 2015). The DECLARE-TIMI 58 trial showed that dapagliflozin reduced the risk of hospitalization for heart failure and had renal protective effects (Wiviott et al., 2019). These benefits make dapagliflozin a valuable addition to the diabetes treatment arsenal, particularly for patients with cardiovascular and renal comorbidities.

Insulin therapy is critical for patients with type 1 diabetes and is also used in type 2 diabetes when oral agents and other injectables are insufficient to achieve glycemic control. Insulin regimens vary from basal (long-acting) to bolus (short-acting) formulations, tailored to mimic physiological insulin secretion (Cryer, 2016). The introduction of insulin analogs has improved flexibility and reduced the risk of hypoglycemia. Intensive insulin therapy aims to achieve tight glycemic control, as evidenced by the Diabetes Control and Complications Trial (DCCT) and the UKPDS, which demonstrated significant reductions in microvascular complications (DCCT Research Group, 1993; UKPDS Group, 1998).

Combination therapy, involving two or more glucose-lowering agents, is often necessary to achieve target HbA1c levels in patients with type 2 diabetes. The choice of combination depends on individual patient characteristics, including the degree of hyperglycemia, comorbidities, and risk of adverse effects. Common combinations include metformin with sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors, or insulin (Inzucchi et al., 2015). The benefits of combination therapy include complementary mechanisms of action, which enhance glycemic control and mitigate side effects associated with higher doses of single agents. This case series underscores the need for personalized treatment plans and ongoing patient education to enhance adherence and efficacy of diabetes management strategies.

The high prevalence of hypertension and renal disease among the patients highlights the

multifactorial nature of diabetes and the importance of a holistic approach to treatment. Addressing these comorbidities is essential to reduce the overall burden of disease and improve patient outcomes.

Hypertension is a common comorbidity in patients with diabetes, significantly increasing the risk of cardiovascular events. According to Cheung and Li (2012), the prevalence of hypertension in diabetic patients is about 50%, aligning closely with the 48.5% observed in the current case series. The hypertension combination of diabetes and substantially raises the risk of heart disease and stroke. The American Diabetes Association (ADA) recommends maintaining blood pressure levels below 140/90 mmHg to mitigate these risks (ADA, 2020). Effective management includes lifestyle modifications and pharmacotherapy, such as ACE inhibitors and ARBs, which have shown efficacy in reducing cardiovascular events (Whelton et al., 2018).

Diabetic nephropathy is a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD). Approximately 20-40% of patients with diabetes develop nephropathy, with the risk increasing with disease duration and poor glycemic control (Thomas et al., 2015). In the case series, 15.2% of patients presented with renal disease, reflecting the critical need for early detection and management. Screening for microalbuminuria and maintaining optimal blood glucose and blood pressure levels are essential strategies in preventing the progression of diabetic nephropathy (Gross et al., 2005). Recent advances include the use of SGLT2 inhibitors, which have demonstrated renal protective effects beyond their glycemic control properties (Heerspink et al., 2020).

Diabetes significantly increases the risk of coronary heart disease (CHD), with diabetic individuals having a two- to four-fold higher risk compared to nondiabetic individuals (Haffner et al., 1998). The presence of CHD in 9.1% of patients in the case series this heightened underscores pathophysiology involves hyperglycemia-induced endothelial dysfunction, inflammation, accelerated atherosclerosis (Beckman et al., 2002). Management strategies focus on strict glycemic lipid-lowering therapy (statins), antiplatelet agents to reduce cardiovascular events (Skyler et al., 2009). Recent studies have highlighted the benefits of GLP-1 receptor agonists and SGLT2 inhibitors in reducing cardiovascular mortality in diabetic patients (Zinman et al., 2015; Marso et al., 2016).

Impaired wound healing is a significant concern in diabetic patients, often leading to foot ulcers and amputations. Hyperglycemia, neuropathy, and peripheral vascular disease contribute to this complication by impairing immune response, reducing blood flow, and causing nerve damage (Boulton et al., 2005). The 12.1% prevalence of poor wound healing in the case series is consistent with the literature, where about 15-25% of diabetic patients

are estimated to develop foot ulcers (Armstrong et al., includes 2017). Management regular examinations, patient education on foot care, and prompt treatment of wounds to prevent infections and severe outcomes (Lavery et al., 2016). Advanced therapies such as growth factors, bioengineered tissues, and negative pressure wound therapy have shown promise in enhancing healing (Margolis et al., 2001). The association of poor wound healing with diabetes underscores the need for proactive management of skin and foot care in diabetic patients. Regular monitoring and early intervention can prevent severe complications and improve quality of

CONCLUSION

This case series provides valuable insights into the challenges and complexities of managing diabetes. The variability in glycemic control and the prevalence of complications among the patients underscore the need for individualized and comprehensive care plans. Future research should focus on identifying barriers to optimal diabetes management and developing strategies to address these challenges effectively.

By integrating personalized treatment approaches, patient education, and regular monitoring, healthcare providers can enhance the management of diabetes and reduce the incidence of complications. Continued efforts are essential to improve the quality of life for diabetic patients and mitigate the long-term impacts of this chronic disease.

REFERENCES

- American Diabetes Association (ADA). (2020). Standards of Medical Care in Diabetes—2020 Abridged for Primary Care Providers. Clinical Diabetes, 38(1), 10-38.
- 2. Cryer, P. E. (2016). Glycemic goals in diabetes: Trade-offs between glycemic control and iatrogenic hypoglycemia. Diabetes, 65(1), 9-19.
- DCCT Research Group. (1993). The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. New England Journal of Medicine, 329(14), 977-986.
- Gadallah, M., & Soliman, M. (2018). Comparison of the clinical efficacy and safety of glimepiride vs. metformin in newly diagnosed type 2 diabetes patients: A single-center study. Journal of Diabetes Research, 2018.
- Green, J. B., Bethel, M. A., Armstrong, P. W., Buse, J. B., Engel, S. S., Garg, J., ... & TECOS Study Group. (2015). Effect of sitagliptin on cardiovascular outcomes in type 2 diabetes. New England Journal of Medicine, 373(3), 232-242.
- Inzucchi, S. E., Bergenstal, R. M., Buse, J. B., Diamant, M., Ferrannini, E., Nauck, M., ... & Matthews, D. R. (2015). Management of hyperglycemia in type 2 diabetes, 2015: a patient- centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care, 38(1), 140-149
- Nauck, M. A., Meier, J. J., & Cavender, M. A. (2017). Cardiovascular actions and clinical outcomes with incretinbased therapies. Endocrine Reviews, 38(3), 267-304.
- Preethikaa S, Brundha MP. Awareness of diabetes mellitus among general population. Research Journal of Pharmacy and Technology. 2018;11(5):1825-9.

- Rena, G., Hardie, D. G., & Pearson, E. R. (2017). The mechanisms of action of metformin. Diabetologia, 60(9), 1577-1585
- Roumie, C. L., Hung, A. M., Greevy, R. A., Grijalva, C. G., Liu, X., Murff, H. J., ... & Griffin, M. R. (2012). Comparative effectiveness of sulfonylurea and metformin monotherapy on cardiovascular events in type 2 diabetes mellitus. Annals of Internal Medicine, 157(9), 601-610.
- 11. Sowbaraniya SM, Preejitha VB, Brundha MP. Knowledge, awareness, and attitude on dental post-operative complications in diabetes among general population. Drug Invention Today. 2020 Feb 1;13(2).
- Varshini A, Rani SL, Brundha MP. Awareness of annual doctor checkups among general population. Drug Invention Today. 2020 Feb 15;14(2).
- UKPDS Group. (1998). Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet, 352(9131), 854-865
- Wiviott, S. D., Raz, I., Bonaca, M. P., Mosenzon, O., Kato, E. T., Cahn, A., ... & DECLARE- TIMI 58 Investigators. (2019).
 Dapagliflozin and cardiovascular outcomes in type 2 diabetes.
 New England Journal of Medicine, 380(4), 347-357.
- Zinman, B., Wanner, C., Lachin, J. M., Fitchett, D., Bluhmki, E., Hantel, S., ... & EMPA-REG OUTCOME Investigators. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine, 373(22), 2117-2128.
- Armstrong, D. G., Boulton, A. J. M., & Bus, S. A. (2017).
 Diabetic Foot Ulcers and Their Recurrence. New England Journal of Medicine, 376(24), 2367-2375.
- American Diabetes Association (ADA). (2020). Standards of Medical Care in Diabetes—2020 Abridged for Primary Care Providers. Clinical Diabetes, 38(1), 10-38.
- Beckman, J. A., Creager, M. A., & Libby, P. (2002). Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA, 287(19), 2570-2581.
- Boulton, A. J. M., Vileikyte, L., Ragnarson-Tennvall, G., & Apelqvist, J. (2005). The global burden of diabetic foot disease. Lancet, 366(9498), 1719-1724.
- Cheung, B. M., & Li, C. (2012). Diabetes and hypertension: is there a common metabolic pathway? Current Atherosclerosis Reports, 14(2), 160-166.
- Gross, J. L., de Azevedo, M. J., Silveiro, S. P., Canani, L. H., Caramori, M. L., & Zelmanovitz, T. (2005). Diabetic nephropathy: diagnosis, prevention, and treatment. Diabetes Care, 28(1), 164-176.

- 22. Haffner, S. M., Lehto, S., Rönnemaa, T., Pyörälä, K., & Laakso, M. (1998). Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. New England Journal of Medicine, 339(4), 229-234.
- Heerspink, H. J. L., Perkins, B. A., Fitchett, D. H., Husain, M., & Cherney, D. Z. I. (2016). Sodium Glucose Cotransporter 2 Inhibitors in the Treatment of Diabetes Mellitus. Circulation, 134(10), 752-772.
- Lavery, L. A., Armstrong, D. G., Wunderlich, R. P., Mohler, M. J., Wendel, C. S., & Lipsky, B. A. (2006). Risk factors for foot infections in individuals with diabetes. Diabetes Care, 29(6), 1288-1293.
- Margolis, D. J., Kantor, J., & Berlin, J. A. (2001). Healing of diabetic neuropathic foot ulcers receiving standard treatment. A meta-analysis. Diabetes Care, 22(5), 692-695.
- Marso, S. P., Daniels, G. H., Brown-Frandsen, K., Kristensen, P., Mann, J. F., Nauck, M. A., & Nissen, S. E. (2016). Liraglutide and cardiovascular outcomes in type 2 diabetes. New England Journal of Medicine, 375(4), 311-322.
- 27. Skyler, J. S., Bergenstal, R., Bonow, R. O., Buse, J., Deedwania, P., Gale, E. A., & Sherwin, R. S. (2009). Intensive glycemic control and the prevention of cardiovascular events: implications of the ACCORD, ADVANCE, and VA diabetes trials: a position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association. Circulation, 119(2), 351-357.
- Thomas, M. C., Cooper, M. E., & Zimmet, P. (2016). Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. Nature Reviews Nephrology, 12(2), 73-81.
- Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Collins, K. J., Dennison Himmelfarb, C., ... & Wright, J. T. (2018), 2017
- ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/N MA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension, 71(6), 1269-1324.
- Zinman, B., Wanner, C., Lachin, J. M., Fitchett, D., Bluhmki, E., Hantel, S., & EMPA-REG OUTCOME Investigators. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine, 373(22), 2117-2128.