RSSDI Indian Diabetes

EDUCATOR JOURNAL

Theme of the Month

Diabetes and Other Endocrine Disorders

To keep Members of Diabetes Care team abreast about
DSME/DSMS - (Diabetes Self management Education/Support) Concepts

2015 2016 2017 2018 2019 2020 2021 2022 2023 2024

Longest Running Monthly Journal

In collaboration with USV

RSSDI

(RESEARCH SOCIETY FOR THE STUDY OF DIABETES IN INDIA)

Launches the Largest Obesity Awareness Campaign

WEIGHT MATTERS

Scan the QR Code to Participate

In Association With

USV

RSSDI
Indian
Diabetes
EDUCATOR JOURNAL

1 st time in India
To keep the members of diabetes care team abreast with DSME and DSMS concepts

EDITORIAL BOARD

Scan the QR code to access full library of IDEJ - **https://usvmed.com/**

*DSME: Diabetes Self-Management Education, DSMS: Diabetes Self-Management Support

NATIONAL ADVISORY BOARD

RSSDI Indian Diabetes
EDUCATOR JOURNAL

1 st time in India
To keep the members of diabetes care team abreast with DSME and DSMS concepts

FOREWORD

Research Society for the Study of Diabetes in India (RSSDI) founded by Prof MMS Ahuja in the year 1972 is the biggest scientific association of healthcare professionals involved in promoting diabetes education and research in India. RSSDI is happy to collaborate with USV to support their endeavour to make India the 'Diabetes care capital of the world'. Through this collaboration, RSSDI would like to strengthen the cadre of diabetes educators by empowering them with recent updates in diabetes management helping bridge the gap between the physician and the patient. Today, the rule of 50% is prevailing in terms of awareness, detection, treatment and control in T2DM. Our aspiration is to achieve 90-90-90-90 i.e.90% of people with diabetes should be made aware, 90% should be detected, 90% of those detected should be treated, and 90% of those treated should reach their goals.

Indian Diabetes Educator Journal (IDEJ) is the first of its kind in India, and the longest running monthly diabetes educator journal since April 2015 & continues its endeavour to spread awareness, knowledge and enable healthcare teams to manage individuals with diabetes and empower them for self-care. RSSDI IDEJ will continue to keep the members of diabetes care team abreast with concepts of Diabetes Self-Management Education/Support (DSME/S) with a reach of 44000 doctors and diabetes educators digitally.

Each year, the 7th of April is celebrated as World Health Day, a significant occasion that sheds light on crucial health issues and promotes united efforts in attaining sustainable development goals related to health. This month's IDEJ aims to explore the connection between diabetes and various endocrine hormones. As a metabolic disorder, diabetes can impact the functionality of specific hormones, while certain hormonal issues may contribute to the occurrence or risk of diabetes. It is imperative for diabetes educators to comprehend the interrelation between different endocrine conditions and diabetes, ensuring a comprehensive approach for individuals dealing with diabetes. We anticipate that this edition will equip diabetes educators with valuable clinical insights within the realm of diabetes and hormonal health.

We sincerely thank our contributors for making this issue delightful reading for our readers. We dedicate this journal to all the healthcare professionals who are working relentlessly towards making "India–The Diabetes Care Capital of the World."

Sincere Regards,

Dr. Sanjay Agarwal
RSSDI Secretary

*DSME: Diabetes Self-Management Education, DSMS: Diabetes Self-Management Support

Expert Contributors
of the month

Dr. V. K. Abichandani

MD, MSc Endocrinology (USW, UK)
Consulting Diabetes and Endocrine Physician, Ahmedabad

Article: Interplay between Pituitary Health and Diabetes Mellitus

Dr. Sanjay P. Shah

MBBS, MD (Medicine)
Consultant Physician, Sun-Deep Nursing Home - Physiotherapy Center, Vadodara

Article: Co-existence and Association of Thyroid Disorders and Diabetes

Dr. Jamil Khanji

MD (Medicine)
Consultant Physician, Sparsh Heart and Medicare Hospital, Modasa

Article: Polycystic Ovary Syndrome – A Risk Factor for Type 2 Diabetes Mellitus

Dr. Sandeep Sudhakaran

MBBS, MSc (Diabetic Foot Surgery), C. DIAB, D. DIAB
Consultant in Diabetic Foot Surgery and Consultant Diabetologist, Medical Director at Dr Sandeep's Diabetes Speciality Centre, Thrissur

Article: Dietary Considerations for Thyroid Disorders

Dr. Mohan T. Shenoy

MBBS, MD, DM - Endocrinology
Senior Consultant Endocrinologist and Unit Chief, Department of Endocrinology, Diabetes and Metabolism, Sree Gokulam Medical College and Research Foundation, Thiruvananthapuram

Article: Interview with Dr. Mohan T. Shenoy

Dr. Brijesh Singh

MBBS, MD (Medicine)
Consultant Diabetologist, Ayush Clinic and Diagnostics, Rae Bareli

Article: Exploring the Dynamics between Diabetes and Menopause

Expert Contributors
of the month

Dr. Rony T. Vempeny

MBBS, MD, DNB (General Medicine)

Consultant Physician and Diabetologist, Vempeny Clinic, Kottayam

Article: Endocrine Disorders that Cause Diabetes

Dr. Rajeev Verma

MD (Medicine)

Assistant Professor, Dept. of General Medicine, AIIMS, Rae Bareli

Article: Association of Leptin, Obesity, and Diabetes

Dr. Dharmadev Ruparel

MBBS, MD (Medicine), PG Dip (Diabetology), FRCP (Cardiff/London)

Consultant Physician and Diabetologist, Sujit Hospital Diabetes and Thyroid Care Center, Bhavnagar

Article: Diabetes and Gonadal Disorders

Dr. Sarthak Gandhi

MBBS, FCCCM, D. Diabetes, D. Endocrine (UK)

Consultant Diabetologist and Endocrinologist, Gandhi Diabetic Care Clinic, Surat

Article: Frequently Asked Questions

To get featured in the Indian Diabetes Educator Journal you can connect with us on the below mail ID for further communication: info@nurturehealthsolutions.com

RSSDI Indian Diabetes
EDUCATOR JOURNAL

Issue No. 109, April 2024

Table of Content

Cover Story: Interplay between Pituitary Health and Diabetes Mellitus

Dr. V. K. Abichandani

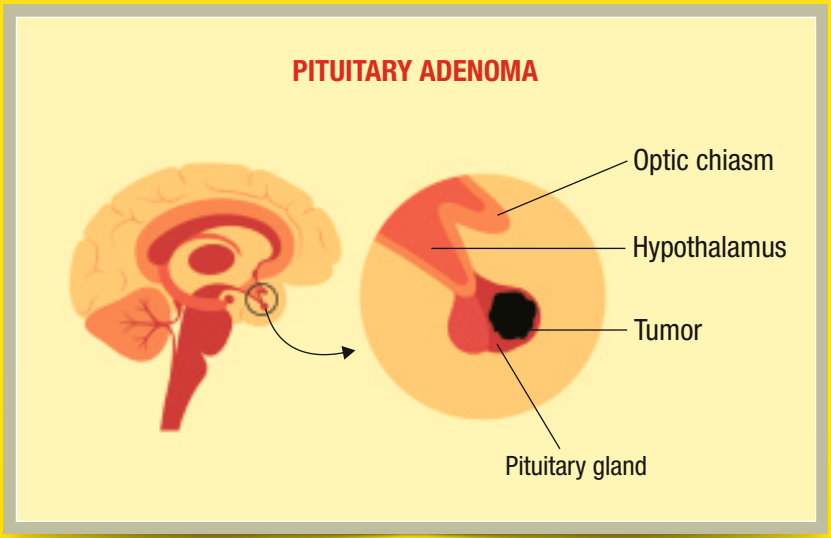
MD, MSc Endocrinology (USW, UK)

Consulting Diabetes and Endocrine Physician, Ahmedabad

Both pituitary hormones, excess and deficiency syndromes, impair the action of insulin to a varying extent by direct and indirect effects. This is most evident in Cushing's disease and acromegaly but also experienced to a lesser extent in prolactinomas, growth hormone (GH) deficiency, hypogonadism, and hypothyroidism.

Interestingly, the pituitary disease can cause hypoglycemia or hyperglycemia; conversely, dysglycemia can disturb pituitary function. Hence, glucose metabolism needs to be closely monitored and treated in individuals with pituitary adenomas. The presence of dysglycemia can represent not only an additional risk factor for cardiovascular mortality but also a factor that influences and personalizes therapeutic decision-making. Correction of the pituitary dysfunction by pituitary surgery, medical, or radiotherapy is generally followed by improvement of glucose homeostasis.

The incidence of pituitary adenomas, which are common benign tumors of the anterior pituitary gland, is increasing annually, accounting for approximately 14% of all intracranial tumors. About 46-64% of these adenomas are functional tumors that secrete hormones. The common secreted hormones are prolactinoma (PRL; 32-51%), GH (9-11%), and adrenocorticotropic hormones (ACTH; 3-6%). The less commonly secreted hormones are follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and melanocyte-stimulating hormone (MSH). Functional adenomas can cause clinical symptoms mediated by the excessive secretion of hormones, leading to galactorrhea, hypogonadism, acromegaly, Cushing's disease, and other symptoms.



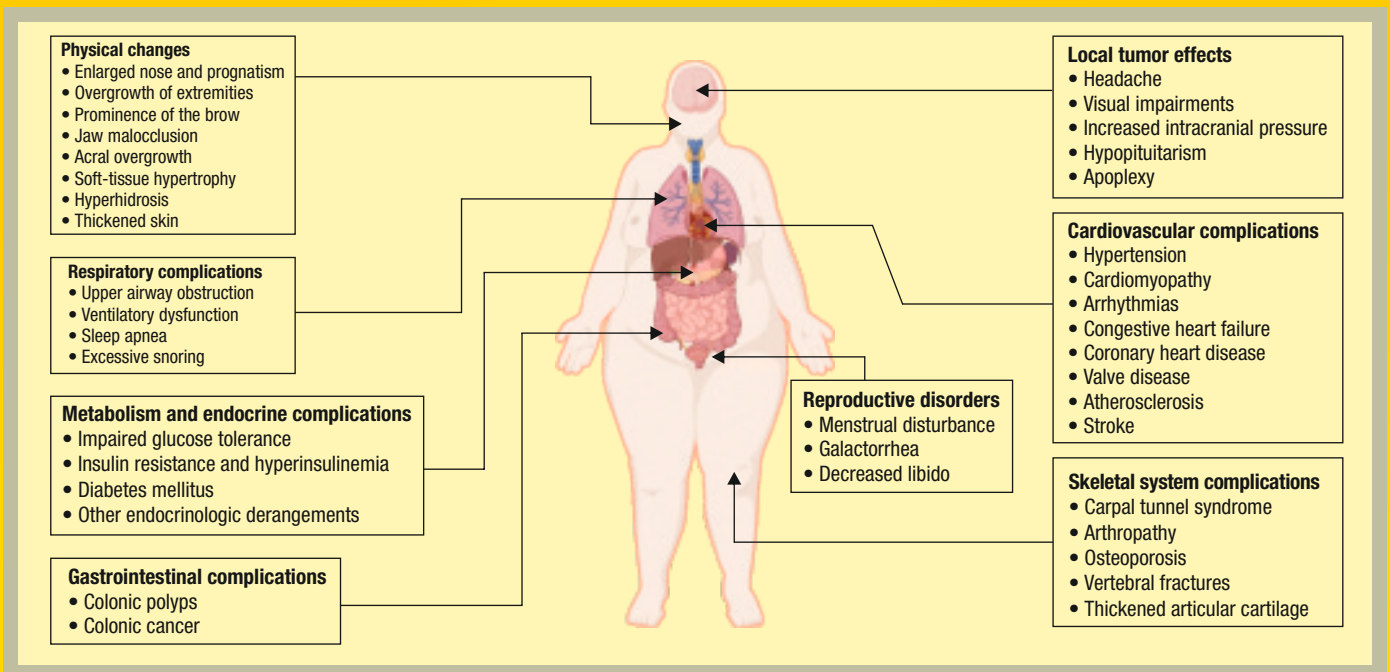
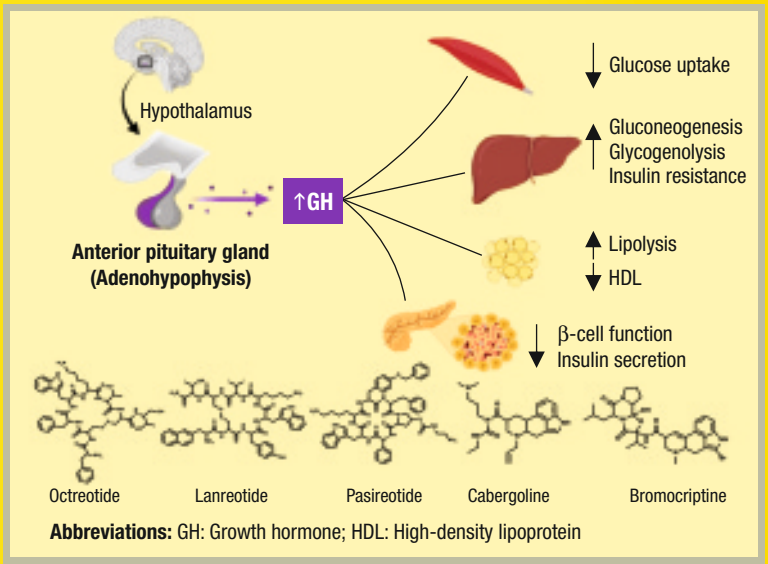


Figure 1. Classic clinical signs and symptoms of acromegaly

Source: Yao, Shun *et al*; (2020). Predictors of postoperative biochemical remission in acromegaly

The diagnosis of acromegaly must be considered in individuals who present an increase in the size of the hands and feet, tightening of facial features with the growth of the mandible and prognathism, frontal bumps, growth of the nasal pyramid, macroglossia, dental diastemas followed by premature teething, excessive sweating, voice thickness, thickened integuments, arthropathy, kyphosis, carpal tunnel syndrome, sleep apnea, and oligomenorrhea. Acromegaly is accompanied by an increased risk of developing diabetes, the appearance of colonic polyps, and colon cancer.

In more than half of the individuals, diabetes is diagnosed before acromegaly. At diagnosis, 22-40.5% of individuals with acromegaly exhibit elevated fasting glucose concentrations and/or impaired glucose tolerance and 12-34.9% diabetes mellitus.



Abbreviations: GH: Growth hormone; HDL: High-density lipoprotein

Legend: Diabetes secondary to acromegaly: Diabetogenic effects of excessive GH in the case of acromegaly and the available therapeutics for acromegaly. Hypothalamus (outlined with a black box): up arrows indicate increase or excess, while down arrows indicate decrease.

Source: Popoviciu MS, Paduraru L, Nutas RM, *et al.* Diabetes Mellitus Secondary to Endocrine Diseases: An Update of Diagnostic and Treatment Particularities. *International Journal of Molecular Sciences*, 2023;24(16).

Glucose homeostasis frequently improves following remission of GH excess by transsphenoidal surgery or pharmacological disease control, but glucose metabolism remains impaired in many individuals. From a pathophysiological viewpoint, substances counteracting insulin resistance appear to be the first choice in acromegaly. As several cases of diabetic ketoacidosis (DKA) have been reported as presenting symptoms/conditions in individuals with acromegaly, SGLT2 inhibitors are not preferred due to their potential to add to GH's effects on glucose metabolism by facilitating the so-called euglycemic ketoacidosis.

Extremely severe insulin resistance, as well as GH's lipolytic action with an increase in free fatty acids and the suppression of insulin secretion, may explain the several cases of DKA that have been reported as presenting symptoms/conditions in individuals with acromegaly. In all reported cases of acromegaly-associated DKA, diabetes resolved after remission of acromegaly. Metformin should be preferred to glitazones due to its adverse effects on bone and fluid retention. DPP4 inhibitors and GLP-1 receptor agonists might be used along with metformin, but insulin remains the therapy of choice in cases with severe hyperglycemia.

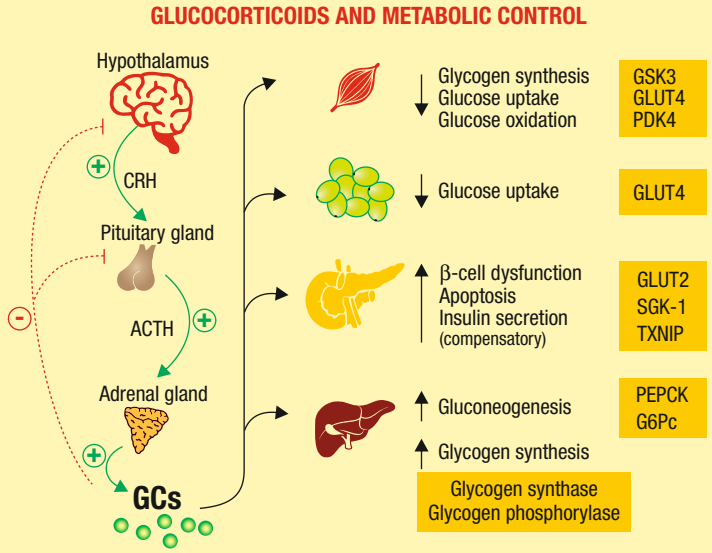
Table 1: Metabolic effects of insulin and alterations in Cushing's disease and acromegaly

Organ	Insulin	Cushing's disease	Acromegaly
Liver			
Gluconeogenesis	↓	↑	↑
Glycogenolysis	↓	↑	↑
Muscle			
Glucose uptake	↑	↓	↓
Proteolysis	↓	↑	↓
Glycogen synthesis	↑	↓	↑
Adipose tissue			
Lipolysis	↓	↑	↑
Glucose uptake	↑	↓	↓

Source: Schernthaner-Reiter, M. H., Wolf, P., Vila, G., & Luger, A. (2021). The Interaction of Insulin and Pituitary Hormone Syndromes. *Frontiers in Endocrinology*

Cushing's disease

Impaired glucose tolerance has been reported in 21-64% at diagnosis and diabetes mellitus in 20-47%. There are several reports on DKA as a presenting symptom of Cushing's disease, where diabetes was cured or remitted with the control of cortisol excess. Diabetogenic effects of cortisol include stimulation of lipolysis with an outpouring of free fatty acids, suppression of insulin secretion, and ketogenesis in the liver.



Abbreviations: GCs: Glucocorticoids; GRs: Glucocorticoid receptors; CRH: Corticotropin-releasing hormone; ACTH: Adrenocorticotropic hormone

Legend: Schematic representation of the HPA axis and the effects of GCs [Glucocorticoids (GCs)/Glucocorticoid receptors (GRs)] on glucose metabolism in the liver, adipose tissue, muscle, and pancreas. Genes/proteins involved (directly or indirectly) in the mentioned events are in shaded boxes.

Source: Magomedova, Lilia & Cummins, Carolyn. (2015). Glucocorticoids and Metabolic Control. Handbook of experimental pharmacology. 233. 10.1007/164_2015_1.

Prolactinoma

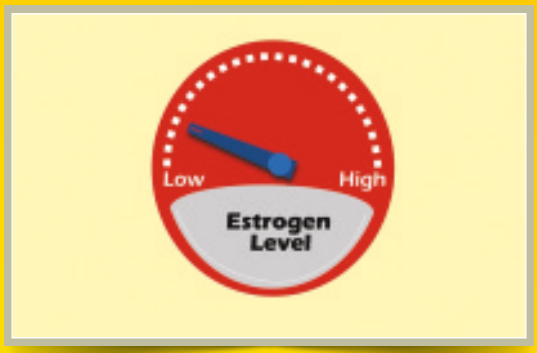
Hyperprolactinemia is associated with insulin resistance, which improves with dopamine agonist therapy, which might be related to the therapy-associated weight loss and activation of insulin signaling. Prolactin-induced hypogonadism might contribute to the metabolic alterations in hyperprolactinemia.

Effects of deficiency of pituitary hormones on glucose homeostasis

Gonadotrophin deficiency due to the mass effects of pituitary adenomas or gonadotrophin suppression due to cortisol or prolactin excess might induce insulin resistance in men and women that can be improved by hormone replacement therapy. Pathophysiological mechanisms by which testosterone deficiency might impair glucose metabolism in men include reduced insulin receptor expression and intracellular insulin signaling, reduced GLUT4 expression, and membrane translocation in skeletal muscle and liver cells, and adipose tissue. In addition, the promotion of differentiation of pluripotent stem cells into adipocytes rather than myocytes in testosterone deficiency and the resulting increase in fat mass and decrease in muscle mass might contribute to the development of insulin resistance.

Estrogen deficiency

Insulin resistance is associated with a low-grade inflammatory state, which may increase the risk of cardiometabolic diseases. Estrogens are involved in the regulation of metabolic processes related to energy balance and can influence inflammatory responses. There is an association between reduced levels of estrogen in postmenopausal women and an increased inflammatory state.



Thyroid hormone disorders

Hypothyroidism has also been associated with insulin resistance and risk of type 2 diabetes. Insulin resistance could be restored by thyroid hormone replacement. Thyroid function is associated with insulin resistance in clinically diagnosed diabetes mellitus and subjects with standard glucose tolerance. Both hyperthyroidism and hypothyroidism can affect insulin resistance, although by different mechanisms. Excess thyroid hormone can increase glucose absorption by the gastrointestinal tract, glucose production in the liver via increasing gluconeogenesis and glycogenolysis, and the concentration of free fatty acids via promoting lipolysis. Hypothyroidism results in impaired glucose absorption from the gastrointestinal tract, delayed peripheral glucose assimilation, and gluconeogenesis.

Conclusion

Disturbances of glucose metabolism are frequently found in individuals with pituitary adenomas and can be especially severe in Cushing's disease and acromegaly. Hyperglycemia and diabetes have serious consequences, increasing cardiovascular morbidity and mortality, and therefore deserve to be meticulously addressed at any stage of the disease.

Resources:

1. Schernthaner-Reiter MH, Wolf P, Vila G, Luger A. The Interaction of Insulin and Pituitary Hormone Syndromes. *Front Endocrinol (Lausanne).* 2021;12:626427. Published 2021 Apr 28. doi:10.3389/fendo.2021.626427.
2. Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005-2009. *Neuro Oncol.* 2012;14(Suppl5):v1–v49. doi:10.1093/neuonc/nos218
3. Schernthaner-Reiter MH, Wolf P, Vila G, Luger A. XI. Diagnosis and treatment of co- morbidities in pituitary tumors. 45. Metabolic disorders. In: Honegger JB, Reincke M,Petersenn S (eds). Pituitary Tumors: A Comprehensive and Interdisciplinary Approach. San Diego, CA, USA: *Academic Press* (2021). pp. 609–16.
4. Tjörnstrand A, Gunnarsson K, Evert M, *et al.* The incidence rate of pituitary adenomas in western Sweden for the period 2001–2011. *Eur J Endocrinol.* 2014;171(4):519–526. doi:10.1530/eje-14-0144
5. Espinosa-de-Los-Monteros AL, Sosa E, Martinez N, Mercado M. Persistence of Cushing's disease symptoms and comorbidities after surgical cure: a long-term, integral evaluation. *Endocr Pract.* 2013;19(2):252-258. doi:10.4158/EP12247.
6. Vila G, Joergensen JOL, Luger A, Stalla GK. Insulin resistance in patients with acromegaly. *Front Endocrinol.* 2019; 10:509. doi: 10.3389/fendo.2019.00509
7. Espinosa-de-los-Monteros AL, Gonzalez B, Vargas G, *et.al.* Clinical and Biochemical Characteristics of Acromegalic Patients with Different Abnormalities in Glucose Metabolism. *Pituitary.* (2011) 14:231-5. doi: 10.1007/s11102-010-0284-x
8. Alexopoulou O, Bex M, Kamenicky P, *et al.* Prevalence and Risk Factors of Impaired Glucose tolerance and Diabetes Mellitus at Diagnosis of Acromegaly: A Study in 148 Patients. *Pituitary.* (2014) 17:81-9. doi: 10.1007/s11102-013-0471-7
9. Giustina A, Barkan A, Beckers A, *et al.* A Consensus on the Diagnosis and Treatment of Acromegaly Comorbidities: An Update. *J Clin Endocrinol Metab.* 2020;105:e937-46. doi: 10.1210/clinem/dgz096
10. Simmons LR, Hughes K, Markovic TP, Chua EL. Diabetic Ketoacidosis as a Presenting Feature of Acromegaly: When Excess Hormone Meets Hormone Deficiency. *Clin Diabetes.* 2012;30:170-2. doi: 10.2337/diaclin.30.4.170
11. Li D., El Kawkgi O.M., Henriquez A.F., Bancos I. Cardiovascular risk and mortality in patients with active and treated hypercortisolism. *Gland Surg.* 2020;9:43–58. doi:10.21037/gs.2019.11.03.
12. Catli G, Abaci A, Tanrisever O, *et al.* An Unusual Presentation of Pediatric Cushing Disease: Diabetic Ketoacidosis. *AACE Clin Case Rep.* (2015);1:e53–8. 10.4158/EP14284.CR
13. Feelders RA, Pulgar SJ, Kempel A, Pereira AM. The Burden of Cushing's Disease: Clinical and Health-Related Quality of Life Aspects. *Eur J Endocrinol.* 2012;167:311-26. 10.1530/EJE-11-1095
14. Scaroni C, Zilio ML, Foti M, Boscaro M. Glucose Metabolism Abnormalities in Cushing Syndrome: From Molecular Basis to Clinical Management. *Endocr Rev.* 2017;38:189-219. 10.1210/er.2016-1105
15. Abildgaard, J., Tingstedt, J., Zhao, Y., Hartling, H. J., Pedersen, A. T., Lindegaard, B., & Nielsen, S. D. (2020). Increased systemic inflammation and altered distribution of T-cell subsets in postmenopausal women. *PLOS ONE*. 15(6):e0235174. https://doi.org/10.1371/journal.pone.0235174
16. Duntas LH, Orgiazzi J, Brabant G. The interface between thyroid and diabetes mellitus. *Clin Endocrinol* (Oxf). 2011;75:1-9.

Co-existence and Association of Thyroid Disorders and Diabetes

Dr. Sanjay P. Shah

MBBS, MD (Medicine)

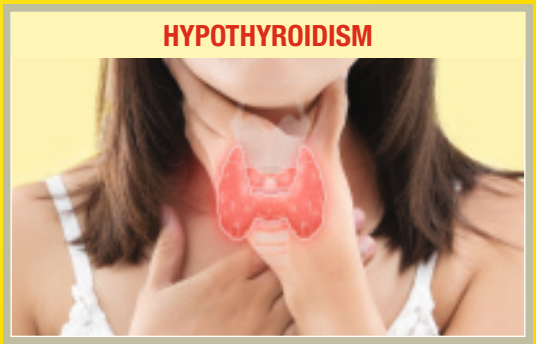
Consultant Physician, Sun-Deep Nursing Home - Physiotherapy Center, Vadodara

Thyroid disorders and diabetes are two prevalent endocrine conditions that affect millions of individuals worldwide. Although they primarily involve different glands and hormones, there exists a compelling association between these two disorders. This intricate interplay has garnered increasing attention in recent years, as researchers delve into the complex relationships and shared mechanisms that underlie the co-existence of thyroid disorders and diabetes. Thyroid hormones significantly influence glucose metabolism, and both hyperthyroidism and hypothyroidism have distinct impacts on this intricate interplay.

Pathophysiology between thyroid disorders and diabetes

In hyperthyroidism, increased insulin degradation and release of biologically inactive insulin precursors contribute to hyperglycemia. Studies show elevated proinsulin levels and impaired proinsulin processing in untreated Graves' disease. Excess thyroid hormones also enhance glucose gut absorption, and increased hepatic glucose output results from elevated GLUT2 levels and heightened lipolysis, stimulating gluconeogenesis. Moreover, hyperthyroidism leads to enhanced non-oxidative glucose disposal, promoting lactate production and impaired glucose tolerance. Individuals with diabetes and hyperthyroidism experience worsened glycemic control, with thyrotoxicosis leading to diabetic ketoacidosis.

Conversely, hypothyroidism decreases liver glucose production, reducing insulin requirements. Individuals with hypothyroidism and diabetes may present with recurrent hypoglycemia. Both clinical and subclinical hypothyroidism are recognized as insulin-resistant states due to impaired insulin-stimulated glucose utilization. Subclinical hypothyroidism is linked to metabolic syndrome and an increased risk of nephropathy in type 2 diabetes.



In diabetes, altered thyroid hormone levels are common, especially with poor glycemic control. The normal nocturnal thyroid-stimulating hormone (TSH) peak is diminished, and TSH response to thyrotropin-releasing hormone

(TRH) is impaired. Uncontrolled diabetes is associated with reduced T3 levels, known as the "low T3 state," potentially linked to impaired T4 to T3 conversion. Despite improved glycemic control, the normal TSH peak may not fully return in some cases, suggesting a diabetes-related impact on TSH control.

The coexistence and association between thyroid disorders and diabetes highlight the complexity of the endocrine system. Shared pathophysiological mechanisms contribute to the intricate interplay between these prevalent conditions. It is crucial to recognize and address the links between thyroid function and glucose metabolism for comprehensive and personalized healthcare. Ongoing research is enhancing the understanding of this relationship, empowering healthcare professionals to better manage and improve outcomes for individuals facing the dual challenges of thyroid disorders and diabetes.

Key points

- Thyroid disorders and diabetes, though involving different glands and hormones, exhibit a compelling association with intricate interplay.
- Hyperthyroidism elevates insulin degradation and releases biologically inactive insulin, leading to hyperglycemia.
- Conversely, hypothyroidism reduces liver glucose production, potentially causing recurrent hypoglycemia.
- Altered thyroid hormone levels in diabetes, especially with poor glycemic control, impact the normal function of TSH, revealing the intricate connections between these prevalent endocrine conditions.
- Managing these conditions necessitates routine screening, multidisciplinary coordination, and addressing insulin resistance.
- Recognizing and managing this association is crucial for delivering personalized healthcare and improving outcomes for individuals navigating both disorders.

Resources:

1. Kalra S, Aggarwal S, Khandelwal D. Thyroid dysfunction and type 2 diabetes mellitus: screening strategies and implications for management. *Diabetes Ther.* 2019;10(6):2035-2044. doi:10.1007/s13300-019-00700-4
2. Biondi B, Kahaly GJ, Robertson RP. Thyroid dysfunction and diabetes mellitus: Two closely associated disorders. *Endocrine Reviews.* 2019;40(3): 789-824.
3. Hage M, Zantout MS, Azar ST. Thyroid disorders and diabetes mellitus. *J Thyroid Res.* 2011;2011:439463. doi:10.4061/2011/439463

Polycystic Ovary Syndrome – A Risk Factor for Type 2 Diabetes Mellitus

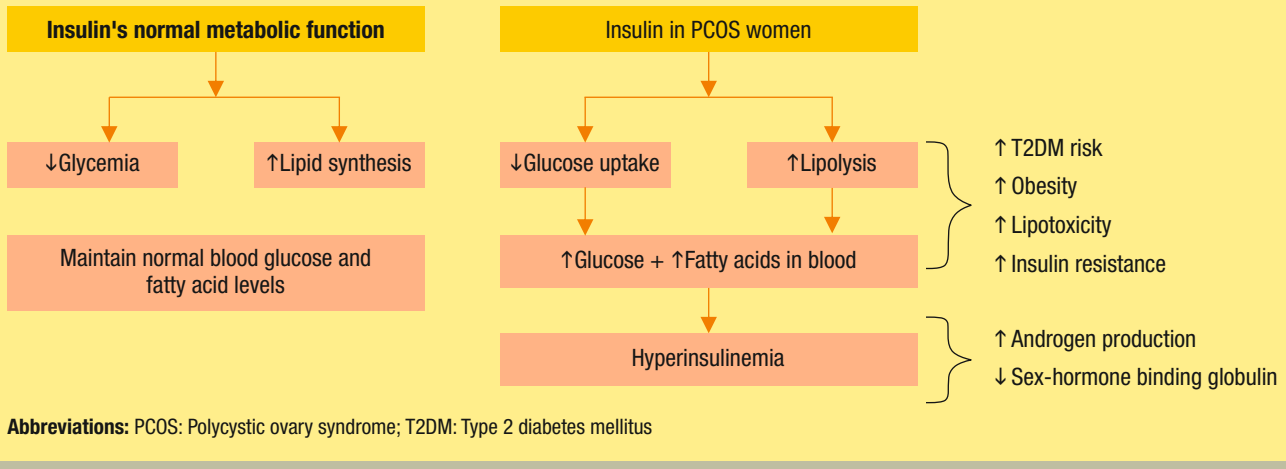
Dr. Jamil Khanji

MD (Medicine)
Consultant Physician, Sparsh Heart and Medicare Hospital, Modasa

Polycystic ovary syndrome (PCOS) is among the most common endocrine disorders observed in women of reproductive age. It is a multifaceted condition. Signs of PCOS include high androgen levels (hyperandrogenism), polycystic ovarian morphology, and ovarian dysfunction leading to menstrual irregularity. Apart from oligo- or amenorrhea and/or clinical or biochemical hyperandrogenism, impaired glucose homeostasis has also been observed in women with PCOS.

The emergence of type 2 diabetes mellitus (T2DM) in PCOS is anticipated to some extent as the two prerequisites for T2DM development-insulin resistance (IR) and β-cell dysfunction, are frequently found to be present in women with PCOS. IR and glucose homeostasis abnormalities have been described in up to 70% of women with PCOS. IR is a key player in underlying PCOS pathophysiology and an additive effect of obesity on the degree of IR further increases risk of T2DM development.

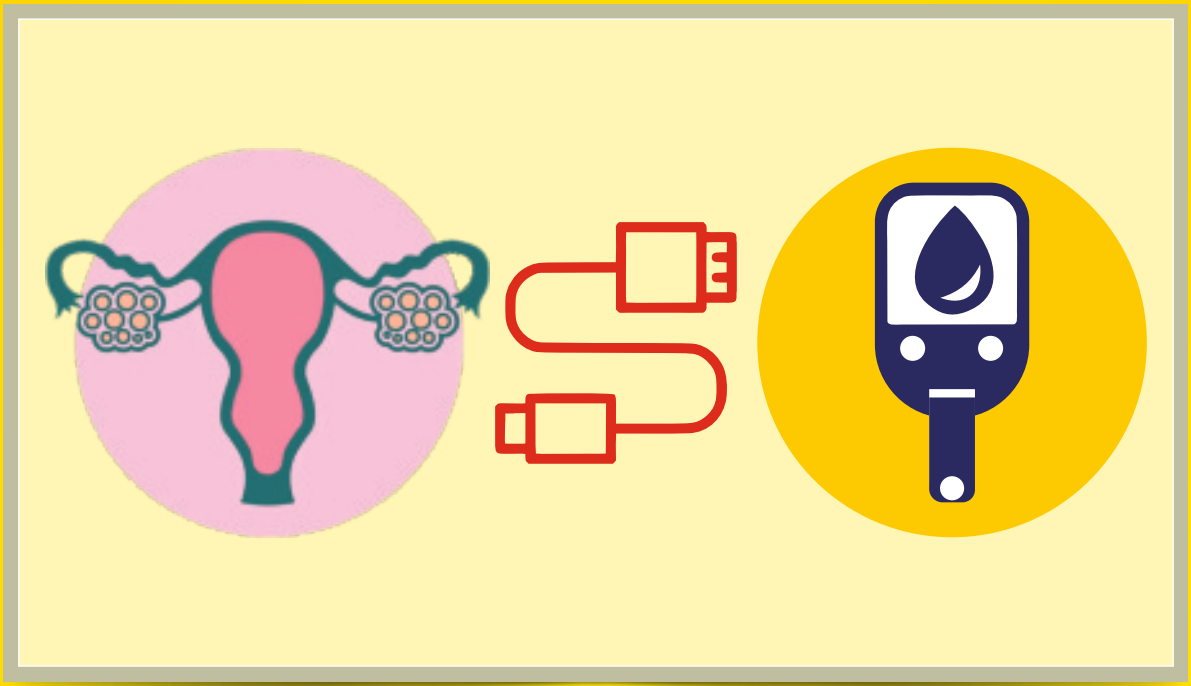
Glucose and fatty acid metabolic pathways are connected via the action of insulin. There is dysregulation of metabolic pathways in women with PCOS. In the insulin pathway, initial steps such as the high uptake of glucose and inhibition of lipolysis, are decreased, resulting in increased glucose and fatty acid levels in the circulation (as described in Fig.1).



Abbreviations: PCOS: Polycystic ovary syndrome; T2DM: Type 2 diabetes mellitus

Figure 1: Schematic representation of insulin action in PCOS

IR refers to a state of disrupted insulin binding to its receptor or ineffective activation of the latter by insulin. To maintain euglycemia, the pancreatic β-cells release more insulin into circulation also called hyperinsulinemia. This chronic state of pancreatic stress results in impaired glucose homeostasis, initially manifesting as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). However, once large numbers of pancreatic β-cells have succumbed to stress, it leads to T2DM. The prevalence of pancreatic β-cell dysfunction is found to higher in women with PCOS compared to their regularly ovulating, non-hyperandrogenic peers. Evidence from large prospective cohorts has also shown progression to either prediabetes or T2DM over time. Adequate measures including medical nutrition therapy, physically active lifestyle, weight loss must be advised, not only to manage PCOS but to reduce future risk of other metabolic disorders like T2DM.



Resources:

1. Livadas S, Anagnostis P, Bosdou JK, *et al*. Polycystic ovary syndrome and type 2 diabetes mellitus: A state-of-the-art review. *World J Diabetes*. 2022;13(1):5-26. doi:10.4239/wjd.v13.i1.5
2. Pani A, Gironi I, Di Vieste G, *et al*. From prediabetes to type 2 diabetes mellitus in women with polycystic ovary syndrome: Lifestyle and pharmacological management. *Int J Endocrinol*. 2020;2020:6276187.
3. Agrawal A 4th, Dave A, Jaiswal A. Type 2 diabetes mellitus in patients with polycystic ovary syndrome. *Cureus*. 2023;15(10):e46859. Published 2023 Oct 11. doi:10.7759/cureus.46859
4. Shabbir S, Khurram E, Moorthi VS, *et al*. The interplay between androgens and the immune response in polycystic ovary syndrome. *J Transl Med*. 2023;21(1):259. Published 2023 Apr 16. doi:10.1186/s12967-023-04116-4

Dietary Considerations for Thyroid Disorders

Dr. Sandeep Sudhakaran

MBBS, MSc (Diabetic foot surgery), C. DIAB, D. DIAB

Consultant in Diabetic Foot Surgery and Consultant Diabetologist, Medical Director at Dr Sandeep's Diabetes Speciality Centre, Thrissur

Dietary guidelines for hypothyroidism

- Iodized salt should be used.
- Cooking neutralizes goitrogens, which are found in foods like soy, peanuts, and cruciferous vegetables (broccoli, cauliflower, and cabbage). These foods can be consumed in the cooked form.

- Protein-rich foods should be included in diet, such as eggs, fish, poultry, curd, dal, and pulses.
- Foods high in selenium, such as amaranth leaves, green gram, dried peas, and brazil nuts should be included in the diet.
- Probiotic sources such as curd/yoghurt should also be included as they foster a healthy gut microflora.
- Hydration is important as it prevents fatigue, sugar cravings, and constipation.
- Take the thyroid medicine with a tall glass of water at the same time every day, on an empty stomach and keep a gap of at least 45 minutes to one hour between thyroid medication and first meal of the day. Do not take thyroid medicine with milk/coffee/tea.
- Avoid taking iron and calcium supplements in the first half of the day as they interfere with thyroid medication.

Nutrition guidelines for Graves' disease/hyperthyroidism

- Iodine supplements should be avoided.
- Include antioxidants rich foods such as blackberries, blueberries, cranberries, raspberries, tomatoes, and bell peppers.
- Increase calcium intake: Osteoporosis and other problems, such as bone loss, can result from Graves' disease. Dairy products like milk, cheese, yogurt (unsweetened) as well as fortified foods like soy milk, whole-grain cereal, etc. are good sources of calcium.

- Protein is important for muscle strength and muscle mass restoration in Graves' disease. Choose protein sources such as fish, salmon, chicken, eggs, dal, pulses, and dairy products.
- Avoid foods high in solid fats, added sugars, and refined grains such as white bread, pasta, sugar, butter, and fried dishes, as they have less nutritious value. Choose whole grains foods over processed foods.
- Steer clear of tea, coffee, chocolate, and soft drinks as they contain caffeine. Anxiety and a fast heartbeat are two symptoms that caffeine may exacerbate.

Resources:

1. Hypothyroidism: Nutrition guide for clinicians. Hypothyroidism | Nutrition Guide for Clinicians. Accessed January 19, 2024.Available at https://nutritionguide.pcrm.org/nutritionguide/view/Nutrition_Guide_for_Clinicians/1342076/all/Hypothyroidism#:~:text=Prevention%20of%20hypothyroidism%20requires%20adequate,normalize%20T3%20and%20TSH%20levels
2. Larsen D, Singh S, Brito M. Thyroid, diet, and alternative approaches. *The Journal of Clinical Endocrinology & Metabolism.* 2022;107(11):2973-2981. doi:10.1210/clinem/dgac473
3. Wiesner A, Gajewska D, Paśko P. Levothyroxine Interactions with Food and Dietary Supplements-A Systematic Review. *Pharmaceuticals (Basel).* 2021;14(3):206. Published 2021 Mar 2. doi:10.3390/ph14030206
4. Andrea Aguilar MSUE. Graves' disease and nutrition recommendations. MSU Extension. September 25, 2018. Accessed January 19, 2024. https://www.canr.msu.edu/news/graves_disease_and_nutrition_recommendations
5. Hyperthyroidism (overactive thyroid) - NIDDK. National Institute of Diabetes and Digestive and Kidney Diseases. Accessed January 19, 2024. https://www.niddk.nih.gov/health-information/endocrine-diseases/hyperthyroidism

In T2DM Uncontrolled on DPP4i + Metformin,SGLT2i + Metformin, SGLT2i + DPP4i,

Uptitrate with

UDAPA-Trio

Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin 500 mg XR

UDAPA-Trio Forte

Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin 1000 mg XR

IMPROVED iCARE STARTS WITH U

Cardio Benefits | **A**1C Control | **R**enal Benefits | **E**nsures Adherence

Abridged Prescribing Information

Indication: It is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus.
Dosage and Administration: The recommended dose is one tablet daily. Each tablet contains a fixed dose of dapagliflozin, Sitagliptin and Metformin Hydrochloride.
Adverse Reactions: Most common adverse reactions reported are: Dapagliflozin- Female genital mycotic infections, nasopharyngitis, and urinary tract infections. Sitagliptin- Upper respiratory tract infection, nasopharyngitis and headache. Metformin- Diarrhea, nausea/vomiting, flatulence, asthenia, indigestion, abdominal discomfort, and headache.
Warnings and Precautions: Dapagliflozin: Volume depletion; Ketoacidosis in Patients with Diabetes Mellitus; Urosepsis and Pyelonephritis; Hypoglycaemia; Genital Mycotic infections
Sitagliptin: General- Sitagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Acute pancreatitis: Hypoglycaemia when used in combination with other anti-hyperglycaemic medicinal product; Renal impairment; Hypersensitivity reactions including anaphylaxis, angioedema, and exfoliative skin conditions- Stevens-Johnson syndrome; Bullous pemphigoid. Metformin Hydrochloride: Lactic acidosis; In case of dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), metformin should be temporarily discontinued and contact with a healthcare professional is recommended.
Contraindications: Hypersensitivity to the active substance of Dapagliflozin, Sitagliptin & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis). Diabetic pre-coma; Severe renal failure (eGFR< 30mL/min); Acute conditions with the potential to alter renal function such as: Dehydration, Severe Infection, Shock; Acute or chronic disease which may cause tissue hypoxia such as: Cardiac or respiratory failure, Recent myocardial Infarction, Shock, Hepatic Impairment, Acute Alcohol Intoxication, alcoholism
Use in a special population: Pregnant Women: Due to lack of human data, drug should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Paediatric Patients: The safety and efficacy of drug has not yet been established. No data are available. Geriatric Patients: In Patients > 65 years, it should be used with caution as age increases.

Additional information is available on request.
Last updated: January 03, 2023

USV | Corvette

In case of any adverse events, kindly contact pv@usv.in For the use of registered medical practitioner, hospital or laboratory

In Uncontrolled Obese T2DM,

START with,

Glycomet®-GP 1 FORTE

Metformin Hydrochloride 1000 mg SR + Glimepiride 1 mg

Glycomet®-GP 2 FORTE

Metformin Hydrochloride 1000 mg SR + Glimepiride 2 mg

Glycomet®-GP 3/850

Metformin Hydrochloride 850 mg SR + Glimepiride 3 mg

January 2023[1]

ESC*
European Society of Cardiology

Long term continuous usage of High Dose Glimepiride:

Inhibits sEH → Increases EET

Greater Cardiovascular Protection

Meta analysis of 21 well established trials[2]

5% Reduction of Weight Vs Baseline Weight[2]

100% Availability

20-50%# Affordable vs other brands

Appropriate to add along with Newer AHAs

1. Glimepiride use is associated with reduced cardiovascular mortality in patients with type 2 diabetes and chronic heart failure, a prospective cohort study | European Journal of Preventive Cardiology | Oxfont Academic (oup.com) 2. Ther Adv Endocrinol Metab 2020. Vol 11:1-12 DOI: 10. 1177/2042018820926000. # Data on file * As compared to non-glimepiride group
EET: Epoxyeicosatrienoic acid; sEH: soluble Epoxide Hydrolase; AHAs: antihyperglycemic agents; T2DM: Type 2 Diabetes Mellitus

Prescribing Information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information **Composition:** Glycomet GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg.• Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg.• Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg.• Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. •Glycomet GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 1mg. • Glycomet GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP mg. **Indication:** For the management of patients with type 2 diabetes mellitus when diet, exercise and single agent (glimepiride or metformin alone) do not result in adequate glycaemic control. **Dosage and Administration:** The recommended dose is one tablet daily during breakfast or the first main meal. Each tablet contains a fixed dose of glimepiride and Metformin Hydrochloride. The highest recommended dose per day should be 8 mg of glimepiride and 2000mg of metformin. Due to prolonged release formulation, the tablet must be swallowed whole and not crushed or chewed. **Adverse Reactions:** For Glimepiride: hypoglycaemia may occur, which may sometimes be prolonged. Occasionally, gastrointestinal (GI) symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur. Hepatitis, elevation of liver enzymes, cholestasis and jaundice may occur; allergic reactions or pseudo allergic reactions may occur occasionally. For Metformin: GI symptoms such as nausea, vomiting, diarrhea, abdominal pain, and loss of appetite are common during initiation of therapy and may resolve spontaneously in most cases. Metallic taste, mild erythema, decrease in Vit B12 absorption, very rarely lactic acidosis, Hemolytic anemia, Reduction of thyrotropin level in patients with hypothyroidism, Hypomagnesemia in the context of diarrhea, Encephalopathy, Photosensitivity, hepatobiliary disorders. **Warnings and Precautions:** For Glimepiride: Patient should be advised to report promptly exceptional stress situations (e.g., trauma, surgery, febrile infections), blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary to maintain good metabolic control. Metformin Hydrochloride may lead to Lactic acidosis; in such cases metformin should be temporarily discontinued and contact with a healthcare professional is recommended. Sulfonylureas have an increased risk of hypoglycaemia. Long-term treatment with metformin may lead to peripheral neuropathy because of decrease in vitamin B12 serum levels. Monitoring of the vitamin B12 level is recommended. Overweight patients should continue their energy-restricted diet, usual laboratory tests for diabetes monitoring should be performed regularly. **Contraindications:** Hypersensitivity to the active substance of glimepiride & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis, diabetic pre-coma). Severe renal failure (GFR<30ml/min). In pregnant women. In lactating women Acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (cardiac or respiratory failure, recent myocardial infarction, shock); hepatic insufficiency; acute alcohol intoxication; alcoholism. **Use in a special population:** Pregnant Women: Due to a lack of human data, drugs should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Pediatric Patients: The safety and efficacy of drugs has not yet been established. Renal impairment: A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g. every 3-6 months.

Additional information is available on request.

Last updated: March 13, 2023

*In case of any adverse events, kindly contact: pv@usv.in

For the use of registered medical practitioner, hospital or laboratory.*

USV Private Limited Corvette Team

Anvind Vithal Gandhi Chowk, B. S. D. Marg, Govandi, Mumbai - 400 088. | Tel.: 91-22-2556 4048 | Fax: 91-22-2558 4025 | www.usvindia.com

Personalized Counseling for Individuals with Diabetes on the Importance of Insulin: A Doctor's Experience on the MyCare Patient Support Program

Dr. Amit Kumar

MBBS, PG Dip Diabetes (Cardiff, UK), PG Diabetology (Boston, USA)

Diabetes Specialist and Consultant Physician

A 38-year-old man with type 2 diabetes, on insulin was managed by Dr. Amit Kumar.

Here's what Dr. Amit Kumar has to say:

A patient with persistently high blood glucose levels was referred for consultation. During assessment it was revealed that his erratic lifestyle had adversely affected his glycemic control, despite ongoing oral antidiabetic medications. The patient had been dealing with type 2 diabetes mellitus since 2014, and had complications such as hyperlipidemia and microalbuminuria. Keeping in mind all his complications, I proposed insulin therapy. However, the patient, was reluctant and fearful about using insulin.

To alleviate his concerns, I sought the guidance of MyCare Diabetes Educator (MDE), Preeti, who played a crucial role in clarifying misconceptions. She explained the insulin administration process and counseled him on role of insulin in glycemic control and assured him of its safety. She emphasized that with a healthier lifestyle, insulin use could be temporary. Stressing the impact of lifestyle changes on blood glucose control, the MDE motivated the patient to adopt positive habits.

In just a month, the patient's fasting blood glucose levels significantly improved 292 mg/dL to 133 mg/dL and 114 mg/dL in a few months. Postprandial glucose decreased from 384 mg/dL to 209 mg/dL and further to 151 mg/dL. In six months, HbA1c went from 10.1 to 6% and triglycerides dropped from 242 mg/dL to 121 mg/dL. His UACR ratio came down from 54 mg/g to 8 mg/g.

Through lifestyle changes and routine check-ups, the patient shifted from insulin to oral medications, and well-controlled blood glucose levels in six months. This proves that personalized education, vigilant monitoring, leads to improved quality of life for those managing diabetes.

Ms. Preeti Kumar

NDEP and T1DE Certified Diabetes Educator

Here's what MDE Preeti has to say:

Continuous monitoring and follow-ups enabled the patient to achieve and maintain good diabetes control. Stress management, knowledge about insulin, proper medication, balanced meals, and regular exercise were crucial in managing his blood glucose levels.

MyCARE

With me, every step of the way

20 weeks personalised and hand-holding support for people with diabetes initiated with Insulin.
Aims to empower PWD* with information and knowledge they need to
ensure a better quality of life while managing their diabetes.

MyCARE Service available at Ahmedabad, Bangalore, Bhopal, Bhuvaneshwar, Burdwan, Chandigarh, Chennai, Cochin, Coimbatore, Delhi, Guwahati, Hubli, Hyderabad, Jaipur, Jodhpur, Kolkata, Lucknow, Ludhiana, Madurai, Meerut, Mumbai, Mysore, Nagpur, Patna, Pune, Siliguri, Surat, Thiruvananthapuram, Varanasi, Vijayawada, Visakhapatnam
*PWD: People with Diabetes

Contact for more information
Nikita Thawarkar | 7304930643 | nikita.thawarkar@usv.in

Interview with Dr. Mohan T. Shenoy

Dr. Mohan T. Shenoy

MBBS, MD, DM - Endocrinology,

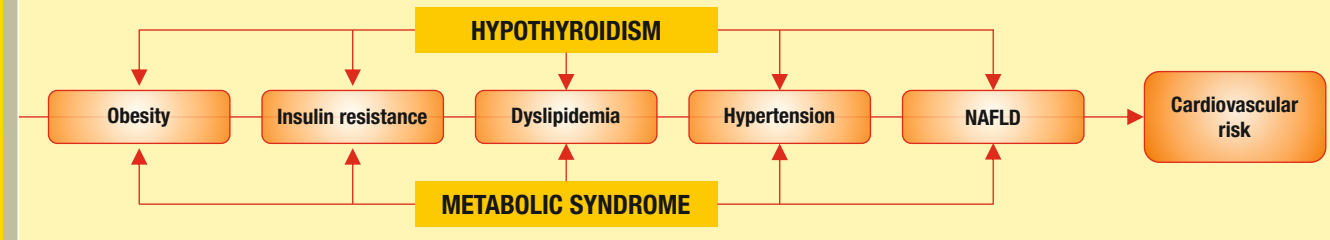
Senior Consultant Endocrinologist and Unit Chief, Department of Endocrinology, Diabetes and Metabolism, Sree Gokulam Medical College and Research Foundation, Thiruvananthapuram

Dr. Mohan T Shenoy is an Endocrinologist with over 20 years of experience. He is a Senior Consultant Endocrinologist at Sree Gokulam Medical College and Research Foundation, SK Hospital and GG Hospital in Thiruvananthapuram and a visiting consultant at KJK hospital, Nalanchira. He is known for his unwavering commitment to delivering exceptional medical care, advancing research in the field of endocrinology, and sharing his extensive expertise through education. He has published and presented in several national and international journals and conferences. Through his work Dr. Shenoy has gained valuable insights into managing complex endocrine disorders and providing specialized care. With a career marked by rigorous training, dedicated clinical practice, and a deep passion for individual well-being, he is a respected figure in the medical community.

Diabetes and Other Hormonal Disorders

1. How diabetes is interconnected with other endocrine disorders, and what commonalities or shared mechanisms exist between them?

Diabetes is recognized as a major endocrine disease worldwide and is characterized by impaired insulin secretion/variable degrees of peripheral insulin resistance (IR) leading to raised blood glucose levels or hyperglycemia. Latest understanding is that diabetes is a complex syndrome, with multiple pathophysiologic connections. Along with pancreatic hormones (insulin and glucagon), glucose homeostasis is regulated by diverse hormones such as thyroxine, glucocorticoids (GCs), growth hormone, and epinephrine. The newly proposed term - 'Glucocrinology', - understands the relationship of glycemia with the endocrine system. IR is the common pathway that links diabetes with the comorbidities – namely, hypothyroidism, obesity, dyslipidemia, hypertension, fatty liver disease, and coronary artery disease.



Abbreviations: NAFLD: Non-alcoholic fatty liver disease

Figure 1: Illustration of the complex interaction of hypothyroidism, metabolic syndrome progressing towards cardiovascular risk

2. How is diabetes insipidus (DI) different from diabetes mellitus (DM) and can they co-exist in an individual?

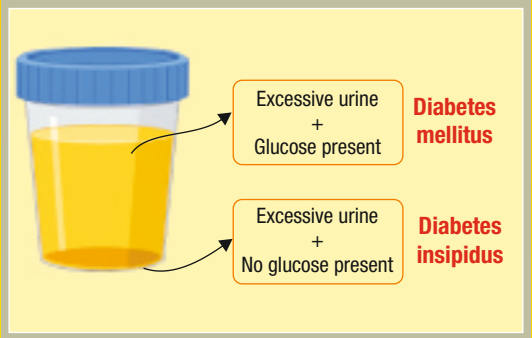


Figure 2: Diabetes mellitus vs diabetes insipidus

DM is taken from the Greek word diabetes, meaning siphon - to pass through and the Latin word mellitus meaning sweet. The hallmark of DI is large volumes of urine excretion, also known as polyuria (typically over 4 L per day). The urine of DI has been classically described as insipid (tasteless), hypotonic and dilute. Though they share the name "diabetes" with similar symptoms (increased thirst and frequent urination), DI and DM are distinct disease states with diverse causes and treatments. DM is due to mainly pancreatic or peripheral causes (insulin deficiency and IR) whereas DI is due to arginine vasopressin deficiency. The role of antidiuretic hormone (ADH) is conservation of the fluid volume of your body by reducing the amount of water passed out in the urine. The causes for DI are either central (pituitary gland-related) or nephrogenic (kidney-related).

Timely referral to endocrinologist is necessary to correct the hormonal deficiencies and prevent complications. DI is much rarer than DM. They can however coexist in some special situations. Genetic association like Wolfram syndrome also known as DIDMOAD (DI, juvenile onset DM, optic atrophy, and deafness). Another possibility is both can be coincident diseases without a common genetic pathway.

Recognition of mixed entity is essential as treatment is different. High sodium levels in DI can lead to seizures. High sugar levels in DM can result in ketoacidosis. Treatment of both is different. DM can be managed by oral hypoglycemic agents and insulin. DI can be managed with *Fluids Ad Libitum* (as per thirst) and supplementation of the hormone vasopressin analogues like *Desmopressin.*

3. Are there specific screening recommendations or protocols for individuals with diabetes to detect the presence of other endocrine disorders early on?

There are no clear guidelines on screening for other endocrinopathies in type 2 diabetes mellitus (T2DM). Thyroid dysfunction is the most common prevalent disorder associated with diabetes. Subclinical hypothyroidism was nearly double in the T2DM population compared with the general population. Individuals with both T2DM and subclinical hypothyroidism were more likely to suffer the complications of diabetes and therefore recommended screening individuals with T2DM for thyroid disorders. There is a lack of clear and consistent recommendations on the screening for thyroid disease in individuals with T2DM. The UK National Screening Committee concluded that thyroid disease screening in the general population is unwarranted as there is lack of agreement as to what is considered a normal thyroid hormone level and some individual's thyroid levels will return to normal without treatment. The British Thyroid Association recommends that individuals with T2DM should be screened for thyroid disease at diagnosis only. The American Thyroid Association recommends that adults aged ≥35 years should be screened for thyroid disorders every 5 years, regardless of whether they have diabetes or not. The National Institute for Health and Care Excellence (NICE) guidelines (2015), provides no mention of monitoring thyroid function in T2DM. Similarly, in the American Diabetes Association Standards of Medical Care in Diabetes (2024). RSSDI-ESI recommendations on T2DM (2020) mentions that patient-centered, structured diabetes self-management education (DSME) is an integral part of the care of all people with T2DM. Reduced insulin reserve and IR may be seen in secondary causes of diabetes like Cushing's syndrome and acromegaly.

These endocrinopathies carry significantly higher mortality and rate of complications as compared with individuals having type 1 diabetes mellitus (T1DM) or T2DM. These individuals with secondary diabetes are exposed to higher risk and demand intensive treatment. However, opportunistic screening is not cost-effective considering the quickly recognizable clinical features associated with these endocrinopathies.

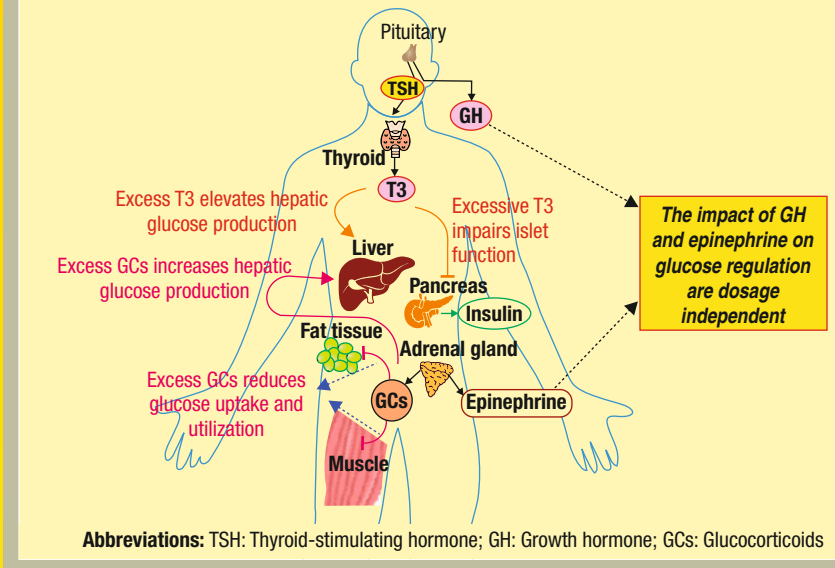


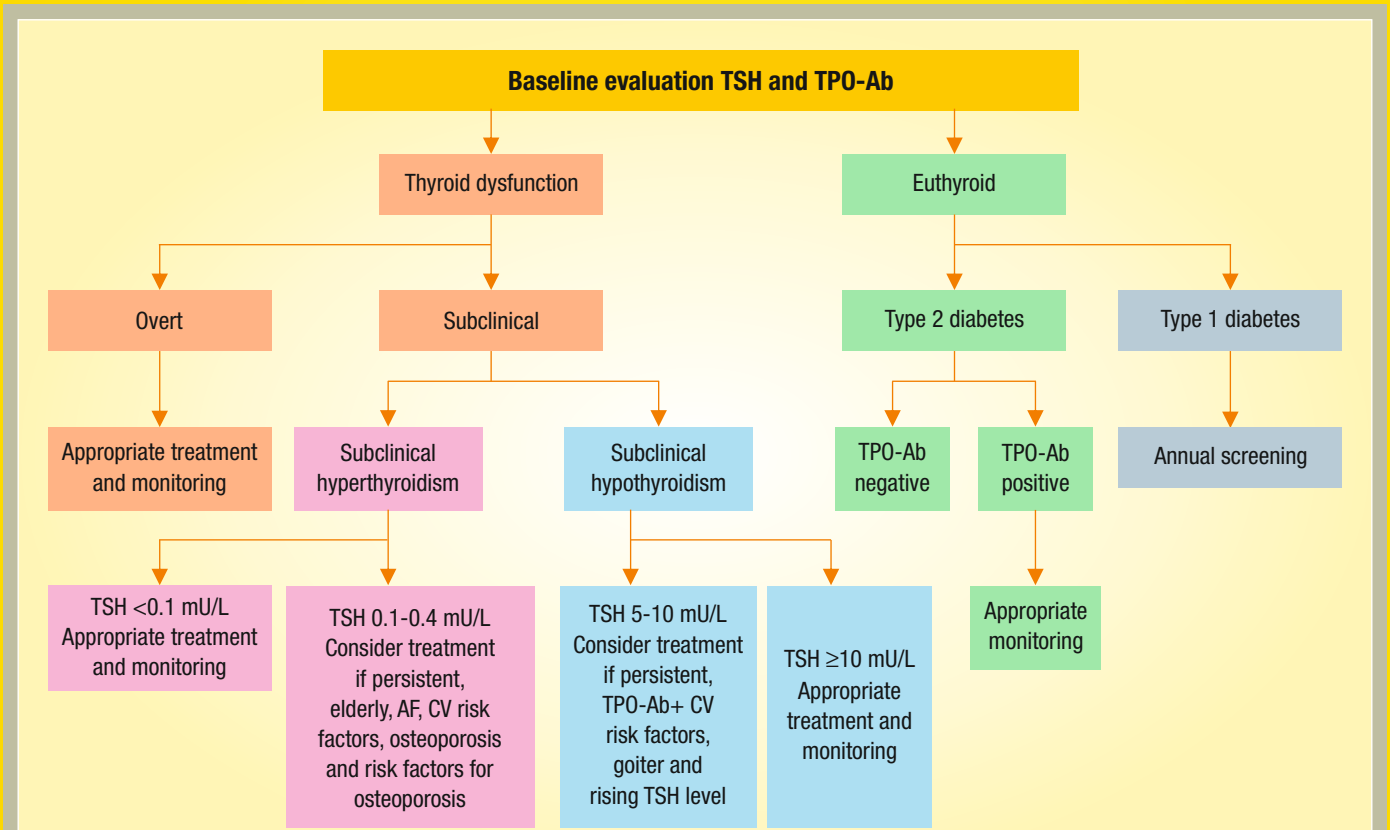
Figure 3: Glucocrinology – Complex interplay with glucose homeostasis

4. In your clinical experience, what is the percentage of women with PCOS who eventually develop T2DM?

Polycystic ovary syndrome (PCOS) is a common disorder in women of reproductive age and is seen in 6-15% of the global population. PCOS constitutes a polygenic trait. Diagnosis and management of PCOS is challenging. There are short-term issues (an ovulatory cycles and infertility) with long-term morbidity of many chronic diseases including diabetes, hypothyroidism, fatty liver disease, obesity, hypertension, and cancer. Impaired glucose homeostasis is a feature with its progression to either prediabetes or T2DM over time. IR and β-cell dysfunction, are frequently present in women with PCOS. There is an ongoing debate as to whether PCOS itself constitutes a risk factor for T2DM or whether T2DM occurs in those with obesity in PCOS. Vitamin D deficiency is frequently seen in PCOS and are associated with higher fasting glucose and insulin concentrations, as well as IR. Sleep quality, mood disorders, and higher prevalence of obstructive sleep apnea in women with PCOS contribute to diabetes. Gut microbiome dysbiosis also contribute to the higher DM in PCOS. In my experience, there is 10-15% ladies with PCOS progressing towards DM. The dictum for treatment is achievement of a significant reduction of T2DM risk by maintenance of a healthy weight.

5. Why is hypothyroidism common in people with T1DM? How often should they screen for thyroid disorders?

Thyroid hormones are crucial for maintaining a healthy metabolism and energy level. There is a complex interdependent interaction/relationship between thyroid disorders and DM. Both underactive and overactive thyroids are more common in people with diabetes than in the general population. Thyroid dysfunction could impact the glucose levels. This can be direct - as in T1DM (pancreatic β-cell destruction, usually leading to absolute insulin deficiency) or indirect mechanism in T2DM (peripheral IR). The major cause of hypothyroidism worldwide is autoimmune thyroid disease occurring in 17-30% of individuals with T1DM. Timely monitoring and recognition ensuring euthyroid state is termed glucovigilance. Screening for autoimmunity is essential at the diagnosis of both individual disorders. At the time of diagnosis, about 25% of children with T1DM have thyroid autoantibodies. Hence, their presence is predictive of thyroid dysfunction and most commonly hypothyroidism, although hyperthyroidism occurs in 0.5% of cases. Annual laboratory determinations of anti-thyroid peroxidase (anti-TPO) antibodies and dosage of TSH should be part of routine tests in the pediatric diabetic population, especially in girls, children with T1DM for more than 5 years and in individuals above 11 years of age or developing dysglycemia without other reasons. In adults with T1DM, female gender, increasing age, and the presence of glutamic acid decarboxylase antibodies (anti-GAD) have been associated with the development of thyroid autoimmunity. All individuals with T1DM should be screened for autoimmune thyroiditis since they are diagnosed with T1DM and every year after that. In case of positive thyroid antibodies, regular follow up of the thyroid function is mandatory. So is the case for screening occasionally for other autoimmune polyendocrinopathy (AP) like celiac disease.



Abbreviations: TSH: Thyroid-stimulating hormone; TPO: Thyroid peroxidase; Ab: Antibody; CV: Cardiovascular; AF: Atrial fibrillation

Figure 5: Illustration of the RSSDI guidelines (2021) on thyroid dysfunction and diabetes

Exploring the Dynamics between Diabetes and Menopause

Dr. Brijesh Singh

MBBS, MD (Medicine)
Consultant Diabetologist,
Ayush Clinic and Diagnostics, Rae Bareli

As women navigate perimenopause and menopause, hormonal fluctuations play a pivotal role in influencing health, particularly blood glucose levels. For women dealing with diabetes, this phase presents distinctive challenges, necessitating careful consideration and proactive management strategies.

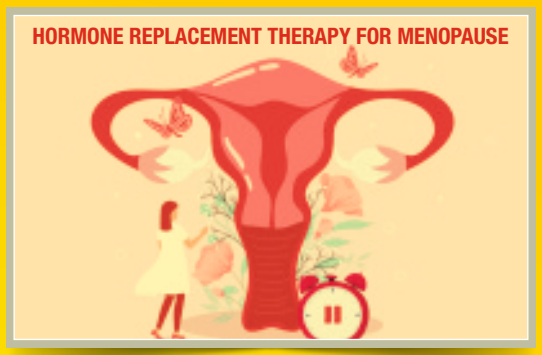
Understanding the link between diabetes and menopause

Menopause marks the permanent end of menstrual cycles due to depleted oocytes, resulting in a significant reduction in natural estrogen production and concluding the reproductive phase. In menopause, there are numerous phenotypic and metabolic shifts, impacting factors like body weight, adipose tissue distribution, energy expenditure, insulin secretion, and sensitivity. These changes may increase women's risk of type 2 diabetes mellitus (T2DM).

Managing blood glucose levels and hormonal impact

In perimenopause, declining estrogen reduces insulin responsiveness, causing sudden blood glucose fluctuations. For women with diabetes, frequent monitoring of blood glucose levels is crucial, as sometimes symptoms like hot flashes can mimic hypoglycemia.

Hormone replacement therapy (HRT)



Doctors may discuss HRT as a potential treatment option. While not universally applicable, research indicates potential benefits, especially for managing menopausal symptoms in women with diabetes. Tailoring treatment adjustments, including the use of medications like metformin, proves instrumental in effectively managing insulin resistance.

Balanced lifestyle choices during menopause

Maintaining a holistic lifestyle becomes pivotal for managing diabetes during perimenopause and menopause. Regular exercise not only aids in blood glucose management but also contributes to overall well-being, supporting essential aspects such as bone strength. Nutrition plays a key role, adopting a diet rich in fruits, vegetables, and whole grains, along with adequate vitamin D and calcium, proves beneficial.

In conclusion, navigating through menopause and diabetes demands a comprehensive strategy. Through active collaboration with healthcare teams, open communication, hormone replacement treatments, and healthy lifestyle choices, women can effectively manage diabetes during the transformative phases of perimenopause and menopause.

Key points

- **Diabetes link:** Menopausal shifts may increase the risk of T2DM.
- **Hormonal influence:** Menopause brings hormonal fluctuations impacting blood glucose levels. Declining estrogen reduces insulin responsiveness, demanding vigilant monitoring for women with diabetes.
- **Treatment:** HRT and tailored medication use, like metformin, play a crucial role.
- **Holistic lifestyle:** Exercise and a nutrient-rich diet support overall well-being and bone strength during menopause and help in maintaining good glycemic control.

Resources:

1. Paschou SA, Papanas N. Type 2 diabetes mellitus and menopausal hormone therapy: An Update. *Diabetes Ther.* 2019;10(6):2313-2320. doi:10.1007/s13300-019-00695-y
2. ADA. Diabetes and early menopause. Available at https://www2.diabetes.org/healthy-living/sexual-health/early-menopause-diabetes
3. BridgetChapple. Menopause and diabetes. *Diabetes UK*. Available at https://www.diabetes.org.uk/guide-to-diabetes/life-with-diabetes/menopause

Endocrine Disorders that Cause Diabetes

Dr. Rony T. Vempeny

MBBS, MD, DNB (General Medicine)

Consultant Physician and Diabetologist,
Vempeny Clinic, Kottayam

Endocrine disorders may be linked to glucose intolerance or diabetes mellitus. Disrupted glycemic balance can result directly or indirectly from the overproduction of hormones. Conditions like acromegaly Cushing's syndrome, pheochromocytoma, hyperthyroidism, hyperaldosteronism, glucagonoma, and somatostatinoma contribute to hyperglycemia, elevating glucose production and inducing insulin resistance. These disorders primarily involve the excessive secretion of "counter-regulatory" hormones, whose metabolic actions antagonize insulin by inhibiting its secretion, action, or both.

Endocrine disorders leading to diabetes

Conditions	Mechanisms
Acromegaly results from the abnormal overproduction of growth hormone (GH), manifesting as a clinical syndrome.	Excess GH in acromegaly leads to insulin resistance through direct and indirect mechanisms. GH directly induces gluconeogenesis, glycogenolysis, and lipolysis, promoting insulin resistance in the liver and peripheral tissues. Indirectly, GH acts through IGF-1 to facilitate insulin action. The lipolytic effect of GH, resulting in increased free fatty acid synthesis, inhibits insulin-mediated glucose uptake in adipose tissue by suppressing glucose transporters. There is increased insulin resistance with increased pancreatic insulin secretion, but over time, as pancreatic secretory capacity decreases, this may progress to prediabetes and diabetes.
Cushing's syndrome is defined by a prolonged overproduction of glucocorticoids.	Excessive glucocorticoids exert multifaceted effects on glucose homeostasis. In the liver, they enhance gluconeogenesis and lipolysis while inhibiting glycogen formation, elevating glucose levels. Skeletal muscles experience insulin resistance due to cortisol interference with insulin signalling, leading to compromised glycogen synthesis and reduced glucose uptake. This hormonal imbalance results in central adiposity, exacerbating insulin resistance and metabolic syndrome. Furthermore, glucocorticoids impact adipose tissue by influencing adipokine release, contributing to insulin resistance. In the pancreas, they inhibit insulin synthesis and secretion, potentially leading to β-cell dysfunction and diabetes.
Pheochromocytoma is an uncommon tumor originating from the chromaffin cells of the adrenal medulla that secretes catecholamines.	Elevated levels of catecholamines lead to the inhibition of insulin secretion from the pancreas, primarily through the activation of α-adrenergic receptors, while simultaneously inducing insulin resistance in peripheral tissues by engaging β-adrenergic receptors. In muscles, catecholamines hinder glucose uptake and utilization. Additionally, at the hepatic level, heightened catecholamine levels promote glucose production by enhancing glycogenolysis and gluconeogenesis processes.
Graves' disease, a thyroid disorder, is acknowledged as the primary cause of hyperthyroidism.	Excessive thyroid hormones contribute to diabetes by impacting insulin secretion and increasing peripheral insulin resistance. Hyperthyroidism is associated with elevated postprandial plasma insulin and proinsulin levels, along with increased apoptosis of pancreatic β-cells. The reduced half-life of insulin is likely attributed to accelerated degradation and high release of biologically inactive insulin precursors. In untreated Graves' disease, there's an elevation in proinsulin levels following food intake.

Conditions	Mechanisms
Primary aldosteronism is marked by an excessive release of aldosterone in the presence of low plasma renin levels.	Studies reveal elevated aldosterone secretion in individuals with obesity. As obesity is a key risk factor for type 2 diabetes, hyperaldosteronism in obese individuals can affect glucose tolerance, affecting both insulin secretion and insulin sensitivity.
Somatostatinomas are tumors that produce somatostatin, are rare neuroendocrine tumors.	Somatostatin, secreted by pancreatic delta cells and in the gastrointestinal tract, inhibits insulin and glucagon release. Elevated somatostatin levels from somatostatinomas can lead to hyperglycemia, progressing from glucose intolerance to diabetes due to inhibited insulin secretion. Additionally, somatostatin's inhibition of glucagon and other blood glucose-elevating hormones may contribute to a potential hypoglycemic effect. These tumors disrupt the delicate balance of insulin and glucagon, playing a significant role in glucose metabolism abnormalities. The intricate interplay between somatostatin and hormones underscores the complexity of effects associated with somatostatinomas.
Glucagonoma is an uncommon neuroendocrine tumor characterized by hypersecretion of glucagon.	The development of diabetes is a consequence of the direct impact of glucagon. Through the stimulation of gluconeogenesis and glycogenolysis, glucagon elevates blood glucose levels and is also involved in amino acid metabolism. The insulin resistance leading to diabetes is a consequence of prolonged exposure to heightened blood glucagon levels.

Conclusion

Diabetes mellitus resulting from endocrine disorders typically presents with mild signs and symptoms, featuring hyperglycemia that is often reversible with treatment of the underlying condition. The significance of screening for diabetes in endocrine disorders stems from its association with an elevated risk of cardiovascular mortality, emphasizing the potential for improved individual quality of life through early detection.

Key points

- Certain endocrine disorders may be linked to glucose intolerance or diabetes mellitus.
- Disrupted glycemic balance may result directly or indirectly from the overproduction of hormones.
- These include conditions like acromegaly, Cushing's syndrome, pheochromocytoma, hyperthyroidism, hyperaldosteronism, glucagonoma, and somatostatinoma.
- Management of dysglycemia is essential to improve prognosis, reduce cardiovascular mortality, and improving quality of life.

Resources:

1. Jennings RE, Hanley NA. Endocrine disorders that cause diabetes. *Textbook of Diabetes.* Published online 2017:272-290. doi:10.1002/9781118924853.ch20
2. Popoviciu MS, Paduraru L, Nutas RM, *et al.* Diabetes Mellitus Secondary to Endocrine Diseases: An Update of Diagnostic and Treatment Particularities. *Int J Mol Sci.* 2023;24(16):12676. Published 2023 Aug 11. doi:10.3390/ijms241612676

Association of Leptin, Obesity, and Diabetes

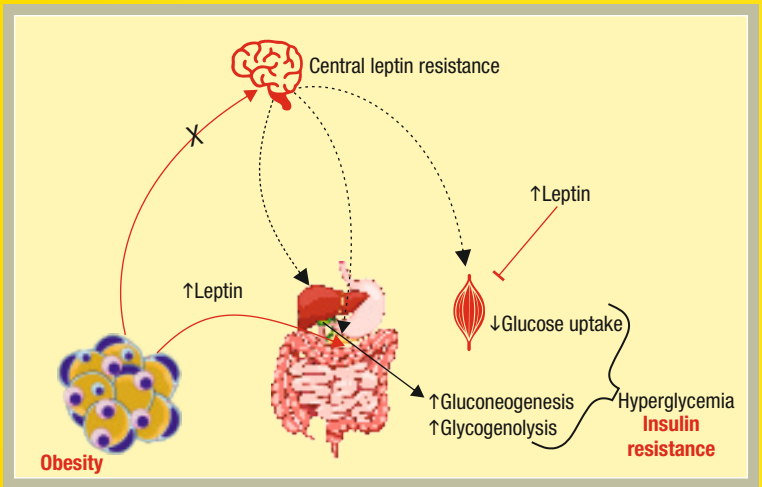
Dr. Rajeev Verma

MD (Medicine)

Assistant Professor, Dept. of General Medicine, AIIMS, Rae Bareli

Leptin is a peptide hormone that regulates food intake, body mass, and other functions (reproductive, fetal growth, proinflammatory immune responses, angiogenesis, and lipolysis). It is released by small intestine cells and adipose tissues to regulate energy balance and inhibit hunger. Due to its mode of action, leptin is thought to play some role in the development of obesity and insulin resistance. Obesity is a complex phenomenon in which there is accumulation of excess amounts of fat. In his review article, Izquierdo AG *et al.*, proposed that obese people have increased serum levels of leptin as explained by leptin resistance in such individuals. Leptin resistance is identified by reduced satiety, over-consumption of nutrients, and increased total body mass and leads to failure of hunger suppression, increased food intake, which eventually leads to obesity. In leptin resistance, insulin resistance develops, which is followed by increase of triglycerides and fat ascites in organs and blood. Thus, obese individuals are also at high risk to develop insulin resistance and have high cholesterol levels, which can lead to development of several chronic illnesses.

Link between leptin, obesity, and diabetes



Source: Freitas Lima LC *et al.* (2015). *Front Physiol.* 2015;6:304.

Obesity, leptin resistance, and insulin resistance are interrelated. According to studies, hyperinsulinemia may eventually develop metabolic syndrome as a result of obesity and leptin resistance in such individuals. Positive correlation between obesity and insulin resistance has been well established. However, they also share another common characteristic in the form of hyperleptinemia. Research has shown that obesity results in elevated amounts of leptin, which acts as a pro-inflammatory cytokine and speeds up the process of insulin resistance.

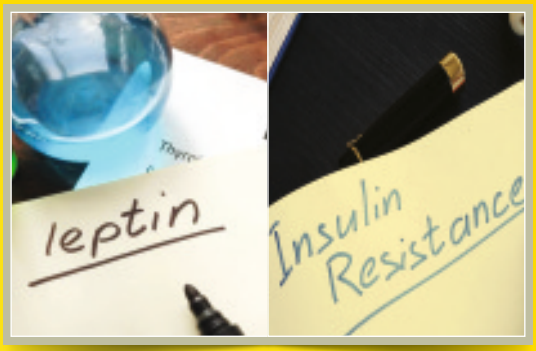
Although the link between type 2 diabetes and leptin has been investigated in many ways, it is still not fully clarified. One of the research reveals that leptin levels are elevated in obese and individuals without diabetes

and are significantly lower in individuals with type 2 diabetes, but other studies have shown that plasma leptin levels in individuals with type 2 diabetes are the same as those without diabetes and have the same body mass index (BMI), and leptin level is associated with BMI. While in obese individuals, serum leptin concentration is positively correlated with BMI and body fat ratio, which are indicators of obesity, numerous studies have shown that there is a positive association between serum fasting leptin and insulin levels and insulin resistance in obese individuals.

Leptin as an important marker

Leptin also plays a role in inflammation. Serum leptin levels are shown to be significantly higher in obese individuals than in normal individuals. Uslu *et al.* also proposed the application of leptin and adiponectin ratio as a cardiovascular disease (CVD) risk factor in individuals with type 2 diabetes.

Leptin is an important marker and may contribute to insulin resistance, obesity, inflammation, type 2 diabetes, and CVD. It's important that people at high risk have their leptin levels monitored periodically and that the proper measures be taken to lower their levels.



Key points

- The hormone leptin, which reduces appetite is the key feature of obesity, although no successful obesity therapy based on this hormone has been developed to date.
- Obesity, leptin resistance and insulin resistance are interrelated. Numerous research is being conducted to determine the role of leptin in obesity and insulin resistance as well as its efficacy in managing obesity.
- Leptin also plays a role in inflammation and is an important marker that may contribute to insulin resistance, obesity, inflammation, type 2 diabetes, and CVD.

Resources:

1. Kumar R, Mal K, Razaq MK, *et al.* Association of leptin with obesity and insulin resistance. *Cureus.* 2020;12(12):e12178. Published 2020 Dec 19. doi:10.7759/cureus.12178
2. Obradovic M, Sudar-Milovanovic E, Soskic S, *et al.* Leptin and Obesity: Role and Clinical Implication. *Front Endocrinol (Lausanne).* 2021;12:585887. Published 2021 May 18. doi:10.3389/fendo.2021.585887
3. Sarı, A., Sadeq, M.B. The relationship between the leptin hormone, obesity and diabetes, physical sciences (NWSAPS). *E-journal of New World Sciences Academy.* 2020; 15(2):40-48, doi: 10.12739/NWSA.2020.15.2.3A0095.
4. Izquierdo AG, Crujeiras AB, Casanueva FF, *et al.* Leptin, obesity, and leptin resistance: where are we 25 years later?. *Nutrients.* 2019;8:2704.
5. Uslu S, Kebapçi N, Kara M, Bal C. Relationship between adipocytokines and cardiovascular risk factors in patients with type 2 diabetes mellitus. *Exp Ther Med.* 2012;4(1):113-120. doi:10.3892/etm.2012.557

Diabetes and Gonadal Disorders

Dr. Dharmadev Ruparel

MBBS, MD (Medicine), PG Dip (Diabetology), FRCP (Cardiff/London)

Consultant Physician and Diabetologist, Sujit Hospital Diabetes and Thyroid Care Center, Bhavnagar

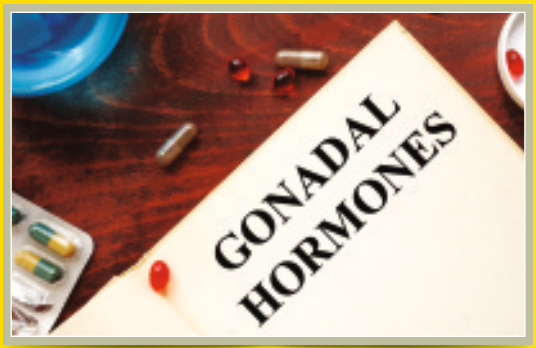
Diabetes and gonadal functions are known to have mutual influence on each other. Hypogonadism (low gonadotropin hormone levels) is a risk factor for onset of diabetes, while diabetes is also a risk factor for the development of hypogonadism.

Effect of diabetes on the hypothalamic-pituitary-gonadal axis

Effect on the hypothalamic-pituitary secretion of hormones

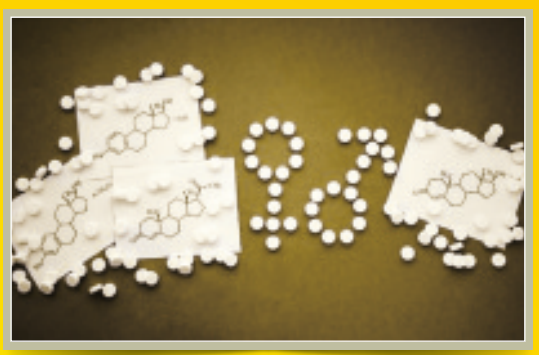
Studies have found the development of hypogonadism to be less frequent in type 1 diabetes as compared to type 2 diabetes. Hypogonadism with low gonadotropic hormone was found to be present in more than 1/3 of the male individuals with type 2 diabetes in a study. It also reported low gonadal function to be associated with low gonadotropic hormone, suggesting that hypogonadism occurs at the hypothalamic-pituitary level. This could be related to the effect of insulin on promoting gonadotropin-releasing hormone (GnRH) secretion and regulating the hypothalamus to inhibit appetite. Insulin resistance and inflammation mediators in type 2 diabetes may also inhibit the hypothalamic secretion of GnRH.

Effect on the gonadal secretion of hormones



The clinical investigations have shown that females with type 1 diabetes have ovarian dysfunction, characterized by menstruation irregularities, delay of menarche age, higher risk of miscarriage and foetal death and adult females with type 1 diabetes are at a higher risk for hyperandrogenism and polycystic ovarian syndrome (PCOS). On the other hand, some studies have shown contradictory results, suggesting that the effect of type 1 diabetes on sex hormones is still unclear. These endocrine abnormalities can be associated with non-physiologic insulin replacement therapy and hyperglycemia and can also vary with the age of the individual.

Effect of sex hormone on onset risk of diabetes



Studies focusing on the role of sex hormones with the onset of diabetes have found androgen to exhibit a protective role in males. The onset risk of type 2 diabetes was found to be reduced by 42% in males with higher testosterone, however, increased risk for type 2 diabetes was reported with increased testosterone in females. Estrogen has been believed to have protective effects in women with the onset risk of diabetes to be increased with reduced estrogen levels.

Clinical studies showed lower incidence of diabetes in females than in males, while the incidence increased significantly after menopause, and the insulin release was only 50% of the premenopausal levels. This could be due to the protective effect of estrogen on B cells. Nevertheless, if estrogen was decreased and androgen was increased in females, then the incidence of diabetes would also increase. A meta-analysis of cross-sectional studies and other prospective studies on diabetes and estrogen, found that estrogen was instead higher in males with type 2 diabetes and post-menopausal females, and it was presumed that this may be related to the fact that the estrogen in males and post-menopausal females was mainly from increased adipose tissues. Another hormone, sex hormone-binding globulin (SHBG) has also been studied in relation to diabetes. SHBG was found to be negatively correlated with the onset risk of type 2 diabetes. Further studies on the clinical application, its plasma level in stratification and intervention of type 2 diabetes are warranted.

Thus, diabetes and gonadal disorders have a bidirectional relationship. Clinically, personalized treatment with considerations to both gonadal disorders and abnormal glucose levels is advised.

Resources:

1. Codner E. The gonadal effects of diabetes. *Int J Pediatr Endocrinol.* 2013;2013(Suppl 1):09. doi:10.1186/1687-9856-2013-S1-09
2. Chen M, Dou J. Diabetes and gonadal disorders. *J Transl Intern Med* 2014;2:119-23.

Frequently Asked Questions

Dr. Sarthak Gandhi

MBBS, FCCCM, D. Diabetes, D. Endocrine (UK)

Consultant Diabetologist and Endocrinologist, Gandhi Diabetic Care Clinic, Surat

1. I am a 34-year-old female. I was diagnosed with type 2 diabetes and hypothyroidism. I am on medication for both. I always take my medicines daily together and never skip a dose, but my thyroid-stimulating hormone (TSH) levels are still elevated. Why is that so?

Ans. If you are taking thyroid medication for hypothyroidism, the timing is crucial for effective absorption. It is generally recommended to take the thyroid medication on an empty stomach, 30-60 minutes before any food intake. Afterward, you can have breakfast, including coffee or milk.

You must also be cautious about potential interactions with certain medications and supplements. To avoid interference with absorption, take fiber supplements, calcium, and iron supplements and multivitamins with minerals 3-4 hours after taking thyroid medication. Always consult your healthcare provider to determine the best timing based on your individual health needs and medications.

2. I am a 51-year-old woman with type 2 diabetes entering menopause. Despite not having significantly low calcium levels, my healthcare provider recommended calcium supplements. Can you explain the specific reasons behind this recommendation in the context of menopause and diabetes?

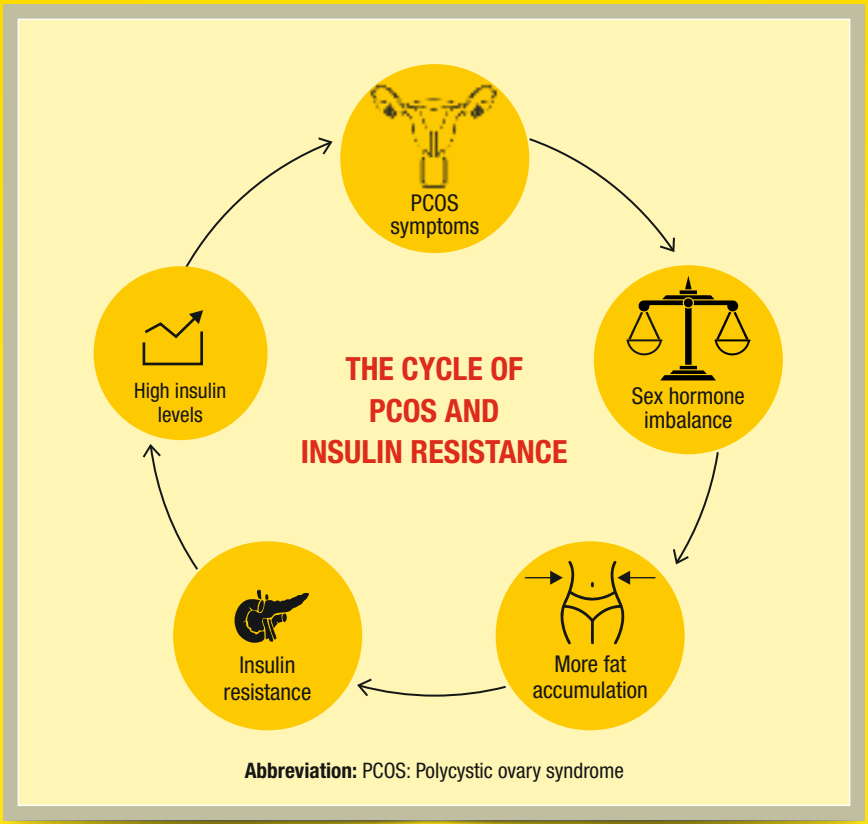
Ans. Calcium, a vital mineral, serves various functions such as maintaining bone and teeth health and regulating muscle contractions. Its significance becomes pronounced during menopause, primarily for bone health. Aging leads to decreased bone density especially in women, elevating the risk of osteoporosis, particularly pronounced in menopausal women. The decline in estrogen during menopause accelerates bone resorption, outpacing bone formation and contributing to risk of osteoporosis.

Calcium extends benefits beyond bone health, potentially alleviating stress in menopausal women with mood swings or sleep difficulties. Adequate intake is linked to positive effects on hypertension, colorectal cancer, obesity, and kidney stones in menopausal women, indicating its broader impact on multiple body systems beyond the skeletal system.

3. I am a 22-year-old female; I am overweight with a BMI of 28kg/m^2. I have been diagnosed with polycystic ovary syndrome (PCOS) 3 years ago. My weight has been increasing in the past 3 years and was advised a blood test by my doctor, in which my HbA1c levels were on borderline for prediabetes. My doctor says that if I don't get my weight under control, I might be at risk of diabetes. How is that possible, I don't even have a family history of diabetes?

Ans. Women with PCOS have a higher risk of diabetes due to a complex interplay between hormonal imbalances and insulin resistance. Increased levels of insulin, triggered by elevated hormones like testosterone, lead to insulin resistance and hyperinsulinemia. This bidirectional relationship between PCOS and prediabetes creates a vicious cycle.

High insulin levels stimulate the ovaries to produce more androgens, contributing to symptoms like irregular menstrual cycles, excess hair growth, and weight gain. Additionally, insulin's effect on appetite and fat metabolism can contribute to weight gain, further heightening the risk of diabetes in women with PCOS.



Abbreviation: PCOS: Polycystic ovary syndrome

Superfood: Brazil Nuts

Native of South America, Brazil Nuts are found growing in amazon region. They are considered a super food due to their impressive micronutrient profile. The nuts are rich in nutrients, with 17% protein and 60-70% oil.

Health benefits

Selenium rich: One of the best natural sources of selenium that has been studied as a potential substitute for selenium supplements. Selenium helps in healthy thyroid functioning and therefore these nuts are good for people having thyroid dysfunction as well.

Nutrient dense: Brazil nuts are not only a good source of fiber and protein but also contain some important nutrients like phosphorus, magnesium, selenium (Se), thiamine, vitamin E, vitamin B_6, calcium, iron, potassium, zinc, and copper.

Antioxidant and anti-proliferative: Brazil nuts have been shown to possess antioxidant and anti-proliferative properties; these properties are mostly attributed to the presence of phenolic and flavonoids present in them.

Better glycemic control: Brazil nuts contains compounds that offer better glycemic control, help in weight management and vascular function.

Brazil nuts are calorie dense, source of proteins, low in carbohydrate with a wide variety of health benefits including better glycemic control, hence can be consumed by people with diabetes in moderation.

Resources:

1. Yang J. Brazil nuts and associated health benefits: A Review. *LWT - Food Science and Technology*. 2009;42(10):1573-80.
2. Cardoso BR, Duarte GBS, Reis BZ, Cozzolino SMF. Brazil nuts: Nutritional composition, health benefits and safety aspects. *Food Res Int.* 2017;100 (Pt 2):9-18. doi:10.1016/j.foodres.2017.08.036
3. Kim Y, Keogh JB, Clifton PM. Benefits of nut consumption on insulin resistance and cardiovascular risk factors: Multiple potential mechanisms of actions. *Nutrients*. 2017;9(11):1271. Published 2017 Nov 22. doi:10.3390/nu9111271

Match the column

A. Column	B. Column
1. Pancreas	A. Estrogen
2. Adipose tissue	B. Thyroxine
3. Thyroid gland	C. Insulin
4. Ovaries	D. Growth hormone
5. Acromegaly	E. Leptin

Answer: 1.C, 2.E, 3.B, 4.A, 5.D

NOTES

NOTES

NOTES

In Newly Diagnosed & Young T2DM,

Start Early with

Glycomet®-GP 0.5

Metformin Hydrochloride 500 mg SR + Glimepiride 0.5 mg

Glycomet®-GP 0.5 FORTE

Metformin Hydrochloride 1000 mg SR + Glimepiride 0.5 mg

Recent Glycomet®-GP Real World SWITCH STUDY 2023' Patients[1]

94% of **T2DM patients Switched** from DPP4i with or without Metformin combination to Low Dose Glimepiride + Metformin

Resulted in

significant **HbA1c reduction** of **1.65%**

Global Innovator with 100% Accessibility

Lesser Risk of Hypoglycemia

Lower Risk of Weight Gain[2]

T2DM: Type 2 Diabetes Mellitus; **HbA1c**: Hemoglobin A1c.

1. SWITCH STUDY (*Data on file*). 2. Diabetes Obes Metab 2017; 19:1180-1192; Endocrine Journal 2014; 61 (12), 1163-1170.

Information

Metformin hydrochloride (as prolonged release) and glimepiride tablets.

Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte.

Abridged Prescribing Information

Composition: • Glycomet GP 0.5 mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 0.5 mg. • Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 0.5 mg. • Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg. • Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. • Glycomet SP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 1 mg. • Glycomet SP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 2 mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 3 mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP mg. **Indications:** Glycomet GP is indicated for the management of patients with type 2 diabetes mellitus (T2DM) when diet, exercise and single agent (metformin hydrochloride or glimepiride alone) do not result in adequate glycemic control. **Dosage and Administration:** Dosage of Glycomet GP should be individualized on the basis of effectiveness and tolerability while not exceeding the maximum recommended daily dose of glimepiride 8mg and metformin 2000 mg. Initial dose: 1 tablet of Glycomet GP should be administered once daily during breakfast or with the first main meal. Do not crush or chew the tablet. In several cases the tablet may remain intact during transit through the gastrointestinal (GI) tract and will be eliminated in feces as hydrated matrix (ghost matrix). Patients should be advised that this is normal as all drug components have already been released during GI transit. **Contraindications:** In patients hypersensitive to glimepiride, other sulfonylureas, other sulfonamides, metformin or any of the excipients of Glycomet GP, pregnancy and lactation; diabetic ketoacidosis, diabetic pre-coma, in patients with eGFR<30 ml/min/ 1.73 m², acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents), acute or chronic disease which may cause tissue hypoxia (myocardial infarction, shock, cardiac/respiratory failure), hepatic insufficiency, acute alcohol intoxication, alcoholism. **Warnings:** Keep out of reach of children. Patient should be advised to report promptly exceptional stress situations (e.g. trauma, surgery, febrile infections). Blood glucose regulation may deteriorate and a temporary change to insulin may be necessary to maintain good metabolic control. In case of lactic acidosis, patient should be hospitalized immediately. **Precautions:** In the initial weeks of treatment, the risk of hypoglycemia may be increased and necessitates especially careful monitoring. Serum creatinine level should be determined before initiating treatment and regularly thereafter, at least annually in patients with normal renal function. Intravascular contrast studies with iodinated materials can lead to acute alteration of renal function. In patients in whom such study is planned, Glycomet GP should be temporarily discontinued at the time of or prior to the procedure, and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal. Use of Glycomet GP should be discontinued 48 hours before any surgical procedure. **Adverse reactions:** For glimepiride – hypoglycaemia; temporary visual impairment; GI symptoms like nausea, vomiting, abdominal pain, diarrhoea may occur; increased liver enzymes; cholestasis and jaundice may occur; allergic reactions may occur occasionally. For metformin – GI symptoms like nausea, vomiting, abdominal pain or discomfort may occur.

In case of any adverse events, kindly contact: pv@usv.in
For the use of registered medical practitioner, hospital or laboratory.

USV Private Limited

Ambedkar Vithal Gandhi Chowk, B. S. D. Marg, Govandi, Mumbai - 400 088. | Tel.: 91-22-2556 4048 | Fax: 91-22-2556 4025 | www.usvindia.com

Beat Diabetes
Win Life

For screening people with High & Moderate Risk of Diabetes

Indian Diabetes Risk Score

Share this simple test with your family & Friends

Users can share it with their family & friends

Video on Suggestive Lifestyle Interventions to minimise risks - for each category

12 Languages

An awareness initiative by USV

USV

is making

Indian Diabetes Risk Score

Accessible to Every INDIAN

For Screening people with High & Moderate Risk of Diabetes

TO KNOW YOUR RISK OF DIABETES SCAN HERE

Beat Diabetes Win Life

USV

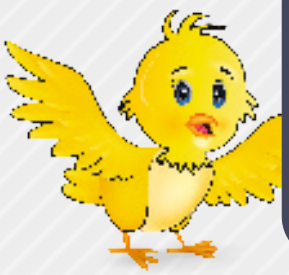
is making

Indian Diabetes Risk Score

Accessible to Every INDIAN

For Screening people with High & Moderate Risk of Diabetes

TO KNOW YOUR RISK OF DIABETES SCAN HERE



Beat Diabetes Win Life

USV

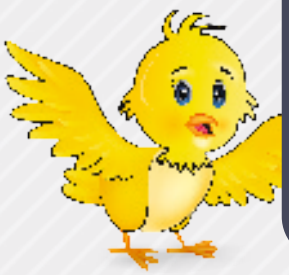
is making

Indian Diabetes Risk Score

Accessible to Every INDIAN

For Screening people with High & Moderate Risk of Diabetes

TO KNOW YOUR RISK OF DIABETES SCAN HERE

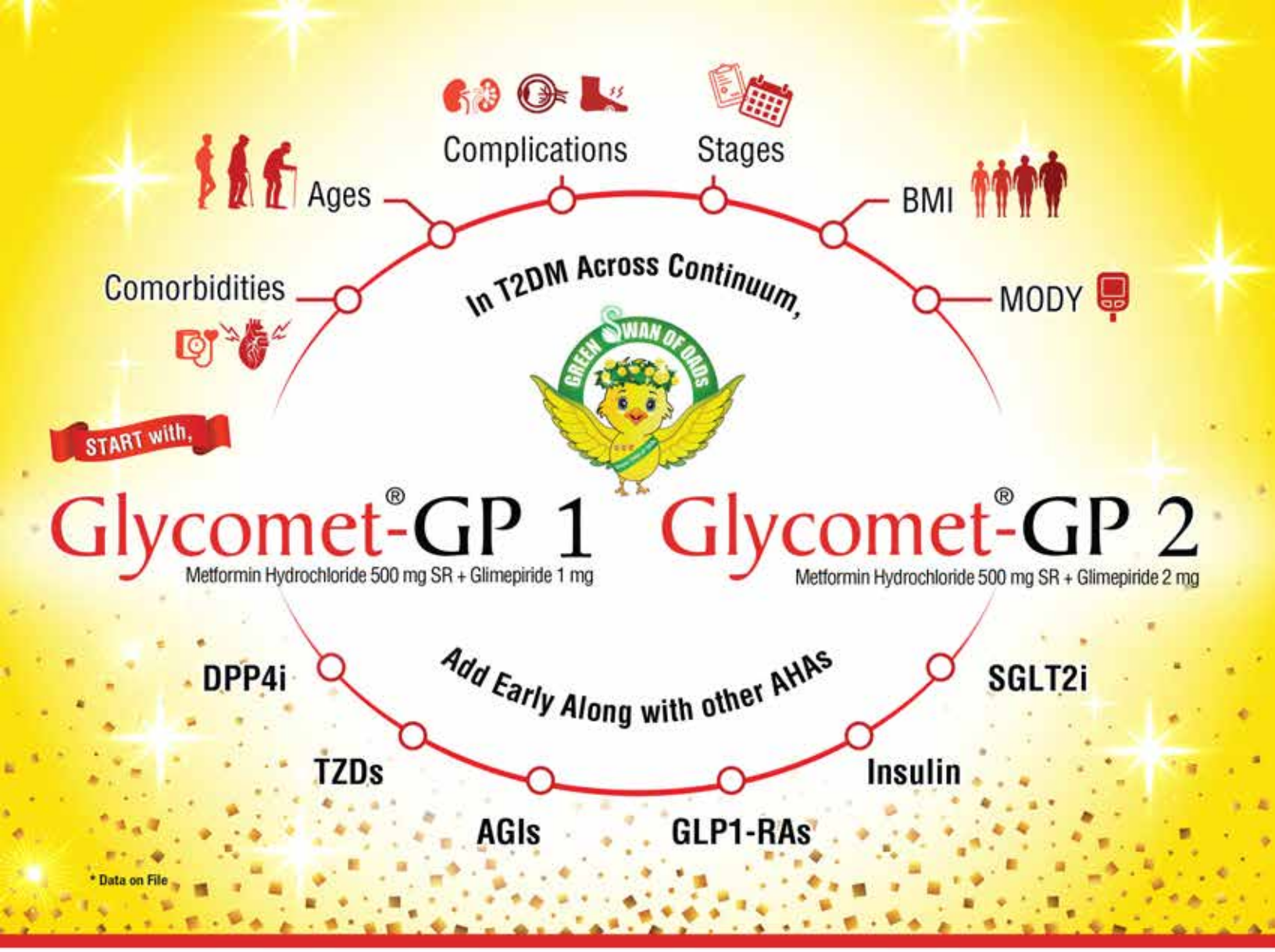


Beat Diabetes Win Life

NOTES

NOTES

NOTES



1. Asian Journal of Diabetology, Vol. 23, No. 2, April-June 2022: YALAMANCHI SADASIVA RAO etal, 2. Asian Journal of Diabetology, Vol. 23, No. 2, April-June 2022; SAUMITRA RAY etal, 3. Cureus 2020; 12(9): e10.7759/cureus.1070 4. CMARC Data 5. Healthplix Data 6. Lim L-L, Lau ESH, Cheung JTK, et al. Real-world usage of sulphonylureas in Asian patients with type 2 diabetes using the Joint Asia Diabetes Evaluation (JADE) register. Diabetes Obes Metab. 2022;1-14. Doi:10. 1111/dom.14865;

Prescribing Information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information **Composition:** Glycomet GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg.• Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg.• Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg.• Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. • Glycomet GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 1mg. • Glycomet GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP mg. **Indication:** For the management of patients with type 2 diabetes mellitus when diet, exercise and single agent (glimepiride or metformin alone) do not result in adequate glycaemic control. **Dosage and Administration:** The recommended dose is one tablet daily during breakfast or the first main meal. Each tablet contains a fixed dose of glimepiride and Metformin Hydrochloride. The highest recommended dose per day should be 8 mg of glimepiride and 2000mg of metformin. Due to prolonged release formulation, the tablet must be swallowed whole and not crushed or chewed. **Adverse Reactions:** For Glimepiride: hypoglycaemia may occur, which may sometimes be prolonged. Occasionally, gastrointestinal (GI) symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur. Hepatitis, elevation of liver enzymes, cholestasis and jaundice may occur; allergic reactions or pseudo allergic reactions may occur occasionally. For Metformin: GI symptoms such as nausea, vomiting, diarrhea, abdominal pain, and loss of appetite are common during initiation of therapy and may resolve spontaneously in most cases. Metallic taste, mild erythema, decrease in Vit B12 absorption, very rarely lactic acidosis, Hemolytic anemia, Reduction of thyrotropin level in patients with hypothyroidism, Hypomagnesemia in the context of diarrhea, Encephalopathy, Photosensitivity, hepatobiliary disorders. **Warnings and Precautions:**: For Glimepiride: Patient should be advised to report promptly exceptional stress situations (e.g., trauma, surgery, febrile infections), blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary to maintain good metabolic control. Metformin Hydrochloride may lead to Lactic acidosis; in such cases metformin should be temporarily discontinued and contact with a healthcare professional is recommended. Sulfonylureas have an increased risk of hypoglycaemia. Long-term treatment with metformin may lead to peripheral neuropathy because of decrease in vitamin B12 serum levels. Monitoring of the vitamin B12 level is recommended. Overweight patients should continue their energy-restricted diet, usual laboratory tests for diabetes monitoring should be performed regularly. **Contraindications:** Hypersensitivity to the active substance of glimepiride & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis, diabetic pre-coma). Severe renal failure (GFR≤30ml/min). In pregnant women. In lactating women.Acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (cardiac or respiratory failure, recent myocardial infarction, shock); hepatic insufficiency; acute alcohol intoxication; alcoholism. **Use in a special population:** Pregnant Women: Due to a lack of human data, drugs should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Pediatric Patients: The safety and efficacy of drugs has not yet been established. Renal impairment: A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g. every 3-6 months.

Additional information is available on request.

Last updated: March 13, 2023

In case of any adverse events, kindly contact: pv@usv.in For the use of registered medical practitioner, hospital or laboratory.

USV Private Limited Corvette Team

Arvind Vithal Gandhi Chowk, B. S. D. Marg, Govandi, Mumbai - 400 088. | Tel.: 91-22-2556 4048 | Fax: 91-22-2558 4025 | www.usvindia.com

Scan the QR code to access full library of IDEJ -
https://usvmed.com/