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level of albumine / creatinine ratio in patient with diabetic retinopathy

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Done by the student

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6th.grade.

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content

- **Acknowledgement** **4**

-Dedication **5**

-List of figures **6**

- list of table **7**

-Abbreviation **8**

-Abstract **9**

-key word **11**

-Introduction **12**

-Aim **28**

-Patients & Methods **29**

-Results **30**

-Discussion **37**

-conclusion **39**

-recommendation **40**

-References **41**

acknowledgment

First I would like to thank

Dr.Abeer Abdul –Amir my supervisor for the assistance and encouragement to pursue to this study that wouldn't complete without her great help and knowledge and be so kind and patient with me.also wish to thank my family for there support and inspiration .last we thank persons with diabetes who would not have succeeded in completing this study on time by cooperation of them.

Dedication :

*I dedicate this research to my **Mam** and **Mad***

Who learn me how to fight and put all my force to reach to my dream and never give up . who stand beside me and never let go me.

*Thank u to be my parents u are the greater gad gift to me **love u***

List of figures

Figure	Title	Page.no
Figure.1	Microaneurysm and dot/blot heamorrhage	19
Figure.2	Retinal hemorrhage.	19
Figure.3	Exudates involving the fovea .	20
Figure.4	clinical appearances of cotton wool spots .	21
Figure.5	Venous change	22
Figure.6	Intra retinal micro vascular abnormalities .	22

List of tables

Table	Title	Page. No
Table(1)	Classification of patent according to gender	30
Table (2)	distribution of age group in our study	31
Table(3)	Duration of diabetic	32
Table (4)	Type of diabetic	32
Table(5)	Control of diabetic	33
Table(6)	Albumin/ creatinine ratio	34
Table(7)	Stage of diabetic	35
Table(8)	Relation of albumin/ creatinin ratio to stage of diabetic	36

Abbreviations :

DM : diabetic mellitus

DR : diabetic retinopathy

A/B : albumin/ creatinine ratio

Abstract

Background:

Diabetes mellitus is reaching epidemic proportions in many countries, and the impact of vision loss due to diabetic eye disease on public health is a major concern ; Unfortunately; there is a lack of awareness about the existing interventions for preventing and the management of complications.

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]

Aim of this study

to assess level of albumine / creatinine ratio in patient with diabetic retinopathy in a sample of iraqi patient

Patient and Methods:

This is across sectional study conducted on 12 iraqi diabetic patients attending Al Immamain Al khadhimain teaching hospital who were examind at the ophthalmology outpatients clinic and found to have diabetic retinopathy aquastionaire including name age sex type of DM , duration of DM ,and control of DM was answered by each patient then sent to investigate there albumin/creatinine ratio, data was collect from first of November 2018 to first of January 2019.

Result:

12 diabetic patient interviewed in this study , most case were female 58.33%, and age group range 20 to 70 years old but most patients were 50 to 70 years and represent 41.66%, the majority of patent have type 2 diabetic 91.66% while only 8.33% have type 1, most patent were have diabetic for more than 20 years 58.33% , the control of diabetic in patent were half of them have good control and the other half poor control ,according to albumin/ creatinine Ratio about 25% of patent have micro albuminurea 8.33% have macro albminurea and 50% have normal kidney function , 66.66% of patent were have pre- proliferative retinopathy and 33.33% have proliferative diabetic retinopathy

Conclusion

We observed that patient with diabetic have a high risk to develop diabetic retinopathy and most patient that have advance stage of diabetic retinopathy also have abnormal renal function and when patient have a long duration and poor control of diabetic increase the risk to have diabetic nephropathy wich effect on treatment of diabetic retinopathy

Key word:

Diabetic mellitus , diabetic retinopathy ,

Albumin/ ceatinine ratio

Introduction:

Diabetic eye diseases refers to a group of eye problems that people with diabetes may face as complication of diabetes ; all diabetic retinopathy ; cataract ; glaucoma can cause severe vision loss or even blindness; moreover diabetics are 25 times more likely to become blind than non-diabetics due to DRP. [1]

Diabetic retinopathy is the leading cause of blindness among working-aged adults, and according to (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. [1]

Ophthalmic complications of diabetes: [2]

Common

- Retinopathy.
- Iridopathy (minor iris transillumination defects).
- Unstable refraction.

• Uncommon

- Recurrent styes.
- Xanthelasmata.

- Accelerated senile cataract.
- Neovascular glaucoma (NVG).
- Ocular motor nerve palsies.
- Reduced corneal sensitivity.

• **Rare**: Papillopathy, pupillary light-near dissociation, wolfram syndrome (progressive optic and mutiple neurological and systemic abnormalites) acute onset cataract;rhino-orbital mucormycosis

Prevalence:

The reported prevalence of diabetic retinopathy in diabetic varies substantially between studies.

Even amongst population in the same countery .

But it probably around (40)% more common in diabetic mellitus type1 than type2 , and sight threating disease in up to 10% .

Proliferative diabetic retinopathy about (5_10)% of diabetic population ,and incidence up to 90% in type 1 diabetic mellitus after30 years .[2]

Risk factor of diabetic retinopathy

1-Diabetes duration

The longer a person suffers from diabetes, the greater the risk of developing retinopathy. Nearly 90% of people who have had type 1 diabetes for over 10 years develop some extent of diabetic retinopathy. The proportion of those who have had type 2 diabetics for over 10 years but do not take insulin is 67% and among type 2 diabetics with a 10 year disease duration who do take insulin, the proportion is 79%.[2]

2-Blood sugar level

The higher a person's blood sugar level is, the greater the risk of developing diabetic retinopathy. People with a persistently raised glycated hemoglobin level (which indicates blood glucose level) are at greater risk of developing diabetic retinopathy.[2]

3-Blood pressure

High blood pressure in itself is detrimental to the retinal blood vessels and can cause hypertensive retinopathy. Therefore, among people with both a raised blood sugar level and high blood pressure, the risk of diabetic retinopathy is [2]greater still

4-Smoking

Smokers are at a greater risk of blood vessel disorders, including retinopathy]2]

5-Gestational diabetes

Pregnant women with gestational diabetes are at a greater risk of developing diabetic retinopathy [2]

6-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.
Diabetic macular usually resolves spontaneously after pregnancy and need not be treated if it develops in later pregnancy .[2]

7- 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. [2]

Pathogenesis

.Hyperglycemia is considered to play an important role in the pathogenesis of retinal microvascular Multiple metabolic pathways have been implicated in hyperglycemia-induced vascular damage .

The earliest responses of the retinal blood vessels to hyperglycemia are dilatation of blood vessels and blood flow changes. These changes are considered to be a metabolic auto regulation to increase retinal metabolism in diabetic patient [3] .

Pericytes loss is another hallmark of the early events of DR. Evidence of apoptosis of pericytes triggered by high glucose has been shown in both in vitro and in vivo studies [4,5]. Since pericytes are responsible for providing structural support for capillaries, loss of them leads to localized outpouching of capillary walls. This process is associated with microaneurysm formation, which is the earliest clinical sign of DR [6].

In addition to pericyte loss, apoptosis of endothelial cells and thickening of the basement membrane are also detected during the pathogenesis of DR, which collectively contribute to the impairment of the BRB Furthermore, pronounced loss of pericytes and endothelial cells results in capillary occlusion and ischemia. [7]

Classification:

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

• **Background diabetic retinopathy (BDR) :** is characterized by micro aneurysms, dot and blot hemorrhages and exudates these are generally the earliest signs of DR, and persist as more advanced lesions appear. [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. [2]

• **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 retinalischemia with a heightened risk of progression to retinal neovascularization. [2]

• **proliferative diabetic retinopathy (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.[2]

• **Advanced diabetic eye disease :** is characterized by tractional retinal detachment significant persistent vitreous hemorrhage. [2]

Symptoms

Patient may have no symptoms in the early stage of diabetic retinopathy . as the condition progress diabetic retinopathy symptoms may include.[8]

-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.

Signs:

-Micro aneurysms:

Are localized out pouchings, mainly saccular, of the capillary wall that may form either by focal dilatation of the capillary wall where pericytes are absent, or by fusion of two arms of a capillary loop; they leak plasma constituents into the retina as a result of breakdown in the blood–retinal barrier is the earliest sign DRP. [2]

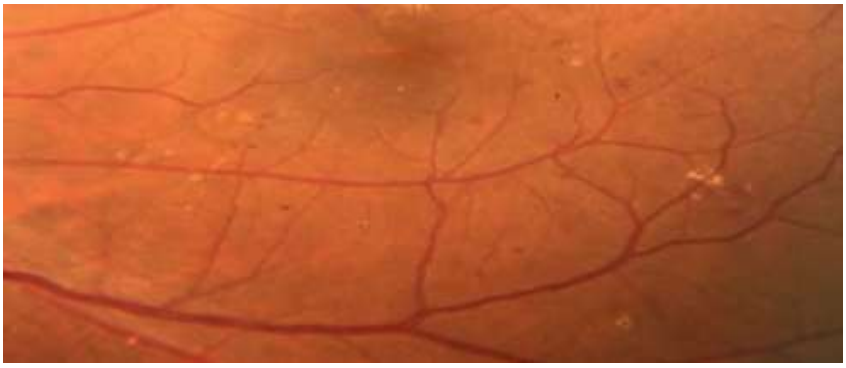
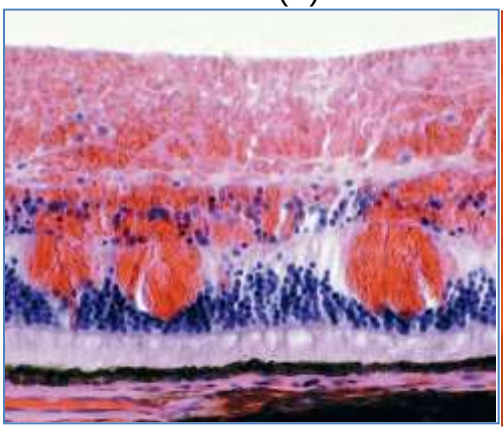


Fig 1 : Micro aneurysms and dot/blot hemorrhage at the posterior pole

-<u>Retinal Hemorrhages</u> *:* either flame shaped ,dot\blot shape or deep dark round hemorrhage. [2]

(A)



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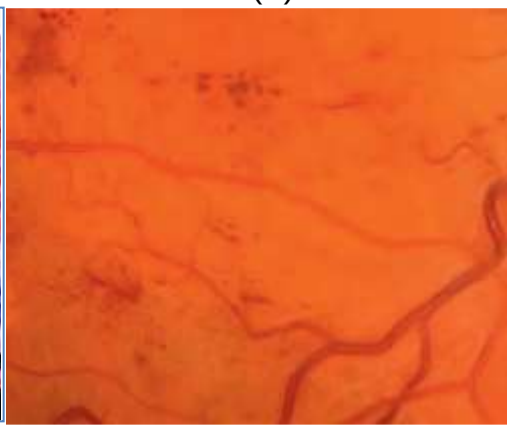

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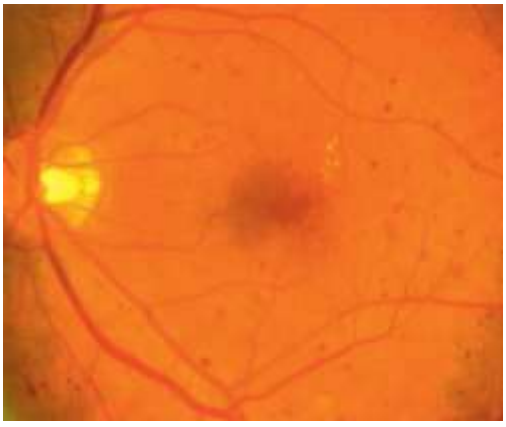

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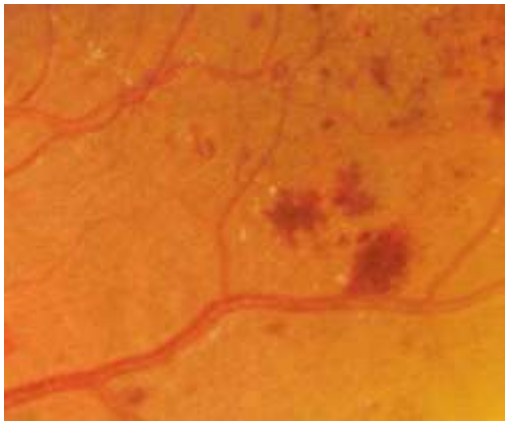


Fig. 2: Retinal hemorrhages. (A) Histology shows blood lying diffusely in the retinal nerve fiber and ganglion cell layers and as globules in the outer layers; (B) retinal nerve fiber layer (flame) hemorrhages; (C) dot and blot hemorrhages(D) deep dark hemorrhages

- **Exudates**: also called hard exudates caused by chronic localized retinal edema ;they composed of lipoprotein and lipid filed macrophage, hyperlipidemia may increase the possibility of exudates formations. [2]

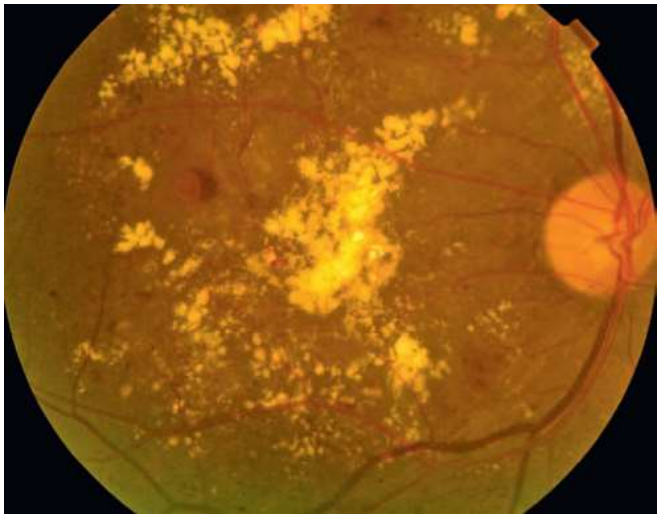


Fig. 3 : exudates involving the fovea, including central crystalline cholesterol deposition – focal laser has recently been applied superio temporal to the fovea.

-Diabetic maculo pathy: includes:
1-foveal edema.
2-foveal exudates.
3-foveal ischemia.

Diabetic maculopathy is the most common cause of visual impairment in diabetic patients ;defuse retinal edema is due to extensive capillary leakage and localized edema by focal leakage from micro aneurysms and dilated capillary segments.[2]

-cotton wool spots :are composed of accumulations of neuron debris they results from disruption of nerve axons. [2]

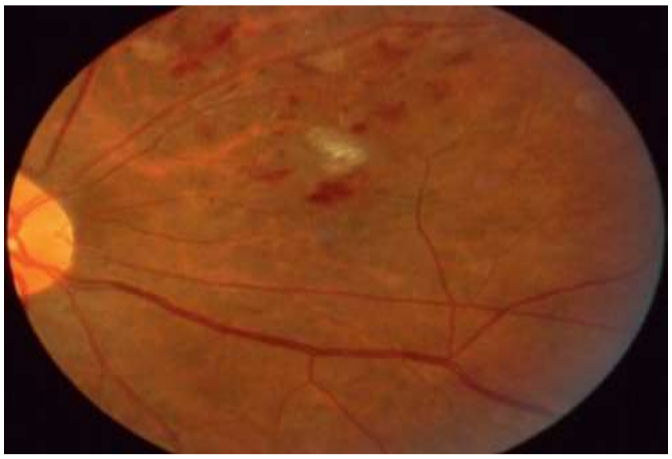
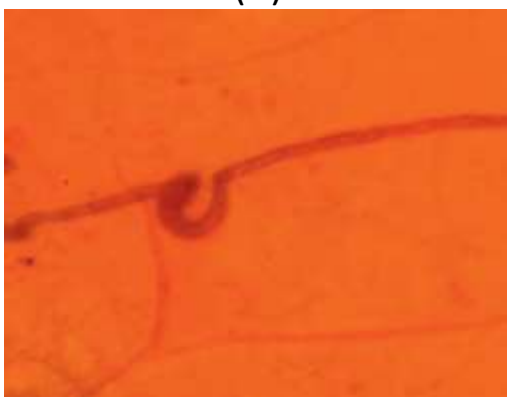


Fig. 4: Cotton wool spots clinical appearance (ischemic changes).

-venous changes : seen in ischemia consists of generalized dilatation and tortuosity; looping and beading. [2]

(A)



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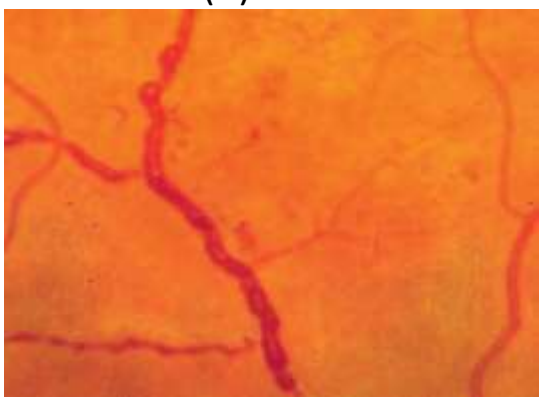
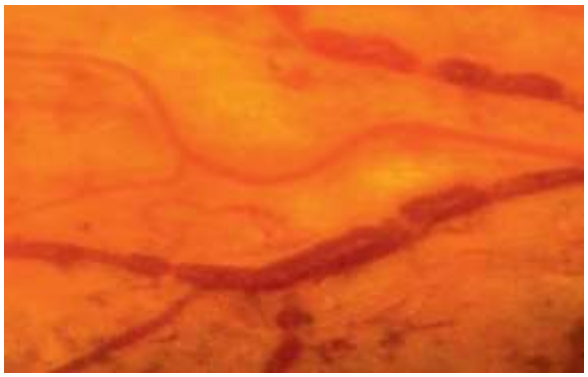




(c)

Fig. 5: Venous changes. (A) Looping; (B) beading; (C) severe segmentation.

-Intra-retinal micro vascular abnormalities(IRMA):

Are arteriolar venular shunts that run from retinal arteriolar to venules. [2]

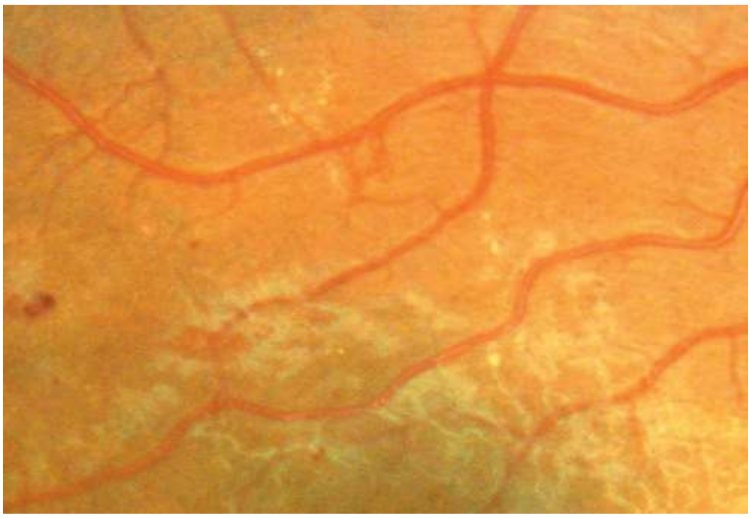


Fig. 6: Intra retinal micro vascular abnormalities clinical appearance

Category/description	Management
Non-proliferative diabetic retinopathy (NPDR)	
No DR	Review in 12 months
Very mild NPDR	Review most patients in 12 months
Microaneurysms only	
Mild NPDR	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	
Moderate NPDR	Review in approximately 6 months Proliferative diabetic retinopathy (PDR) in up to 26%, high-risk PDR in up to 8% within a year
• 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	
Severe NPDR	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: • Severe haemorrhages in all 4 quadrants • Significant venous beading in 2 or more quadrants • Moderate IRMA in 1 or more quadrants	
Very severe NPDR	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)	
Mild–moderate PDR	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	
High-risk PDR	Treatment advised – see text Should be performed immediately when possible, and certainly same day if symptomatic presentation with good retinal view
• New vessels on the disc (NVD) greater than ETDRS standard photograph 10A (about ⅓ disc area) • Any NVD with vitreous haemorrhage • NVE greater than ½ disc area with vitreous haemorrhage	
Advanced diabetic eye disease	See text

Table. managment of diabetic retinopathy

Nephropathy

Diabetic nephropathy is a serious kidney-related complication of type 1 diabetes and type 2 diabetes. It is also called diabetic kidney disease. Up to 40 percent of people with diabetes eventually develop kidney disease.[9]

Diabetic nephropathy affects the ability of your kidneys to do their usual work of removing waste products and extra fluid from your body. The best way to prevent or delay diabetic nephropathy is by maintaining a healthy lifestyle and treating your diabetes and high blood pressure.

Over many years, the condition slowly damages kidneys' delicate filtering system. Early treatment may prevent or slow disease progression and reduce the chance of complications.

kidney disease may progress to kidney failure, also called end-stage kidney disease. Kidney failure is a life-threatening condition. At this stage treatment options are dialysis or a kidney transplant.

Symptoms

In the early stages of diabetic nephropathy, may not notice any signs or symptoms. In later stages, the signs and symptoms include:

*Worsening blood pressure control *Protein in the urine

*Swelling of feet, ankles, hands or eyes

*Increased need to urinate

*Less need for insulin or diabetes medicine

*Confusion or difficulty concentrating

*Loss of appetite

*Nausea and vomiting

*Persistent itching

Risk factors

Several factors may increase your risk of diabetic nephropathy, including:

*Diabetes, type 1 or 2

*High blood sugar (hyperglycemia) that's difficult to control

*High blood pressure (hypertension) that's difficult to control

*Being a smoker and having diabetes

*High blood cholesterol and having diabetes

*A family history of diabetes and kidney disease0

Complications

Complications of diabetic nephropathy may develop gradually over months or years. They may include:

*Fluid retention, which could lead to swelling in your arms and legs, high blood pressure, or fluid in your lungs (pulmonary edema)

*A sudden rise in potassium levels in your blood (hyperkalemia)

*Heart and blood vessel disease (cardiovascular disease), possibly leading to stroke

*Damage to the blood vessels of the retina (diabetic retinopathy)

*Anemia

*Foot sores, erectile dysfunction, diarrhea and other problems related to damaged nerves and blood vessels

*Pregnancy complications that carry risks for the mother and the developing fetus

*Irreversible damage to your kidneys (end-stage kidney disease), eventually requiring either dialysis or a kidney transplant for surviva

Prevention

To reduce your risk of developing diabetic kidney disease:

Treat your diabetes. With effective treatment of diabetes, you may prevent or delay diabetic kidney disease.

Manage high blood pressure or other medical conditions. If you have high blood pressure or other conditions that increase your risk of kidney disease, work with your doctor to control them. Ask your doctor about tests to look for signs of kidney damage.

Follow instructions on over-the-counter medications. When using nonprescription pain relievers, such as aspirin, ibuprofen (Advil, Motrin IB, others) and acetaminophen (Tylenol, others), follow the instructions on the package. For people with diabetic kidney disease, taking these types of pain relievers can lead to kidney damage.

Maintain a healthy weight. If you're at a healthy weight, work to maintain it by being physically active most days of the week. If you need to lose weight, talk with your doctor about strategies for weight loss. Often this involves increasing daily physical activity and reducing calories.

Don't smoke. Cigarette smoking can damage your kidneys and make existing kidney damage worse. If you're a smoker, talk to your doctor about strategies for quitting smoking. Support groups, counseling and medications can all help you to stop.

Aim

to assess level of albumin / creatinine ratio in patient with diabetic retinopathy in a sample of iraqi patient

patient and methods

This is across sectional study conducted on a sample of iraqi diabetic patients attending ophthalmology outpatient unit in Al- Immamain Al -Khadhimain teaching hospital from the period first of novmber 2018 to first of January 2019,

Atotal number of 12 iraqi diabetic patients who had adilated fundus examination by slit lamp biomicriscope and 90 D fundus lens and found to have diebetic retinopathy of different stages then aquastionaire including. Name ,age ,sex ,type of DM ,duration of DM ,control of DM by the last HbA1c level was answerd by those patients ,then those patient sent for Albumin/creatinine ratio to assess their renal function,

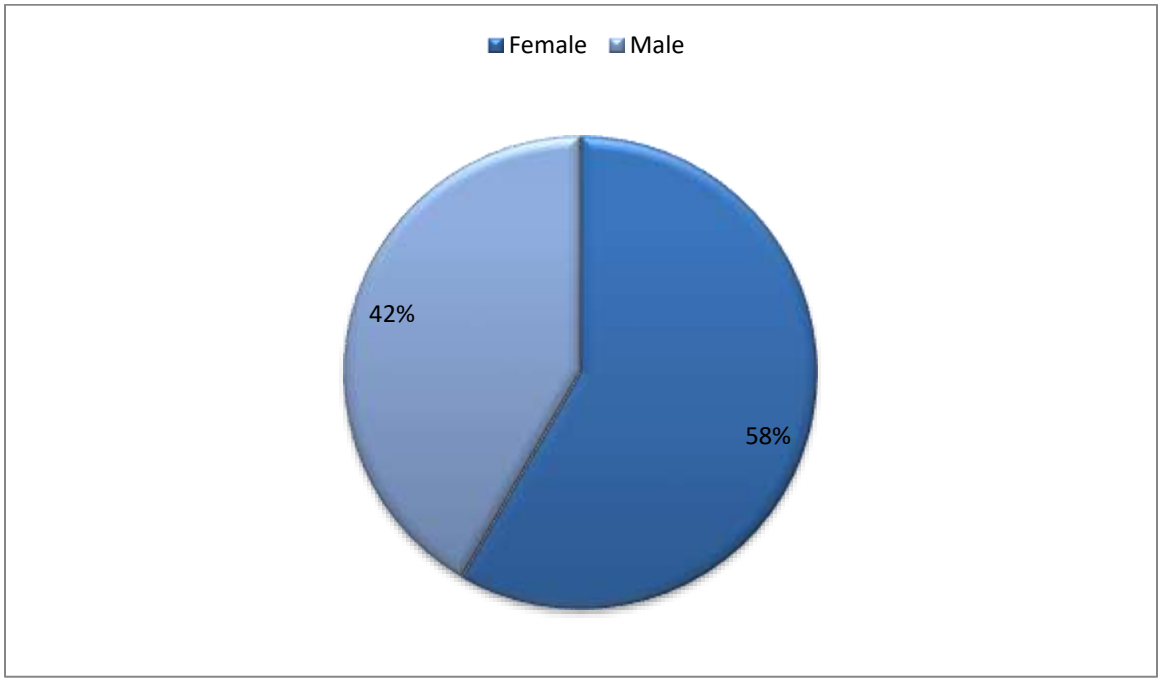
Data from aquastionaire was used in addition to the finding of examination and investigation , complete data was analyzed by microsoft Excel program.

Result

Tale(1):showing distribution of age group in our study we took 12 case found that most patients are female as showing below

Gender	No	Percentage
Female	7	58.33%
Male	5	41.66%

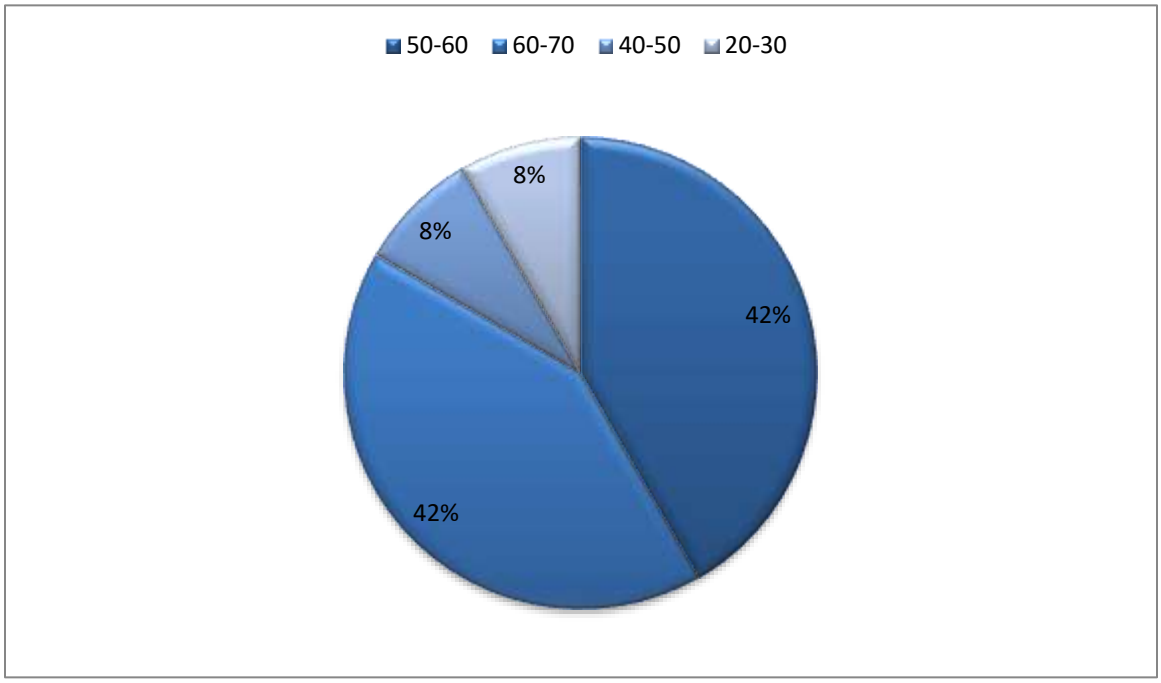
Table(1)



Table(2): showing distribution of age group in our study

Age group	Percentage
10-20 years	0%
20-30 years	8.33%
40_50 years	8.33%
50-60 years	41.66%
60-70 years	41.66%

Table.2



Table(3): show duration of diabetis

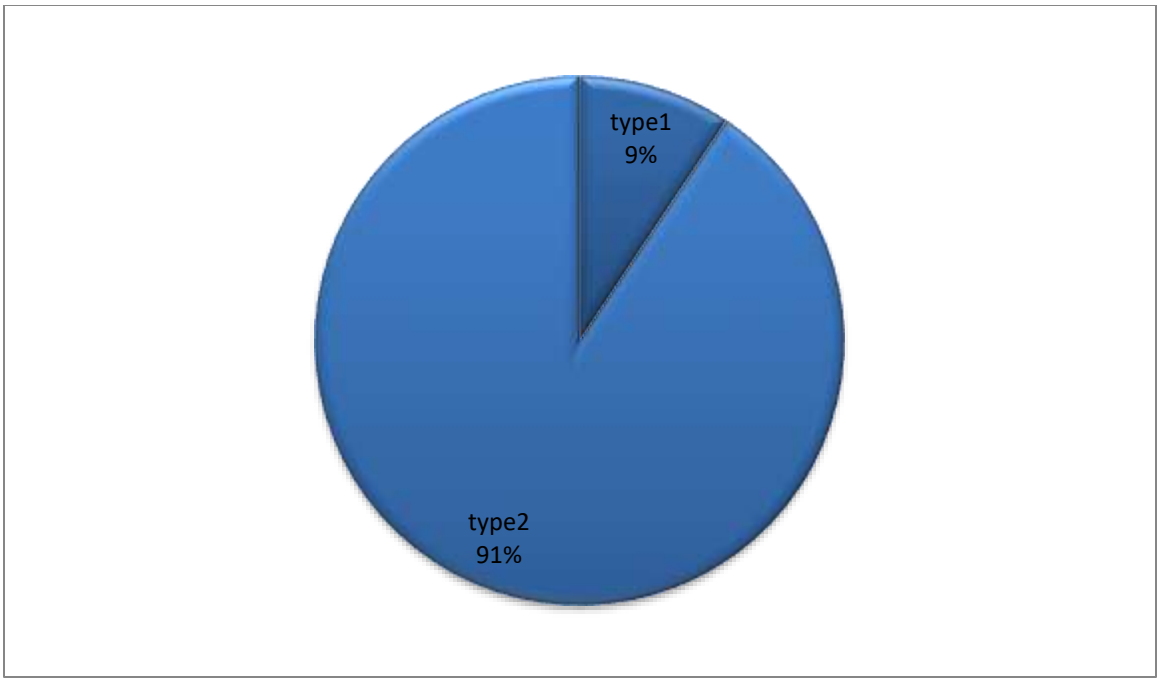
Duration of diabetic	Percentage
5-10 years	16.66%
10_20 years	25%
20_30 years	58.33%

Table(3)

Table (4): show type of diabetic in our patient we found that most patient was diagnosed with type 2 diabetic mellitus and only one have type1 diabetis

Type of diabetic	No	Percentage
Type 1	1	8.33%
Type 2	11	91.66%

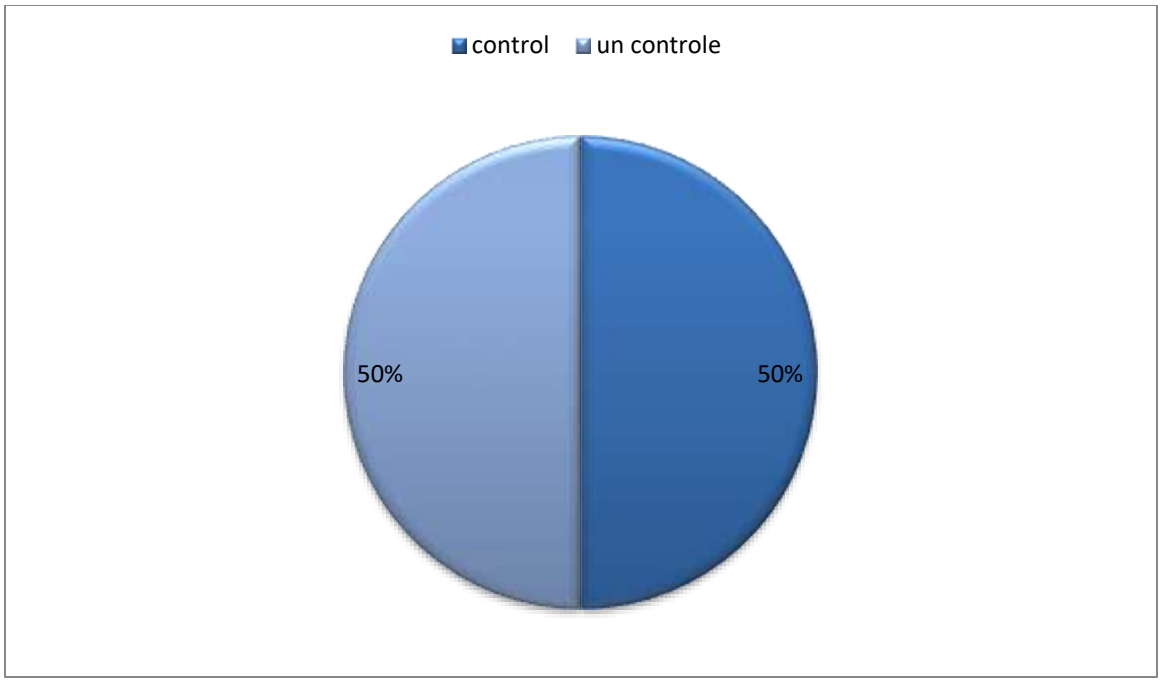
Table(4)



Table(5):show control of diabetic acording to level of HBA1c we conceder level from 5.6 to 7 is a good control

Control of Diabetic	No	Percentage
Control	6	50%
Un control	6	50%

Table(5)



Table(6): of show renal function according to level

albumin\ creatinine ratio

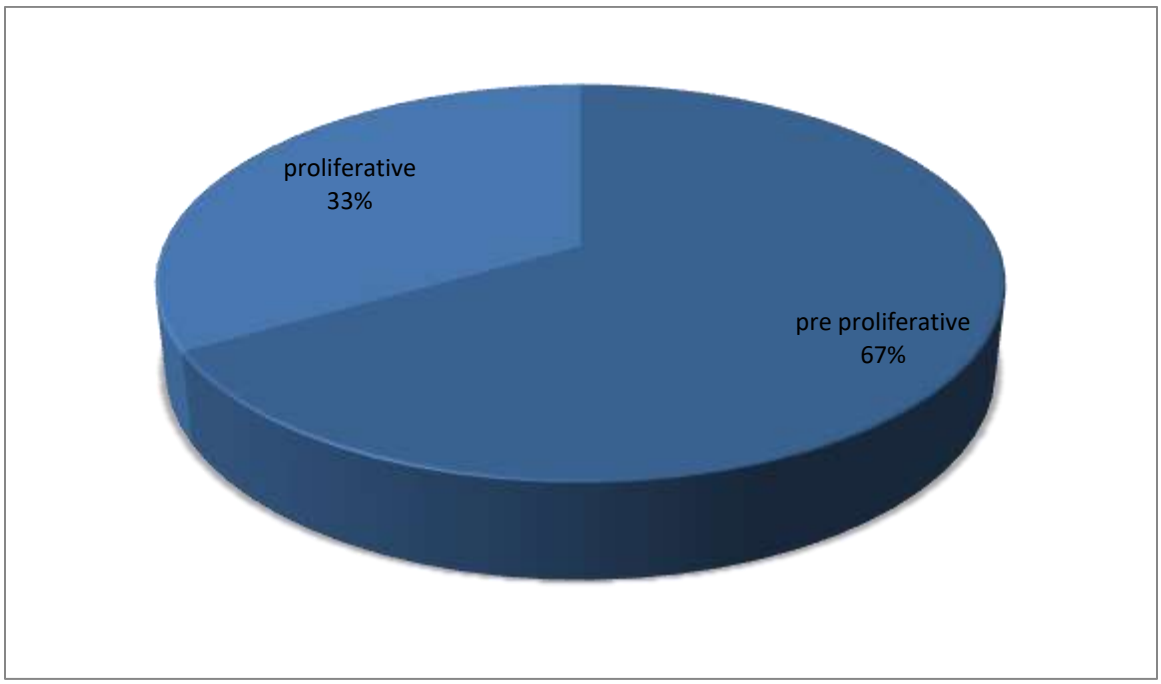
Category	ACR(mg \g)	Term	No	Percentage
A1	<30	normal	8	66.66%
A2	30_300	Micro albumin urea	3	25%
A3	>300	Macro albumin urea	1	8.33%

Table(6)

Table (7):shows number of patiens and stage of DR

Type of presentation	No	Percentage%
Pre proliferative retinopathy	8	66.66%
Proliferative retinopathy	4	33.33%

Table(7)



Table(8) relation of albumin/ creatinine ration to the stage of diabetic retinopathy

Albumin / creatinine ratio	No.	Pre-proliferative retinopathy	Proliferative retinopathy	
normal	8(66.66%)	8(66.66%)	----------	
Micro albumin urea	3(25%)	----------	3(25%)	Totally.
Macro albumin urea	1(8.33%)	----------	1(8.33%)	33.33%

Table(8)

Discusion

This study was conduct on selected patient who visit Al_ Kadhymia teaching hospital who present with variable duration of diabetic and variable stage of diabetic retinopathy .

in our study found that most patient were female gender**58.33%** and male gender was**41.66%** we compare our result with other research done on Caucasian patient with diabetic retinopathy was male more than female **56.13%** male percentage **Journal of Diabetes Research**[10]

Most patent were age more than **50** years old **41.66%** and have diabetic more than 10 years **16.66%between5-10 years** ,**25%between 10-20 years** and most of them **58.33% were more than 20 years** , the same result were observed in study on Wisconsin patient with diabetic Said that the prevalence of them that have diabetic retinopathy **28.8%** if have diabetic **less than 5 years** , **77.8%**if have diabetic **more than 15** years **Prevalence and Risk of Diabetic Retinopathy** [11] on Americans patient with diabetic that said there is risk of developing diabetic retinopathy by increase **age 20-74 years and risk about 3.6%** of developing retinopathy if have diabetic for long duration more than **10 years** and 1.6% risk if have it less than 10 years **Retinopathy in Diabetes** [12], and other research in US observe that most patient **40.3% percent were older than 40** years **The Prevalence of Diabetic Retinopathy Among Adults in the United States**[13]

Most patent have type2 diabetic**91.66%** and only **8.33** have type1diabetic mellitus

Half of patient in our study 50% were poor control of diabetic **HBA1c>7** and half of them were good control50% Compare these result with other research that said poor control of diabetic have **95%** risk of developing and progression of diabetic retinopathy**- Relationship of Hyperglycemia to the Long-term Incidence and Progression of Diabetic Retinopathy** [14], and other study said that poor control of diabetic have a risk about 45%of developing diabetic retinopathy in high risk group and 43% in low risk group **The Relationship of Glycemic Exposure (HbA1c) to the Risk of Development and Progression of Retinopathy in the Diabetes Control and Complications Trial**[15]

In our study **25%**of patient were albumin/ creatinin ratio between **30-300mg/g** have micro albumin urea and **8.33%** have macroalbuminurea these patient were have proliferative diabetic retinopathy while patient who have normal albumin/ creatinine ratio **66.66%**have pre proliferative diabetic retinopathy we observed the same result in study on japanes patient who have diabetic retinopathy and nephropathy it was shown that only **36%** had no diabetic retinopathy, while **53%** had non proliferative, **9%** moderate to severe, and **2%** severe diabetic retinopathy **Japan Diabetes Complications**[16].and other study on Caucasian patient with diabetic in the study observe there is relation between diabetic retinopathy and abnormal albumin/creatin ratio **Glomerular Filtration Rate and/or Ratio of Urine Albumin to Creatinine as Markers for Diabetic Retinopathy**[10]

Conclusion

We observed that patient with diabetic have a high risk to develop diabetic retinopathy and most patient that have advance stage of diabetic retinopathy also have abnormal renal function and when patient have a long duration and poor control of diabetic increase the risk to have diabetic nephropathy wich effect on treatment of diabetic retinopathy

Recommendations :

Diabetic retinopathy is a serous diseases and one of cause of blindness world wide every patent with diabetic should highly control of there blood sugar and have annual visit ophthalmological clinic they should also investigate their renal function to notice if there any abnormality for early control to decrease risk and progression of diabetic retinopthy

Also improving the renal function will improve response to treatment of diabetic retinopathy.

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