



49TH ANNUAL MEETING OF
**RESEARCH SOCIETY FOR THE
 STUDY OF DIABETES IN INDIA**
RSSDI 2021 11TH-14TH NOV, 2021

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11TH-14TH NOVEMBER 2021

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The Makers of:





Why Do Some Develop Diabetes Complications and Others Don't?

Dr. Vijay Vishwanathan (Vice-President RSSDI) during his talk highlighted the differential complication risk pattern in different diabetic patients. An excerpt of his talk are presented below-

Introduction

Diabetes is a vascular disease and is marked by various complications. The risk can be mitigated with intensive blood glucose control however the average glucose control is poor in diabetic patient and more so in India.

A correlation to identify high risk individuals and treat them accordingly in terms of prevention and management can help physicians to reduce the risk of long term complications.

Data Suggesting Familial Aggregation of Diabetic Nephropathy

- In one of the original papers published by Dr V Vishnathan and colleagues in the official IDF journal concluded that there is a familial aggregation of diabetic nephropathy. It was observed that if a patient is suffering from diabetic nephropathy, the risk of developing the complication is higher in patient's siblings if they are also diabetic
- Also in another original research paper published earlier, Dr Vishwanathan and colleagues had shown association between ACE gene polymorphism and diabetic nephropathy in South Indian patients
- As concluded in the paper, the ACE gene present on chromosome 17 has two alleles – DD (Deletion) or ID (Insertion) genotype. If the Patient has DD Allele, then there is a greater fall in eGFR, even after treating with ACEI

- The outcome was further reinforced in another paper presented in 2018
- Along with ACE gene, TNF alpha is another gene which is responsible for increasing the risk of nephropathy as its presence of this gene leads to increased levels of circulating TNF alpha
- Beyond the genes, there is also a cross between endoplasmic reticulum stress and oxidative stress which plays a part in the progression of nephropathy as was shown in latest paper presented in 2020 by Dr. Vishwanathan and colleagues
- Another factor responsible for nephropathy progression is TGF beta (through underlying mechanism as mentioned below) –
- TGF beta is an important determinant in predicting the risk of nephropathy and patients with higher levels of TGF beta have an increased risk.
- Another biomarkers identified in a paper published by Dr. Vishwanathan and colleagues, is YKL-40 whose expression increases with the severity of nephropathy

Biomarkers for Risk Related to Diabetic Foot

- Risk of diabetic foot or ulcer or amputation is also related to the genetic background
- Those who have SDF-1 (Stromal cell Derived Factor) polymorphism do have a higher level of cytokines in serum and also resultant higher risk of diabetic foot ulcers
- SDF-1 is associated with major amputation even after adjusting for confounding variables
- Another gene identified related to risk of diabetic foot is HSP (Heat Shock Protein)

Association of HSP with Diabetic Foot Ulcer

Is HSP70-hom (C2437T) Single Nucleotide Polymorphism (SNP) associated with Diabetic Foot Ulcer (DFU) among South Indian population?

Authors: Dharmodharan Umapathy M.Phil,¹ Ezhilarasi Krishnamoorthy M.Phil,¹ Parthiban Muthukumar Ph.D,¹ Rama Rajaram Ph.D,² Indira Padmalayam Ph.D,³ Vijay Viswanathan MD, PhD, FRCP^{1*}

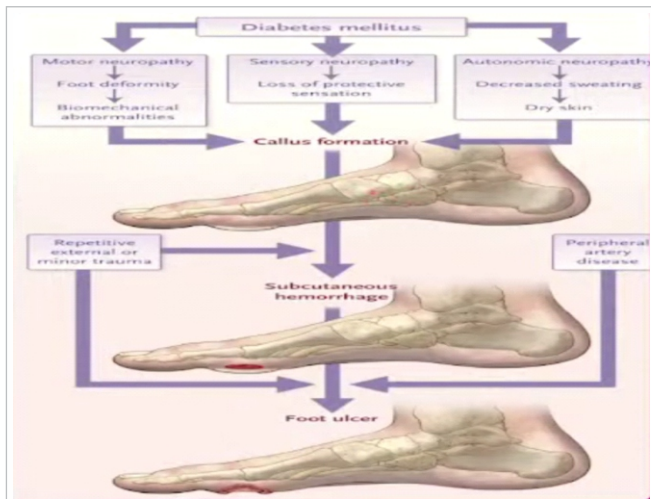
The Journal of Diabetic Foot Complications, 2012; Volume 4, Issue 2, No. 3, Pages 57-62 © All rights reserved.

SNP	Diabetic Foot Ulcer (DFU) (n=95) (f)	Healthy Controls (n=124) (f)
C2437T Genotype		
HSP70-hom C/C	2 (2.0 %)	20 (16.1 %)
HSP70-hom C/T	34 (36.0 %)	92 (74.2 %)
HSP70-hom T/T	59 (62.0 %)	12 (9.7. %)
Allele		
C	38 (2.0 %)	132 (5.0 %)
T	152 (8.0 %)	116 (5.0 %)

HSP=Heat shock protein;
f=genotype frequencies.

Table 2 - Genotype and allelic frequencies of the HSP70-hom (C2437T) SNP in Diabetic Foot Ulcer Patients and Healthy Controls

Biomechanical Factors Leading to Diabetic Foot Ulcers



Limited Joint Mobility in the feet Leading to Diabetic Foot Ulcers

- Limited joint mobility in the feet can be determined by the dorsi-flexion of the big toe (if dorsiflexion movement can't be flexed by 360°, then it's a sign of limited mobility)



Genetic Predisposing Factor for Type 2 Diabetes

- Genetic predisposing factors can not only determine the risk of complications but also the prevalence of diabetes
- TCF7L2 polymorphism can lead to increased risk of Type 2 diabetes in patients with positive family history of diabetes



Summary

- Along with biomechanical causes, genetics also play a major role in determining the risk factors in diabetes
- Complications like nephropathy, diabetic foot ulcer are related to presence of particular genetic structure which predisposes patients to have higher risk of developing these complications
- Genetics not only predisposes to complication risk but can also higher risk of prevalence of diabetes
- Early identification of risk factors in patients can help us to effectively manage the long-term complications in diabetes

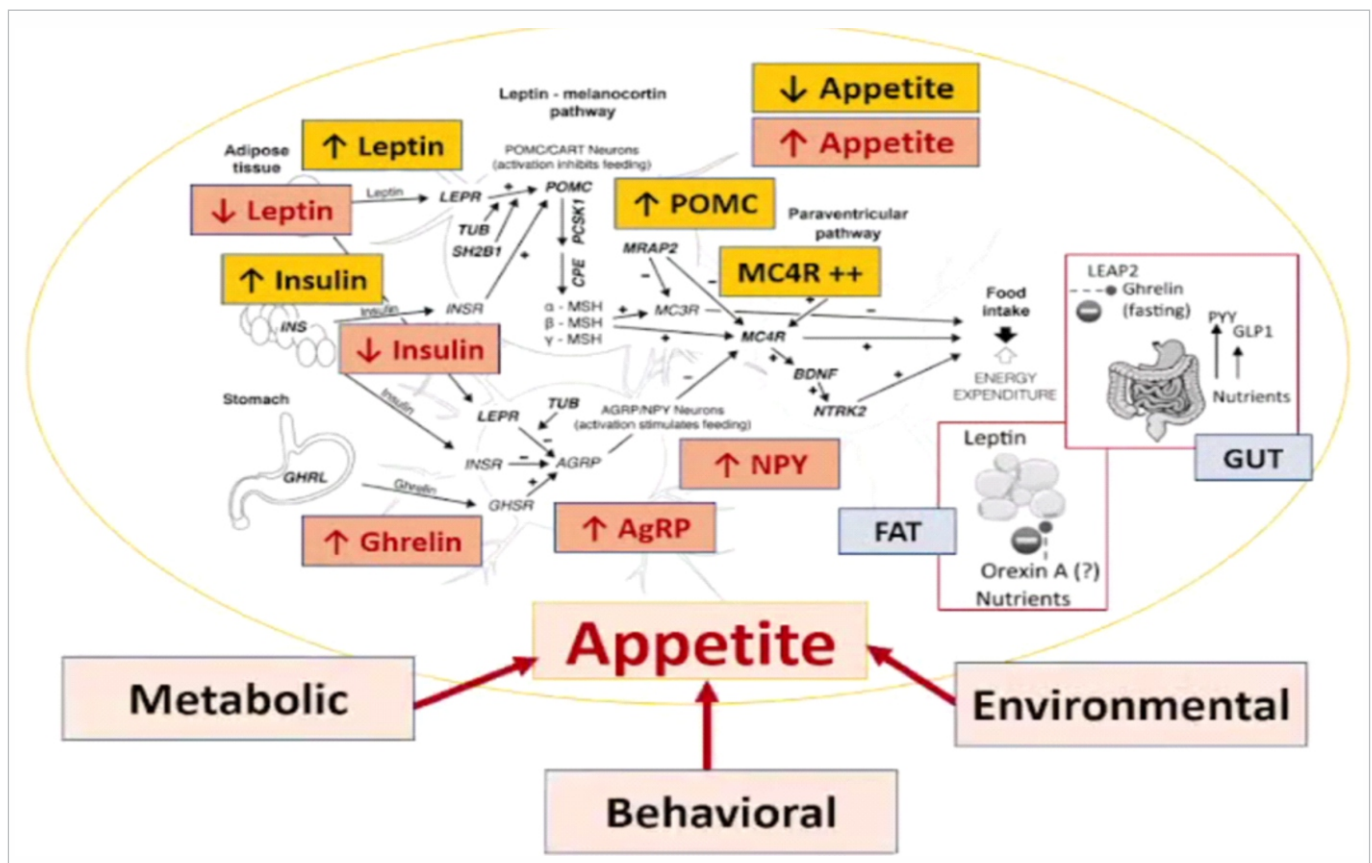
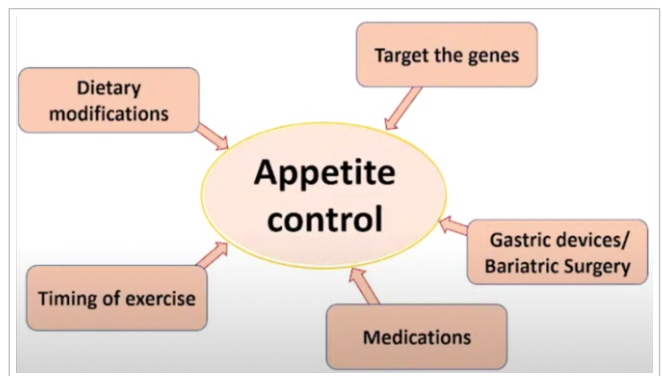
Methods to Control Appetite in Patients with Diabetes: A Clinical Perspective

Dr. Nitin Kapoor from Vellore shed some light on appetite control from a clinical perspective and ways to adopt the same. An excerpt of his presentation are mentioned below -

- Epidemiological data (National Family Health Survey, published June 2021) has revealed that prevalence of obesity in Indian adults is around 35-40%
- Diabetes along with Obesity has become a twin pandemic reaching enormous proportions
- Obesity mainly arises due to energy imbalance (in form of intake vs expenditure)
- This energy (calorie) intake is not only related to the will-power but also related to certain hormones in the hypothalamus which play a crucial role in impacting the appetite

- Certain hormones can increase the appetite (like ghrelin) while others can reduce (like leptin)
- An imbalance of these hormones can lead to differential appetite as well

5 approaches to Regulate Appetite in Patients





A. Dietary Modifications

As per the recent (Apr 2021) paper published by Dr Kapoor and colleagues on consensus on Medical Nutrition Therapy for diabetes in adults: A South Asian perspective, there are 6 major points to be considered –

1. Eat by the clock
2. No skipping of meals
3. Have small, frequent meals
4. Regulate oil intake per month
5. Should not impair quality of life
6. **Ensure Recommended Protein Intake – Very important** (a small dose of whey protein, co-ingested with mixed-macronutrient breakfast and lunch meals, is shown to improve postprandial hyperglycemia and suppresses appetite in men with Type 2 diabetes)

B. Timing of Exercise

Literature have shown the following patterns with respect to the effect of timing of exercise on appetite –

1. Early morning walk or near to lunch time works better for reducing appetite
2. With respect to timing, 30-min walk 60-min before lunch works better than 180-min before lunch

C. Medications

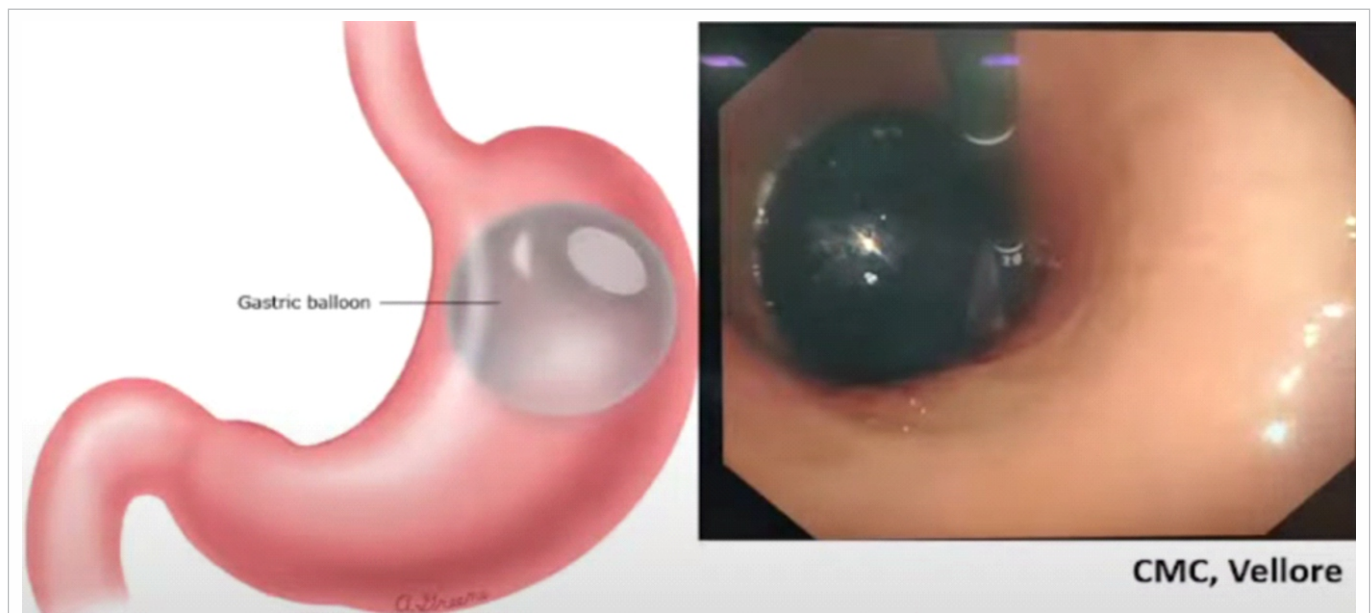
1. Contemporary medication like GLP-RA 1 have shown to have beneficial effect on weight beyond HbA1c reduction
2. Semaglutide have shown best effect of weight reduction in the class
3. Future diabetic drugs with beneficial effect on appetite includes Tirzepatide and Cagrisema (weight loss in phase 2 trials is almost equal to bariatric surgery)

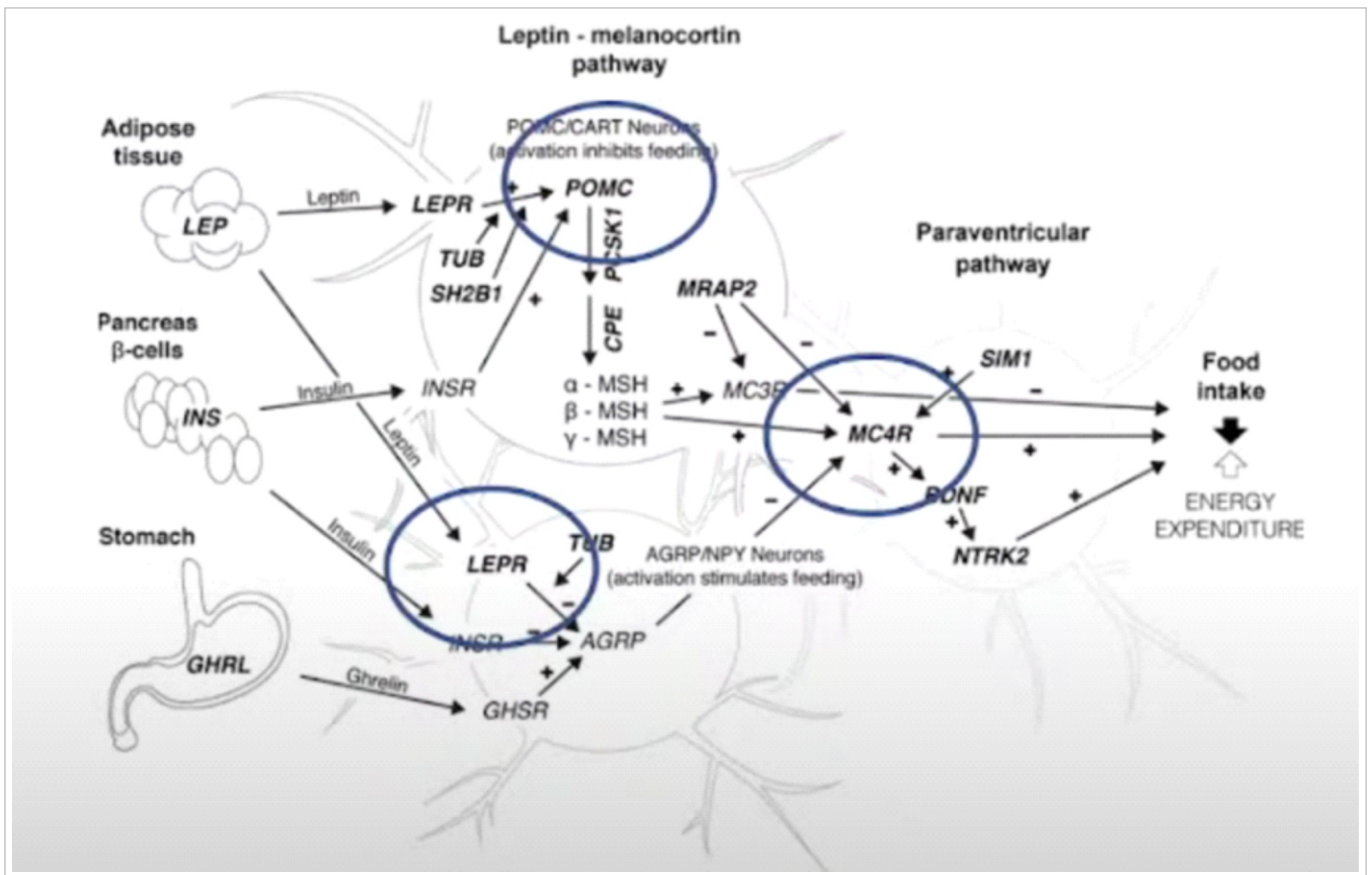
D. Gastric Devices and Bariatric Surgery

1. The taste function and ingestive behavior changes significantly post bariatric surgery with reduction in cravings for energy-dense foods
2. Gastric devices like intra-gastric balloon is shown to have positive impact
3. Bariatric surgery have shown to reduce the levels of ghrelin however gastric balloon doesn't change the hormone levels

E. Target the Genes

1. Genetic factors are linked to the risk of appetite regulation
2. There are drugs available now which can target these genes. Eg Setmelanotide targets severe obesity due to lack of LEPR or POMC gene deficiency





When to ask for genetic testing –

- Age of onset of obesity < 10 years
- Presence of comorbid obesity
- Family history of consanguinity
- Family history of young onset obesity
- History of hyperphagia
- Mild/moderate development delay
- Clinically evident visual impairment/hearing defect
- Macrocephaly

Summary

- Obesity is an important risk factor in diabetes and is related to increased risk of complications
- Regulating appetite can help us reduce the burden of obesity and resulting complications
- Several factors can impact appetite regulation including diet, exercise timing, medications, surgery/devices and genetics

Gaps in Diabetes Care: Challenges and Solution

Dr. P V Rao from Hyderabad highlighted the gaps in the current diabetes care and effective ways to overcome them to improve the standard of care. Few salient points from his talk are presented below -

Introduction

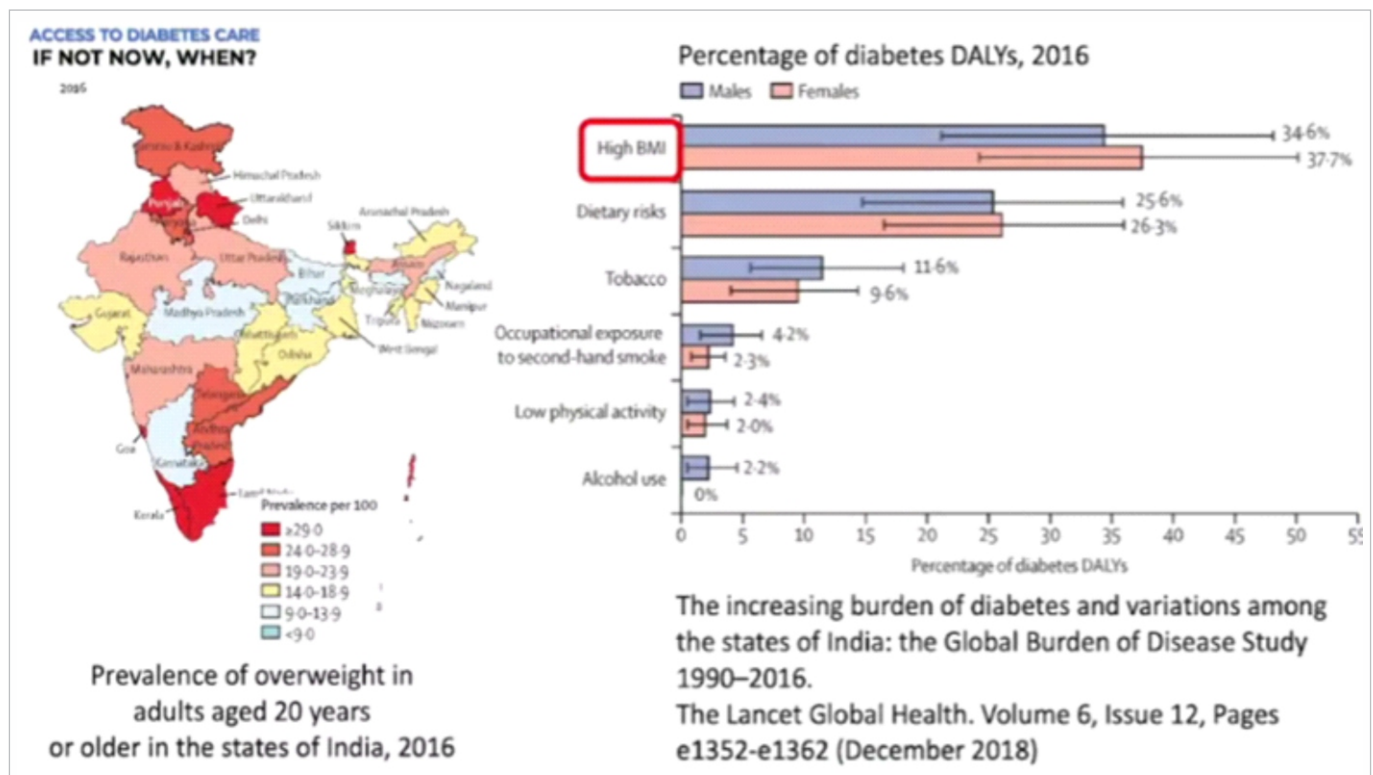
Overall diabetes care is a decisive factor in managing diabetes and its long-term complications not only with medications but beyond that as well.

With respect to comprehensive diabetes care, the theme of World Diabetes Day 2021-23 revolves around access to 5 major components including –

- Insulin
- Oral medicines
- Self-monitoring
- Education and psychological support and
- Healthy food and safe place to exercise

Challenges in Providing Optimal Diabetes Care

1. Gap in optimal number of diabetes specialist doctors
 2. Overweight population
 3. High prevalence Fatty liver
 4. Consumption of unhealthy food (non-balanced diet)
 5. Self-monitoring
 6. Oral medicines
 7. Insulin practices
1. India needs a large number of trained diabetologists to provide minimal diabetes care. Currently the ratio of diabetologists to patients is poor which can cause a major hindrance to provide optimal care if not addressed well
 2. Overweight or obesity is increasing in prevalence in India and is associated with many





other comorbid conditions and should be aggressively treated early stage

Life-Time Risk of Diabetes at Different Stages of Obesity at Different Ages

A recent study have demonstrated that even young people having obesity have a high-life time risk of developing diabetes

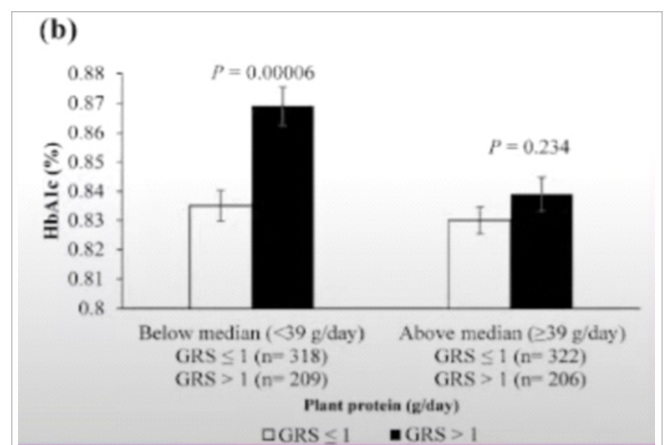
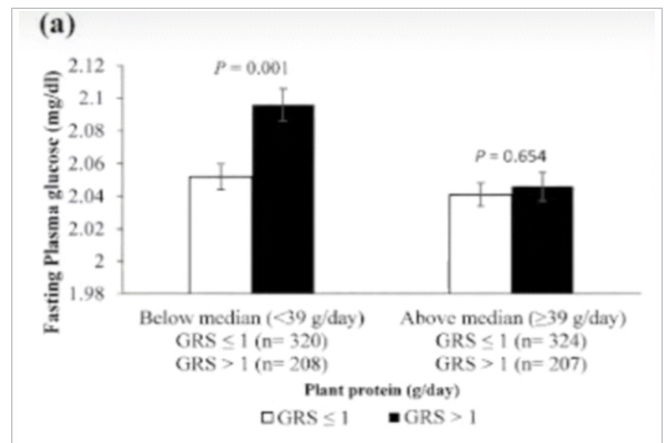
ACCESS TO DIABETES CARE
IF NOT NOW, WHEN?

Lifetime risk of diabetes (%) at ages 20, 40 and 60 years by global BMI and WC cut points in Indian metropolitan cities
* Relative risk of dying among those classified as centrally obese relative to those classified as not centrally obese extracted from Cerhan et al (2014)

BMI group	Age (years)	Lifetime risk (%)	
		Men	Women
Normal weight (BMI<25kg/m ²)	20	40.0 (36.4-43.3)	40.6 (35.9-45.2)
	40	35.7 (32.2-39.8)	36.9 (32-41.4)
	60	23.2 (19.28-6.1)	23.9 (19.1-28.7)
Overweight (BMI>=25 & <30kg/m ²)	20	69.9 (63.7-75.1)	69.3 (62.8-75.2)
	40	63.4 (55.7-71.1)	63 (53.2-70.6)
	60	44.2 (34.1-56.3)	43.6 (33.2-56.1)
Obese (BMI>=30kg/m ²)	20	88.9 (82.2-93.3)	85.3 (77.3-92.4)
	40	82.1 (70.2-89)	79.3 (66.1-88.1)
	60	62.1 (41.4-78.7)	59.0 (43-73.9)

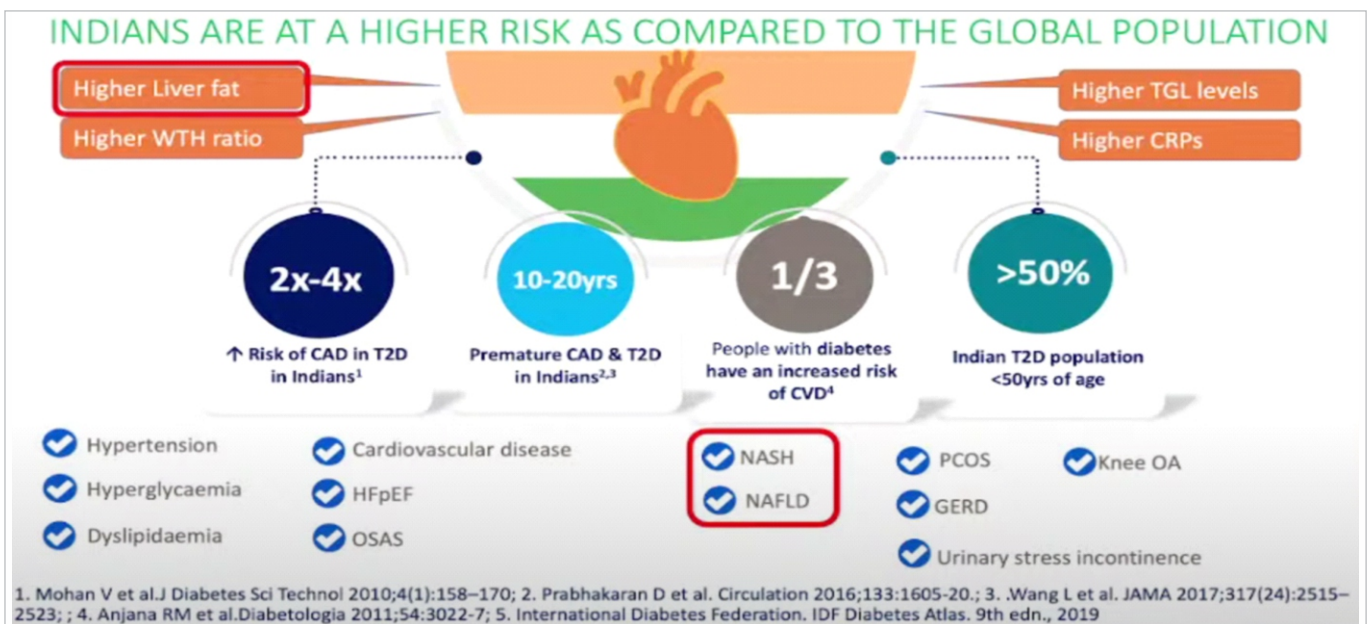
Waist circumference	Age (years)	Lifetime risk (%)	
		Men	Women
WC <90cm (men); WC <80cm (women)*	20	45.2 (40.5-48.8)	44.5 (39.6-49.4)
	40	38.0 (34-42.4)	39.5 (34-44.7)
	60	23.3 (19.28-4)	25.0 (19.3-32.4)
WC>= 90cm (men); WC>=80cm (women)	20	71.0 (64.4-80.9)	75.5 (65.2-84.2)
	40	60.5 (51.7-72.2)	67.8 (54.4-79.1)
	60	39.4 (29.5-3)	46.4 (31.3-62.4)

Luhar S, Kondal D, Jones R, Anjana RM, Patel SA, Kinra S, Clarke L, Ali MK, Prabhakaran D, Kadir MM, Tandon N, Mohan V, Narayan KMV. Lifetime risk of diabetes in metropolitan cities in India. Diabetologia. 2021 Mar;64(3):521-529.



- Indians are at higher risk of having fatty liver as compared to the global population with prevalence going as high as 2nd/3rd of the diabetic population
- Indian meals is commonly high on carb but at the same time low on protein which is even more critical than high carb diet. As shown in a recent paper, a low protein diet is associated with increased risk of developing and progression of diabetes. Also less fiber and more fat consumption leads to increased risk

- Self monitoring is increasing as more and more people are getting aware about the complications however there is scope for improvement and also newer technologies like dried blood spot should be adopted to avoid any gaps in collection and transportation and thus resultant misreading



6. Oral medication recommendation as per global guidelines is for GLP-1 RA or SGLT2i for high risk patients however they are not affordable to most of Indian patients and thus use of SUs or TZDs should be continued as recommended by guidelines as well
7. Regarding the use of Insulin, the RSSDI-ESI 2020 guidelines recommend initiation of insulin therapy with a long-acting insulin and then adding short-acting, making it like basal-bolus which is a standard practice globally. However in India still 70% insulin patients are on pre-mix insulin, which should not be the case

Summary

- There are several gaps to be addressed in providing comprehensive diabetes care
- Theme of world diabetes day is to create awareness around 5 major points for improving standard of care
- In India there are multiple challenges around providing optimal care not only in terms of diagnosis and medication but also in terms of diet and lifestyle
- A coordinated effort is required to address and overcome these challenges

Diabetes and Hypertension

Dr. A Murugunathan presented his talk on diabetes and hypertension and highlighted the need to addressing these conditions to minimize complication risk. Few salient points from his presentation are mentioned below -

- Prevalence of diabetes and hypertension is very common
- Several pathophysiological factors contribute to the higher prevalence of hypertension in diabetes including -
 - Metabolic syndrome
 - Excessive RAAS activity
 - Renal Scarring
 - Hyperinsulinemia
 - Increased salt and water retention
 - Increased sympathetic tone
 - Endothelial dysfunction
 - Genetic factors

BP Goals

- Major global guidelines recommend more stringent BP goals (130/80) in diabetes as compared to non-diabetic (140/90) hypertensives
- However, these BP targets should be individualized considering –
 - Age
 - Life expectancy
 - Associated comorbidities
 - Overall treatment burden
 - Risk of hypotension
 - Drug side effects
 - Cost compliance
 - Patient's attitude
 - Support system
- Ideally in diabetics, we should target lowest BP which patient can tolerate without postural hypotension

Management of Diabetic Hypertensive Patients

- First we should target adequate blood glucose control
- Aggressively treat to achieve the BP goals
- Regular screening for early detection of complications and adapting strategies for prevention or delay in progression to improve the patients' quality of life
- Even if diabetic patients have normal BP, they should be advised aggressive lifestyle modification measures and should be monitored carefully. Pharmacotherapy should be used in case of BP above targets

Lifestyle Modifications that have been Proven to have Positive Impact on BP -

- Weight reduction (even mild reduction can work)
- DASH Diet (addition of fruits/fiber)
- Sodium restriction
- Physical activity
- Alcohol abstinence

Components of an Ideal Anti-Hypertensive Drug in Diabetics

- Decrease BP to the targeted levels
- Reduce RAAS activity
- Prevent/improve or arrest proteinuria
- Prevent/protect from CKD/CVD/CHF
- Have favorable glycemic profile
- Improve dyslipidemia
- Must not worsen PAD
- Improve ED and not cause impotency
- Decrease eGFR and/or increase creatinine
- Do not increase uric acid and/or serum potassium
- Do not increase insulin resistance
- Well tolerated and cost-effective



General Principles of Treatment in Diabetic Hypertensives

- All patients should receive ACEi or ARBs
- Combination drug therapy is generally required to achieve target BP pressure
- Statin therapy should be initiated to achieve the LDL-C goals
- Beta-blockers should be used with caution due to risk of–
- Masking of hypoglycemia
- Prolonged/worsening of hypoglycemia
- Less protection for nephropathy
- Increase in insulin resistance
- At the same time, withholding beta or underusing them can also increase risk of CAD especially should be used in patients with CAD/Post-MI/LVD/Tachyarrhythmias/HF
- Newer generation beta-blockers like Carvedilol, offers lesser negative impact on diabetes condition as compared to atenolol

Practical tips for using diuretics in diabetic hypertensives

- Particularly useful in ISH in elderly patients
- Low-dose should be preferred – using combination is better than increasing the dose
- Best combined with ACEi or ARBs
- Avoid combination with Beta-blockers
- Use Chlorthalidone if creatinine is less than 2 or otherwise use loop diuretics

Summary

- Diabetes and hypertension have increased prevalence and should be managed with aggressive control
- Early screening, adequate treatment should be priority
- Patient education should be imparted for improving adherence
- Cost and compliance should be considered for long-term management
- Team care should be provided and home BP / glucose monitoring should be promoted
- Hypertension clinics should be promoted



Body Composition Analysis: How Important for Clinician It Is?

Dr. Hemant Antani discussed about the factors involved in body composition analysis and their relevance in optimizing care in diabetes. Few highlighting points from the talk are presented below -

Body composition analysis takes into consideration the following parameters. The crux of body composition is the ratio of body fat vs lean mass –

- Total body water (intracellular and extracellular)
- Lean body mass
- Dry lean mass
- Body fat mass
- Weight

Methods Used to Do Body Composition Analysis

- Anthropometric measurements (weight, height, waist and hip circumference, waist-to-hip ratio, BMI – however as doesn't distinguish between body fat and muscle mass, it can lead to misreading. Body fat percentage is more accurate, comprehensive and realistic measure)
- Skin fold test (Skin fold thickness measurement provides an estimated size of the subcutaneous fat deposit with the help of which an estimation of the total body fat can be made. However, it has limitation of not being very accurate and gives incorrect results if skin thickness is > 5cms)
- Hydrostatic weighing (Weighing underwater calculates the total body fat by the density of the body using the Archimede's principle. It's regarded as gold standard)
- Computed tomography (Can provide accurate, high quality information on body composition, including muscle mass, visceral fat, subcutaneous fat)

- Air displacement plethysmography (Measures the body volume by measuring the volume of air according to the changes in pressure in a chamber)
- Dual energy X-ray absorptiometry (DEXA) (Measures body weight in terms of BMC, lean and fat based on decrement of X-ray on the images obtained by exposing to 2 different x-rays. It can measure body composition of bone density, body fat and muscle mass for different parts)
- Bioelectric impedance analysis (BIA) (Method of measuring impedance by applying alternating electric currents to a user to measure their volume of water through impedance values. The method provides estimation of body water from which body fat can be calculated using selected equations)

Importance of Body Composition Analysis

- Most diet and fitness goals focus on weight however two individuals with same weight can have very different body composition which can lead to a different levels of overall health and wellness
- Body composition analysis allows documenting the efficiency of nutrition support, tailoring the choice of disease-specific and nutritional therapies and evaluating their efficacy. It guides the patient to focus on fat loss and not just weight loss

Parameters for Measurement

- Percentage Body Fat (PBF)
 - More accurate than BMI,
 - For a healthy body fat level, aim for PBF – 10- 20% (for males) and 18-28% for females
- Skeletal Muscle Mass (SMM) – Crucial for mobility, posture, and strong immunity for long-term health



- Body Water – Both Intra and Extra cellular body water are crucial but ECW particularly can give insight regarding inflammation. Desirable ECW/TBW is below 0.39
- Lean Body Mass (LBM) – It's the sum of ICW, ECW, and Dry lean mass. LBM is the weight of everything in the body (muscle, water, bones and organs) except fat and thus also called Fat-free mass. Increase in LBM is considered an improvement in body composition (except in case if body water ratio is abnormally increased)

Summary

- Body composition describes the amount of fat, one, water and muscle in the body
- It is very vital to know all components of body to guide patients with specificity
- BMI is not very reliable indication of health
- Percent body fat is the most important marker to predict health. The focus must be on fat loss and not just weight loss
- Skeletal muscle mass is crucial determinant of immunity
- Various accurate methods are now available to estimate the body composition

Estimating CV Risk in DM: Use of Scoring Systems

Dr. Sonali Patange in her presentation shared ways to estimate the CV risk in diabetes patients and their clinical relevance. Few highlighting points from his talk are presented below -

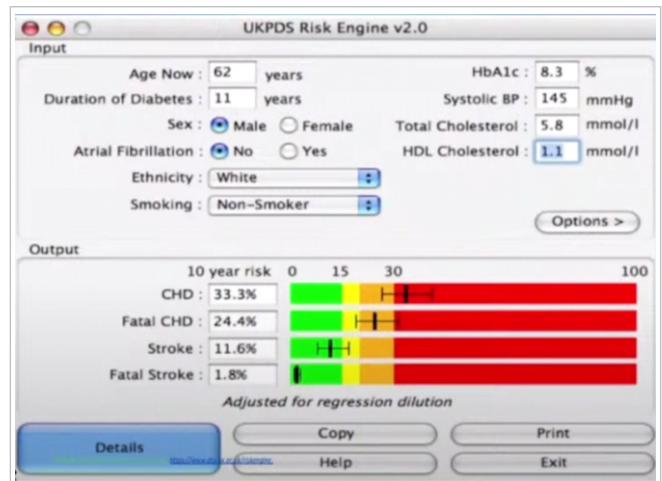
- CVD is considered to be the leading cause of morbidity and mortality in diabetes
- CAPTURE was the first study to uncover the high prevalence of CVD in diabetes
- Life expectancy reduces in diabetic patients with history of CVD

CVD Risk Calculators

- They are used to generate a patient's score for the absolute risk of specific CV outcomes, based on the weighing of independent risk factors

- UKPDS and ADVANCE are common diabetes-specific CVD risk calculators

UKPDS Risk Calculator



ADVANCE Risk Calculator

Step 1		Step 5		Step 11																																							
Age at diagnosis (years)	Points	Retinopathy	Points	Sum-up points from steps 1 to 10 Look up predicted four-year risk of major CVD in the table																																							
29-34	0	No	0	<table border="1"> <thead> <tr> <th>Total points</th> <th>Four-year risk (%)</th> </tr> </thead> <tbody> <tr><td>5 or less</td><td>< 0.5</td></tr> <tr><td>6</td><td>0.5</td></tr> <tr><td>7</td><td>0.7</td></tr> <tr><td>8</td><td>1.0</td></tr> <tr><td>9</td><td>1.4</td></tr> <tr><td>10</td><td>2.1</td></tr> <tr><td>11</td><td>3.0</td></tr> <tr><td>12</td><td>4.3</td></tr> <tr><td>13</td><td>6.2</td></tr> <tr><td>14</td><td>8.9</td></tr> <tr><td>15</td><td>12.6</td></tr> <tr><td>16</td><td>17.8</td></tr> <tr><td>17</td><td>24.7</td></tr> <tr><td>18</td><td>33.7</td></tr> <tr><td>19</td><td>41.9</td></tr> <tr><td>20</td><td>57.8</td></tr> <tr><td>21</td><td>71.4</td></tr> <tr><td>22</td><td>Above 83</td></tr> </tbody> </table>		Total points	Four-year risk (%)	5 or less	< 0.5	6	0.5	7	0.7	8	1.0	9	1.4	10	2.1	11	3.0	12	4.3	13	6.2	14	8.9	15	12.6	16	17.8	17	24.7	18	33.7	19	41.9	20	57.8	21	71.4	22	Above 83
Total points	Four-year risk (%)																																										
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11-15	3	9 +	2																																								
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21-25	5	Albuminuria	Points																																								
26-30	6	Normoalbuminuria	0																																								
31-35	7	Microalbuminuria	2																																								
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Women	-1	3 - < 6	1																																								
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Atrial fibrillation	Points	9 +	5																																								
No	0	Step 11																																									
Old or present	2	Predicted four-year risk of major CVD																																									

The Risk Discussion Should be Done Considering

- Potential for ASCVD risk reduction benefit
- If decision is unclear, then consider high LDL (>160)/family history of premature ASCVD, lifetime ASCVD risk, abnormal CAC score or hs-CRP=>2
- Potential adverse effects and drug-to-drug interactions
- Healthy lifestyle
- Management of other risk factors
- Patient preferences

Risk Stratification Considerations

- Aspirin therapy in appropriate patients, BP control, cholesterol management and smoking cessation

Risk Enhancing Factors

- Family history of premature ASCVD
- Primary hypercholesterolemia
- Metabolic syndrome
- Chronic kidney diseases
- Chronic inflammatory conditions

- History of premature menopause (before age 40) and history of pregnancy-associated conditions such as pre-eclampsia
- High-risk race ethnicities
- **Lipid biomarkers associated with ASCVD risk like**
 - Elevated hs-CRP
 - Elevated Lp(a)
 - Elevated ApoB
 - ABI (ankle-brachial index) < 0.9

Summary

- Prevalence of ASCVD is very high in diabetes
- Indians are at higher risk for CVD as compared to the global population
- UKPDS and ADVANCE are the common diabetes-specific CVD risk calculators
- Risk assessment tools can be used as a guide for decision-making in the primary prevention of CVD
- CVD in diabetes follows a gradient which can be captured with timely identification risk factors



DSME: Concept and Components

New technologies that are getting integrated into hospitals and clinics include

- Artificial intelligence
- Robotics
- Precision medicine
- 3-D printing
- Augmented and virtual reality
- Genomics
- Telemedicine

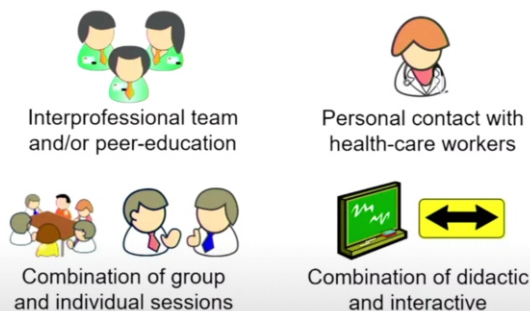
- Such support may include frequent follow-up by a healthcare provider, diabetes coaching, peer support or community health workers, linkages with community support groups or interest groups
- Evidence suggests that combining SME and SMS is most advantageous for improving glycemic control, self-efficacy and self-care behaviors, and reducing diabetes stress and foot complications



By using powerful new technologies and data analytics, healthcare administrators can better understand the need of both the patients and the staff, in order to create a more seamless experience and higher standards of care.



How should SME be delivered?



Self-Management Support (SMS)

- SMS are strategies that augment an individual's ability to self-manage their diabetes

4 critical times to provide and modify DSME

1. At diagnosis
2. Annually and/or when not meeting treatment targets
3. When complicating factors develop
4. When transition in life and care occur

Summary

- There are many evidence-based benefits of DSME including psychosocial benefits and behavioral improvements
- DSME is grossly underutilized
- Health systems and providers should mobilize to ensure all people with Type 2 diabetes have easy access to DSME including nutrition, physical and emotional health support



ADA Standards of Medical Care in Diabetes recommends all patients be assessed and referred for:



Four critical times to assess, provide, and adjust diabetes self-management education and support

1 At diagnosis	2 Annual assessment of education, nutrition, and emotional needs	3 When new <i>complicating factors</i> influence self-management	4 When <i>transitions</i> in care occur
When primary care provider or specialist should consider referral:			
<ul style="list-style-type: none"> <input type="checkbox"/> Newly diagnosed. All newly diagnosed individuals with type 2 diabetes should receive DSME/S <input type="checkbox"/> Ensure that both nutrition and emotional health are appropriately addressed in education or make separate referrals 	<ul style="list-style-type: none"> <input type="checkbox"/> Needs review of knowledge, skills, and behaviors <input type="checkbox"/> Long-standing diabetes with limited prior education <input type="checkbox"/> Change in medication, activity, or nutritional intake <input type="checkbox"/> HbA_{1c} out of target <input type="checkbox"/> Maintain positive health outcomes <input type="checkbox"/> Unexplained hypoglycemia or hyperglycemia <input type="checkbox"/> Planning pregnancy or pregnant <input type="checkbox"/> For support to attain and sustain behavior change(s) <input type="checkbox"/> Weight or other nutrition concerns <input type="checkbox"/> New life situations and competing demands 	<p>Change in:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Health conditions such as renal disease and stroke, need for steroid or complicated medication regimen <input type="checkbox"/> Physical limitations such as visual impairment, dexterity issues, movement restrictions <input type="checkbox"/> Emotional factors such as anxiety and clinical depression <input type="checkbox"/> Basic living needs such as access to food, financial limitations 	<p>Change in:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Living situation such as inpatient or outpatient rehabilitation or now living alone <input type="checkbox"/> Medical care team <input type="checkbox"/> Insurance coverage that results in treatment change <input type="checkbox"/> Age-related changes affecting cognition, self-care, etc.

Summary of DSMES benefits to discuss with people with diabetes

- Provides critical education and support for implementing treatment plans.
- Reduces emergency department visits, hospital admissions and hospital readmissions.
- Reduces hypoglycemia.
- Reduces all-cause mortality.
- Lowers A1C.
- Promotes lifestyle behaviors including healthful meal planning and engagement in regular physical activity.
- Addresses weight maintenance or loss.
- Enhances self-efficacy and empowerment.
- Increases healthy coping.
- Decreases diabetes-related distress.
- Improves quality of life.

No negative side effects | Medicare and most insurers cover the costs

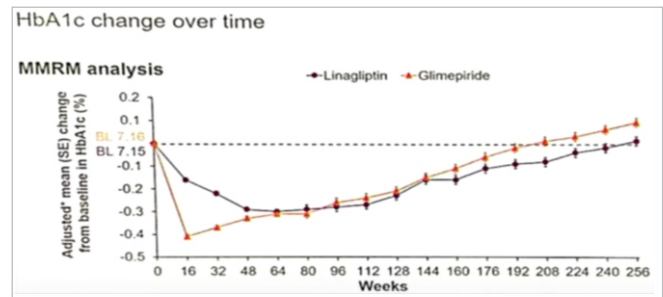


Have We Been Unfair to Sulfonylureas

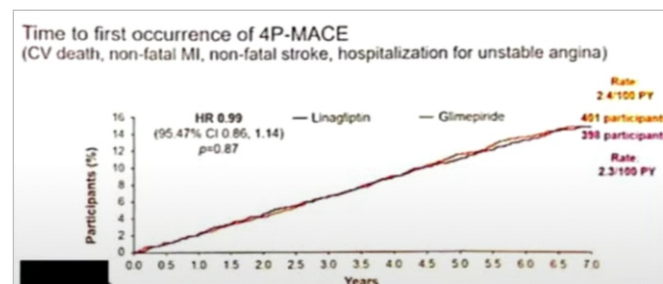
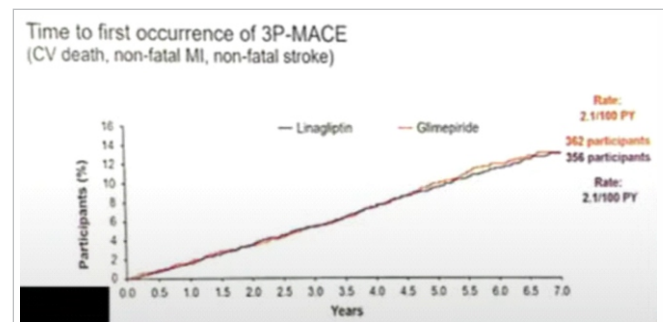
Dr. Vivek Arya (For) and Dr. Piyush Desai (Against) participated in a debate on the use of sulfonylurea (SU) and their status in light of recent data and guidelines. Few highlighting points from the debate are presented below -

Dr. Vivek Arya (For)

- First and foremost risk associated with SUs is the perceived risk of hypoglycemia however the risk can be mitigated by judicious use of SUs as the risk is related to individual patient. Moreover, the risk is mainly associated with older generation of SUs and not much reported with second and third generation SUs
- Cost-effectiveness of therapy is another advantage with SUs. India is placed at rank 99 in terms of per capita income and cost of therapy plays an important role for long-term adherence
- SUs were first made available in 1956 and that shows the longevity of the efficiency of drug. However, in the last few years availability of DPP4i and SGLT2i have raised questions regarding the use of SUs
- Landmark trials like UKPDS have shown the reduction of even 1% HbA1c can reduce all related diabetic micro and macrovascular complications to great extent and out of the available OADs, SU are one of the most effective drugs for reduction of HbA1c
- Newer generation drugs including DPP4i and SGLT2i are weak as compared to SU in terms of HbA1c reduction
- **In terms of CV safety, recently conducted Carolina trial has shown that**
 - Glimepiride was more effective than Linagliptin in reducing the HbA1c



- Linagliptin does not provide more durability for glycemetic control than Glimepiride
- Glimepiride was weight neutral during the trial period
- **In terms of CV safety, recently conducted Carolina trial has shown that -**
 - In this trial 42% patients had established CVD and 37% patients had => 2 defined CV risk factors still no significant difference observed between the two groups in terms of blood pressure, lipids and Glimepiride has shown at-par CV safety as compared to Linagliptin



- There was no significant difference in the CV safety observed even in different subgroups



- of patients based on their age, gender, prior anti-diabetic treatment, baseline HbA1c and baseline eGFR
- There was no difference in the mortality rates as well between the Glimepiride arm and Linagliptin arm. In fact more hospitalization rates due to heart failure were reported in the Linagliptin arm
- Even the incidences of severe hypoglycemia and hospitalization due to hypoglycemia were minimal in both the groups

- SGLT2i have robust data regarding CV and renal outcomes benefits
- Certain set of patients with high risk of hypoglycemia SU should be avoided

	EMPA-REG OUTCOME ¹ (empagliflozin)	CANVAS Program ² (canagliflozin)	DECLARE-TIMI 58 ³ (dapagliflozin)
HHF	HR 0.65* (95% CI 0.50, 0.85)	HR 0.67* (95% CI 0.52, 0.87)	HR 0.73* (95% CI 0.61, 0.88)
CV death	HR 0.62 (95% CI 0.49, 0.77)	HR 0.87 (95% CI 0.72, 1.06)	HR 0.98 (95% CI 0.82, 1.17)
3P-MACE	HR 0.86* (95% CI 0.74, 0.99)	HR 0.86* (95% CI 0.75, 0.97)	HR 0.93* (95% CI 0.84, 1.03)
Renal Outcomes ⁵	HR 0.54* (95% CI 0.40, 0.75)	HR 0.59* (95% CI 0.44, 0.79)	HR 0.55* (95% CI 0.41, 0.75)

Remogliflozin - No CVOT

Comparison of studies should be interpreted with caution due to differences in study design, populations and methodology. Testing for superiority for 3P-MACE was the primary endpoint (co-primary for dapagliflozin).
Epidemiary outcome
* Composite of Renal Worsening, End-stage renal disease, or Renal death (in patients with atherosclerotic CVD)
1. Zinman B et al. N Engl J Med 2015;373:2117-2. Neal B et al. N Engl J Med 2017;377:844. 3. Vivott 5 et al. N Engl J Med 2019;380:347

Summary

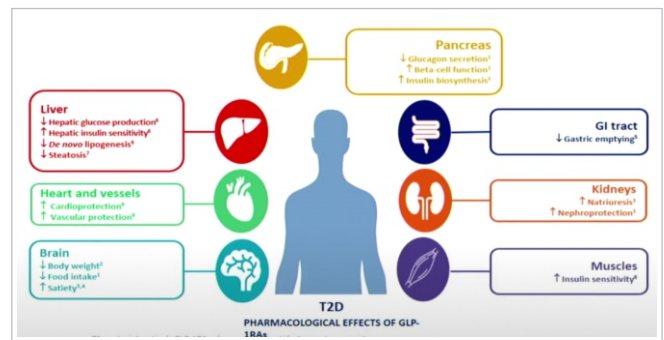
In the light of recent evidences, we should forget to reap the benefits of SU which offers the following advantages –

- Time tested
- Potent
- Most affordable
- Safe

Dr. Piyush Desai (Against)

- Globally SU are still the second largest prescribed OAD after metformin

- Also GLP-1 RA have myriad beneficial effects in diabetes



Summary

- Dr. Vivek Arya in his final comments mentioned that even though newer generation drugs have certain benefits, it comes at a cost of side effects like Genito-urinary infections, Diabetic ketoacidosis, gangrene, boxed warning (in US) for risk of amputation with SGLT2i, retinopathy risk with GLP-1 RA and its very early to understand their side effects and safety profile
- Dr. Piyush Desai in his final comments mentioned that we continue to use SU is our daily practice however as now different drug classes are available, we should personalize the treatment for each patient based on individual profile and need and the desired outcome. If cost is the issue, then even today SU is the answer.

Long-term Trends in Antidiabetes Drug Usage in the U.S.: Real-world Evidence in Patients Newly Diagnosed With Type 2 Diabetes
Olga Montvida,^{1,2} Jonathan Shaw,¹ John J. Atherton,³ Frances Stringer,⁴ and Sanjay K. Paul^{1,2}
<https://doi.org/10.2337/dk17.1414>

Despite the introduction of newer therapies, sulfonylureas remained the most popular second-line agent, and the rates of intensification with sulfonylureas and insulin remained consistent over time

Global **Treatment patterns for 1st, 2nd line management of T2DM: DISCOVER**

Table: Antidiabetic medications in the DISCOVER-MENA region cohort, alone or in combination
n (%)

	1 st Line (prior to enrolment) N=3525	At enrolment N=3525
MET*	2955 (83.8%)	2570 (72.9%)
SU	1101 (31.2%)	1550 (44.0%)
DPP-4i	160 (4.5%)	911 (25.8%)
TZD	75 (2.1%)	150 (4.3%)
Meglitinides	63 (1.8%)	126 (3.6%)
SGLT-2i	7 (0.2%)	114 (3.2%)
Alpha-glucosidase	24 (0.7%)	70 (2.0%)
GLP-1 RA	0 (0.0%)	94 (2.7%)
Insulin (basal)	NA	247 (7.0%)

Most common 2nd line therapies were metformin in combination with either a sulphonylurea (SU): 24.0%, or DPP-4i: 22.0%, or triple therapy with metformin, an SU and a DPP-4i: 14.4%

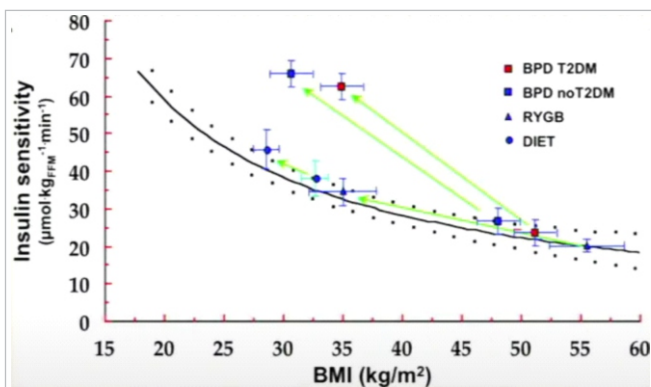
However to reduce the long-term risk we need to be more cautious

- Head-to-head trial of SU and Gliptins have shown favourable results in terms of CV hazards for gliptin

Important Tips On Diet - A Must for Practicing Clinicians

Dr. Heti Verma in her presentation shared some practical diet tips to be adopted for enhancing the control in diabetes. Few highlighting points from his talk are presented below -

- Obesity promotes diabetes and at the same time weight loss counteracts it
- Weight loss through diet / surgery have shown to improve insulin sensitivity
- Same outcomes were reinforced in the recent Magnetic Cohort study



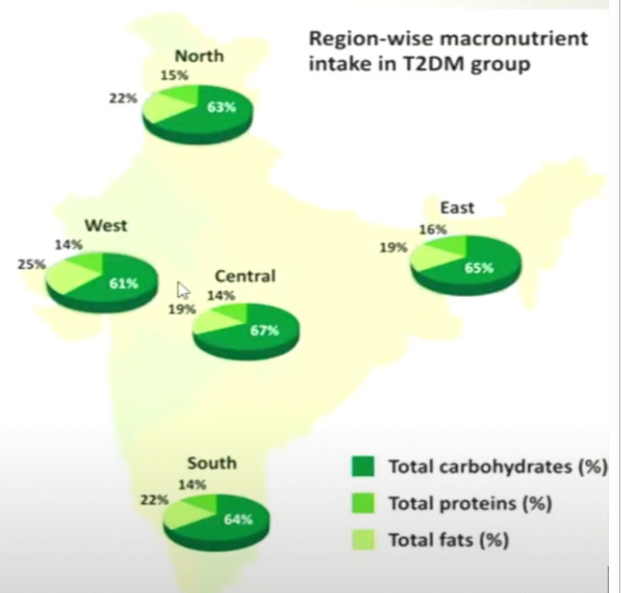
- Some additional parameters along with BMI / waist circumference / waist-to-hip ratio can also be used like the ideal waist size (in cms) should be equal to Height (in cms) / 2
- Some diet tips that can be recommended to patients
 - Diagnose the case well and take action accordingly
 - Make 1 citrus fruit a day compulsory
 - Handful of nuts – for good fats
 - Ask patients to have their own affordable multigrain atta
 - Teach importance of nutrition and practice the same at home from an early age
 - Teach the art of balancing the plate where every meal has enough fiber and protein
 - Small and frequent meals – with GI snacking options like nuts, seeds chana, boiled pulses, sprouts, eggs, milk

BALANCING OF THE PLATES



Your diet plan will be customized based on your urine, blood tests and medical conditions when you are followed by a nutritionist

Region-wise macronutrient intake in T2DM group



- Reduce the amount of caffeine as well as comfort food in the diet

Summary

- Diet plays an important role in managing diabetes
- A healthy diet can help the patient to manage the glucose levels well over long term
- Even a small reduction in weight can help the patient to improve insulin sensitivity and resultant glycemic control
- Small and effective tips which are easy to implement should be given to patients for adoption in day to day life

Diabetes Related Vascular Complications in Pre-Diabetes

Dr. S V Madhu during his talk highlighted the degree of risk vascular complications in pre-diabetes and possible reasons and implications of the same. An excerpt of his talk are presented below -

Introduction

- Prevalence of pre-diabetes in India is around 10.3%, which is higher than diabetes.
- Long-term comorbidities associated with diabetes like vascular complications could also be found in pre-diabetes stage.
- An intervention at early stage of pre-diabetes can help us stratify the risk factors associated with diabetes.

Comparison of diabetes Related Vascular Complications at Different Stages of Diabetes

- A recent paper (2021) published by Dr. Madhu and colleagues compared the prevalence of diabetes related vascular

complications in people with normal glucose tolerance, pre-diabetes, newly detected diabetes and known diabetes

Presence of Micro and Macro Vascular Complications at Different Stages of Diabetes

	NGT (n = 72)	Prediabetes (n = 72)	NDDM (n = 72)	KDM (n = 80)	Total (N = 296)
1.Macrovascular	0	3 (4.2%)	3 (4.2%)	5 (6.3%)	11(3.7%)
a) CAD	0	2 (2.8%)	1 (1.4%)	4 (5%)	7 (2.4%)
b) PVD	0	1 (1.4%)	2 (2.8%)	1 (1.3%)	4 (1.3%)
c) CVA	0	0	0	0	0
2.Microvascular	1(1.4%)	5 (6.9%)	7 (9.7%)	14 (17.6%)	27 (9.1%)
a) Retinopathy	1 (1.4%)	0	0	5 (6.3%)	6 (2%)
b) Nephropathy	0	3 (4.1%)	6 (8.3%)	7(8.8%)	16 (5.4%)
c) Neuropathy	0	2 (2.8%)	1 (1.4%)	2 (2.5%)	5 (1.7%)

Presence of Cardiometabolic Risk Factors at different Stages of Diabetes

CV Risk Factors	NGT (n = 72)	Prediabetes (n = 72)	NDDM (n = 72)	KDM (n = 80)
1.Hypertension	4 (5.6%)	6 (8.3%)	6 (8.3%)	14 (17.5%)
2.Dyslipidemia				
a. TC (>150 mg/dl)	6 (8.3%)	17 (23.6%)	35 (48.6%)	26 (32.5%)
b. HDL c (<50 mg/dl in females <40 mg/dl in males)	59 (81.9%)	64 (88.9%)	60 (83.3%)	77 (96.2%)
c. LDL c (mg/dl)	24 (33.3%)	30 (41.7%)	31(43.1%)	31(38.7%)
3.Smoking	7 (9.7%)	2 (2.7%)	2 (2.7%)	5 (6.3%)
4.Total number of CV risk factors observed in different groups	213	236	261	408
5.Metabolic Syndrome	7 (9.8%)	44 (61.1%)	61 (84.7%)	67 (83.8%)

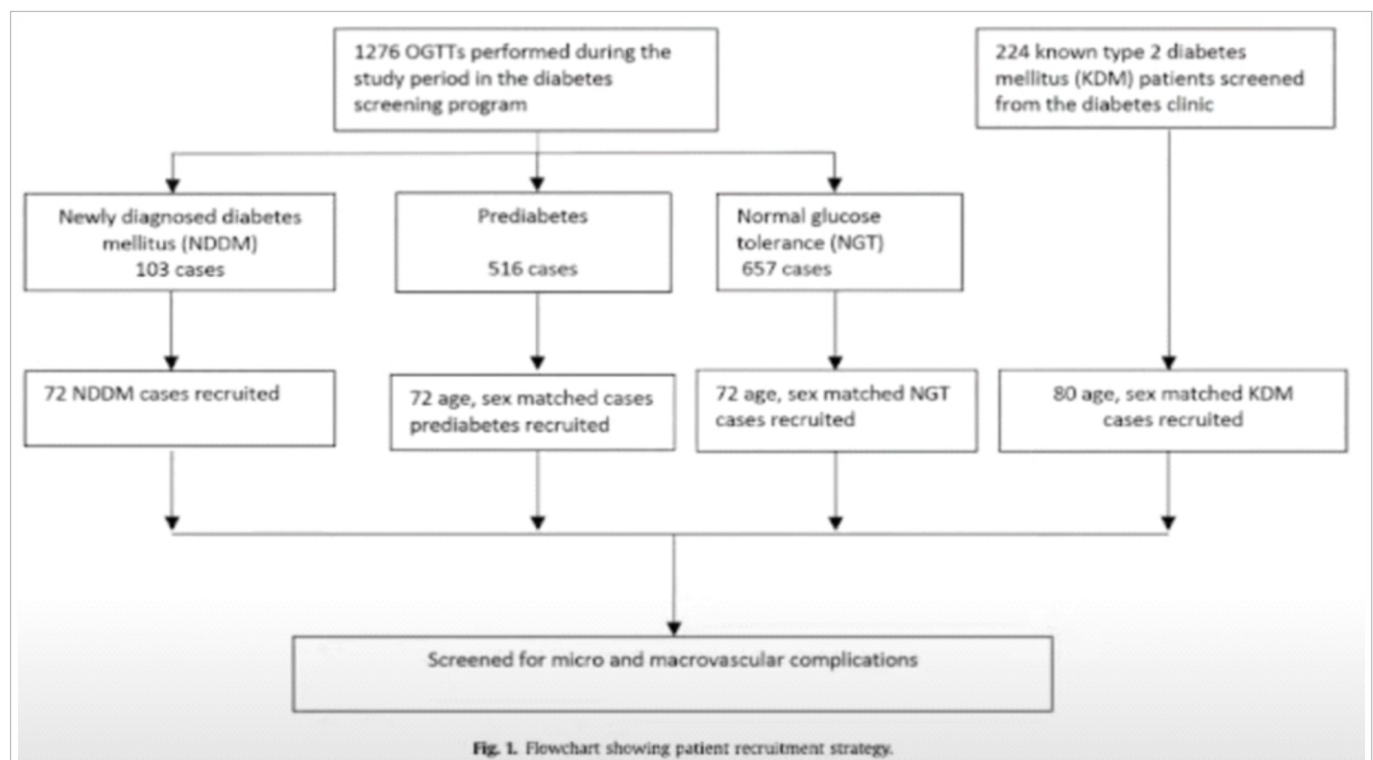


Fig. 1. Flowchart showing patient recruitment strategy.



Presence of Metabolic Syndrome Factors at different Stages of Diabetes

No. of metabolic syndrome features	NCT (n = 72)	Prediabetes (n = 72)	NDDM (n = 72)	IDDM (n = 80)
0	4	0	0	0
1	19	3	0	2
2	41	25	9	10
3	8	35	40	36
4	0	9	23	32

Study Outcomes

- Vascular complications related to diabetes were present in over 10% of subjects with pre-diabetes
- Proportion of pre-diabetes subjects with vascular complications was about 50% of those with known diabetes and almost similar to those with newly detected diabetes
- Over 90% of the pre-diabetes subjects were observed to have one or the other risk factor for macrovascular complications

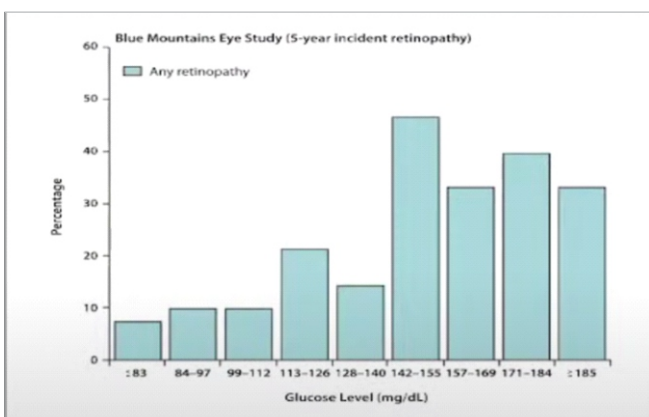
Global Data on Prevalence of Microvascular Complications in Pre-diabetes

The prevalence rate varies in different studies however it ranges

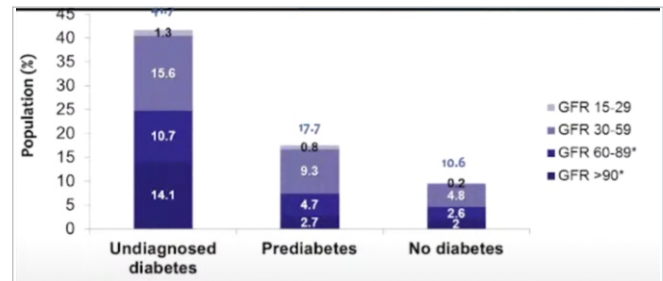
- Retinopathy in 7.9% to 20.9%
- Nephropathy in 15.5% to 17.7%
- Neuropathy in 13% (IGT) and 11% (IFG)

Diabetes Prevention Programme Research Group. *Diabet Med* 2007;24:137e44
Chen et al. *Eye Lond Engl* 2012;26:816e20.
Bahar et al. *Nephro-Urol Mon* 2013;5:741e4.
Plantinga et al. *Clin J Am Soc Nephrol CJASN* 2010;5:673e82.
Deigler et al. *Diabetes Care* 2008;31:464e9

Relationship Between FPG and 5 Years Incident Retinopathy



Prevalence of CKD in US Adults with Undiagnosed Type 2 Diabetes or Pre-diabetes



Pre-diabetes and Risk of CVD

Definition of Pre-diabetes	Risk of CVD	Notes
IFG (100-125 mg/dl)	1.18	* Meta-analysis of 18 studies
IFG (110-125 mg/dl)	1.20	* 175,152 participants
IGT	1.20	

Ford, E. S., G. Zhao, et al. (2010). *J Am Coll Cardiol* 55(13): 1310-7.

Summary

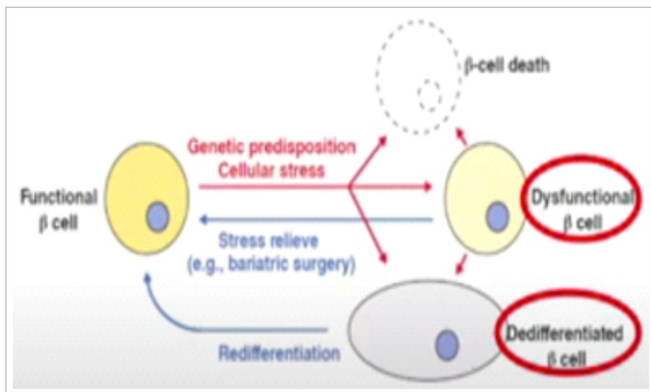
- The prevalence of vascular complications and risk factors in subjects with pre-diabetes highlights the importance of initiating effective preventive measures at an early stage itself
- Significant range of dysglycemia (as observed by CGMS) in some individuals with pre-diabetes could result in the development of vascular complications in diabetes
- Even non-pharmacological approaches can be considered for managing pre-diabetes stage.

Beta Cell: Dysfunction to Dedifferentiation

Dr. Sudhir Bhandari shed some light on the physiology of beta cell functioning in diabetes. An excerpt of his presentation are mentioned below -

- Insulin resistance and beta cell dysfunction are the core defects of Type 2 diabetes

Possible Beta Cell Fates in Type 2 Diabetes and Ways for Recovery of Functional Beta Cell Mass



- Beta cell abnormalities might also contribute to Type 1 diabetes pathogenesis, **leading to notion of so-called beta cell suicide**
- Beta cell HLA **class I overexpression is common in pancreatic sections** from cadaveric donors with Type 1 diabetes
- Overexpression serves as a **homing signal for cytotoxic T lymphocytes**
- Additionally, evidence also exists for **increased beta cell endoplasmic reticulum stress** linked with accelerated beta cell death
- Endoplasmic reticulum stress in beta cells has also been associated with alterations in mRNA splicing and errors in protein translation and folding; resultant protein products have been proposed as **potential immunogenic neoantigens**

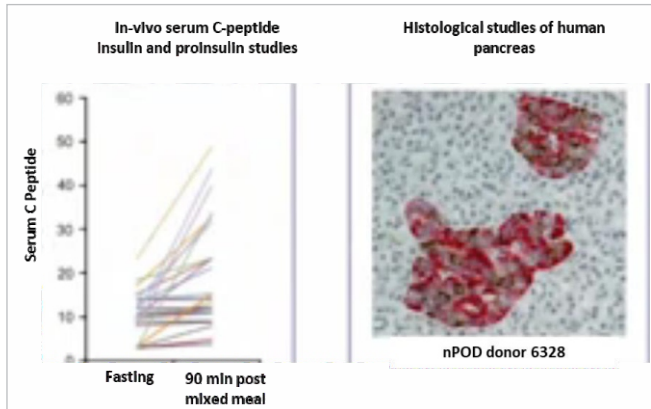
Key Points

- Innate immunity and inflammatory mediators have a broad and important role in the pathogenesis of Type 1 diabetes
- Activation of both endogenous and exogenous ligands of pattern recognition receptors can induce islet inflammation and death of pancreatic beta cells
- Amplification of insulinitis might depend on a dialog between immune cells and beta cells that is mediated by local production of chemokines and cytokines, and danger signals from dying beta cells
- After transition to adaptive immune response, inflammatory mediators such as cytokines might contribute to prolonged functional suppression and death of beta cells, modulation of beta cell regeneration and insulin resistance
- Some inflammatory mediators might promote the survival and proliferation of beta cells, especially in the absence of autoimmune reaction

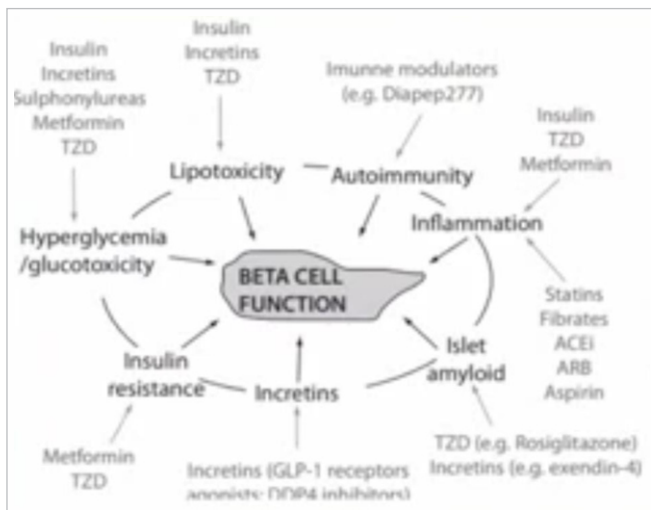
Life and Death of Beta Cells in Type 1 Diabetes

- During progression of Type 1 diabetes beta cell most likely die from a combination of necrosis and apoptosis
- Methods to visualize beta cell inflammation and beta cell mass are being developed
- Molecular techniques have been applied to identify beta cell killing in-vivo
- Use of these methods suggest revision of previous models of the pathogenesis of the disease
- The basis for the long term loss of beta cell remains unclear. It is possible that ongoing beta cell destruction is intrinsic

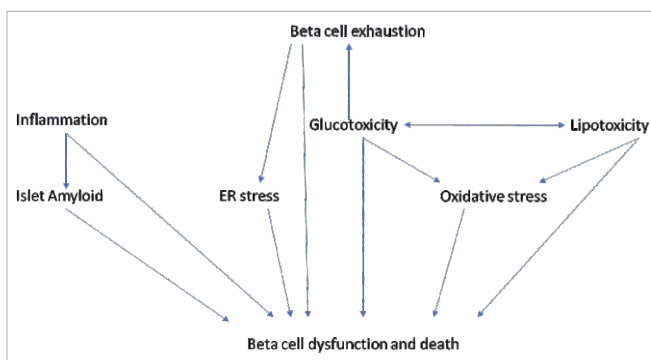
Evidence for Persistent Beta Cells in Long Duration Type 1 Diabetes



Factors Associated with Progressive Reduction of Beta Cell Function and Mass



Proposed Mechanism of Beta Cell Failure



Beta Cell Exhaustion

- Strongest support exhaustion concept comes from studies examining benefits of "beta cell

rest" strategies. When inhibitors of insulin secretion, such as diazoxide or somatostatin are given to animals or humans with diabetes, paradoxical increases in beta cell function are observed following a period of "rest"

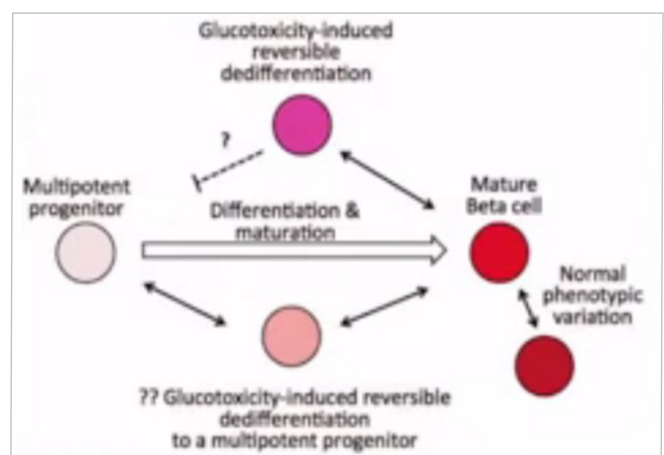
- Furthermore, human subjects with poorly controlled diabetes demonstrate a dramatic improvement in beta cell function following a brief period of intensive glycemic control

Understanding of Beta Cell Failure in Type 2 Diabetes

- Renewed focus on beta cell differentiation
 - How this may be prevented or reversed
 - Extend to which other islet cells can be induced to differentiate into beta cells
- Recent therapeutic developments – Possibility of restoring endogenous beta cell function although long-term stability, safety and efficacy of these approaches is are not yet known

Beta Cell Dedifferentiation in Diabetes

- Differentiation state of a fully mature beta cell can change with national reversible events and during progression to death
- Hyperglycemia of diabetes is thought to be major determinant causing beta cells to lose their differentiation (also termed dedifferentiation), which leads to dysfunctional insulin secretion



Summary

- Beta cell dysfunction plays a pivotal role in progression of diabetes
- Many factors that influence beta cell function altering natural course of disease
- A correct assessment of beta cell function requires concomitant evaluation of insulin sensitivity, because two variables need to be judged in relation to each other
- Clinical considerations are made regarding the therapeutical options which impact on various factors/mechanisms that contribute to the progressive loss of beta cell function/mass
- Ultimately it the failure of beta cells to respond to the insulin requirements posed by the prevailing level of insulin resistance that leads to the development of Type 2 diabetes
- Various genetic and environmental factors conspire together in this state of beta cell susceptibility and decompensation
- C-peptide could be the simplest step to check the status of beta cell function and should be routinely adopted in clinical practice



Diabetes & Metabolic Disorders: Lessons Learnt from ICMR-INDIAB Study

Dr. Pradeepa Guha in her talk summarized the key outcomes and clinical pointers of the ICMR-INDIAB study. An excerpt of her presentation are mentioned below -

Primary Objective

To determine the national prevalence of diabetes mellitus and pre-diabetes in India, by estimating the state-wise prevalence of the same

Additional Objectives

- To determine the prevalence of hypertension and dyslipidemia in urban and rural India
- To determine the prevalence of coronary artery disease among subjects with and without diabetes
- To assess the level of diabetes control among self reported diabetic subjects in urban and rural India

Study design

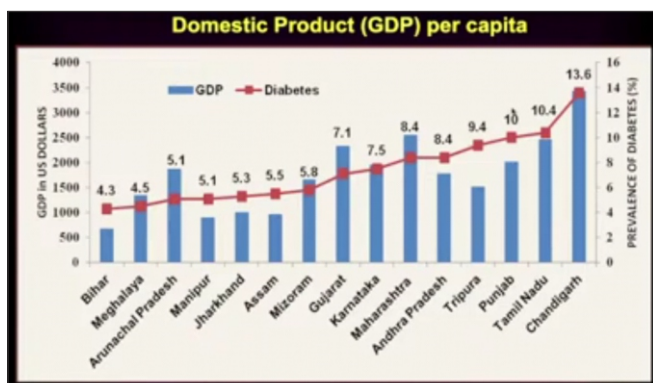
Cross-sectional door to door survey
Sample size – 1,13,043 from 27 states, 2 union territories and national capital territory of Delhi

Study subjects

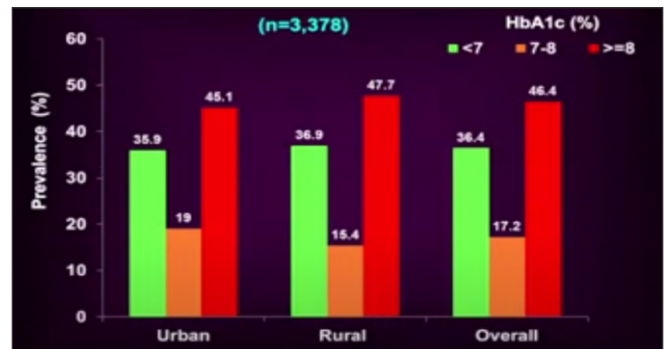
Individuals aged 20 years and above recruited for the study

Outcomes

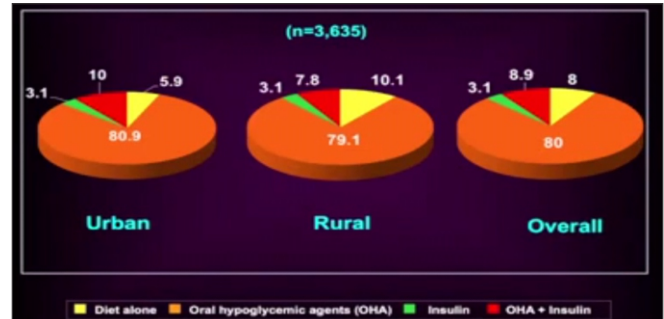
- Burden of diabetes in adult population of India – 77.8 million
- States with higher GDP have higher prevalence of diabetes



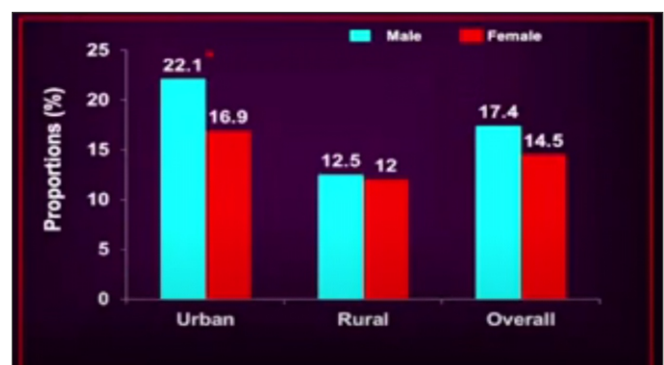
Glycemic Control in Known Diabetes Individuals



Management of Diabetes Among Subjects with self-Reported Diabetes in India

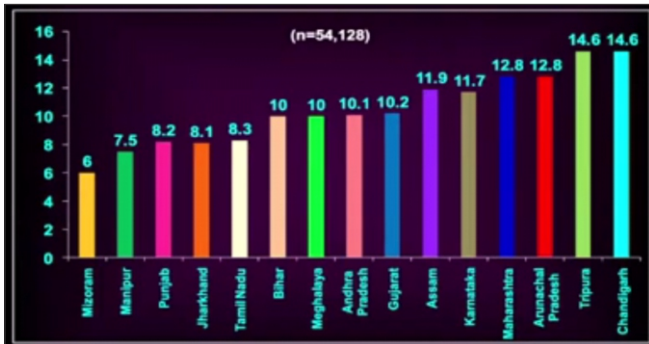


Self Monitoring of Blood Glucose Among Subjects with Self-Reported Diabetes in India

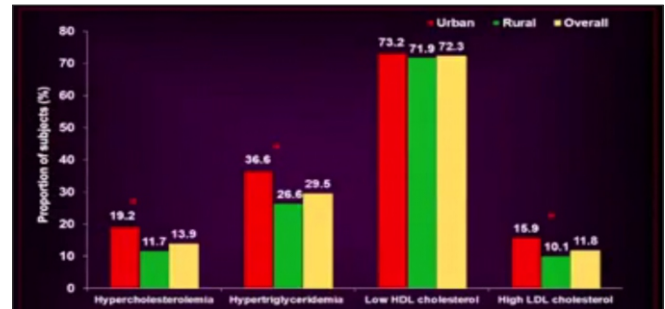




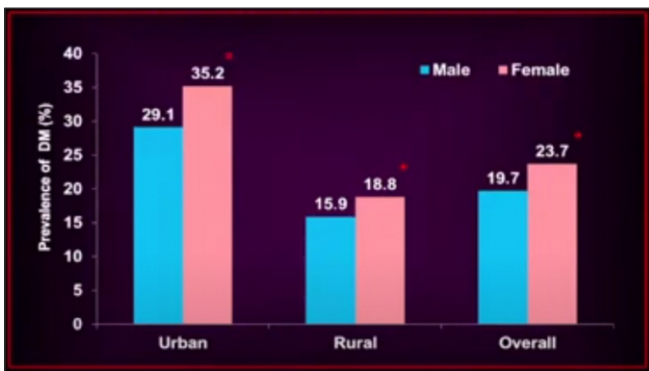
Weighted Prevalence of Pre-diabetes



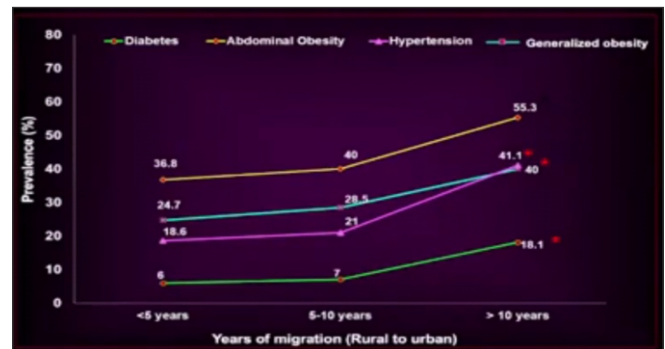
Prevalence of Components of Dyslipidemia



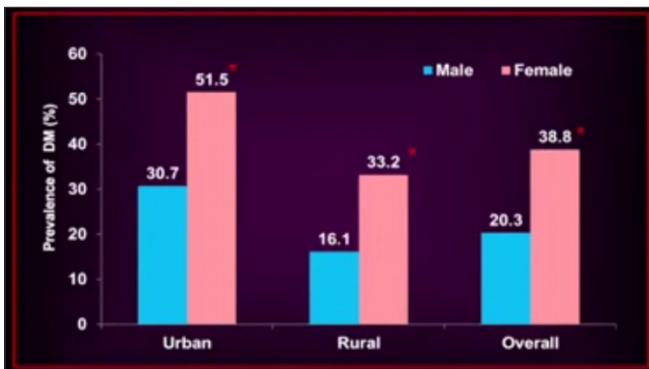
Prevalence of Generalized Obesity



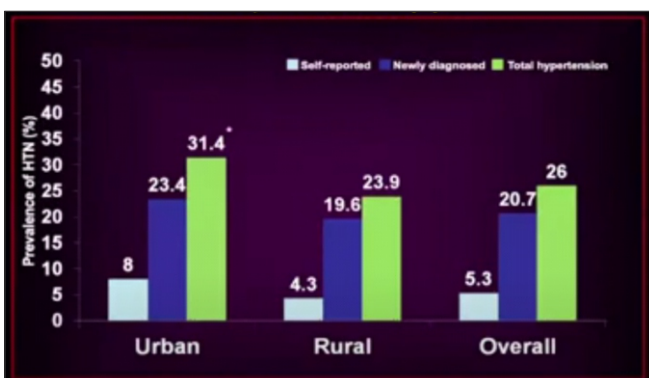
Relationship of Duration of Migration with Prevalence of Type 2 Diabetes and Related Metabolic Parameters Among Rural to Urban Migrants



Prevalence of abdominal obesity



Age Standardized Prevalence of Hypertension in Urban and Rural Population



Major Learning Outcomes of the Study

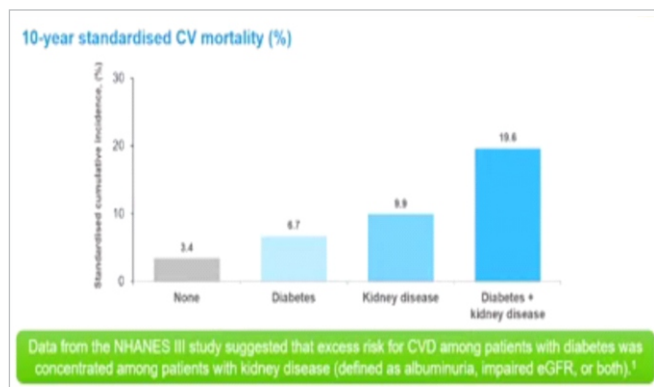
- The prevalence of diabetes is high in both urban and rural areas
- Explosion in diabetes is inevitable with increasing prevalence of pre-diabetes
- Only a third of those with diabetes have an HbA1c of <7%
- Only 16% of the known diabetic individuals reported doing SMBG
- Insulin use is extremely low
- Prevalence of hypertension, obesity and dyslipidemia are high
- Rural-urban migrants had higher prevalence rates of diabetes, hypertension and abdominal obesity than rural non-migrants
- The risk for diabetes was 2 times higher in rural-urban migrants compared to non-migrant rural dwellers
- The results from the ICMR study have important implications for cities and health systems, especially in developing countries like India

Unmet Needs in the Treatment of Diabetic Kidney Disease (DKD)

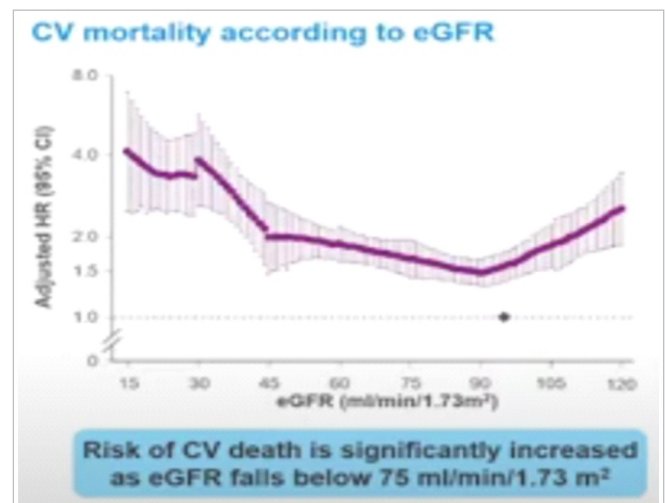
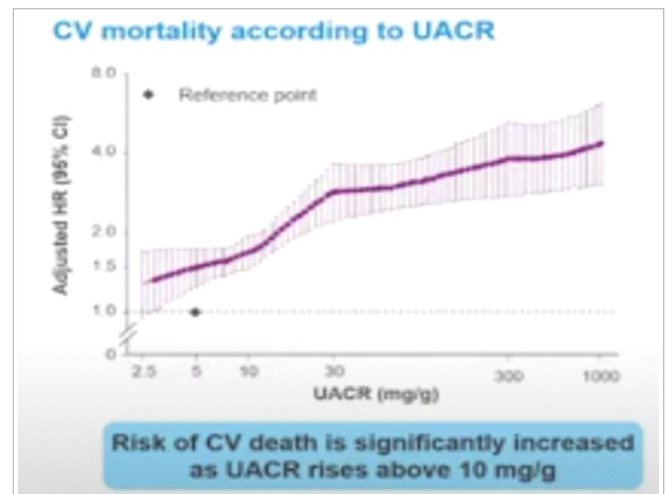
Dr. Shashank Joshi during his talk pointed out and highlighted the unmet needs in the treatment of DKD. An excerpt of his talk are presented below -

- Identification of unmet needs is important to delay the onset and progression of DKD
- Approximately 1/3rd of patients with diabetes will develop CKD
- Although the natural history of CKD and Type 2 diabetes varies, patients eventually progress to end-stage kidney disease
- Compared with healthy individuals, having CKD and diabetes can shorten the life expectancy by 16 years

Kidney Disease Approximately Doubles the risk of CV Mortality in Patients with CKD and Type 2 Diabetes Compared to Patients with CKD Alone



Risk of CV Events in Patients with Diabetes Increases as Albuminuria Progresses and eGFR Declines

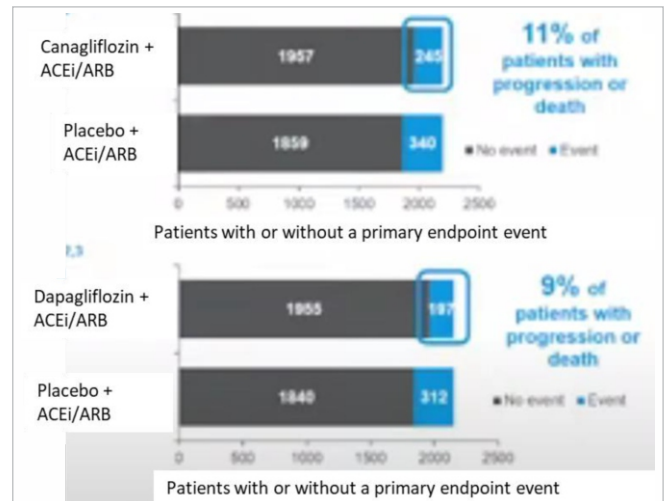
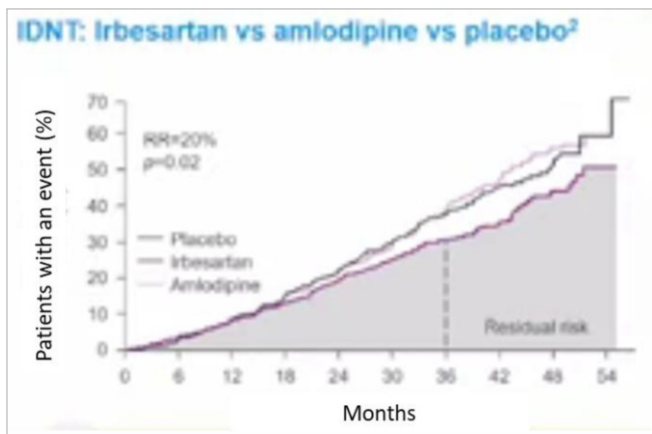
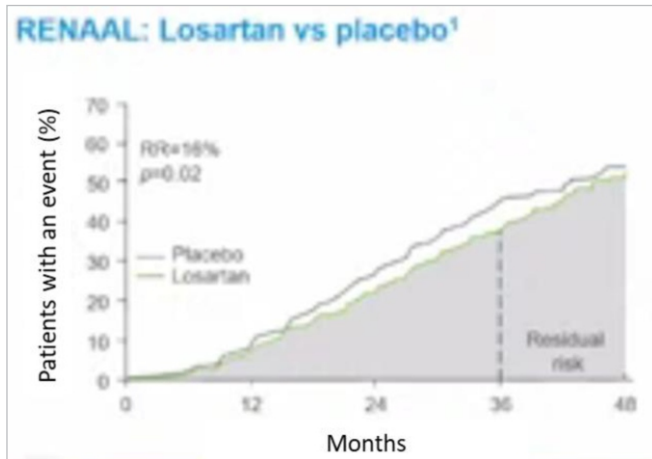


Diagnosis of CKD Relies on Assessment of Kidney Damage and/or Function

- Early-stage kidney disease is usually asymptomatic, requiring lab tests for detection
- Guideline-recommended lab tests to evaluate end stage kidney disease include eGFR (index of kidney function) and Albuminuria – UACR (marker of kidney damage)

- UACR and eGFR should be assessed annually in all patients with Type 2 diabetes regardless of treatment and twice annually in patients with UACR >30 mg/g and/or eGFR <60 ml/min/1.73m²

Patients with Type 2 diabetes and Advanced CKD are at risk of CKD Progression Even when Treated with Current Standard of Care Despite RAAS Blockade and SGLT2 inhibition, patients with Type 2 Diabetes and Advanced CKD are at-Risk of CKD Progression



Summary

- CKD in Type 2 diabetes significantly increases risk of CV morbidity and mortality over Type 2 diabetes alone
- Risk of CV events increases as CKD progresses
- Assessment of both albuminuria and eGFR is required for early CKD diagnosis and identification of patients at increased CV risk
- Improved early diagnosis of CKD through UACR screening may improve outcomes in patients with CKD and Type 2 diabetes
- Current treatments are associated with a high residual risk of cardiorenal events in patients with CKD and Type 2 diabetes

Self Monitoring of Blood Glucose (SMBG): Current Evidence and Implications for Clinical Practice

Dr. Nikhil Tandon during his talk highlighted the significance of SMBG in effective control of diabetes and it's complication. An excerpt of his talk are presented below -

SMBG Overview

- SMBG is an optimal way to confirm and appropriately treat hypoglycemia
- Provides feedback and results on behavioral and pharmacological interventions
- Can increase patient adherence and empowerment
- Provides insights on day-to-day fluctuations in glucose levels
- Helps intensify blood glucose control during physical activity, exercise, illness etc
- Detects clinically silent hypoglycemia

SMBG Points to Consider

- Accuracy of the detecting device
- Probability of analytical errors (glucostrips/ glucometers/interfering substance)
- Possible errors in enzymatic methods
- Sources of errors beyond analytical (contaminated surface/sampling error/site/ others like hypotension/incorrect reading/ incorrect recording/incorrect transmission)

Benefits of SMBG in Type 1 Diabetes

- In DCCT trial, intensive insulin therapy guided by frequent SMBG delayed the onset and slowed the progression of microvascular complications compared with conventional therapy in patients with Type 2 diabetes
- More structured, focused SMBG intervention in sub-optimally controlled patients can provide significant improvements in HbA1c

Benefits of SMBG in Type 2 Diabetes

- Kumamoto study showed that intensive

insulin therapy guided by SMBG can reduce the risk of microvascular complications

- Diabetes Outcomes in Veterans Study (DOVES) showed intensified SMBG improved glycemic control in patients whose SMBG compliance exceeded 75% or those with baseline HbA1c > 8%

Evidence of SMBG in Type 2 Diabetes

- In meta-analyses of trails comparing SMBG with no SMBG in **non-insulin treated patients** with Type 2 diabetes, there was improvement in A1c in the short term (Cochrane Database Sys Rev 2010)
- In economic analysis, use of SMBG in **non-insulin-treated Type 2 diabetes** was associated with diminished initial quality of life; considered unlikely to be cost effective (Simon et al., BMJ 2008)

ADA 2020 Recommendation on Frequency of SMBG in Type 1 Diabetes

- At least 4 times daily (before meals and at bedtime), occasionally post-prandially (90 10 180 minutes after meals), prior to exercise and occasionally at 3 AM
- The frequency of testing may vary based on individual needs
- Patients with hypoglycemia unawareness may need to test more frequently; prior to driving or operating any machinery, watching small children, and other activities where compromise of cognitive function may be dangerous
- When low blood glucose is suspected and after treating low blood glucose (until glucose levels are normal)
- This can require checking as often as 6 to 10 times daily in some patients on specific days, but the frequency can vary between

individuals and in the same individual on different days

Record Keeping in SMBG

The record book is required at the time of consultation and should contain time and date of

- Glucose levels
- Carbohydrate intake
- Insulin dosage
- Note of special events affecting glycemic control (e.g., illness, exercise, menses, alcohol intake)
- Hypoglycemic episodes, description of severity, and potential alterations in the usual routine to help explain the cause for the event
- Episodes of hyperglycemia, ketonuria/ketonemia

Summary

- SMBG is fundamental for optimal diabetes self-management
- SMBG devices have become smaller, more accurate, require less blood
- Standards required to gain FDA clearance have become more stringent and more accurate glucometers are now available in the market
- SMBG is only helpful if the patient and the caregivers know how to view, interpret and act on their results
- The recommended frequency of SMBG should be individualized



Is Diabetes An Inflammatory Disease? Biomarkers Tell the Story

Dr. A Ramchandran during his presentation discussed the role of biomarkers and their significance in diabetes management. Few salient points from his talk are presented below -

- Biomarkers are not only predictors of diseases, but are also involved in the pathogenesis and therefore modifying them has a potential to change the course or onset of disease like diabetes
- An ideal biomarker should refine identification of those at risk of a disease or progression, improve prediction of complications of disease and/or guide and help tailor responses to different therapies

Biomarkers in Diabetes

- Biomarkers for diabetes should predict onset of diabetes in non-diabetic subjects
- Biomarkers for complications should identify subjects with high risk of developing complications of diabetes, namely CVD and or micro-angiopathy
- In some instances a biomarker may be added to conventional risk variables to improve power of association or prediction

Biomarkers in Prediction of Diabetes in Studies by Dr. Ramchandran and Colleagues Include

- Adiponectin
- Retinol binding protein-4
- Gamma-glutamyltransferase (GGT) & alanine transaminase (ALT)
- Interleukin-6
- Leptin
- Vistafin
- Fetuin-A

Study Outcomes Showing Role of Biomarkers in Predicting Diabetes

- Low adiponectin concentration is indicative of low insulin sensitivity and is a strong independent predictor of future development of diabetes in subjects with IGT. Adiponectin may have a central role in the pathogenesis of Type 2 diabetes
- Retinol binding protein 4 levels are shown to independently associated with diabetes after adjusting for known metabolic covariates such as GGT, triglycerides, BMI and insulin resistance
- GGT is an independent predictor of incident diabetes and combination of GGT and FPG offers a simple and sensitive tool to identify subjects at high risk of developing diabetes

Mechanistic Role of Biomarkers in Pathophysiology of Diabetes

- Adiponectin improves peripheral insulin sensitivity
- Interleukin-6 alters insulin signaling in hepatocytes/adipocytes and impaired energy regulation in CNS
- Leptin is related to insulin resistance

VISFATIN / NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE (NAMPT) / PRE-B CELL COLONY ENHANCING FACTOR
Source of Origin: Visceral Adipose (Adipokine)

Tissue, Macrophages, Leukocytes, Hepatocytes

Biological Significance: Regulated by hormones and cytokines influencing glucose homeostasis, correlated with markers of obesity, parallel increase with insulin in hyperglycaemic state.

FETUIN A / ALPHA - 2 HEREMANS -SCHMID GLYCOPROTEIN

Source of Origin: Liver (Hepatokine)

Biological Significance: Elevated levels in obesity, T2DM, metabolic syndrome, NAFLD. Correlated with parameters of metabolic homeostasis and pro / anti inflammatory factors



Combination of biomarkers increases the risk prediction of Diabetes.

Variables	β (SE)	OR (95%CI)
Visfatin (ng/ml)	1.88 (0.56)	6.56 (2.21-19.5)
Fetuin-A (μ g/ml)	0.03 (0.01)	1.01 (1.01 – 1.04)
Visfatin ng/ml.+FetuinA μg/ml	2.54 (0.64)	12.63(3.57-44.63)

Influence on the incidence of diabetes was higher when elevated levels of visfatin and fetuin-A co-existed

Conclusion

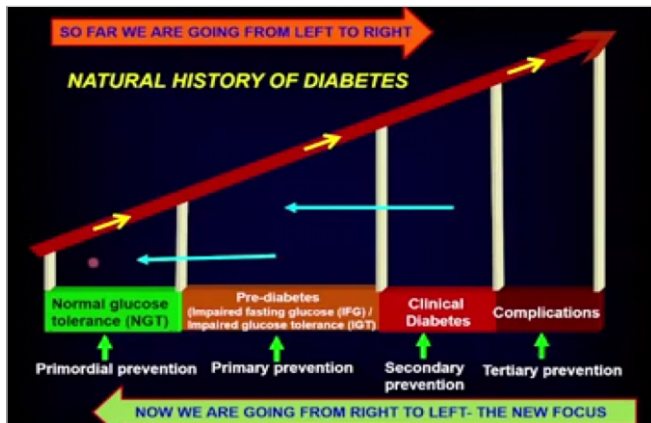
- The high levels of pro-inflammatory cytokines/ biomarkers in those who develop diabetes indicate that they have a role in the pathogenesis of diabetes

- Therefore diabetes is an inflammatory disease
- They help in identifying people with high risk of diabetes and targeting them may prove useful in prevention of diabetes
- The association of some of these biomarkers with CVD probably indicate that they have a role in the development of complications of diabetes
- The future success of biomarker strategies may depend on the discovery of new biomarkers to complement the best existing ones

Reversal of Diabetes: How, When and for Whom?

Dr. V Mohan shared insights on an intriguing topic on various aspects related to the reversal of diabetes. An excerpt of his talk are presented below -

- Reversal of diabetes is possible up to the clinical stage and not from complications stage
- Also, certain forms of diabetes are currently not possible to reverse including Type 1



Examples of Reversal of Type 2 Diabetes

- After severe weight loss
- Post gestational diabetes
- After bariatric surgery
- Stress induced diabetes
- Drug induced diabetes

Definition of Remission/Reversal of Diabetes

Guidelines for remission	Partial or complete?	Glucose lowering agents	Glycemic parameters	Duration
ADA	Remission	No diabetes medication	HbA1c<6.5% and/or FPG<126mg/dL	>3 months
DIRECT / DIADEM-1	Remission	No diabetes medication	HbA1c<6.5%	>1 year

2 Proposed Diet Routes to Achieve Reversal of Diabetes

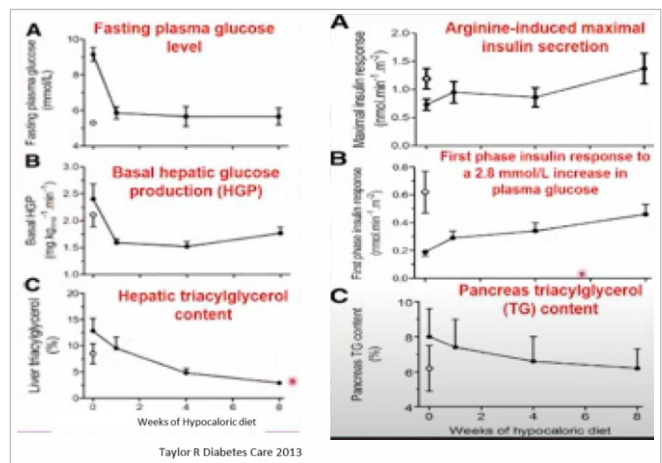
- Low Carbohydrate diet (LCD) – less than 10% carbohydrate or 20-50 gm/day and replace it with fat however it's extremely difficult to implement.

- Very low calorie diet (VLCD) – fewer than 800 calories/day for not more than 12-weeks

Can VLCD Reverse Diabetes

- Within 7 days of instituting a substantial negative calorie balance by either dietary intervention or bariatric surgery, fasting plasma glucose levels can normalize
- This rapid change relates to a substantial fall in liver fat content and return of normal hepatic insulin sensitivity
- Over 8 weeks, first phase and maximal rates of insulin secretion steadily return to normal, and this change correlates with the decreased pancreatic fat content

Effects of VLCD on Diabetes



TRIVIAS

- It is likely that Type 2 diabetes is caused by less than 1gm of fat in pancreas
- 15 kgs weight loss is needed to reverse diabetes

Conclusions

- Almost half of obese/overweight individuals with Type 2 diabetes with <6 yrs duration who had lost 10kgs or more, achieved diabetes remission



- Recovery of first-phase insulin response defined responders, sustained at 12 mos
- First study to suggest that the ability of beta cells to recover, persists after diagnosis, and is linked to Type 2 diabetes duration

Who Does Reversal Works for ?

Remember the ABCDE

- **A** – A1c not very high
- **B** – Body weight with high BMI
- **C** – C-peptide high indicating good insulin secretion
- **D** – Duration of diabetes to be short
- **E** – Enthusiasm of patient who should be motivated to follow the directives

However Following Points Should be Kept in Consideration

- Effectiveness beyond 2 years is limited
- More data is needed in an ethnically diverse population
- Most importantly 're-reversal of diabetes' occurs in large percentage of people

Conclusion

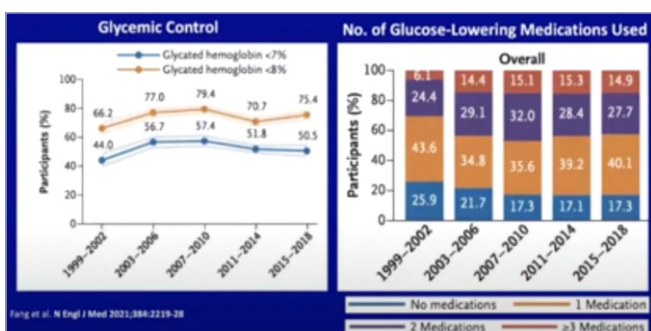
- Conversation with people with Type 2 diabetes should include discussing remission
- The dietary approach to achieve remission is less important. VLCD and LCD can be equally effective
- Programs supporting people towards achieving remission need to be structured and should offer continued, regular support, including the involvement of dietitians for long-term success
- In many cases, re-reversal of diabetes occurs and should be managed accordingly

American Diabetes Association Update for Management of Type 2 Diabetes

Dr. Guillermo Umpierrez discussed on the ADA updates regarding prevalence, trends and algorithm for the management of diabetes and its complications. An excerpt of his talk are presented below -

- There is a trend in decrease in prevalence of diabetes in the recent past in the adult US population after an incremental trend for around 20 consecutive years
- The decrease can be attributed to increased awareness, education programs, improved lifestyle
- The same trend was observed in children and adolescents
- Similar observations are recorded even in terms of trend of diabetes complications including MI, stroke, amputation, hypoglycemia, ESRD and the CV events

Trends in Diabetes Treatment and Control in US Adults, 1999-2018

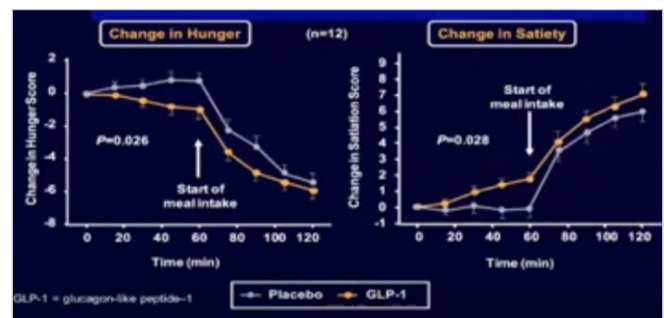


- Metformin is the most prescribed anti-diabetic agent in the world
- SUs, even after the launch of newer generation drugs, remains the second most prescribed oral antidiabetic drug
- In 2018, only 7% of patients with diabetes were treated with SGLT2i and GLP-1 RA

Test	Glycemic Control Targets		
	ADA	AACE	ACP
A1C	<7%	≤6.5% ³	7-8%
FPG	80-130 mg/dL	<110 mg/dL ³	Targets closer to 7% may be appropriate for patients with >15 year life expectancy and who prioritize more intensive control over risk, cost, burden
PPG	<180 mg/dL	<140 mg/dL ³	Clinicians should consider deintensifying pharmacologic therapy in patients with T2D who achieve HbA1c < 6.5%.

Additional Benefits of GLP-1 RA Class of Drugs Beyond Glycemic Control

- Delays gastric emptying
- Reduces hunger and enhances satiety
- Exerts positive effect on weight loss
- Beneficial effect on BP parameters
- Demonstrated positive CV outcome data
- Shows favorable renal profile



ADA 2021 Recommendation for Intensifying Injectable Therapies

- If injectable therapy needed to reduce HbA1c, consider GLP-1 RA in most patients prior to insulin
- If above HbA1c target, add basal insulin (at 0.1-0.2U/day)

Studies with CV Outcomes with SGLT2i

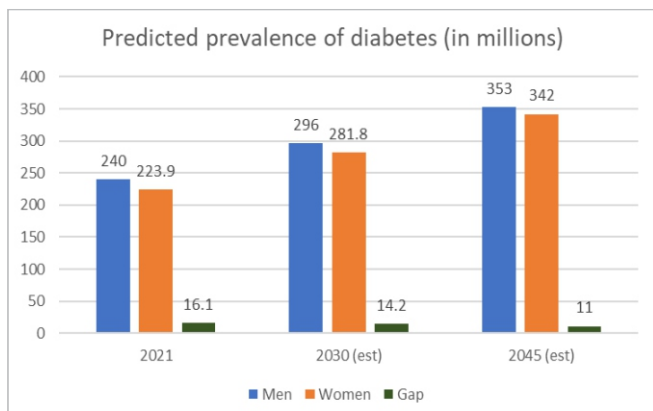
	MACE	CV Death	HHF
	HR (95% CI)	HR (95% CI)	HR (95% CI)
EMPA-REG OUTCOME ¹	0.86 (0.74, 0.99)	0.62 (0.49, 0.77)	0.65 (0.50, 0.85)
CANVAS Program ²	0.86 (0.75, 0.97)	0.87 (0.72, 1.06)	0.67 (0.52, 0.87)
DECLARE-TIMI 58 ³	0.93 (0.84, 1.03)	0.98 (0.82, 1.17)	0.73 (0.61, 0.88)
VERTIS CV	0.97 (0.85, 1.11)	0.92 (0.77, 1.11)	0.70 (0.54, 0.90)

Women and Diabetes: Myths, Misconception and Realities

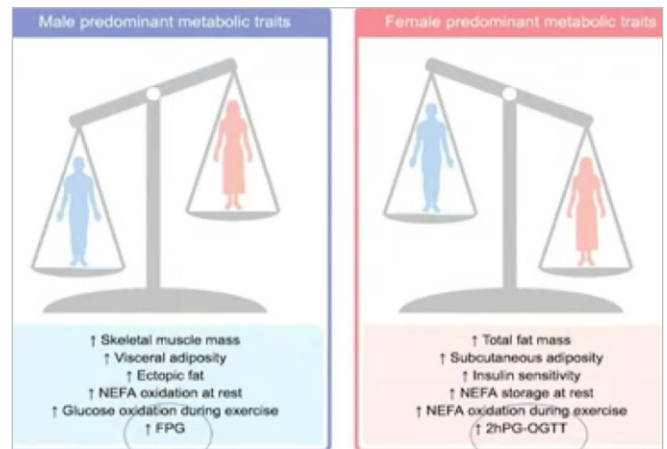
Dr. Usha Shiram busted the myths and misconception related to various aspects of management of diabetes in women. An excerpt of her presentation are mentioned below -

- Major focus on women and diabetes started from 2017 with the theme of “Women and diabetes: our right to healthy future
- **Common myths and misconceptions**
 - Diabetes is more prevalent among men
 - Diabetes is caused by same genetic and/or environmental factors in men and women
 - Heart diseases are also more prevalent among men
 - Diabetes care is largely ignored by women
 - All diabetes are same
 - All women are same
 - All treatments work the same way
 - What approach is good for men will be good for women too

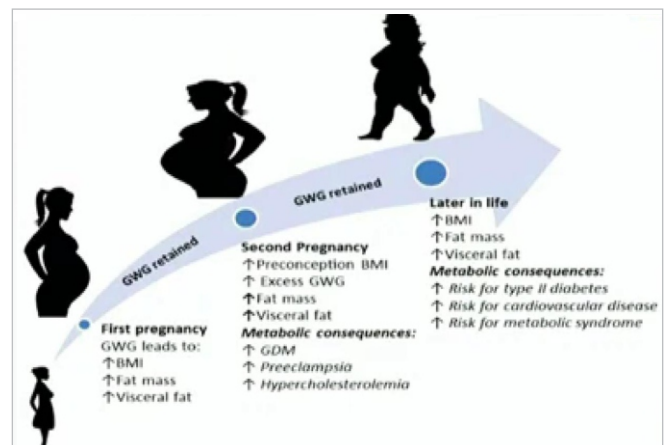
1. Gap Between Men and Women Prevalence of Diabetes is Predicted to Get Closure and Closure in the Next 25 years



2. The metabolic Traits are Different and Screening for Post-prandial or HbA1c Rather Than Only FPG or Random is Necessary to Early Diagnose Women with Diabetes



3. Gestational Weight Gain (GEG) Persists in Majority of the Women Resulting in Incremental Long-Term Risk of Developing Diabetes and Its Complications



4. Mortality rates are much higher in women than men, which is mainly due to higher risk of vascular disease associated with diabetes in women compared to men, including CAD, Stroke, CKD, ESRD



Mortality over 2 decades

years by sex

Mortality rate per 100,000 persons	1995		2005		2015	
	M	F	M	F	M	F
Globally	12.9	15.9	16.2	19.1	20.1	21.1
High-income countries	15.0	18.9	18.6	21.2	18.7	19.6
Middle-income countries	13.4	18.0	18.8	21.5	23.5	25.8
Low-income countries	9.8	10.0	10.3	10.9	11.9	12.7

M Males, F Females

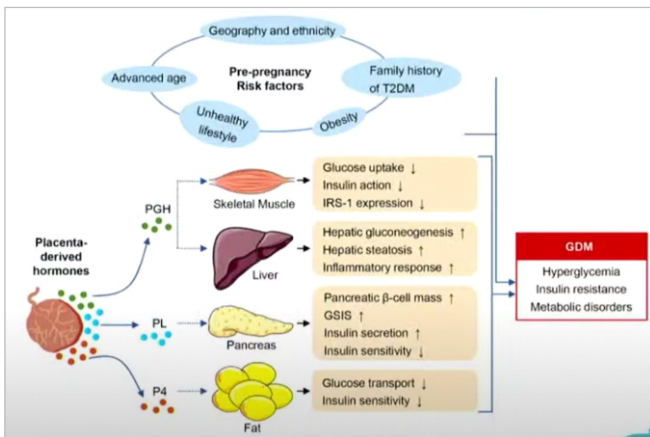
Risk factors for cardiovascular disease in women

Well-established, sex-specific, and under-recognised risk factors

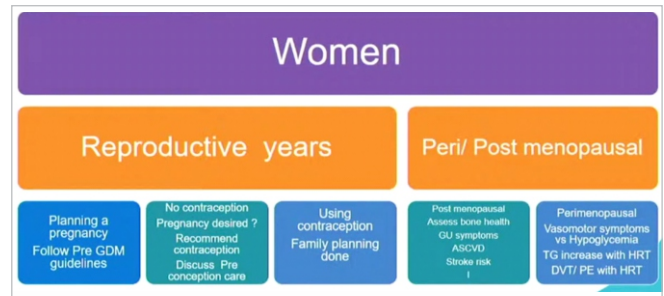


Women do spend more time in pre-diabetes state due to late diagnosis resulting from delayed (around 2 years) development of visceral obesity as compared to men

Pregnancy is another unique aspect in women related to the development of diabetes and related complications



Points to Consider While Tailoring Treatment in Women



The Paradox

- 85% Of women agree that regular medical checkup is a must to prevent and control diabetes
- 50% Of the surveyed women have not had themselves examined for diabetes
- 50% Of women believe that exercise and yoga are beneficial in controlling diabetes
- 35% Of them admit to lack of exercise in their daily life
- 35% Of women do not consult a specialist when suspected of diabetes but consult friends

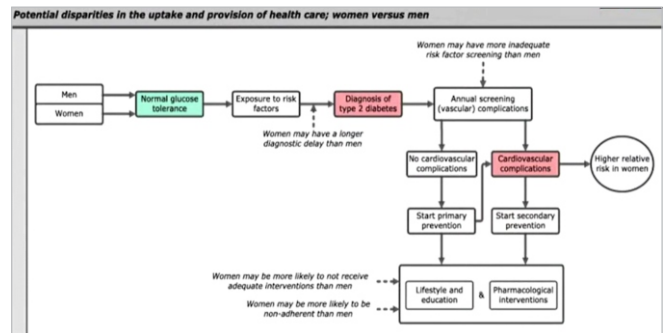
Lack of Management

- 60% Of Indian women are aware of diabetes linked to pregnancy (gestational diabetes)
- 44% Of women are cognizant of prediabetes
- 70% Of women acknowledge that regular meals and regular exercise are important for a healthy body
- 60% Of them confessed to skipping meals often
- 20% Of them say their eating habits are irregular

Despite these awareness levels, Indian women remain hesitant to adopt lifestyle and make dietary adjustments

Diabetes can be prevented through simple lifestyle and dietary choices

Proper testing, treatment, lifestyle changes, healthy eating, walking and other physical activities are beneficial in preventing diabetes





Care of People with Diabetes Post COVID-19 in Primary Care

Dr. Urman Dhruv discussed an interesting and relevant topic of providing primary care in post-COVID patients with diabetes. Few highlights of his presentation are mentioned below -

- People with diabetes have been disproportionately affected because of COVID
- Around 12-25% of COVID patients had diabetes
- Diabetes was found to have 2-folds increased association for COVID
- Severity of COVID was also found to be higher in patients with hypertension and chronic kidney diseases

Challenges in Managing COVID in Diabetic Patients

- More burden on patients and physicians
- Balance between hypo and hyper is difficult to manage
- Accessibility to medicines, diagnostic tools and manpower is very low
- POC is not easily available

Patient Related Challenges

- Inadequate fluid and food intake
- Volume depletion
- Drug induced side effects
- Steroid induced hyperglycemia
- Ketotic milieu
- Hypoglycemia unawareness
- Failure to get help which was otherwise 'regularly' available (like neighbours/friends)
- Patients are reluctant to visit clinics resulting in underdiagnosis – there was reduction in new diagnosis cases of diabetes over previous year. Even HbA1c monitoring and other care processes like lipid check) have been reduced

Management of Diabetes in Post-COVID Era

- Failure to seek help
- Failure to attend hospitals
- Neglecting symptoms of other diseases till late
- Investigations and treatment in hospitals delayed due to COVID protocols
- Overall physical and mental health of patients can also decline due to socioeconomic impacts as shown with increased levels of anxiety in diabetic patients
- Ongoing inflammation after resolution of COVID
- COVID is also linked to fluctuating levels of glucose
- There is always a future risk of readmission as full recovery is not sure

First Priority – Risk Stratification Tools

- **Identify high risk patients early to stratify risk. These patient class includes patients having**
 - HbA1c > 10%
 - Uncontrolled hypertension
 - Complete unawareness of hypoglycemia (Gold score 7 if available)
 - History of severe hypoglycemia in last 12 months
 - Diabetes related admission for DKA or unstable cardiac or cerebrovascular diseases in last 12 months
 - eGFR < 30 min/mL
 - Active diabetic foot disease

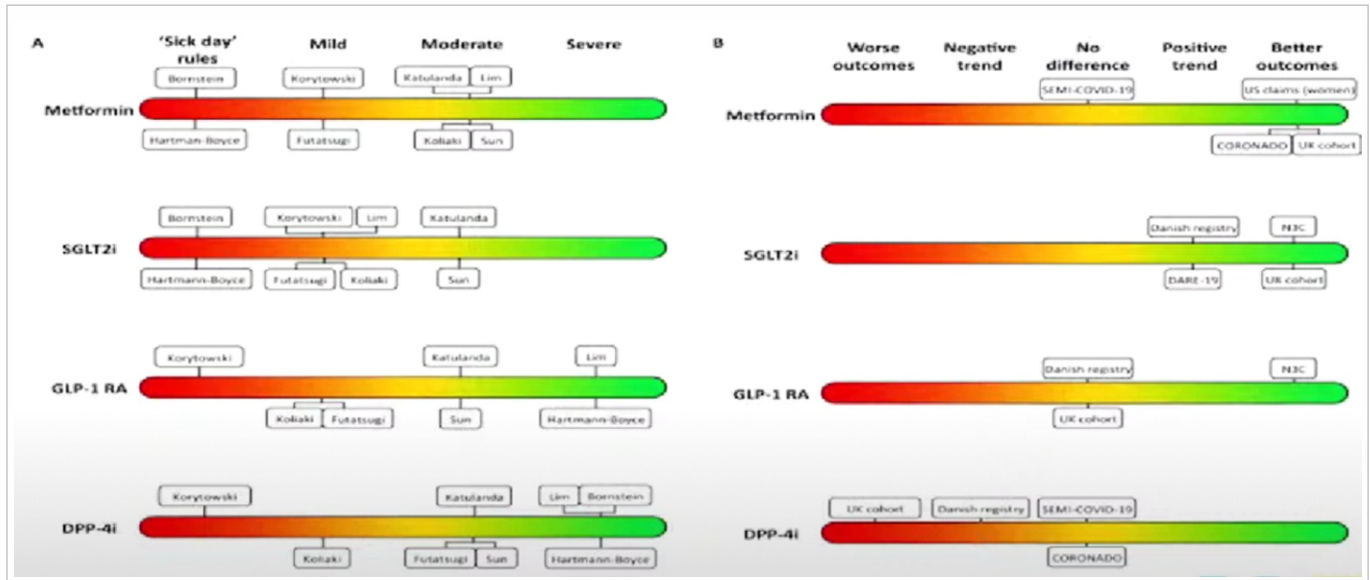
Opportunity to Modify Management

- Opportunity to change management as patients will be willing to adjust to minimize risk associated with COVID



- Opportunity to change the drug regimen
- Encourage use of POC including SMBG/digital BP instrument
- Reemphasize lifestyle changes including alcohol and smoking cessation and encourage exercise and healthy eating habits

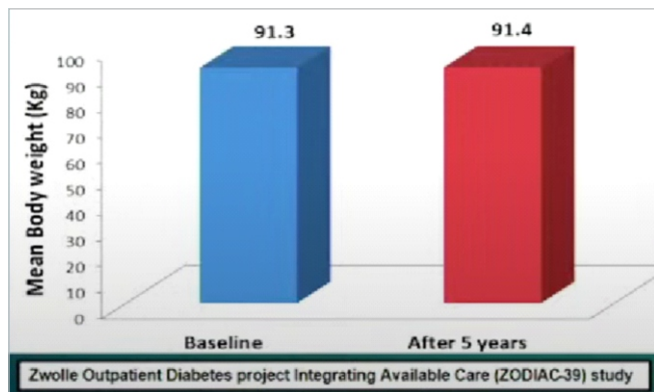
Pharmacotherapy Recommendations



Type 2 Diabetes: Recent Clinical Trials Translating into Practice

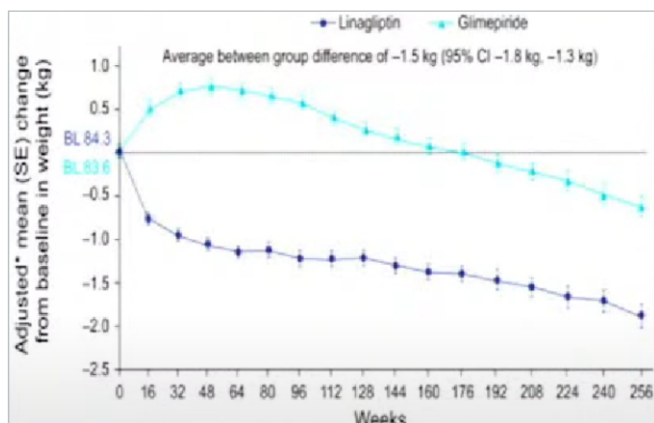
Dr. Anuj Maheshwari shared the practical aspects and application of the outcomes of clinical trials in diabetes. An excerpt of his presentation are mentioned below -

- Existing molecules (like Metformin and SUs) continue to be studied extensively and newer data highlights the benefits of these drugs even in recent light of introduction of newer molecules
- Strict glycemia control can be maintained with modern sulfonylurea and metformin in a real life setting without relevant weight changes



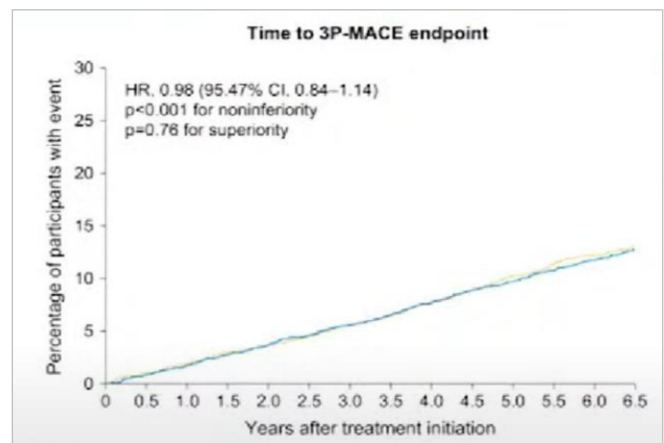
CAROLINA Trial Reassured Body Weight Neutrality with Modern SU

- By the end of trial period, both the groups had reduction of weight from baseline



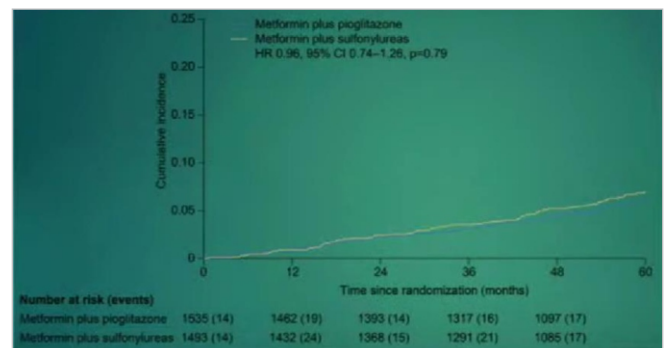
CAROLINA Trial Also Reassured the CV Safety of Modern SU

- There was no significant difference in occurrence of 3P-MACE in patients treated with Glimepiride as compared to those treated with Linagliptin



TOSCA.IT Trial – Focusses on the Long-Term CV Safety of Modern Sus

- The incidence of CV events were similar in patients treated with SUs (mostly Glimepiride and Gliclazide) and those treated with Pioglitazone as an add-on to Metformin



Review of 177 RCTs Showing Cost-effectiveness of SUs – Genere et al., Annals of Int Med, 2018

- In patients with Type 2 diabetes inadequately controlled on metformin monotherapy,

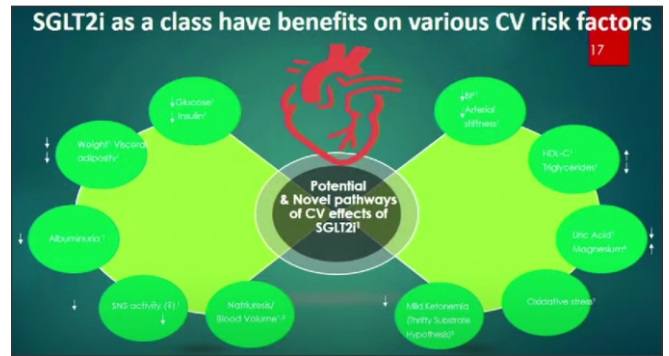
sulfonylureas were the most cost-effective add-on therapy

SU – Stands Strong As The Second Line

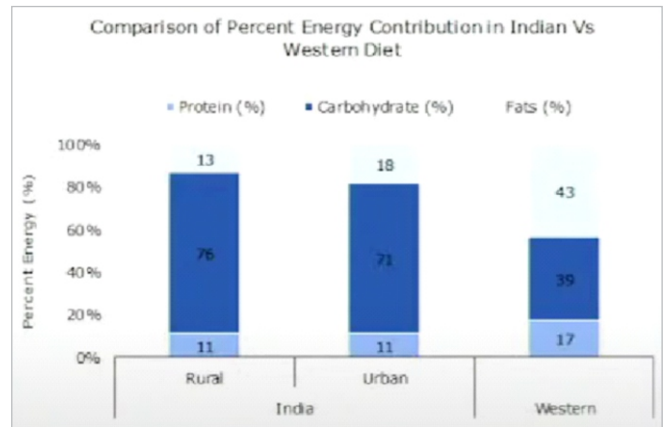
Second-Line Agents for Glycemic Control for Type 2 Diabetes: Are Newer Agents Better?

Diabetes Care 2014;37:1338–1345 | DOI: 10.2337/dc13-1901

Conclusions:
Use of sulfonylurea as second-line therapy for type 2 diabetes generated glycemic control and QALYs comparable with those associated with other agents but at lower cost. The regimen with sulfonylurea resulted in the longest time to insulin dependence.



Higher Post-Prandial Glucose Excursions in Indian Population



Pioglitazone – Best Insulin Sensitizer

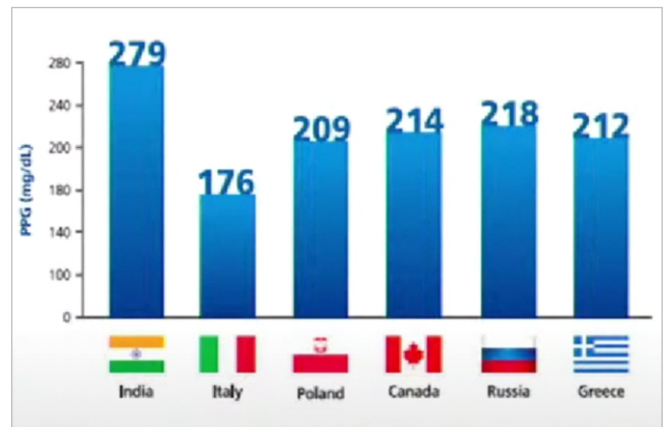
Pros

- Rare hypoglycemia
- Relatively higher A1C efficacy
- Durability
- ↓ Triglycerides
- ? ↓ CVD events (PROactive, pioglitazone)
- ↓ Risk of stroke and MI in patients without diabetes and with insulin resistance and history of recent stroke or TIA (IRIS study)

Cons

- ↑ Weight
- Edema/heart failure
- Bone fractures

Important agent from Indian perspective due to the high prevalence of Insulin Resistance

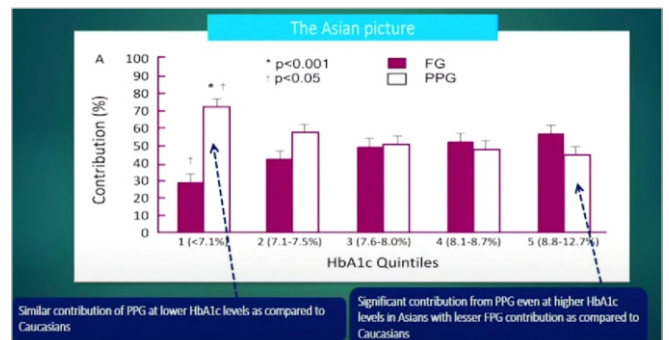


Consensus Statement on Management of Post-Prandial Hyperglycemia in Clinical Practice in India

- AGIs have a crucial role in Indian T2DM patients due to the high carbohydrate diet.
- AGIs effectively control PPHG and provide additional benefits.
- AGIs can be used as first-line drug in early type 2 diabetes, as well as in combination with nearly all established oral antidiabetic and insulin
- AGIs have favorable effect on PPG, FBG and HbA1c which reflect the overall improvement in glucose control of the patients

Arora D et al. Journal of the Association of Physicians of India, Vol. 63, August 2015.

Significant Contribution from PPG Even at Higher HbA1c Levels in Asians



VERIFY. Primary endpoint

Time to initial treatment failure
two consecutive values of HbA1c ≥7%

HR 0.51 [0.45, 0.58]; p<0.0001.

More people benefit in longer term

Sequential
Combination

Initial failure. ~15% never achieve control

Median time to treatment failure
Met monotherapy: 36.1 months
Met + Vilda combo: >61.9 months

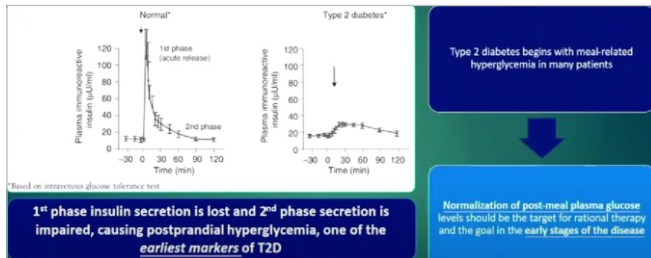
Early combo greatly extends time in good control

Patients at risk	0	6	12	18	24	30	36	42	48	54	60
Metformin + placebo	989	937	733	661	576	503	434	377			
Metformin + vildagliptin	983	960	862	815	752	671	597	551			

Matthews et al. Diabetes Obes Metab 2019. DOI: 10.1111/dom.13800; Matthews et al. Lancet 2019. http://dx.doi.org/10.1016



Type 2 Diabetes Begins with Meal-Related Hyperglycemia in Many Patients



Way Forward after Merging Evidences with Experiences

- Make the patient follow diet
- Ensure patient exercise regularly
- Up-titrate metformin
- Use modern SUs / choose right gliptin
- Know the pros and cons of Pioglitazone and AGIs
- Identify right place for SGLT2i in our patients
- Prefer combination therapy
- Patient adherence to treatment in most important
- Keep a check whether the patient is achieving the goal

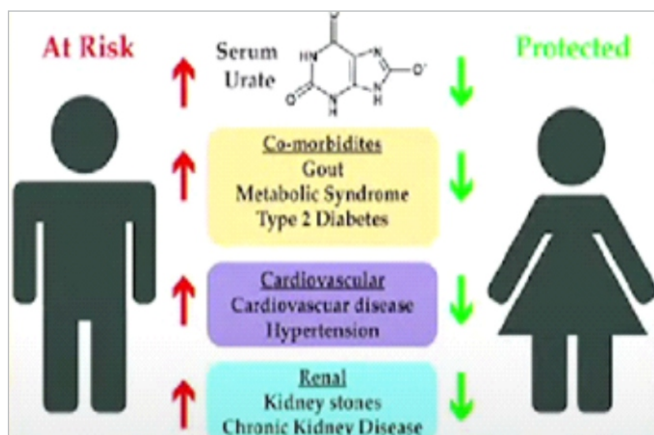
Diabetes Mellitus and Hyperuricemia

Dr. V K Abhichandani in his talk highlighted the correlation and underlying link between diabetes and hyperuricemia and ways to deal with it. An excerpt of his presentation are mentioned below-

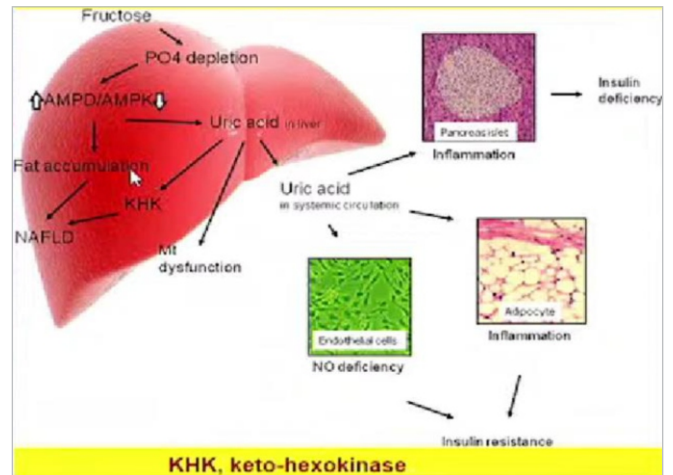
- Hyperuricemia has been attributed to hyperinsulinemia in metabolic syndrome and to decrease uric acid excretion in kidney dysfunction
- It is now also being acknowledged as an important mediator of metabolic syndrome, renal disease, and cardiovascular disorders
- Its association with nephrolithiasis and preeclampsia is widely accepted
- Intracellular uric acid, which leads to ATP depletion and mitochondrial injury, and reduced nitric oxide synthesis, is the major cause for complications like nephropathy

Sex Difference in Urate Handling

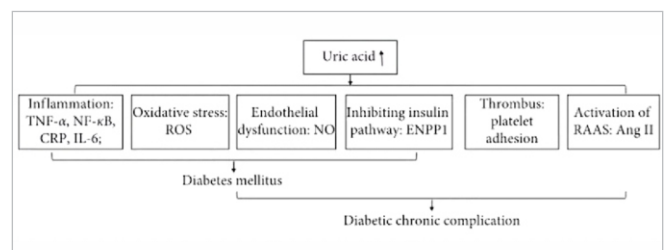
- Males tend to have higher serum urate levels than women and therefore have an increased risk of associated co-morbidities



Uric Acid: Potential Mechanism for Insulin Resistance and Diabetes



Pathological Mechanism of Uric Acid on Diabetes and Its Chronic Complications



Commonly Used Drugs Can Cause Increase in Uric Acid Levels

- Diuretics
- AKT – Pyrazinamide and Ethambutol
- Low-dose aspirin
- Immuno-suppressant drugs like Cyclosporin
- Nicotinic acid
- Cancer chemotherapy
- Levodopa
- High-dose TRT



Cardiometabolic drugs which can reduce uric acid levels

- OADs (Metformin/SGLT2i)
- Lipid lowering drugs (Statin/Fibrates)
- Appetite suppressant (Orlistat)
- Anti-platelets (high-dose Aspirin)
- Anti-hypertensives (Losartan, Amlodipine)

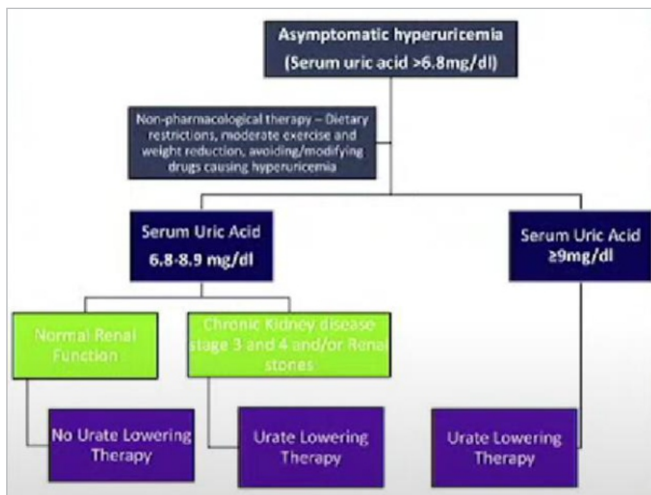
Non-Pharmacological Management Aspect of Hyperuricemia

Harmful	Beneficial	No restriction
Animal protein: Red meat, Organ meat(Liver), Shellfish & Seafood	Coffee, caffeinated drinks in moderation	Vegetable protein: peas, lentils, spinach, beans, mushroom, asparagus
Beer & Liquor	Cherries	
Sweetened soft drink, juices, fructose & table sugar	Vitamin C	Red wine in judicious quantities
Sudden weight loss	Gradual weight reduction	
Dehydration	Exercise in moderation	
Extremely vigorous exercise		

Summary

- Uric acid is a risk factor for the development of metabolic, renal and cardiovascular diseases
- The intracellular uric acid seems to be more pathogenic
- Both hyperuricemia and prediabetes are associated with purine-rich food and patients need to be advised on appropriate diet
- The prevalence of hyperuricemia is common among patients with obesity, long duration of diabetes, increased diastolic blood pressure and excess alcohol consumption
- There is a need to raise awareness of lifestyle modifications, healthy behavior and early diagnosis of hyperuricemia in patients with Type 2 diabetes

Algorithm for the Management of Asymptomatic Hyperuricemia



Glycemic Pentad

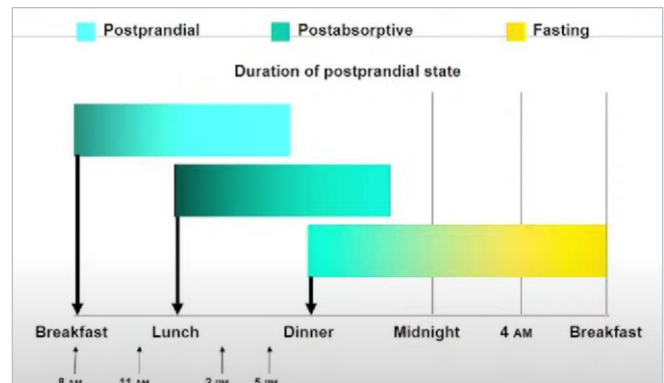
Dr. Ami Sanghvi discussed during the meeting, the evolving concept of glycemic pentad to provide comprehensive care in diabetes. An excerpt of her talk are presented below -

- The management of diabetes is evolving from conventional triad – HbA1c, FPG and PPG to pentad including variability and quality of life (QoL) – which is a measurable target
- This early glycemic pentad highlighted the importance of patient-reported outcomes and underlined the biopsychosocial model of health of diabetology
- This pentad was patient-centric and was meant to achieve better outcomes



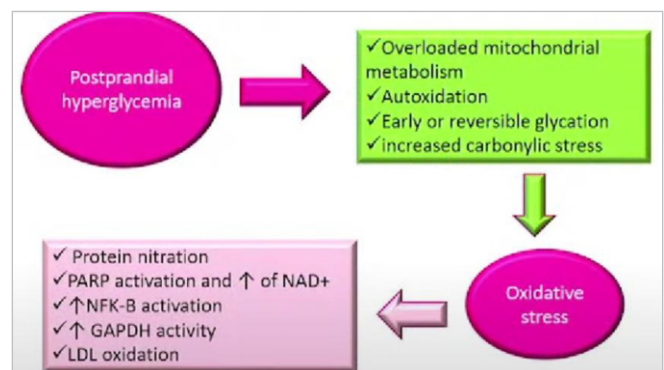
Various Components of Pentad

1. FPG – “Fix Fasting First” is the ideal approach
2. PPG – Is critical as Type 2 diabetic patient may spend more than 12 hrs a day in post-prandial state



Various Components of Pentad

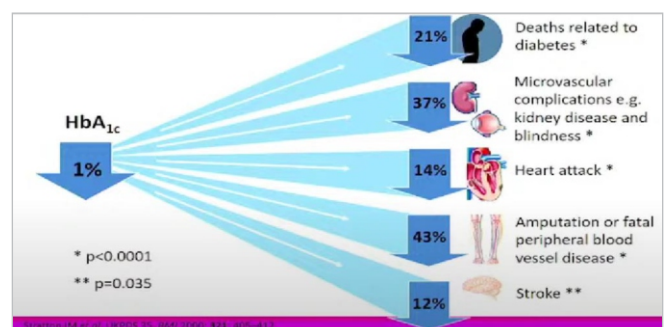
- PPG – leads to increased oxidative stress through various mechanisms



Various Components of Pentad

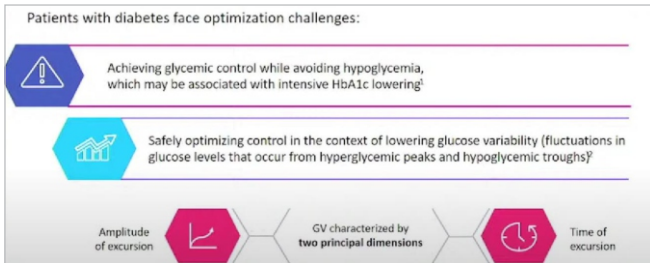
3. HbA1c – Tight glycemic control is known to reduce complications

Epidemiological Extrapolation Showing Benefit of 1% Reduction in Mean HbA1c

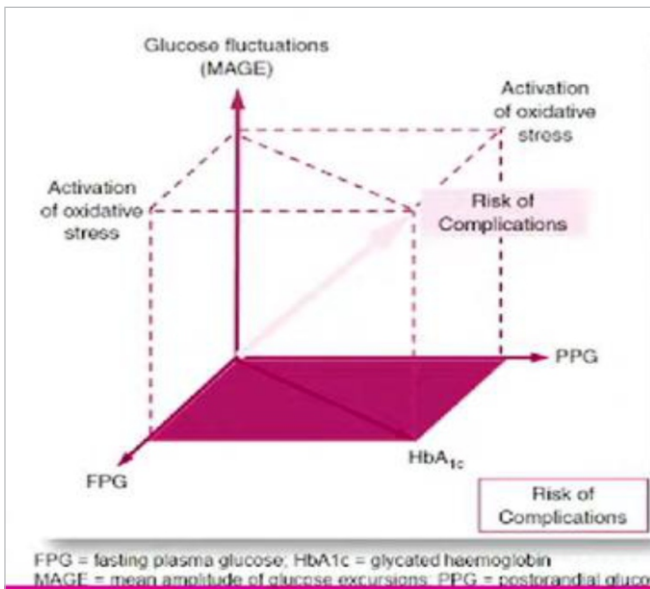


Various Components of Pentad

4. Glycemic variability – Going beyond HbA1c



Impact of Hyperglycemia and Glucose Fluctuations on the Risk of Complications



Various Components of Pentad

5. Quality of Life (QoL) –

WHO Definition

Broad ranging concept affected in a complex way by the person’s physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment

CDC Definition

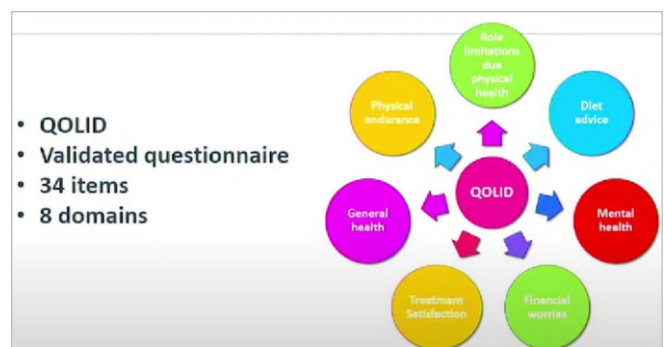
Health Related QoL is defined as an individual’s or group’s perceived physical and mental health over time

- QoL perception can get affected by person’s background including socioeconomic status, dietary and lifestyle habits, gender, and culture
- QoL in diabetes could be affected by “Disease-derived” factors (duration of diabetes and emergence of complications) or “Therapy-derived” factors (adverse events, cost, lifestyle restrictions imposed by the treatment)

Importance of QoL



QoL instrument for Indian Diabetic (QoLID) Patients



Management of Glycemic Pentad

- Improve diet compliance by individualizing diet therapy
- Encourage regular physical exercise
- Provide self-management education and support

- Judicious use of anti-diabetic agents with abilities to reduce components of glycemic pentad

Alternate Glycemic Pentad / Hexad

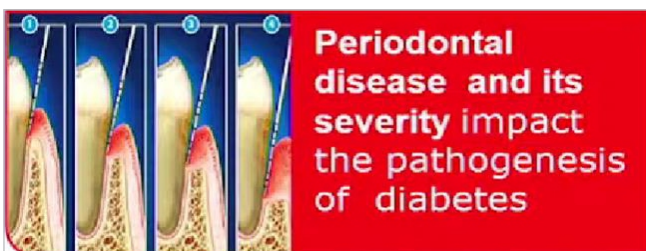
- As QoL is not a glycemic parameter in strict sense, an alternate pentad is proposed which replaces QoL with minimal hypoglycemia
- Thus, in this alternate pentad all five investigations listed are related to glycemia, are independently related to cardiovascular outcomes and are important targets of glucose-lowering therapy
- Later with an objective of enhanced safety and tolerability, another parameter was proposed to the above list – Nocturnal hypoglycemia, making it a hexad or Glycemic Sixer

Diabetes & Oral Health

Dr. Manoj Chawla highlighted the importance of oral health in diabetes. An excerpt of his talk are presented below -

- Periodontitis is a chronic inflammatory disease triggered by bacterial infection
- Like diabetes Periodontitis is highly prevalent and is currently the 6th most prevalent disease in the world
- Inverse relationship has been observed between Periodontitis and income levels with lower-income individuals having 1.8 times increased odds of severe Periodontitis
- Also Periodontitis has higher prevalence in patients with > 40 years

Diabetes and Periodontitis – the Two Chronic Diseases, Adversely Affect Each Other



Poorly Controlled Diabetes – A Good Predictor of Periodontal Disease

Poorly controlled diabetes

- **Significantly worsens periodontal disease**
- **Increased risk of tooth loss (odds ratio of 1:3, after adjusting for potential confounding factors)**

Good glycemic control

- **Consistent maintenance of glycemic level improves periodontal health**

Prediabetes and Periodontal Disease – Evidence is Evolving

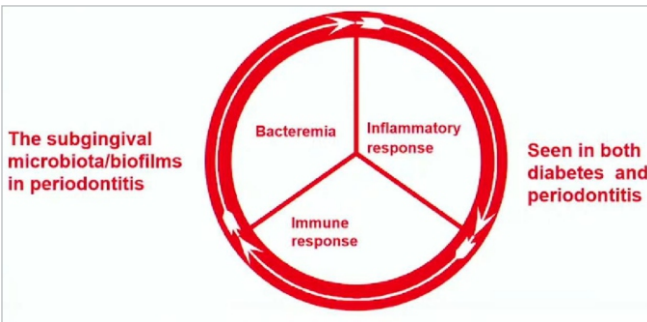
- In patients with prediabetes, higher periodontal parameters have been recorded
- Also strong association between prediabetes with “Bleeding on probing” was found
- Vice-a-versa, bacterial dysbiosis in periodontal disease may contribute to prediabetes development
- Thus, screening prediabetes risk test can be used for suspected diabetic patients visiting dental clinics

Periodontal Disease Affects the Pathogenesis of Diabetes – the Evidence Link

Periodontitis adversely affects: glycemic control diabetes complications promotes the development of type 2 diabetes.	People with poor periodontal health and type 2 diabetes at greater risk of developing poorer glycemic control	Patients with severe periodontitis might increase the incidence of developing type 2 diabetes
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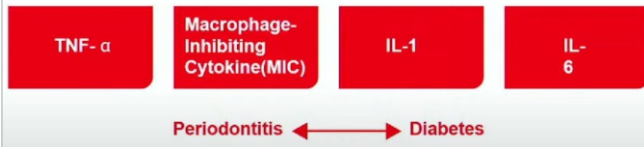
Diabetes and Periodontitis Status - Correlation

- Severe periodontitis worsens diabetes as it's associated with increased risk of hyperglycemia, increased HbA1c levels and is associated with higher incidence of complications

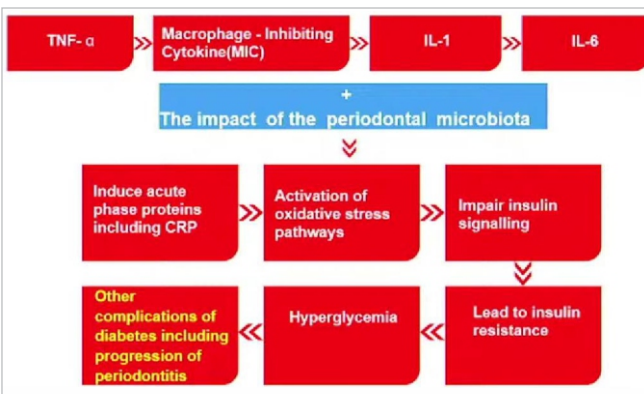


Inflammatory Response Connects the Pathophysiological Pathways Between Diabetes and Periodontitis

Diabetes and periodontitis lead to elevated levels of cytokines or pro-inflammatory biomarkers



Elevated inflammatory Markers Lead to a Cascade of Events



Summary

- The link between diabetes and periodontal disease is triggered by a triad of inflammation, immune response and dysbiosis
- Inflammatory mediators cause periodontal destruction
- Inflammation can lead to insulin resistance worsening glycemic control

Diabetes impacts Periodontitis

- Diabetes patients are at 3 times higher risk of Periodontitis than normal individuals
- Uncontrolled diabetes increases risk of Periodontitis
- The increased risk of ONSET and PROGRESSION
- Longer the diabetes – more severe is Periodontitis

Periodontitis impacts Diabetes

- Presence of Periodontitis results in poor glycemic control
- Could be considered an early indicator of pre-diabetes and diabetes
- Periodontitis doubles the risk of development of T2DM
- Can facilitate progression / worsening of diabetes
- Increases risk of complications of diabetes

Interprofessional Responsibilities

Role of Physicians

- Patients with DM should be referred to a dentist to have their oral health assessed as part of the overall evaluation of DM
- Physicians should seek evidence for the presence of oral health problems in high-risk patients, as part of their initial evaluation and ask about **signs and symptoms of oral/periodontal diseases** (bleeding gums, halitosis, drifting of teeth, tooth mobility, etc.)
- Assist their dental colleagues by providing the results of laboratory tests such as HbA1c to dentists on request.
 - Dentists can use this information to assess risk of progressive periodontal destruction
 - Dentists also can use HbA1c results to help assess the risk of hypoglycemia in the dental office

Role of Dentists

- Evaluate patients for signs/ symptoms of DM and then refer them to a physician for formal medical evaluation and diagnosis
- Ask for a detailed patient's family history of DM
- Should inform physicians about any oral signs of infection or other problems that may affect glycemic control



49TH ANNUAL MEETING OF
RESEARCH SOCIETY FOR THE
STUDY OF DIABETES IN INDIA
RSSDI 2021 11TH - 14TH NOV, 2021

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