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Incidence of diabetic retinopathy in diabetic foot patients

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Dedication

I dedicate this research to my Mom and Dad

Who learn me how I should be patience ..who learn me the steps of success and support me always.... I have been blessed to had my parent .. you were always and still the greatest parents for me and my inspiration.....

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Abstract

Background :

The reported prevalence of diabetic retinopathy (DRP) in diabetics varies substantially between studies even amongst contemporary populations in the same country but is probably around 40% it is more common in type 1 diabetes than type 2 and sight threatening disease is present in up to 10% proliferative diabetic retinopathy(PDR) affects 5–10% of the diabetic population; type 1 diabetic are at particular risk of with an incidence of up to 90% after 30 years .¹

Duration of diabetes is the most important risk factor beside to glycyemic control , hypertension ,pregnancy ,nephropathy ¹ .

Foot ulcer are one of the main complications of Diabetes mellitus with 15% life time risk of foot ulcers in all diabetic patients.

Diabetic foot ulcer precede 85% of lower limb amputations & there is two folds increase in the mortality rate in patient with diabetic foot ulcers. ⁴

Aim of this study :

To know the incidence of diabetic retinopathy in diabetic foot patients

Patient and Methods:

This study is descriptive cross sectional study; in which 26 adult diabetic patients with diabetic foot were interviewed in out patients clinic of Al-imamain Al-Kadhyimain medical city; The period of data collection was 3 months started from 23th of september 2018 to 23th of December 2018. with cooperation of diabetic and endocrine unit by referring diabetic patients with diabetic foot to ophthalmology unit for dilated fundus examination were patients were given mydriatic eye drops then fundus examination was done with slit lamp biomicroscope with 90D lense to assess the presence of diabetic retinopathy .

Results

A total of 26 patients (12 females and 14 males) were included in this study. 3 (11.5%) of them were type I DM , and 23 (88.5%) were type II DM . The age there was no patient between 20-30 years , 1 (3.8%) of them was between 31-40 , 10 (38.5%) were between 41-50 , 11(42.3%) were between 51-60 , and 4 (15.4%) of them were 61 year and above. The duration of diabetes was between 6-10 years in 12.5 % of them , between 11-15 years was 33% , between 16-20 years was 29.2% ,and it forms 25% equal and more than 21 years. **92.3 %** Of the patients were had DR and 100% poorly control there DM .

Conclusion

data from this study demonstrated a high prevalence of DR complications among patients with DF with high HbA1c levels.

the results of this study support recommendations for early complications screening and aggressive targeting of glycemic control in patients with diabetes.

Key Words

DM	diabetes mellitus
DR , DRP	diabetic retinopathy
DF	diabetic foot

Introduction

Diabetes mellitus is a clinical syndrome characterized by hyperglycaemia due to absolute or relative deficiency of insulin.²

Long-standing metabolic derangement can lead to the development of complications of diabetes, which characteristically affect the eye, kidney and nervous system.²

1-1 Epidemiology of diabetic retinopathy and diabetic foot:

The reported prevalence of diabetic retinopathy (DRP) in diabetics varies substantially between studies even amongst contemporary populations in the same country but is probably around 40% it is more common in type 1 diabetes than type 2 and sight threatening disease is present in up to 10% proliferative diabetic retinopathy(PDR) affects 5–10% of the diabetic population; type 1 diabetic are at particular risk of with an incidence of up to 90% after 30 years .¹

Diabetic retinopathy is the leading cause of blindness among working-aged adults, and according to world health organization (WHO) is responsible for 3.9% (1.8 million) of the 45 million cases of blindness worldwide although it is not totally preventable or curable, many cases of blindness can be avoided through early detection ; treatment; and follow up care.³

Foot ulcer are one of the main complications of Diabetes mellitus with 15% life time risk of foot ulcers in all diabetic patients.

Diabetic foot ulcer precede 85% of lower limb amputations & there is two folds increase in the mortality rate in patient with diabetic foot ulcers.⁴

1-2 Pathogenesis:

Pathophysiology of DF:

The pathophysiology of primary diabetic lower limb complications has three main components: peripheral neuropathy (motor, sensory, and autonomic), peripheral vascular disease, and immunodeficiency (

Tissue necrosis in the feet is a common reason for hospital admission

in diabetic patients. Foot ulceration occurs as a result of often trivial trauma in the presence of neuropathy (peripheral and autonomic) and/or peripheral vascular disease; infection occurs as a secondary phenomenon. ²

Pathogenesis of DRP:

The exact cause of diabetes microvascular disease is unknown . it is believed that exposure to hyperglycemia over an extended period results in a number of biochemical and physiologic changes that ultimately cause endothelial damage . specific retinal capillary changes include selective loss of pericytes and basement membrane thickening, which favor capillary occlusion and retinal non perfusion as well as, decompensation of the endothelial barrier function , which allow serum leakage and retinal edema to occur .

A large number of haematologic and biochemical abnormalities have been correlated with the prevalence and severity of retinopathy ⁷:

- 1 – increased platelet adhesiveness
- 2- increased erythrocyte aggregation
- 3- abnormal serum lipid
- 4- defective fibrinolysis
- 5- abnormal level of growth hormone .

1-3 Risk factors:

DF risks

important risk factors for ulceration, namely deformity, swelling and callus, are frequently also present. Deformity, swelling and callus do not commonly lead to ulceration in patients with intact protective pain sensation and a good blood supply, but when they are found in combination with neuropathy or ischaemia they significantly increase the risk of ulceration.⁶ There are other factors that increase risk, including diabetic complications, comorbidities and social problems. Important among these are ⁶ :

- Poor vision
- Old age
- Poverty
- Ignorance
- Intellectual deficit
- Concurrent psychiatric illness

- Obesity.

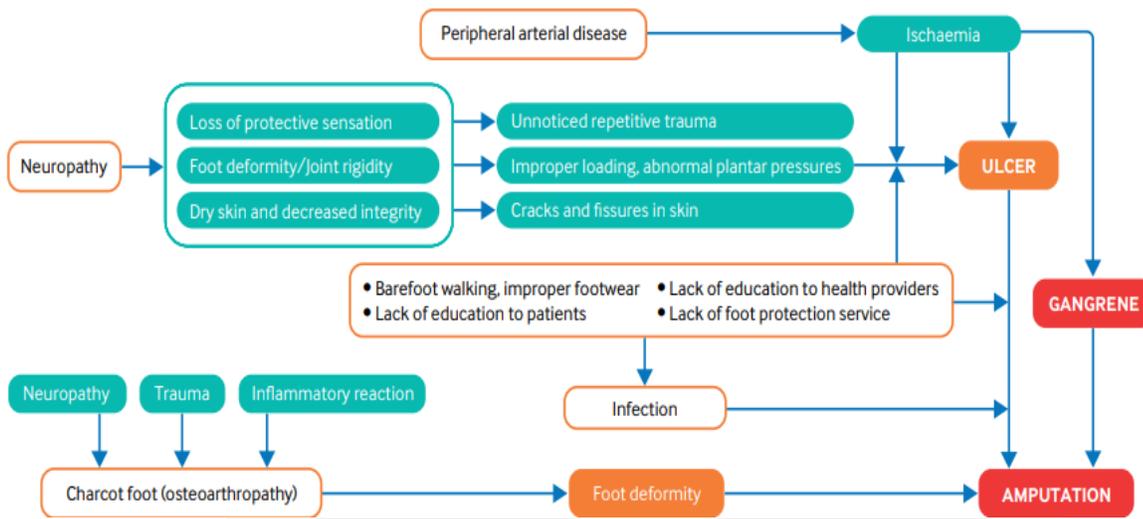


Figure 1 : risk factors and mechanism for foot ulcer and amputation. ⁵

DRP risks

- **Duration of diabetes** : is the most important risk factor. 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.¹

- **Poor control of diabetes** : It has been shown that tight blood glucose control, particularly when instituted early, can prevent or delay the development or progression of DR. However, a sudden improvement in control may be associated with progression of retinopathy in the near term.

Type 1 diabetic patients appear to obtain greater benefit from good control than type 2. Raised HbA1c is associated with an increased risk of proliferative disease.¹

- **Pregnancy** : is sometimes associated with rapid progression of DR; Predicating factors include greater pre-pregnancy severity of retinopathy; poor pre-pregnancy control of diabetes, control exerted too rapidly during the early stages of pregnancy, and pre-eclampsia.

The risk of progression is related to the severity of DR in the first trimester, If substantial DR is present, frequency of review should reflect individual risk, and can be up to monthly. ¹

Diabetic macular usually resolves spontaneously after pregnancy and need not be treated if it develops in later pregnancy ¹

- **Hypertension** : , which is very common in patients with type 2 diabetes, should be rigorously controlled (<140/80 mmHg), Tight control appears to be particularly beneficial in type 2 diabetics with maculopathy, Cardiovascular disease and previous stroke are also predictive. ¹

- **Nephropathy**, if severe, is associated with worsening of DR, Conversely, treatment of renal disease (e.g. renal transplantation) may be associated with improvement of retinopathy and a better response to photocoagulation. ¹

- **Other risk factors** : include hyperlipidaemia, smoking, cataract surgery, obesity and anemia.

1-4 Classifications

DF classification :

Most ulcers are **neuropathic or neuroischaemic** in type. They usually develop at the site of a plaque of callus skin, beneath which tissue necrosis occurs, eventually breaking through to the surface. Charcot neuro-arthropathy, with destructive inflammation of neuropathic joints, is usually caused by diabetes.²

1- Neuropathic foot

- The neuropathic foot is a warm, well-perfused foot with bounding pulses and distended dorsal veins due to arteriovenous shunting
- Sweating is diminished so skin and any callus tend to be hard and dry and prone to fissuring
- Toes are clawed and the arch of the foot may be raised
- Ulceration commonly develops on the sole of the foot, associated with neglected callus and high plantar pressures
- Despite the good circulation, necrosis can develop secondary to severe infection

- The neuropathic foot is also prone to bone and joint problems which we refer to as Charcot's osteoarthropathy. ⁶

2- Neuroischaemic foot

- The neuroischaemic foot is a cool, pulseless foot with poor perfusion and almost invariably also has neuropathy

The colour of the severely ischaemic foot can be a deceptively healthy pink or red caused by dilatation of capillaries in an attempt to improve perfusion. The neuroischaemic foot develops necrosis in the presence of infection or if tissue perfusion is critically diminished.

- Even if neuropathy is present and plantar pressures are high, plantar ulceration is rare. This is probably because the foot does not develop heavy callus, which requires good blood flow. ⁶

The natural history of the diabetic foot can be divided into six stages as shown:

- Stage 1: Normal foot
- Stage 2: High-risk foot
- Stage 3: Ulcerated foot
- Stage 4: Infected foot
- Stage 5: Necrotic foot
- Stage 6: Unsalvageable foot.

Figure 2 : natural history of neuropathic and neuro ischemic foot



Classification of DRP

The classification used in the Early Treatment Diabetic Retinopathy Study (ETDRS– the modified Airlie House classification) is widely used internationally ¹:

- **Background diabetic retinopathy (BDR)** : is characterized by microaneurysms, dot and blot hemorrhages and exudates these are generally the earliest signs of DR, and persist as more advanced lesions appear.

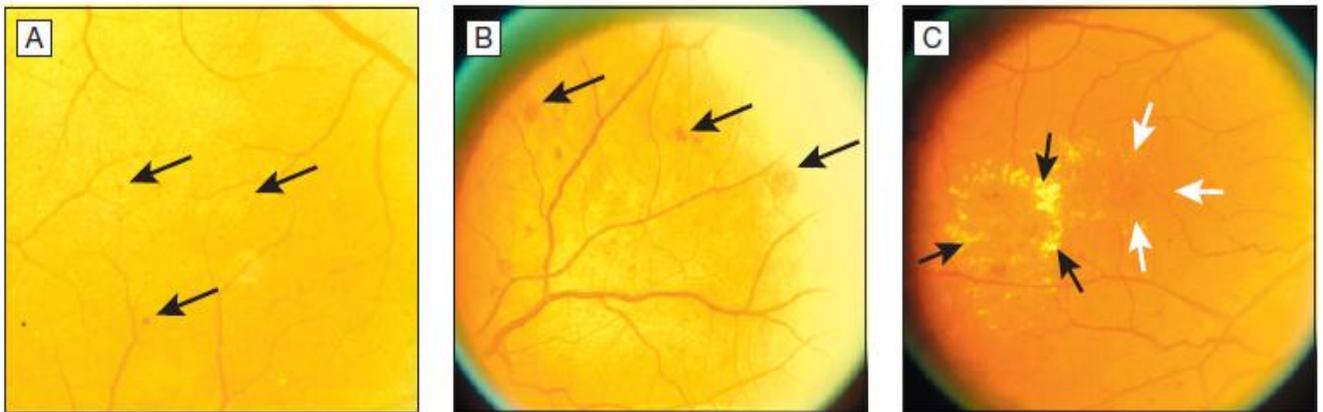


Figure 3 : A,b :dots/blots hemorrhages , C: exudate ²

- **Diabetic maculopathy** strictly refers to the presence of any retinopathy at the macula but is commonly reserved for significant changes, particularly vision-threatening edema and ischemia. ¹

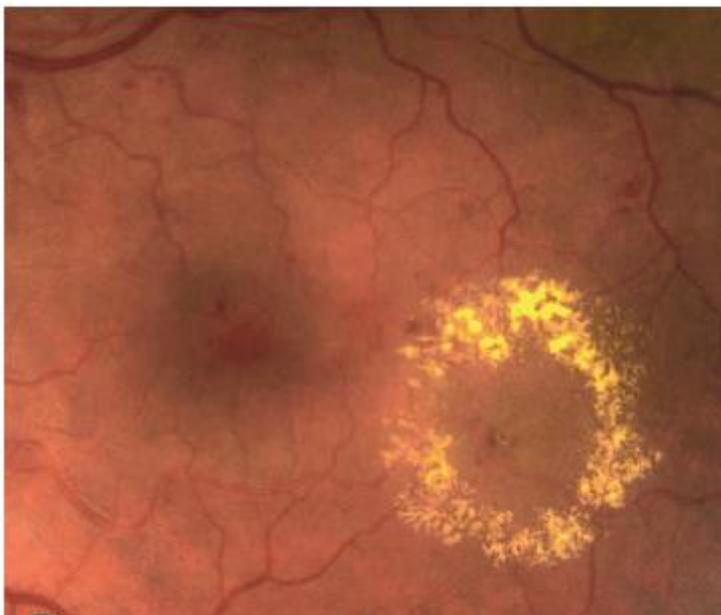


Figure 4: maculopathy ,exudate ring around macula.¹

- **Pre proliferative diabetic retinopathy (PPDR)** manifests with cotton wool spots, venous changes, intra retinal micro vascular anomalies (IRMA) and often deep retinal hemorrhage PPDR indicates progressive retinal ischemia with a heightened risk of progression to retinal neovascularization. ¹

Cotton wool spots

Cotton wool spots are composed of accumulations of neuronal debris within the nerve fibre layer. They result from ischaemic disruption of nerve axons, the swollen ends of which are known as cytooid bodies, seen on light microscopy as globular structures in the nerve fibre layer (Fig. 5). As cotton wool spots heal, debris is removed by autolysis and phagocytosis.¹



Figure 5 : cotton wool spots. (A) Histology shows cytooid bodies in the retinal nerve fibre layer; (B) clinical appearance; (C) red-free photography showing differing appearance of cotton wool spots and haemorrhages, the latter appearing black – the smaller well-defined white lesions are exudates. ¹

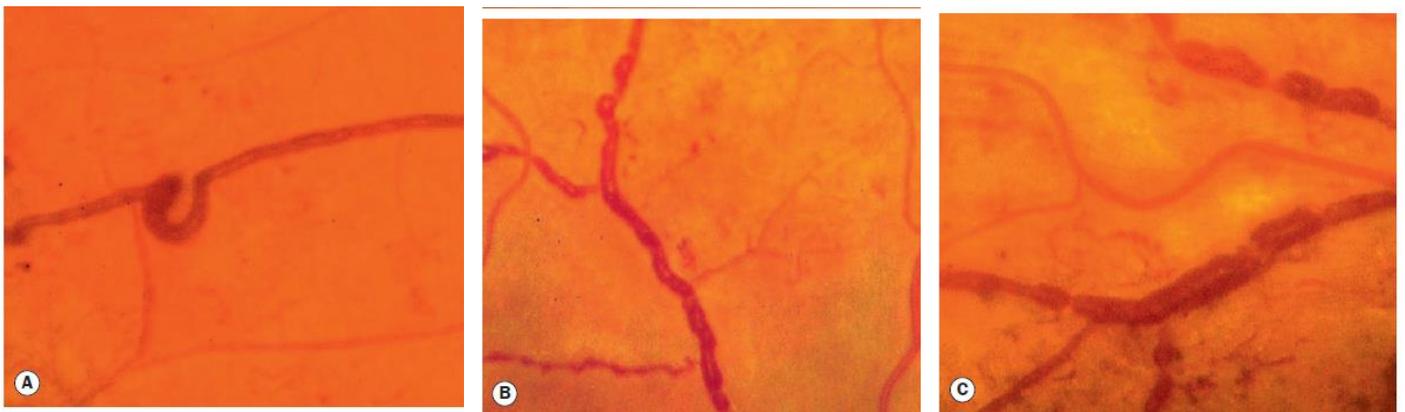


Fig. 6 : Venous changes. (A) Looping; (B) beading; (C) severe segmentation. ¹

- **PDR** : is characterized by neo vascularization on or within one disc diameter of the disc (NVD) disc diameter of the disc (NVD) and/or new vessels elsewhere (NVE) in the fundus.¹



Fig. 7 :DRP growth of new blood vessels on the retina .²

- **Advanced diabetic eye disease** ; is characterized by tractional retinal detachment significant persistent vitreous hemorrhage.¹

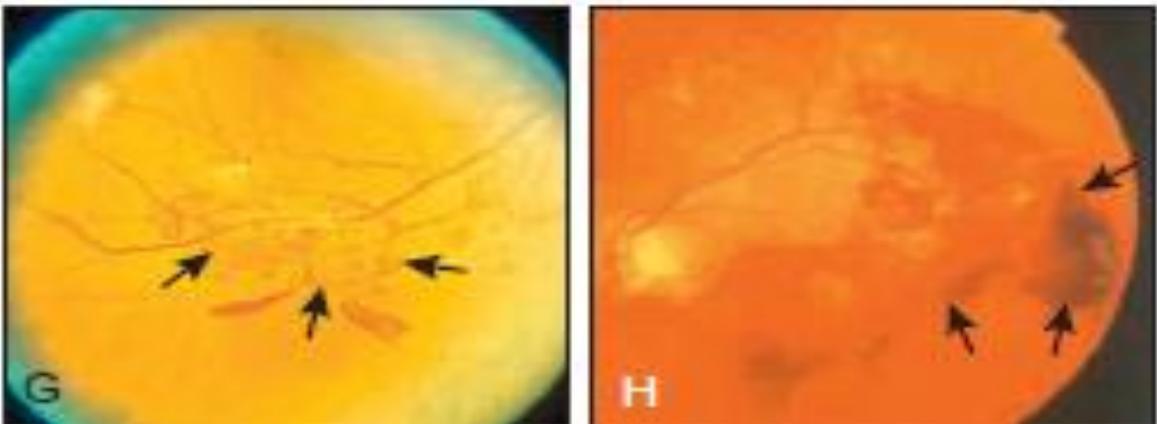


Fig. 8 : vitreous hemorrhage.²

Table 1 : Abbreviated Early Treatment Diabetic Retinopathy Study (ETDRS) classification of diabetic retinopathy. ¹

Category/description	Management
Non-proliferative diabetic retinopathy (NPDR)	
<i>No DR</i>	Review in 12 months
<i>Very mild NPDR</i>	Review most patients in 12 months
Microaneurysms only	
<i>Mild NPDR</i>	Review range 6–12 months, depending on severity of signs, stability, systemic factors, and patient's personal circumstances
Any or all of: microaneurysms, retinal haemorrhages, exudates, cotton wool spots, up to the level of moderate NPDR. No intraretinal microvascular anomalies (IRMA) or significant beading	
<i>Moderate NPDR</i>	Review in approximately 6 months Proliferative diabetic retinopathy (PDR) in up to 26%, high-risk PDR in up to 8% within a year
<ul style="list-style-type: none"> • Severe retinal haemorrhages (more than ETDRS standard photograph 2A: about 20 medium–large per quadrant) in 1–3 quadrants or mild IRMA • Significant venous beading can be present in no more than 1 quadrant • Cotton wool spots commonly present 	
<i>Severe NPDR</i>	Review in 4 months PDR in up to 50%, high-risk PDR in up to 15% within a year
The 4–2–1 rule; one or more of: <ul style="list-style-type: none"> • Severe haemorrhages in all 4 quadrants • Significant venous beading in 2 or more quadrants • Moderate IRMA in 1 or more quadrants 	
<i>Very severe NPDR</i>	Review in 2–3 months High-risk PDR in up to 45% within a year
Two or more of the criteria for severe NPDR	
Proliferative diabetic retinopathy (PDR)	
<i>Mild–moderate PDR</i>	Treatment considered according to severity of signs, stability, systemic factors, and patient's personal circumstances such as reliability of attendance for review. If not treated, review in up to 2 months
New vessels on the disc (NVD) or new vessels elsewhere (NVE), but extent insufficient to meet the high-risk criteria	
<i>High-risk PDR</i>	Treatment advised – see text Should be performed immediately when possible, and certainly same day if symptomatic presentation with good retinal view
<ul style="list-style-type: none"> • New vessels on the disc (NVD) greater than ETDRS standard photograph 10A (about ½ disc area) • Any NVD with vitreous haemorrhage • NVE greater than ½ disc area with vitreous haemorrhage 	
<i>Advanced diabetic eye disease</i>	See text

1-5 Clinical Features:

Table 2 : symptoms of DF. ²

21.44 Clinical features of the diabetic foot		
	Neuropathy	Ischaemia
Symptoms	None Paraesthesiae Pain Numbness	None Claudication Rest pain
Structural damage	Ulcer Sepsis Abscess Osteomyelitis Digital gangrene Charcot joint	Ulcer Sepsis Gangrene

Symptoms of DRP ⁸:

patient with DR may complaint from:

- Blurred vision
- Both eyes are usually affected.
- Color vision becomes impaired
- Floaters - transparent and colorless spots that float in the patient's field of vision. Sometimes they may appear as dark strings
- Patches or streaks block the person's vision; sometimes described as empty or dark areas
- Poor night vision
- Sudden total loss of vision.

1-6 Management :

General ¹:

- **Patient education** is critical, including regarding the need to comply with review and treatment schedules in order to optimize visual outcomes.
- **Diabetic control** should be optimized.
- **Other risk factors**, particularly systemic hypertension (especially type 2 diabetes) and hyperlipidaemia should be controlled in conjunction with the patient's diabetologist.

- **Fenofibrate** 200 mg daily has been shown to reduce the progression of diabetic retinopathy in type 2 diabetics and prescription should be considered; the decision is independent of whether the patient already takes a statin.
- **Smoking** should be discontinued, though this has not been definitively shown to affect retinopathy.
- **Other modifiable factors** such as anaemia and renal failure should be addressed as necessary. ¹

Management of DRP

Novel agents are emerging, including ranibizumab, a monoclonal antibody fragment that is anti-angiogenic; it is used for diabetic macular oedema. Severe non-proliferative and proliferative retinopathy is treated with retinal photocoagulation, which has been shown to reduce severe visual loss by 85% (50% in maculopathy). Argon laser photocoagulation is used to:

- Seal leaking microaneurysms.
- Destroy areas of retinal ischaemia.
- Reduce macular oedema.
- Gliose new vessels on the retinal surface.

Patients must be reviewed regularly to check for recurrence.

Extensive bilateral photocoagulation can cause visual field loss, interfering with driving and night vision. Vitrectomy may be used in recurrent vitreous haemorrhage that has failed to clear, or tractional retinal detachment threatening the macula. Rubeosis iridis is managed by early pan-retinal photocoagulation. ²

Management of diabetic foot

Preventative treatment is the most effective method of managing the diabetic foot. Patient education is crucial. Annual screening should include formal testing of sensation and removal of callus (by podiatrist). Further management includes:

- Débridement of dead tissue.
- Prompt and prolonged antibiotics in the presence of infection.
- Bespoke orthotic footwear (preventing pressure and deformity)
- Vascular assessment: angiography/vascular reconstruction if the foot is ischaemic.
- Charcot foot: cast immobilisation and avoidance of weight-bearing.
- Amputation: if there is extensive tissue/bony destruction, or intractable ischaemic pain when vascular reconstruction is not possible or has failed. ²

Aim

To know the incidence of diabetic retinopathy in diabetic foot patients in sample of Iraqi patients.

The study

Patients and method

Study setting and design : The study was conducted in out patients ophthalmology of AL-Imamain AL-Kadhymiyain medical city .

A hospital based cross sectional study with an attempt to evaluate the incidence of diabetic retinopathy among patients who had diabetic foot.

The period of data collection was 3 months started from 23th of september 2018 to 23th of December 2018.

Selection of the study sample: A total number of 26 diabetic patients with diabetic foot were interviewed from both sexes , age from 20-70 years old who have diabetes .

HbA1c was used to assess the control , less than 7 % considered good control ,and above 7% considered poor control.

Data collection: with cooperation of diabetic and endocrine unit by referring diabetic patients with diabetic foot to ophthalmology unit for dilated fundus examination were patients were given mydriatic eye drops then fundus examination was done with slit lamp biomicroscope with 90D lense to assess the presence of diabetic retinopathy .

A Questioners was used to get information from studied population , which included : name .age ,sex ,type of ,duration and control(HbA1c) of diabetes

Completed Data was entered in Microsoft Excel program 2016.

Results

A total of 26 patients (12 females and 14 males) were included in this study.

3 (11.5%) of them were type I DM , and 23 (88.5%) were type II DM .

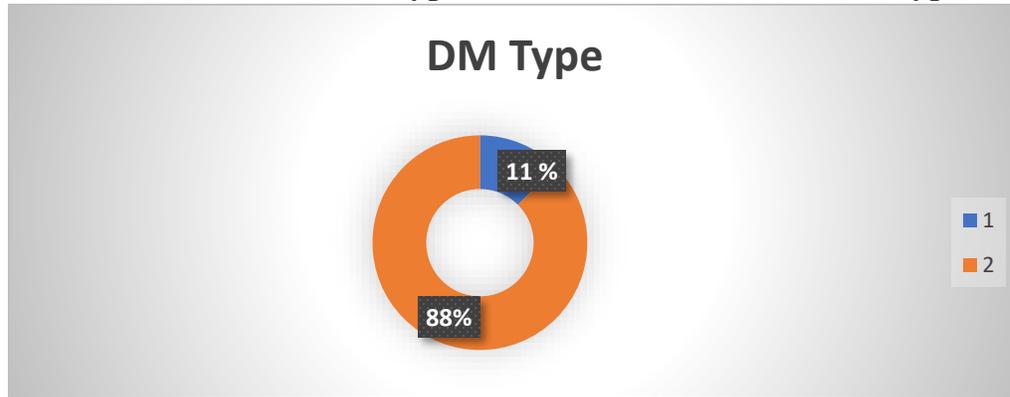


Fig. 9 : percent of diabetic type.

Regarding the age there was no patient between 20-30 years , 1 (3.8%) of them was between 31-40 , 10 (38.5%) were between 41-50 , 11(42.3%) were between 51-60 , and 4 (15.4%) of them were 61 year and above .

Table 3 : number and percent of each age group with number of types .

Age category	NO. & % of each	DM I	DM II
20-30	0	0	0
31-40	1 (3.8%)	1	0
41-50	10 (38.5%)	2	8
51-60	11 (42.3%)	0	11
>=60	4 (15.4 %)	0	4

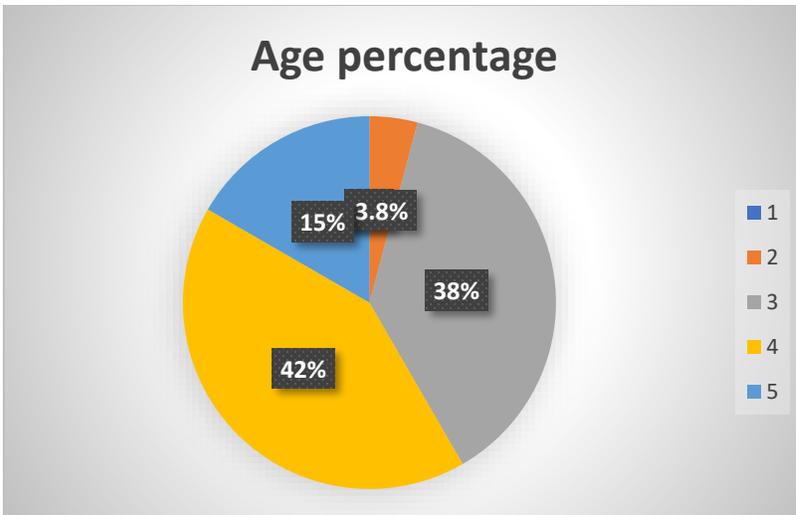


Fig.10 : percent of each age category . (1= 20-30 yr. , 2=31-40yr , 3=41-50yr , 4=51-60yr , 5>= 61yr)

The presence of DR percent in all patients was **92.3% (24 patients had DR)**

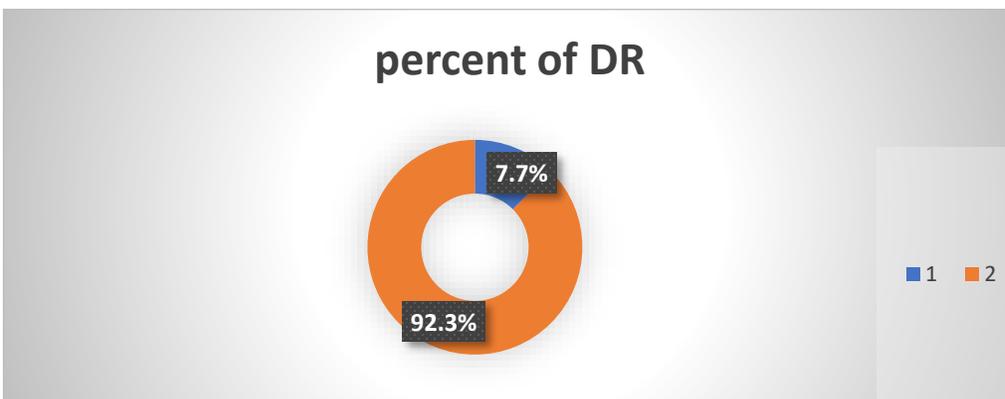


Figure 11 : percent of DR (1= do not have DR , 2= have DR)

Table 4 : relationship between control of DM and retinopathy with each age group.

Age category	NO. & % of each	Poor control %	Good control %	Retinopathy %
20-30	0	0	0	0
31-40	1 (3.8%)	100 %	0 %	100 %
41-50	10 (38.5%)	100 %	0 %	90 %
51-60	11 (42.3%)	100 %	0 %	91 %
>=61	4 (15.4%)	100 %	0 %	100 %

The duration of diabetes was between 6-10 years in 15.3 % of them , between 11-15 years was 34.6% , between 16-20 years was 30% ,and it forms 23% equal and more than 21 years .

Table 5 : percent of diabetic duration with control and DR .

Duration of DM (years)	NO. of patients for each duration	Poor control %	Good control %	Retinopathy %
<= 5	0	0	0	0
6-10	4 (15.4%)	100 %	0%	75 %
11-15	9 (34.6%)	100 %	0%	89 %
16-20	7 (30%)	100 %	0%	100 %
>= 21	6 (23 %)	100 %	0%	100 %

Discussion

Our study to demonstrate the percent of DR among DF patients in our hospital which was 92.3 % , which is nearly similar results that shows 90% of DF patients had DR changes in South Korea.¹⁵

But other study was carries in south India shows less prevalence which was 67.58% · this difference in percent may be due to larger sample size and longer period of data collection

it is more than other study ,Other Numerous studies were carried out to determine the prevalence of retinopathy yielded different rates between 26.3 % - 93.6%^{9,10,11,12,13,14} .The variation in rate between other studies and our study could be as a result of different methods used in those studies, the population and or the races involved, or variation in controlling blood sugar level , the sample size and duration of data collection and absence of DF.

Our results shows a significant association between DR and diabetes control which is similar to other studies that suggest the presence and severity of DR correlate with high level of HbA1c^{17,18} .

Our study showed a significant association between prevalence of DR and diabetes duration, this pattern was seen in Klein et al. As the prevalence of DR varied from 28.8% in persons who had diabetes for less than five years to 77.8% in persons who had diabetes for 15 or more years¹⁸ .

Since all patients in our study had DF so the had other microvascular complication other than DR due to poor glycemic control which goes with other study found there is Relationships between glycaemic control and development of microangiopathy¹⁹. this may explain the high percent of DR in our study (present of complication and poor control)

Limitations of this study include the possibility of selection bias, where more patients with worse disease control (including high HbA1c values and those with complications) were recruited into the program, while others with inadequate control or multiple comorbidities have been referred to secondary care. The intention of the program was to include all diabetic patients irrespective of their current disease control status.

Conclusion

data from this study demonstrated a high prevalence of DR complications among patients with DF with high HbA1c levels.

the results of this study support recommendations for early complications screening and aggressive targeting of glycemic control in patients with diabetes.

Recommendations

we can reduce the prevalence of diabetic retinopathy by developing an integrated health and social care pathway, further education and better communication between all the relevant parties hence it is extremely crucial to spread knowledge regarding diabetic retinopathy through television, newspaper, posters in all hospitals and other health centres as it will motivate and encourage the diabetic patients to undergo a timely eye examination and thus engage individuals so an initial details and comprehensive eye examination should be performed shortly after the diagnosis for all type 2 diabetic patients. Subsequent examinations for type 1 and type 2 diabetic patients should be repeated annually in the absence of retinal changes , otherwise shorter intervals are recommended ²⁰ .

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