PATHOGENESIS AND CLASSIFICATION OF DIABETIC RETINOPATHY

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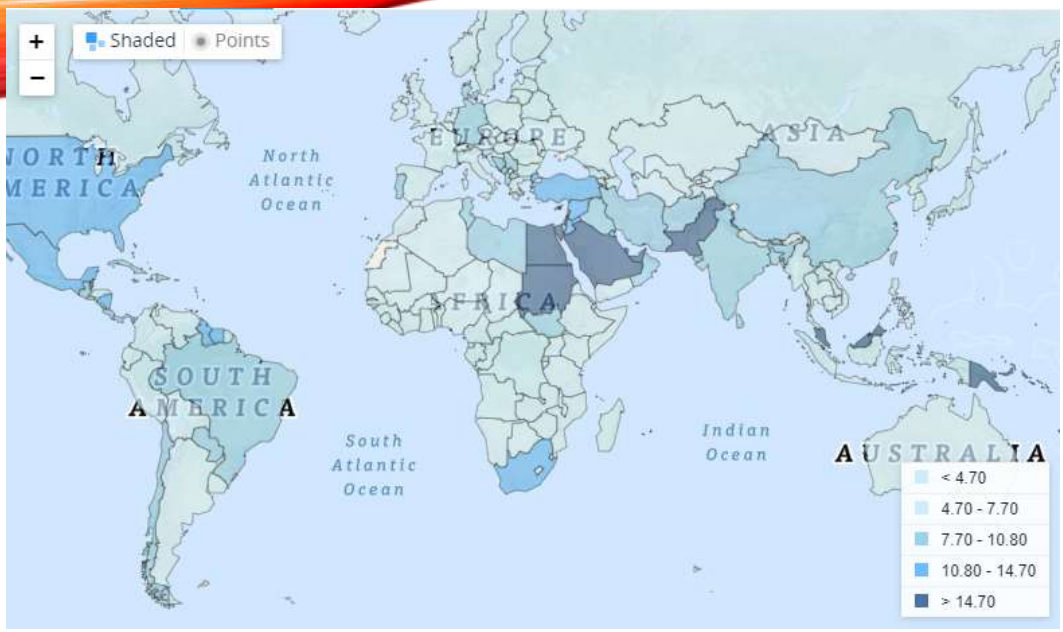
PREVALENCE OF DIABETES IN EGYPT

- **Diabetes is a fast-growing health problem in Egypt with a significant impact on morbidity, mortality, and health care resources**.
- Currently, the prevalence of type 2 diabetes (T2D) in Egypt is around 17.2% of all adults aged 20 to 79 in 2019 (The world average is 8.8%)
- The International Diabetes Federation (IDF) has identified Egypt as the ninth leading country in the world for the number of patients with T2D.
- The prevalence of T2D in Egypt was almost tripled over the last 2 decades. This sharp rise could be attributed to either:
  - an increased pattern of the traditional risk factors for T2D such as obesity and physical inactivity and change in eating pattern or
  - other risk factors unique to Egypt. These include increased exposure to environmental risk factors like pesticides and increased prevalence of chronic hepatitis C.



PREVALENCE OF DR IN EGYPT

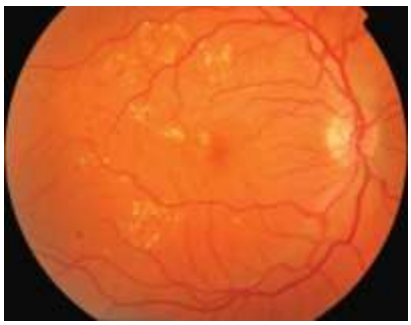
- Approximately one-half of individuals with diabetes will develop retinopathy in time
- with DME being the commonest cause of visual loss.
- It is more common in type 1 diabetes than in type 2
- Sight-threatening disease is present in up to 10%.
- PDR affects 5–10% of the diabetic population. Type 1 diabetics are at particular risk, with an incidence of up to 90% after 30 years

CLINICAL OBJECTIVES

- Identify patients at risk of developing diabetic retinopathy.
- Encourage a collaborative approach between the patient, the primary care physician, and subspecialists in the management of the patient's systemic disorder, with specific attention to control of blood sugar (hemoglobin A_{1c} [HbA_{1c}]), blood pressure, serum lipids, body weight, and management of renal disease, coronary artery disease,[4] and neuropathy.
- Encourage and provide lifelong monitoring of retinopathy progression.
- Treat patients with visual loss or those at risk for visual loss from diabetic retinopathy.
- Minimize the side effects of treatment that might adversely affect the patient's vision and/or vision-related quality of life.
- Provide or refer for visual rehabilitation services when a patient has visual impairment from the disease.

SCREENING FOR DR

- Patients with type 1 diabetes should have an initial dilated and comprehensive eye exam within 3–5 years of the diagnosis
- Those with type 2 diabetes should have an eye exam shortly after diagnosis.
- All diabetics should have subsequent eye exams annually



OCULAR MANIFESTATIONS OF DM

1. Anterior segment:
    - Eyelids:
        - Recurrent styes
        - Xanthelasma
    - Conjunctiva and Cornea:
        - Dry eye
        - Corneal hypoesthesia (risk of neurotrophic keratitis)
        - Decrease corneal healing (risk of recurrent corneal erosion)
    - Iris and pupils:
        - Iridopathy (minor iris transillumination defects).
        - Ectropion uvea
        - Increase pigment at angles
        - Difficulty in dilating pupils
        - Argyll Robertson pupils (light-near dissociation)
    - Glaucoma:
        - POAG and neovascular glaucoma
    - Lens:
        - Cataract

* Common

OCULAR MANIFESTATIONS OF DM

2. Posterior segment:
    - Retinopathy: DME, macular ischaemia and sequelae arising from retinal ischaemia (retinal new vessels, vitreous haemorrhage and tractional retinal detachment)
    - Retinal vascular occlusions
    - Asteroid hyalosis
    - Lipemia retinalis
3. Neurological manifestations:
    - Papillopathy
    - Wolfram syndrome (progressive optic atrophy, neurological and systemic abnormalities)
    - CN palsies (classically pupil sparing III CN palsy)
    - Anterior ischemic optic neuropathy
4. Others:
    - Unstable refraction
    - Orbital mucormycosis

* Common

DR WORKUP

1. Check fasting blood sugar and PP, hemoglobin A1c, and lipid panel.
2. Check blood pressure.
3. Slit lamp examination and gonioscopy with careful attention for NVI and NVA, preferably before pharmacologic dilation.
4. Dilated fundus examination by using a
   - 90- or 60-diopter or fundus contact lens with a slit lamp to rule out neovascularization and ME.
   - Use indirect ophthalmoscopy to examine the retinal periphery.
5. Consider FA to determine areas of perfusion abnormalities, foveal ischemia, microaneurysms, and subclinical neovascularization, especially if considering focal macular laser therapy.
6. Consider OCT to evaluate for presence and extent of DME.
7. OCT angiography (OCTA) can be useful to check for presence of significant central macular ischemia.

RISK FACTORS DURATION OF DIABETES

- The most important risk factor.
- Almost all type 1 diabetic patients and over three fourths of type 2 diabetic patients will have some form of DR after 20 years of the disease
- In patients diagnosed with diabetes before the age of 30 years, the incidence of DR after 10 years is 50% and after 30 years 90%.
- DR rarely develops within 5 years of the onset of diabetes or before puberty, but about 5% of type 2 diabetics have DR at presentation.
- It appears that duration is a stronger predictor for proliferative disease than for maculopathy

RISK FACTORS GLYCEMIC CONTROL

- The American Diabetes Association (ADA) recommends
  - Pre-prandial capillary glucose (fasting) of 70–130 mg/dL.
  - The postprandial glucose goal is <180 mg/dL
  - hemoglobin (Hb) A1C goal of less than 7%.
  - The ADA target for blood pressure is <140/90 mmHg.
- The American Association of Clinical Endocrinology recommends
  - Pre-prandial glucose (fasting) of <110,
  - postprandial <140
  - HbA1C <6.5%
  - The blood pressure goal is <130/80 mmHg
- By decreasing the HbA1c by 1% the microvascular complications can be reduced by one-third.
- Patients with diabetes should be referred to an endocrinologist
- All patients should be advised to adhere to a healthy lifestyle consisting of
  - attention to diet,
  - regular physical activity
  - and stop smoking

DCCT (Diabetic Control and complications trial)	**Aim:** *In Type 1 DM, assess the effect of intensive glycaemic control on complications (nephropathy, neuropathy, DR) and on rate of progression of complications*
	• Inclusion criteria: Type 1 DM
	• Treatment: Tight vs normal control
	• Results
	  ◦ In pts with no DR: decreased risk of developing DR by 76%
	  ◦ In pts with mild-mod NPDR
	  • Slowed progression of DR by 54%
	  • Decreased risk of developing PDR or SNPDR by 47%
	  ◦ Decreased risk of neuropathy by 60%
	Conclusion: Tight control is beneficial, but after prolonged hyperglycaemia, can lead to initial worsening of DR

UKPDS (UK Prospective diabetes study)	**Aim:** *Ascertain if improved DM/HT control reduces complications* • Method: Intensive vs conventional blood glucose management AND Tight BP vs less tight BP control in T2DM • Inclusion criteria: T2DM +/- HT • Treatment: Tight vs normal control • Results ◦ Control of both slows the progression and reduces the risk of DR, neuropathy and nephropathy **Conclusion:** Tight control beneficial T2 DM

OTHER RISK FACTORS

- Hypertention
- Cardiovascular disease and previous stroke
- Pregnancy
- Nephropathy
- Hyperlypidemia
- Smoking
- Cataract surgery
- Obesity
- Anaemia
- Ethnic and genetic

CLASSIFICATION

- **Background diabetic retinopathy (BDR)**
  - microaneurysms,
  - dot and blot haemorrhages
  - exudates.
- **Diabetic maculopathy**
  - retinopathy at the macula (oedema & ischaemia)
- **Preproliferative diabetic retinopathy (PPDR)** indicates progressive retinal ischaemia
  - cotton-wool spots,
  - venous changes,
  - intraretinal microvascular anomalies (IRMA)
  - deep retinal haemorrhages.
- **PDR**
  - neovascularization (NVD & NVE)
- **Advanced diabetic eye disease** is characterized by
  - tractional retinal detachment,
  - significant persistent vitreous haemorrhage
  - neovascular glaucoma.

CLASSIFICATION (EDTRS)

Definition	Criteria	Treatment
Mild NPDR	• 1 microaneurysm	• Observe (ETDRS)
Moderate NPDR	• Microaneurysm, hard exudates, hemorrhages, cotton wool spots, etc. (not meeting criteria below)	• Observe (ETDRS)
Severe NPDR (Preproliferative)	• Blot hemorrhages in four quadrants < photo 2A • Venous bead in two quadrants • IRMA in one quadrant > photo 8A	• PRP (ETDRS)
Early PDR	• NVD or NVE (not fulfilling criteria below) < photo 10A	• PRP (ETDRS)
High risk PDR	• NVD > ¼ disc diameter • NVD < ¼ disc diameter with VH • NVE > ½ disc diameter with VH	• PRP (DRS)
Advanced PDR and VH	• High risk PDR with tractional RD involving macular or with VH	• Early vitrectomy for Type I DM (DRVS)
Macular edema	• Retinal thickening or **hard exudates** within 1 disc diameter from fovea	• Observed at 6-monthly intervals (ETDRS)
CSME	• Retinal edema < 500 micron from fovea • Hard exudates < 500 micron from fovea with adjacent retinal thickening • Retinal edema > 1,500 micron, any part of which is within 1,500 micron of fovea	• Focal/grid laser (ETDRS)

INTERNATIONAL CLINICAL DISEASE SEVERITY SCALE

This disease severity scale is based upon the findings of the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) and the ETDRS.

- No apparent retinopathy
- Mild NPDR
  - Microaneurysms
  - Dot and blot hemorrhages
  - Hard (intra-retinal) exudate
- Moderate-to-severe NPDR

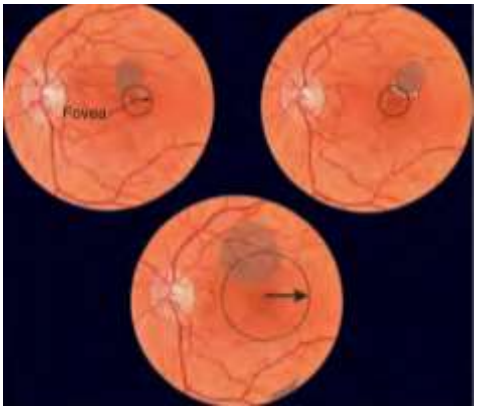
  Is mild NPDR plus:
  - Cotton-wool spots
  - Venous beading and loops
  - Intraretinal microvascular abnormalities (IRMA)
- PDR
  - Neovascularization of the retina, optic disc or iris
  - Fibrous tissue adherent to vitreous face of retina
  - Retinal detachment
  - Vitreous hemorrhage
  - Pre-retinal hemorrhage

DIABETIC MACULAR EDEMA

- Focal maculopathy: well-circumscribed retinal thickening associated with complete or incomplete rings of exudates. FA shows late, focal hyperfluorescence due to leakage, usually with good macular perfusion.
- Diffuse maculopathy: diffuse retinal thickening, which may be associated with cystoid changes. There are typically also scattered microaneurysms and small haemorrhages. Landmarks may be obscured by oedema, which may render localization of the fovea impossible. FA shows mid- and latephase diffuse hyperfluorescence and demonstrates CMO if present
- Ischemic maculopathy. FA shows capillary non-perfusion at the fovea (an enlarged FAZ) and frequently other areas of capillary non-perfusion at the posterior pole and periphery.
- Mixed maculopathy

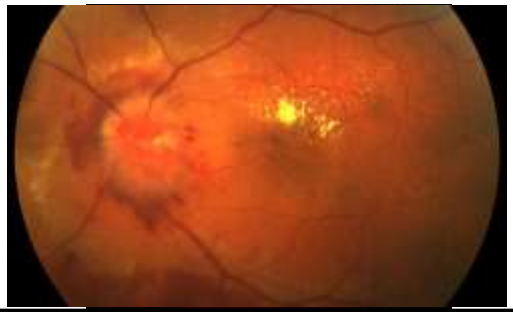
CSME (ETDRS)

- Retinal thickening within 500 µm of the centre of the macula.
- Exudates within 500 µm of the centre of the macula,
  - if associated with retinal thickening.
  - The thickening itself may be outside the 500 µm.
- Retinal thickening one-disc area (1500 µm) or larger
  - any part of which is within one disc diameter of the centre of the macula



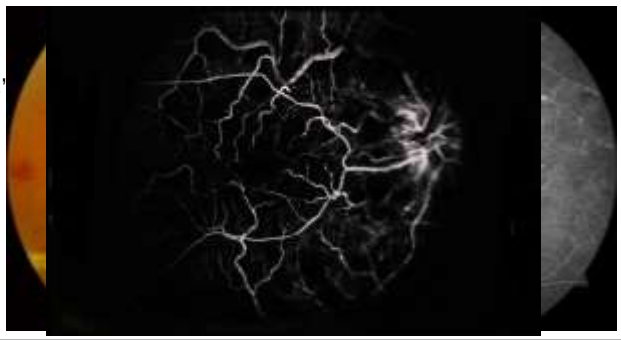
DD OF NPDR

- **CRVO:**
  - Optic disc swelling
  - veins are more dilated and tortuous,
  - hard exudates and microaneurysms usually not found
  - hemorrhages are nearly always in the NFL ("splinter hemorrhages")
  - generally unilateral and of more sudden onset.
- **BRVO:**
  - Hemorrhages are distributed along a vein and do not cross the horizontal raphe (midline).
- **OIS:**
  - Hemorrhages mostly in the midperiphery and larger;
  - exudates are absent.
  - Usually accompanied by pain;
  - mild anterior chamber reaction;
  - corneal edema;
  - episcleral vascular congestion; a
  - mid-dilated, poorly reactive pupil;
  - iris neovascularization.
- **Hypertensive retinopathy:**
  - Hemorrhages fewer and typically flame-shaped,
  - Cotton wool spots, macular star.
  - arteriolar narrowing, AV crossing changes "AV nicking".
  - Microaneurysms are rarely present.
- **Radiation retinopathy:**
  - Usually develops within a few years of radiation.
  - Microaneurysms are rarely present.



DD OF PDR

- Neovascular complications of CRAO, CRVO, or BRVO
- Sickle cell retinopathy:
  - Peripheral retinal neovascularization.
  - "Sea fans" of neovascularization present.
- Embolization from intravenous drug abuse (talc retinopathy):
  - Peripheral retinal neovascularization in patient with history of intravenous drug abuse. Typically see talc particles in retinal vessels.
- Sarcoidosis:
  - May have uveitis,
  - exudates around veins "candlewax drippings"
  - NVD & NVE
  - systemic findings.
- Other inflammatory syndromes (e.g., SLE).
- OIS: OIS/Carotid Occlusive Disease.
- Radiation retinopathy
- Hypercoagulable states
  (e.g., antiphospholipid syndrome).



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