Diabetes Mellitus, Diagnosis and Complications
The Great Diabetes Epidemic

Top 10 countries/territories of number of people with diabetes (20-79 years), 2013

1. China: 98.4 million
2. India: 65.1 million
3. USA: 24.4 million
4. Brazil: 11.9 million
5. Russian Federation: 10.9 million
6. Mexico: 8.7 million
7. Indonesia: 8.5 million
8. Germany: 7.6 million
9. Egypt: 7.5 million
10. Japan: 7.2 million

ICMR-INdia DIABetes Study

National study (Phase I) estimated the prevalence of diabetes and pre-diabetes from urban and rural inhabitants from 3 States and 1 UT

Extrapolated to all of India, these estimates translate to 62.4 million individuals with diabetes

Anjana et al. Diabetologia 2011;54(12):3022–7
Diabetes Mellitus: Definition

• Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.

• The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.
Diabetes Classification

- Type 1 Diabetes
- Type 2 Diabetes
- Gestational Diabetes (GDM)
- Other types related to other causes
  - Exocrine diseases (i.e. cystic fibrosis)
  - Genetic defects affecting insulin action or production
  - Drug/chemically induced (i.e. HIV/AIDs treatments)

## Etiologic Classification of Diabetes Mellitus

<table>
<thead>
<tr>
<th>I. Type 1 diabetes (beta-cell destruction, usually leading to absolute insulin deficiency)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Immune-mediated</td>
</tr>
<tr>
<td>B. Idiopathic</td>
</tr>
<tr>
<td>II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)</td>
</tr>
<tr>
<td>III. Other specific types of diabetes</td>
</tr>
<tr>
<td>A. Genetic defects of beta-cell function (MODY, others)</td>
</tr>
<tr>
<td>B. Genetic defects in insulin action</td>
</tr>
<tr>
<td>C. Diseases of the exocrine pancreas—pancreatitis, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibrocalcus pancreatopathy</td>
</tr>
<tr>
<td>D. Endocrinopathies—acromegaly, Cushing’s syndrome, glucagonoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma</td>
</tr>
<tr>
<td>E. Drug- or chemical-induced</td>
</tr>
<tr>
<td>F. Infections—congenital rubella, cytomegalovirus, coxsackie</td>
</tr>
<tr>
<td>G. Uncommon forms of immune-mediated diabetes—”stiff-man” syndrome, anti-insulin receptor antibodies</td>
</tr>
<tr>
<td>H. Other genetic syndromes sometimes associated with diabetes (Down’s syndrome, others)</td>
</tr>
<tr>
<td>IV. Gestational diabetes mellitus (GDM)</td>
</tr>
</tbody>
</table>
Features Of Type 1 Diabetes

- < 5% of diabetic population
- Younger (< 20 yrs) & lean patients
- Progressive autoimmune (self) destruction of beta cells
- Absolute insulin deficiency
- Prone to ketosis
- Exogenous insulin - necessary for survival
Symptoms of Type 2 Diabetes

- Usually slow onset
- May be asymptomatic
- 3 P’s:
  - polyuria,
  - polydipsia,
  - polyphagia
- Weakness/fatigue
- Dysuria
- Dry, itchy skin
- Visual changes
- Skin and mucous membrane infections
Symptoms of Diabetes

Main symptoms of Diabetes

Central
- Polydipsia
- Polyphagia
- Lethargy
- Stupor

Eyes
- Blurred vision

Breath
- Smell of acetone

Systemic
- Weight loss

Respiratory
- Kussmaul breathing (hyper-ventilation)

Gastric
- Nausea
- Vomiting
- Abdominal pain

Urinary
- Polyuria
- Glycosuria
<table>
<thead>
<tr>
<th>Feature</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Acute</td>
<td>Gradual</td>
</tr>
<tr>
<td>Occurrence</td>
<td>Less common (5-25%)</td>
<td>More common (75-95%)</td>
</tr>
<tr>
<td>Age at onset</td>
<td>Younger patients (&lt;35yrs)</td>
<td>Older patients (&gt;35yrs)</td>
</tr>
<tr>
<td>Defect</td>
<td>Insulin deficiency (absolute)</td>
<td>Insulin deficiency or insulin resistance or both</td>
</tr>
<tr>
<td>Weight of patient</td>
<td>Mostly Lean</td>
<td>Mostly obese</td>
</tr>
<tr>
<td>Family history</td>
<td>Present</td>
<td>Strongly present</td>
</tr>
<tr>
<td>Management</td>
<td>Insulin is essential for survival</td>
<td>OHA or most patients require Insulin (not essential for survival)</td>
</tr>
<tr>
<td>Ketosis</td>
<td>Prone to ketosis</td>
<td>Generally not prone to ketosis</td>
</tr>
</tbody>
</table>
Type 1.5 Diabetes or LADA

- Clinically present as having type 2 diabetes
- Age > 40 years
- Have autoimmune antibodies (feature of type 1 diabetes)
- These patients eventually require insulin therapy
## Diagnosis Of Diabetes: Values For Diabetes/Pre-diabetes

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Criteria for Diabetes</th>
<th>Criteria for Pre-Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG</td>
<td>≥ 126 mg/dL</td>
<td>100 - 125 mg/dL</td>
</tr>
<tr>
<td>OGGTT</td>
<td>≥ 200 mg/dL</td>
<td>140 - 199 mg/dL</td>
</tr>
<tr>
<td>A1C</td>
<td>≥ 6.5%</td>
<td>5.7 - 6.4%</td>
</tr>
<tr>
<td>Random PG</td>
<td>≥ 200 mg/dL</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Pre-Diabetes Diagnosis

- Plasma glucose and/or A1C level between normal range and diabetes
  - Risk for developing DM and CVD
  - Estimates for developing diabetes over 5 years range from 9% - 50%
  - Evaluate and treat other risk factors:
    - Obesity/overweight, dyslipidemia, and hypertension

Who to Test/Screen for Diabetes?

• For which patients should you be recommending testing/screening for Diabetes?

• When/How often should they be screened?
  – Evaluate individual patient risk
  – Assess previous screening results

• What risk factors can you name?
<table>
<thead>
<tr>
<th>Risk Factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity/overweight (BMI ≥ 25 kg/m²)</td>
<td>History of CVD</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>Prior diagnosis of pre-diabetes</td>
</tr>
<tr>
<td>First degree relative with DM</td>
<td>HDL cholesterol &lt; 35 mg/dL</td>
</tr>
<tr>
<td>High risk ethnicity/race:</td>
<td>Triglycerides &gt; 250 mg/dL</td>
</tr>
<tr>
<td>• African American</td>
<td>Hypertension: BP ≥ 140/90 mmHg or on treatment</td>
</tr>
<tr>
<td>• Latino</td>
<td>Conditions associated with insulin resistance:</td>
</tr>
<tr>
<td>• Native American</td>
<td>• Severe obesity (BMI ≥ 40 kg/m²)</td>
</tr>
<tr>
<td>• Asian American</td>
<td>• Acanthosis Nigricans</td>
</tr>
<tr>
<td>• Pacific Islander</td>
<td></td>
</tr>
<tr>
<td>Women with history of GDM or delivering a baby weighing &gt; 9 lbs</td>
<td></td>
</tr>
<tr>
<td>Women with Polycystic Ovarian Syndrome (PCOS)</td>
<td></td>
</tr>
</tbody>
</table>
Who to Screen for Diabetes?

- All adults (≥ 18 years old) with BMI ≥ 25 kg/m\(^2\) and 1 or more additional risk factors
- In adults without additional risk factors
  - Screening should start at age 30 years
- If results of screening are normal; repeat in 3 years
  - Repeat yearly in those with Pre-diabetes values
- For diagnosis screening test must be repeated
  - Is better to use same test (i.e. A1C, FPG, etc) for repeat

Screening in Children & Adolescents

- Test for type 2 diabetes and pre-diabetes in children/adolescents
  - Overweight (BMI > 85th percentile for age and gender or > 120% of ideal weight for height)
  - Plus 2 risk factors:
    - Family history in 1st or 2nd degree relative
    - Race/ethnicity (same as in adults)
    - Signs of insulin resistance or associated conditions
    - Gestational DM in mother while child was in utero

Screening for Gestational Diabetes

- Screen all pregnant women at first antenatal visit
- Without risk factors screen at 24-28 weeks
  - Use OGTT for diagnosis (fasting, 1 hour, and 2 hour)
    - FPG $\geq 92$ mg/dL
    - 1 hour $\geq 180$ mg/dL
    - 2 hour $\geq 153$ mg/dL
- DIPSI criteria for screening - 2hr plasma glucose after 75 gm glucose of $>140$mg/dl
- In women with gestational DM, screen for type 2 DM at 6-12 weeks post-delivery then every 3 years

## Target BG Levels

<table>
<thead>
<tr>
<th>Parameters</th>
<th>AACE</th>
<th>IDF</th>
<th>ADA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1C</td>
<td>≤ 6.5</td>
<td>≤ 6.5</td>
<td>&lt; 7</td>
</tr>
<tr>
<td>Fasting/Preprandial (mg/dL)</td>
<td>&lt; 110</td>
<td>&lt; 100</td>
<td>70 - 130</td>
</tr>
<tr>
<td>Postprandial (mg/dL)</td>
<td>&lt; 140</td>
<td>&lt; 135</td>
<td>&lt; 180</td>
</tr>
</tbody>
</table>

AACE: American Association of Clinical Endocrinology  
IDF: International Diabetes Federation  
ADA: American Diabetes Association
## Target Blood Glucose for Gestational Diabetes

<table>
<thead>
<tr>
<th>FPG</th>
<th>PPG</th>
<th>Mean PG level</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 mg %</td>
<td>110 mg %</td>
<td>95 mg %</td>
</tr>
<tr>
<td>90 mg %</td>
<td>120 mg %</td>
<td>105 mg %</td>
</tr>
</tbody>
</table>

Birth weight between 2.5 and 3.5 Kg

V. Seshiah, AK Das, Balaji V, Shashank Joshi, MN Parikh, Sunil Gupta for DIPSI. GDM- Guidelines. JAPI vol 54, 2006, 622-28
Complications of Uncontrolled Diabetes
Acute Complications

- Hypoglycemia
- Diabetic ketoacidosis
- Hyperosmolar non-ketotic coma
- Lactic acidosis
Hypoglycemia

- Hypoglycemia - a major burden in people with diabetes
- It increases morbidity (ACCORD, VADT)
- Increasing duration of both types of diabetes leads to vulnerability to hypoglycemia
- It might cause sudden death through a number of plausible mechanisms
- It seems to behave as a marker of disease burden rather than as a direct cause of death
Neurological Consequences Of Hypoglycaemia

- Hypoglycemia deprives the brain of glucose, promoting an autonomic response (e.g., sweating, trembling, anxiety) & neuroglycopenic-induced behavioral changes & cognitive impairment

- Normal counter-regulatory responses to hypoglycaemia can be impaired following repeated hypoglycemia

- Normal chronic cognitive impairment is rare

2. DCCT. N Eng J Med 2007;356;1842–52
Diabetic Ketoacidosis (DKA)

Diabetic ketoacidosis is a state of metabolic decompensation which occurs as a consequence of an absolute deficiency of insulin.

Features:
- Hyperglycemia
- Ketosis
- Metabolic Acidosis

Diagnostic Criteria:
- Plasma Glucose > 250 mg/dL
- Arterial pH < 7.3
- Serum bicarbonate < 15mEq/l
- Ketonuria / ketonemia
Hyperosmolar Non Ketotic Coma

HHS or HONK is an acute clinical syndrome of diabetes characterized by hyperglycemia, hyperosmolarity, and dehydration without significant ketoacidosis. Most patients present with severe dehydration and focal or global neurologic deficits.
Lactic Acidosis (LA)

- A serious condition characterized by excessive accumulation of lactic acid & metabolic acidosis
- Presence of tissue hypoxemia, which leads to enhanced anaerobic glycolysis & to increased lactic acid formation.
- Normal blood lactic acid concentration is 1mmol/l, and the pyruvic to lactic ratio is 10:1. An increase in lactic acid without concomitant rise in pyruvate leads to LA of clinical importance.
Microvascular Complications

- Nephropathy
- Retinopathy
- Neuropathy
  - Foot ulcers/lesions
  - Numbness, pain
  - Sexual dysfunction
  - Gastroparesis
Macrovascular Complications

- Cardiovascular Diseases (CVD)
  - Coronary Artery Disease (CAD)
  - Myocardial Infarction (MI)
  - Stroke or transient ischemic attack (TIA)

- Peripheral Artery Disease (PAD)
Macrovascular disease
- Transient ischaemic attack
- Stroke
- Angina
- Myocardial infarction
- Cardiac failure

Microvascular disease
- Diabetic retinopathy
  - non-proliferative
  - proliferative
  - macular oedema
- Microalbuminuria
- Macroalbuminuria
- End-stage renal disease
- Erectile dysfunction
- Autonomic neuropathy
- Peripheral neuropathy
- Osteomyelitis
- Amputation

Peripheral vascular disease
# Diabetes Complications in India: The Numbers

<table>
<thead>
<tr>
<th>Complication</th>
<th>Percentage</th>
<th>Millions (2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary Artery Disease (CAD)</td>
<td>21.4%</td>
<td>10.9</td>
</tr>
<tr>
<td>Peripheral Vascular Disease (PVD)</td>
<td>6.3%</td>
<td>3.2</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>17.6%</td>
<td>8.9</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>2.2%</td>
<td>1.1</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>26.1%</td>
<td>13.3</td>
</tr>
</tbody>
</table>

**References**

Mohan V et al, J Am Coll Cardiol. 38; 682-687, 2001
Premalatha G et al, Diabetes Care. 23; 1295-1300, 2000
Pathogenesis of Complications

Hyperglycemia

- ↑ AGE’s
  - Altered protein function

- ↑ sorbitol
  - Altered cell function

- ↑ DAG
  - ↑ Gene, enzyme expression

- ↑ F6PO4
  - ↑ GF expression

Complications
Mechanisms

- Genetic susceptibility
- Hyperglycemia
- *Repeated acute changes in cellular metabolism
- Tissue damage
- **Cumulative long term changes in stable macromolecules
- Independent accelerating factors
Why are People with Diabetes at Increased Risk For CVD?

People with diabetes, often have the following conditions that contribute to their risk for developing cardiovascular disease:

- High blood pressure (hypertension)
- Abnormal cholesterol and high triglycerides
- Obesity
- Lack of physical activity
- Poor glycaemic control
- Smoking

Heart disease and stroke are the No. 1 causes of death and disability among people with type 2 diabetes. In fact, at least 65 percent of people with diabetes die from some form of heart disease or stroke.

http://www.heart.org/HEARTORG/Conditions/Diabetes/WhyDiabetesMatters/Cardiovascular-Disease-Diabetes_UCM_313865_Article.jsp
The "Common Soil" Hypothesis Of Diabetes Complications

Pathogenesis of Diabetes – Related Vascular Changes and Tissue Damage

Hyperglycaemia

Irreversible glycation of intra- and extracellular proteins

Alteration in signaling pathways

Changes in gene expression

Induction of oxidative stress

Vascular pathologic changes and tissue damage

Obesity, Insulin Resistance & Endothelial Dysfunction

Obesity

- Hyperinsulinemia
- FFA
- TNF-α
- leptin
- resistin
- adiponectin

Insulin Resistance

- FFA
- IL-1
- IL-6
- PAI-1
- TNF-α
- leptin
- adiponectin

Endothelial Dysfunction

- Hyperglycemia
- Hypertension
- Dyslipidemia
- Altered coag/fib

CRP

Caballero AE. Obes Res. 2003; 11: 1278-1289
Macrovascular Complications of T2D

- 80% of people with type 2 diabetes (T2D) die from CVD
  - Peripheral vascular disease
    - e.g., intermittent claudication, gangrene, amputations
  - Cerebrovascular disease
    - e.g., stroke, transient ischemic attacks
    - 2- to 4-fold increased mortality risk
  - Coronary heart disease (CHD)
    - e.g., angina, heart attack, heart failure
    - 2- to 4-fold increased mortality risk

Thus, diabetes must take its place alongside the other major risk factors as important causes of CVD. In fact, it may be appropriate to say, “diabetes is a cardiovascular disease”.
Risk of CVD Events in Patients with Diabetes Relative to Non-Diabetic Subjects: Framingham Heart Study

- Any CVD event
- Stroke
- Intermittent claudication
- Cardiac failure
- CHD
- Myocardial infarction
- Angina pectoris
- Sudden death
- Coronary mortality

Age-adjusted risk ratio

- Male
- Female

* $p<0.001$
† $p<0.05$
‡ $p<0.01$
§ $p<0.1$

Adapted from Kannel. Am Heart J. 1990;120:672–6
Cardiovascular Disease & Diabetes

~65% of deaths are due to CV disease

Coronary heart disease deaths ↑2- to 4-fold

Stroke risk ↑2- to 4-fold

Heart failure ↑2- to 5-fold

Cardiovascular complications of T2DM

T2DM = type 2 diabetes mellitus

‘Glucose Triad’ of Diabetes Management

HbA$_{1c}$
Average long-term glucose level

FPG
Basal glucose level

PPG
Prandial glucose level
Glycaemic Variability in Diabetes management

HbA$_{1c}$
Average long-term glucose level

FPG
Basal glucose level

PPG
Prandial glucose level

Glycaemic Variability
SMBG
Fasting and Post-load Glucose Levels Identify Different Individuals with Asymptomatic Diabetes. FPG, Fasting Plasma Glucose; 2H PG, 2H Postload Plasma Glucose

adapted from the DECODE Study Group
The Association between Post-Challenge Glycaemia and Mortality

Adjusted for age, centre, sex, cholesterol, body mass index (BMI), systolic blood pressure (SBP), smoking

Relation between Postprandial Blood Glucose Levels and Cardiovascular Mortality


Cavalot F et al. *J Clin Endocrinol Metabol* 2006;91:813–9

ppBG = postprandial blood glucose
CV = cardiovascular
Glycaemic Triad & CV Risk: Recent Studies

- San Luigi Gonzaga Diabetes Study\(^1\)
  - 505 T2D patients (14 year follow-up)
  - HbA\(_{1c}\) & 2hr PPG predict cardiovascular events (not FPG)

- Strong Heart Study\(^2\)
  - 3,850 female adults (15 year duration)
  - “HbA\(_{1c}\) is more convenient than FPG in diagnosing diabetes, neither test adds to conventional CVD risk factors in predicting CHD or total CVD”

1. Cavalot et al. Diabetes Care 2011;34
2. Wang et al. Diabetes Care 2011;34(12):2576-80
Cardiovascular Disease Risk in Type 2 Diabetes

- Individuals with type 2 diabetes mellitus have increased cardiovascular disease risk compared with those without diabetes.
- Treatment of the residual risk, other than blood pressure and LDL-cholesterol control, remains important as the rate of diabetes increases worldwide.
- The accelerated atherosclerosis and cardiovascular disease in diabetes is likely to be multifactorial and therefore several therapeutic approaches can be considered.
Micro vascular Complications
Eye Complications

Cataracts

• Non enzymatic glycation of lens protein and subsequent cross linking

• Sorbitol accumulation could also lead to osmotic swelling of the lens but evidence of involvement in cataract formation is less strong
Eye Complications

Retinopathy
- Non proliferative diabetic retinopathy (NPDR)
  - Mild, Moderate, Severe
- Proliferative diabetic retinopathy (PDR)

Glaucoma
Diabetic Retinopathy (DR)

- DR is the leading cause of blindness in the working population of the Western world
- The prevalence increase with the duration of the disease (few within 5 years, 80 – 100% will have some form of DR after 20 years)
- Maculopathy is most common in type 2 patients and can cause severe visual loss
### Classification of Diabetic Retinopathy

#### Classification of Diabetic Retinopathy in the Early Treatment of Diabetic Retinopathy

<table>
<thead>
<tr>
<th>Disease Severity Level</th>
<th>Findings Observable upon Dilated Ophthalmoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild nonproliferative retinopathy</td>
<td>At least one microaneurysm, and definition not met for moderate nonproliferative retinopathy, severe nonproliferative retinopathy, early proliferative retinopathy, or high-risk proliferative retinopathy</td>
</tr>
<tr>
<td>Moderate nonproliferative retinopathy</td>
<td>Hemorrhages and/or microaneurysms $\geq$ standard photograph 2A*; and/or soft exudates, venous beading, or intraretinal microvascular abnormalities definitely present; and definition not met for severe nonproliferative retinopathy, early proliferative retinopathy, or high-risk proliferative retinopathy</td>
</tr>
<tr>
<td>Severe nonproliferative retinopathy</td>
<td>Soft exudates, venous beading, and intraretinal microvascular abnormalities all definitely present in at least two of fields four through seven; or two of the preceding three lesions present in at least two of fields four through seven and hemorrhages and microaneurysms present in these four fields, equaling or exceeding standard photo 2A in at least one of them; or intraretinal microvascular abnormalities present in each of fields four through seven and equaling or exceeding standard photograph 8A in at least two of them; and definition not met for early proliferative retinopathy or high-risk proliferative retinopathy</td>
</tr>
<tr>
<td>Early proliferative retinopathy (i.e., proliferative retinopathy without Diabetic Retinopathy Study high-risk characteristics)</td>
<td>New vessels; and definition not met for high-risk proliferative retinopathy</td>
</tr>
<tr>
<td>High-risk proliferative retinopathy (proliferative retinopathy with Diabetic Retinopathy Study high-risk characteristics)</td>
<td>New vessels on or within one disc diameter of the optic disc (NVD) $\geq$ standard photograph 10A* (about one-quarter to one-third disc area), with or without vitreous or preretinal hemorrhage; or vitreous and/or preretinal hemorrhage accompanied by new vessels, either NVD &lt; standard photograph 10A or new vessels elsewhere (NVE) $\geq$ one-quarter disc area</td>
</tr>
</tbody>
</table>
Background Retinopathy

- Micro aneurysms
- Scattered exudates
- Hemorrhages (flame shaped, Dot and Blot)
- Cotton wool spots (<5)
- Venous dilatations

Background retinopathy
Pre-Proliferative Retinopathy

- Rapid increase in amount of micro aneurisms
- Multiple hemorrhages
- Cotton wool spots (>5)
- Venous beading, looping and duplication

Proliferative retinopathy
Proliferative Retinopathy

- New vessels (on disc, elsewhere)
- Fibrous proliferation (on disc, elsewhere)
- Hemorrhages (preretinal, vitreous)

Panretinal photo-coagulation
Vitreous Bleeding
Rubeosis Iridis
Advanced Diabetic Eye Disease

- Retinal detachment with or without retinal tears
- Rubeosis iridis
- Neovascular glaucoma
Maculopathy

- Macular edema (focal or diffuse)
- Ischaemic maculopathy
Diabetic Nephropathy (DN)

• Diabetes has become the most common cause of end stage renal failure in the US and Europe
• In India also diabetes certainly is the leading cause of ESRD
• About 20 – 30% of patients with diabetes develop evidence of nephropathy
Stages of Diabetic Nephropathy

GFR (ml/min) = Kidney Function

Proteinuria (mg/24hr)

Years of diabetes (on average)
Stages of DN

**Stage I**

↑ glomerular filtration and kidney hypertrophy

**Stage II**

u-albumin excretion < 30mg/24h

**Stage III**

Microalbuminuria (30 – 300 mg/24h)
Stages of DN (cont)

**Stage IV**
Overt nephropathy (＞300mg/24h, positive u dipstick)

**Stage V**
ESRD characterized by ↑ blood urea and creatinine levels, hyperkalaemia and fluid overload
# Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min per 1.73 m² body surface area)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage* with normal / increased GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage* with mildly decreased GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

GFR = glomerular filtration rate

*Kidney damage defined as abnormalities on pathologic, urine, blood, or imaging tests.

ADA. VI. Prevention, Management of Complications. *Diabetes Care* 2013;36(suppl 1):S35-S36; Table 12.
Diabetic Neuropathy

- Sensorimotor neuropathy (acute/chronic)
- Autonomic neuropathy
- Mononeuropathy
  - Spontaneous
  - Entrapment
  - External pressure palsies
- Proximal motor neuropathy
Sensorimotor Neuropathy

- Patients may be asymptomatic / complain of numbness, paresthesias, allodynia or pain
- Feet are mostly affected, hands are seldom affected
- In diabetic patients sensory neuropathy usually predominates
Complications of Sensorimotor Neuropathy

- Ulceration (painless)
- Neuropathic edema
- Charcot arthropathy
- Callosities
Autonomic Neuropathy

Symptomatic
- Postural hypotension
- Gastroparesis
- Diabetic diarrhea
- Neuropathic bladder
- Erectile dysfunction
- Neuropathic edema
- Charcot arthropathy
- Gustatory sweating

Subclinical Abnormalities
- Abnormal pupillary reflexes
- Esophageal dysfunction
- Abnormal cardiovascular reflexes
- Blunted counter-regulatory responses to hypoglycemia
- Increased peripheral blood flow
Mononeuropathies

- Cranial nerve palsies (most common are n. IV, VI, VII)
- Truncal neuropathy (rare)
Entrapment Neuropathies

- Carpal tunnel syndrome (median nerve)
- Ulnar compression syndrome
- Meralgia paresthetica (lat cut nerve to the thigh)
- Lat Popliteal nerve compression (drop foot)

All the above are more common in diabetic patients
Proximal Motor Neuropathy

Amyotrophy: Most common proximal neuropathy, affects the Quadriceps muscles with weakness & atrophy

(synonym: Diabetic Femoral radiculo-neuropathy)
Additional Concerns

• Depression and other mental disorders

• Tuberculosis in diabetic patients

• Skin and soft tissue infections

• Increased risk of ear nose throat infections, urinary tract infections, pneumonia, cholecystitis etc.

• Can affect fertility

• Dental disease
Thank You...!!!