

Narrative Review: Pathogenesis and Management Of Diabetic Retinopathy

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ABSTRACT

Diabetic Retinopathy is a microvascular disorder that occurs due to the long-term effects of diabetes mellitus. Diabetes mellitus (DM) is caused by metabolic disorders that occur in the pancreas organ which is characterized by increased blood sugar or often referred to as hyperglycemia which is caused by a decrease in the amount of insulin from the pancreas. This can cause damage to the retina that threatens vision and can cause blindness. Effective management requires a multidisciplinary approach that includes glucose control, medical intervention, and patient education. This study aims to determine the pathogenesis and management of Diabetic Retinopathy. This research is a literature study with a narrative review approach. The literature reviewed is literature obtained from databases that have been accredited or indexed by Sinta. The results of this literature study show that vascular dysfunction including loss of pericyte cells, formation of acellular capillaries (endothelial cell death), thickening of the basement membrane and increased capillary permeability to the closure of blood vessels leading to retinal ischemia-infarction is the pathogenesis of diabetic retinopathy. Management of diabetic retinopathy depends on the severity of the symptoms. Treatment does not only consist of observing blood sugar control, systemic hypertension and hypercholesterolemia, but also therapy such as laser photocoagulation, administration of Anti-Vascular Endothelial Growth Factor (Anti-VEGF), intravitreal steroids or IVTA (Intra Vitreous Triamcinolone Acetonide), and other procedures. pars plana vitrectomy.

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INTRODUCTION

Retinopathy Diabetes is a complex health problem with diverse pathogenetic mechanisms. Effective management requires a multidisciplinary approach that includes glucose control, medical intervention, and patient education (Abdelhady, A et et al., 20 19). Retinopathy Diabetic retinopathy is a microvascular disorder that occurs due to the long-term effects of

diabetes mellitus. It can cause damage to the retina that threatens vision, and can lead to blindness. Retinopathy Diabetic retinopathy is the most common cause of vision loss in adults in the working age group. ¹ Classification of retinopathy Diabetic has several stages, namely non- proliferative and proliferative. (Douglas, B. et al., 2018)

Based on *International Agency for the Prevention of Blindness (IAPB)* in 2015, 145 million people suffered from retinopathy diabetic retinopathy (DR). In Europe, it is estimated that between 20% and 35% of people with diabetes will experience retinopathy. diabetic and about 2% will experience retinopathy diabetic proliferative. Prevalence of retinopathy Diabetics in Indonesia are 10-32% of the total population of diabetes mellitus. (Coughlin, B. et al., 2017) Meanwhile in Makassar City, research conducted at Wahidin Sudirohusodo Hospital in 2016 showed that results prevalence sufferer retinopathy diagnosed diabetic is 28.89%. (Douglas, B. et al., 2018)

Based on the description above, researchers are interested in researching literature that discusses the pathogenesis of retinopathy. diabetic and what treatments can be performed on retinopathy patients diabetic. This is used as a background in the creation of a scientific paper entitled " *Narrative Review: Pathogenesis and Management of Retinopathy Diabetic.*"

METHOD

Types of research in research This use studies literature with approach *narrative review*. Research This done with review in a way narrative to related articles with pathogenesis and management diabetic retinopathy. Reviewed literature is literature that has been published on existing databases accredited Synta such as DOAJ, Springerlink, Cochrane, Biomed, Garuda Portal, Google Scholar, Elsevier / Clinical Key, PubMed and other database sources. The literature used in the form of studies report cases that have been rise in 10 years final since study This started. The literature obtained in accordance with objective study This obtained totaling 10 pieces of literature later arranged in a way narrative.

RESULTS

Based on results search obtained as many as 3,240 articles. Journal or article filtered on base title, abstract, and keyword search " Retinopathy Diabetic ", "Diabetic Retinopathy", " Pathogenesis Retinopathy Diabetic ", "Pathogenesis of Diabetic Retinopathy", " Management Retinopathy Diabetic ", " Management of Diabetic Retinopathy ", 72 articles were obtained which will be processed back. All journal or article filtered return see overall the appropriate text, namely 12 journals or article in the form of a case study report. Search results after filtered,, that is 10 years the last one then filtered return with see conformity Contents articles and accessibility article. Final result from search and filter found 10 relevant articles For used in this narrative review.

Table 1. Results table literature review

No.	Journal (Year, Origin, Author)	Title	Methods and diagnosis	Symptom Clinical	Pathogenesis	Management	Conclusion
1.	Guide Husada (Southeast Asia, Indonesia, 2023) Nabila Hana, et al.	Retinopathy Diabetic Proliferative : Risk Factors and Management	Case Report Retinopathy Diabetic :	OD : papilla difficult assessed, neovascularization of the optic disc, bleeding (+). OS : papilla limited firm, exudate (+), micro aneurysm (+) and also neovascularization (+).	Disturbance microcirculation vessels blood. Patient suffering from Type II DM since 9 years ago, the patient's KGD often No controlled	The handling that has been given to the patient is administration of Anti VEGF and Pan Retinal Photocoagulation (PRP) laser.	Retinopathy diabetic is one of common complications occurs in patients with type I DM and Type II. Detection early detection in patients is very important For prevent severity diseases that can cause blindness. At the time detection early role manpower in the facility health level First very much important. Management from retinopathy diabetic covering medication and non- medication. In addition to proper management control factor risk to the patient also plays a role important on the patient's prognosis.

2.	Journal Medical Unila (Southeast Asia, Indonesia, 2017)	Retinopathy Diabetic : Case Review Diagnosis and Management	Case Report Retinopathy Diabetic :	OD : Microaneurysms in 4 quadrants (more from 20 on each quadrants), venous beading in 2 quadrants, flame shape hemorrhage, and hard exudate in the area macula and NVE. OS : vitreous cloudiness, pre retinal hemorrhage and NVD	Disturbance microcirculation vessels blood. Patient with history of diabetes mellitus since 4 years ago with blood sugar levels who does not controlled. The patient also has history blood high and hypercholesterolemia.	Patient planned For done laser photocoagulation procedure panretinal and focal laser/intravitreal anti VEGF for eye right and vitrectomy with endolaser on the eye left.	Retinopathy diabetic is one of complications microvascular in DM. Establishing a diagnosis of retinopathy diabetic as early as Possible need done through effort routine screening in DM patients. Some examination that can done For Diagnosis enforcement includes examination biomicroscopy, angiography fluorescein, ultrasonography and Optical Coherence Tomography (OCT). There are a number of RD management efforts, namely laser photocoagulation, intravitreal steroids, surgical procedures vitrectomy and intravitreal administration of anti-Vascular Endothelial Growth Factor (VEGF).
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3.	Asian Journal of Biomedical and Pharmaceutical Sciences (South Asia, India, 2022) Mayur Raka, et al.	A clinical case report of diabetic retinopathy.	Case Report Retinopathy Diabetic :	ODS : flame shaped hemorrhages, retinal edema and tough exudates, cotton-wool spots, boat- shaped pretinal hemorrhage associates neovascularization	Disturbance microcirculation vessels blood. Patient also have history diabetes mellitus disease in 5 years final	Governance with Pan-Retinal Photocoagulation	This is report case retinopathy diabetic type proliferative in the eye left. Cause general retinopathy diabetic is history of diabetes and hypertension. For prevent condition said, continuous examination is very important and diagnosis and treatment, especially in 3 years First after findings Positive in diabetes sufferers is very important for the best prognosis.
4.	BMC Ophthalmology (East Asia, Japan, 2017) Ryohsuke Kohmoto, et al.	A case of proliferative diabetic retinopathy in which scintillated particles appeared in the intravitreal cavity after laser photocoagulation	Case Report Retinopathy Diabetic :	ODS: preretinal macular hemorrhage	Disturbance microcirculation vessels blood. Have high HbA1c levels (more from 10%).	Treatment performed on the eyes right with photocoagulation panretina	To the best of our knowledge, this is case first where the particles sparkling found appears in the intravitreal cavity after laser photocoagulation for DR. Although particle sparkling This No show symptoms and possible can followed up without treatment, we believe that it is very important For

							investigate change in these cases furthermore.
5.	Korean Journal of Ophthalmology (East Asia, Korea, 2022) Jae Ryong Han, et al.	Spontaneous Regression of Neovascularization at the Disc in Diabetic Retinopathy	Case Report Retinopathy Diabetic :	ODS: bilateral NVD, microaneurysms, dot shaped retinal hemorrhages, abnormalities microvascular intraretinal, and hemorrhage preretina of the eye left	Disturbance microcirculation vessels blood. Suffering from diabetes mellitus and controlled with agent oral hypoglycemic.	Photocoagulation panretinal done three times on the eye left. Treatment during One month with steroid eye drops	Retinal neovascularization is caused by many factors, such as retinal ischemia and inflammatory stimuli. With Thus, neovascularization Possible is response end from various varying stimuli. Reports previously also linked neovascularization discus optics with inflammation.
6.	Indian Journal of Ophthalmology - Case Report (South Asia, India, 2023) Zubin D'Souza, et al.	Bacillary layer detachment in a case of diabetic retinopathy	Case Report Retinopathy Diabetic :	ODS : hemorrhages in all quadrant	Disturbance microcirculation vessels blood. Suffering from diabetes mellitus	anti-VEGF injection	Release layer basilar (BLD) is feature tomography coherence new optics (OCT) just described in various disturbance inflammation
7.	Case Reports in Ophthalmology	Exacerbation of Diabetic Retinopathy Following Hypoxia-	Case Report	ODS : scattered retinal hemorrhages and	Disturbance microcirculation vessels blood. Three twelve year before	Patient undergo pan-retinal photocoagulation. Darbeoetin alfa	Patient with retinopathy advanced stage diabetes who use HIF-PH inhibitors should be be aware

	(East Asia, Japan, 2024) Nobuaki Ariyoshi, et al.	Inducible Factor-Prolyl Hydroxylase Inhibitor Administration: A Case Report	Retinopathy Diabetic :	hard and soft exudates	visit First to our department, he diagnosed suffering from diabetes mellitus type 2 at age 18.	was initially given and replaced with roxadustat HIF-PH inhibitor	exacerbation retinal hemorrhage. If observed, the plan treatment, including termination HIF-PH inhibitors or switch to drug other, must discussed with doctor diabetes specialist, nephrologist, and physician specialist eye.
8.	Clinical & Refractive Optometry (North America, USA, 2024) Victoria Branca, et al.	Proliferative Diabetic Retinopathy: A Case Review	Case Report Retinopathy Diabetic :	ODS : neovascularization disc (NVD), dot/blot hemorrhages in the macula, neovascularization elsewhere (NVE)	Disturbance microcirculation vessels blood. Medical history patient significant For history of DM type II who is insulin dependent for 25 years and has hypertension.	Medications consumed patient including dulaglutide 0.75mg pen injection, insulin glargine 42 units, losartan 100mg, and amlodipine 10mg, intravitreal bevacizumab (IVB) injection and PRP laser therapy	Retinopathy diabetic proliferative is a life-threatening disease vision and is reason main lost vision in the United States. Dilated fundus examination in a way regular together with use imaging a wise diagnostic can resulting in rapid diagnosis and treatment. Improvement control of diabetes mellitus and comorbidities systemic together with anti-VEGF and/ or PRP, can prevent disturbing complications vision term long such as NVG, VH, and TRD.

9.	Journal of Ophthalmic and Vision Research (Southeast Asia, Malaysia, 2022) Syed Shoeb Ahmad, et al.	Florida Diabetic Retinopathy in a Young Patient	Case Report Retinopathy Diabetic Florid	ODS : neovascularization colored discus (NVD) redness, “coralliform” NVD, neovascularization others (NVE), bilateral edema with some hard exudates, macular edema,	Disturbance microcirculation vessels blood. Patient has diagnosed suffering from diabetes mellitus three month previously	100 milligrams of metformin every day and 80 milligrams gliclazide twice daily orally, which is consistent maintain level glucose his blood between 72-90 mg/dl. bilateral panretinal laser photocoagulation (PRP) and laser photocoagulation	FDR is representation aggressive from retinopathy diabetic ; therefore that is all diabetes sufferers age young must undergo screening as soon as possible maybe. Patients This need monitored in a way strict For identify condition since early. After FDR develops, the patient need handled in a way aggressive with laser photocoagulation and possibly vitrectomy. However, FDR is still is presentation that is not beneficial for diabetic patients aged young and portends a poor prognosis Good.
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Discussion

Based on review library pathogenesis retinopathy diabetic started with change microvascular. High sugar levels trigger damage vascular through polyol pathway, accumulation results end of the glycation process, the protein kinase C pathway, and the hexosamine pathway. Management retinopathy diabetic No only done observation just but given therapy like laser photocoagulation, administration *Anti- Vascular Endothelial Growth Factor* (Anti-VEGF), intravitreal steroids, and other actions pars plana vitrectomy. From the results findings, criteria eligibility filled by 10 studies published 10 years final that is 2014 to 2024 and take 100% case report based journal.

Mechanism the occurrence disease microvascular diabetes still Not yet clear, but condition hyperglycemia chronic can change physiology and biochemistry vessels blood, so that happen damage endothelial. Hyperglycemia chronic cause damage microvascular through four track change biochemistry that is protein kinase C pathway, hexosamine pathway, polyol pathway and improvement product glycation (*Advanced Glycation End Products* / AGEs). Fourth track This will culminating in an increase stress oxidative beside track another path as intermediary stress oxidative. (Doctoral Study Program) Knowledge Udayana Medical School, 2021)

AGEs are product reaction non- enzymatic chemistry with amino groups of proteins, lipids, and acids triggered nucleic acid hyperglycemia. Accumulation of AGEs induces cell apoptosis. retinal pericytes, affecting the occurrence thickening retinal capillary basement membrane, and increases permeability vessels blood on cells retinal endothelium. Under normal conditions, AGEs begin formed since from development embryogenic and cumulative along with time, but will increase in condition hyperglycemia. AGEs are glycosylated amino acids or lipids or oxidation without enzymatic process, after exposed to aldose sugars. AGE formation through three step, initial, medium, and advanced. At stage early, glucose react with free amino acids so that formed Which *Schiff base* will be will formed return become more products stable, called product amadori. At the stage medium, product amadori degraded become various type dicarbonyl. And at the stage continued glycation process will AGEs are formed which are product irreversible. (Doctoral Study Program Knowledge Udayana University Medicine, 2021)

Microaneurysm is protrusion wall capillary especially vein area with in the form of spots red small located near vessels blood especially posterior pole. In the phase beginning retinopathy happen change retinal capillaries such as thickening basement membrane and loss cell pericyte. Pericyte cells Alone play a role in maintain stability vessels blood. The loss of cell pericyte will weaken wall capillary so that cause microaneurysm, namely the exit bag small from the lumen of the vessel blood. Microaneurysm the Can break and form bleeding

deep within the retina, which is bounded by a membrane internal boundary (ILM). (Doctoral Study Program Knowledge Udayana University Medicine, 2021)

Soft exudate, often called *cotton wool patches* is retinal ischemia. On examination ophthalmoscopy give description spots diffuse jaundice. Hyperglycemia cause stress oxidative that is with improvement intracellular *reactive oxygen species* (ROS) originating from from chain transport electron mitochondria, cytochrome p450, *nicotinamide adenine dinucleotide phosphate* (NADPH), and oxidation *nitric oxide synthase* (NOs). Improvement ROS levels are related with dysfunction vascular including the disappearance pericytes, formation capillary acellular, thickening basement membrane and increased permeability capillary. *Hard exudate* happen consequence improvement permeability vessels blood that allows leakage fluid and lipoproteins to the retina so cause thickening macular and edema resorption is usually produce precipitation lipid residue in layer plexiform outside (Henle).(Yusran, 2017)

Cotton-wool spots (CWS) are likely caused by the reduction flow blood (ischemia) to the retina. Retina is layer network in part behind eye. The retina changes light become signal nerves, which then sent to brain. Blockage in the supplying arteries blood to the retina can cause ischemia that creates CWS. Spots cotton formed from swollen flakes from cells local. (Yusran, 2017)

At the stage retinopathy diabetic more proliferative severe, blood vessels abnormal blood can grows on the surface of the retina or on the nerves optics. This process called " neovascularization ". This condition This based on because the occurrence dysfunction cell endothelium which ultimately will compensate become capillary acellular and start emergence non- perfused capillaries. This is induced by adhesion leukocytes to cell endothelium so that happen death cell endothelium, loss cell perisite and closure vessels blood that leads to ischemia. Adhesion leukocytes to cell endothelium mediated by molecules adhesion such as ICAM-1 (*Intercellular Adhesion Molecule-1*) and VCAM-1 (*Vascular Cell Adhesion Molecule-1*). (Yusran, 2017)

Capillary acellular cause the disappearance retinal perfusion, closure vessels blood and retinal ischemia-hypoxia. Hypoxia will increase expression *Hypoxia Inducible Factor-1* alpha (HIF-1 α) which is factor transcription and arrangement expression various pro- angiogenic genes such as VEGF, VEGF-receptor, and angiopoietin-1 (Ang-1). Activation various factor angiogenic produce neovascularization pathological as occurs in proliferative DR.(Preethi, S. et al., 2015)

Neovascularization or vessels blood this new abnormal can break and fill eyeball part with blood, which is called bleeding vitreous. Condition this can also cause formation network scars that can interesting retina and causes retinal ablation, namely release network nerve from part behind eye. (Preethi, S. et al., 2015)

Macular edema Diabetic / *Diabetic Macular Edema* (DME) can also occurs in diabetic patients. The macula is part the eyes used For vision center that allows We see the object in

front eyes, play a role in vision colors and fine details from objects seen. In DME occurs accumulation fluid to retinal macular interstitial tissue of capillary. Fluid crossing the BRB (*Blood Retinal Barrier*) through two pathways that is paracellular and transcellular. Movement fluid in the capillaries affected by pressure hydrostatic and oncotic gradient based on Starling's law. Damage to the BRB causes accumulation of protein in the interstitial tissue so that increase pressure oncotic causing movement fluid to interstitial space. This is can cause swelling or thickening macula which can lower function from macula so that Can happen decline vision. (Raka, M. et al., 2022)

Flame shaped hemorrhages is part from retinal hemorrhage that occurs inside layer fiber retinal nerve. Bleeding This related with pathology plexus superficial retinal capillaries, including retinopathy hypertension and retinal vein occlusion. In general, bleeding triggered by damage wall vessels blood Because instability wall vessels blood caused existence improvement pressure blood, pressure physique due to trauma or surgery, inflammation, weak connective tissue, and/ or pathology coagulation systemic. (Raka, M. et al., 2022)

Governance The main RD is blood sugar control, hypertension systemic, and hypercholesterolemia. Nonproliferative RD light-moderate No need therapy, but observation done every years and done blood sugar control. In nonproliferative RD heavy need monitoring every 6 months For detect signs progressiveness become proliferative. In macular edema without manifestation clinically significant done observation without laser action. CSME (*clinically significant macular edema*) requires focal laser action or diffuse, intravitreal injection of triamcinolone or intravitreal injection of anti- VEGF.(Han, et al, 2014)

proliferative RD given Cito laser action. Panretinal photocoagulation (PRP) for regression vessels blood new so that lower number blindness. Vitrectomy performed on bleeding vitreous and traction vitreoretinal. Preoperative intravitreal anti-VEGF can lower incident bleeding repeat and improve sharp post- operative vision.

a. Laser Photocoagulation

Laser action (laser photocoagulation) will be one of choice main when happen progressiveness in the form of retinopathy diabetic type proliferative or complications in the form of macular edema. This is aiming For close leakage vessels blood and prevent progressiveness neovascularization so that decline sharp vision can pressed. However, it is necessary known existence risk effect side consequence characteristic destructive from laser in the form of disturbance vision central and decline function vision dark. (Balasopoulou A, et al., 2017)

Laser therapy is usually For nonproliferative diabetic retinopathy accompanied by CSME and proliferative diabetic retinopathy. The purpose of laser photocoagulation is prevent leakage microaneurysms and inhibit extravasation fluid to macula. The use of laser photocoagulation in CSME has shown repair results with remainder disturbance sharp vision moderate *visual loss* (MVL) between inspection initial and inspection continued. MVL is duplication visual angle, from 20/20 to 20/40 or 20/100 from 20/50, an improvement of 15 or more letters on the ETDRS chart, or repair more of 3 lines on

the Snellen chart. Laser therapy can postponed after macular edema has resolved.^{2,10} Laser therapy is accompanied by intravitreal injection significant repair sharp vision and decline thickness macula (anatomy) vs. laser therapy within 6-24 months.(Sellechio J. et al., 2021)

Panretinal laser photocoagulation (PRP) in proliferative diabetic retinopathy aiming For regression neovascular. PRP damages the ischemic area of the retina and increases pressure oxygen eye. Ischemic area of the eye can produce *vascular endothelial growth factor* (VEGF), so progressive damage the retina. PRP therapy can One or a number of session, using a green Argon laser or blue burn as many as 1200 or more from 500 µm separated One with other with distance One half wide wound burn. Effect next to the PRP scatter, namely decline sharp vision Evening day, change vision color, sensitivity light, sharp vision peripheral, and dilation pupil.(Sellechio J. et al., 2021)

b. *Anti-Vascular Endothelial Growth Factor* (Anti-VEGF)

In retinopathy diabetic type proliferative or accompanied by with macular edema. then under consideration administration of anti-VEGF. This is aiming For prevent progressiveness, but there is limitations in the form of time short half so that need done injection every month. The important thing For under consideration is complications in the form of endophthalmitis related injection and load financial experienced patients. Some anti-VEGF options are ranibizumab, pegaptanib, aflibercept, and bevacizumab.(Sellechio J. et al., 2021)

Anti- angiogenic therapy using anti-VEGF can repair sharp vision diabetic macular edema patients. Aflibercept improves sharp vision and anatomy more Good than ranibizumab. Ranibizumab is humanized monoclonal antibody fragments against all VEGF isoforms, are useful as choroidal neovascularization therapy in age-related macular edema. Bevacizumab is a humanized monoclonal IgG antibody that binds to and inhibits all VEGF isoforms and have been patented For therapy carcinoma colorectal, however off label use in therapy ophthalmology. Pegatanib is a 28-base ribonucleid acid aptamer that binds and inhibits extracellular VEGF action, especially amino acid 165 (VEGF165). Aflibercept (VEGF Trap-Eye) is a 115- kDa recombinant fusion protein that binds with VEGF receptors 1 and 2. (Ahmad SS, et al., 2017)

c. Corticosteroids

Corticosteroid drugs has proven hinder gene expression factor growth endothelium vascular and anti-inflammatory mediators others (such as prostaglandins). Triamcinolone, fluocinolone, and dexamethasone is the main steroid that has been studied For macular edema treatment. Network Study Clinical Retinopathy Diabetic (DRCR Net) is a clinical trial random multicenter comparing triamcinolone intravitreal acetamide as monotherapy with photocoagulation focal / grid for DME treatment. Research This randomize 840 eyes with DME for received 1 mg IVTA (*Intra Vitreous Triamcinolone Acetonide*) vs. 4 mg IVTA vs. focal /grid laser. Group IVTA 4 mg has

greater visual acuity good on four months ; however, at 16 months, two years, and three year, the laser group has greater visual acuity Good than second IVTA group. In addition, the laser group has more A little incident cataracts and glaucoma. (Ahmad SS, et al., 2017) IVTA provides effect maximum on increase sharpness vision in three month, and benefits This lost on six month, so that need frequent intravitreal injections. IVTA is injected to in cavity vitreous as a bolus, not as formulation release continuous. Each IVTA bolus exposes eyes on high doses of steroids, which increases risk improvement pressure intraocular and formation cataracts. For reduce risk cataracts and increased IOP, system possible intravitreal steroid delivery release a number of small steroids during period continuous time has developed. (Ahmad SS, et al., 2017) Ozurdex (dexamethasone intravitreal implant) is one of the formulation corticosteroids off slow injected intravitreally. Ozurdex has approved by the FDA for macular edema treatment consequence retinal vein occlusion. Research also shows benefit Ozurdex in treating macular edema diabetic. Analysis subgroup against 171 eyes with persistent DME ≥ 90 days treated with Ozurdex 0.7 mg or 0.35 mg indicates sharpness more vision good (10 letter increase) or more), decrease Central Foveal Thickness (*CFT*) and **decreased** leakage on fluorescein angiogram at 90 days compared to with observation. However, at 180 days, no found difference between group treatment and observation. Both the 0.7 mg and 0.35 mg groups experienced increased IOP, but the numbers more low compared to with the reported for IVTA. A studies prospective evaluating Efficacy of 0.7 mg Ozurdex For treatment of resistant DME to treatment in 55 eyes that underwent vitrectomy show improvement sharpness vision and CFT reduction at 26 weeks compared to with early.(Ahmad SS, et al., 2017) Insertion ophthalmic fluocinolone acetonide (Retisert) which does not can unraveled in a way biological has FDA approved for non-infectious uveitis treatment and is designed For releases 0.59 mg/ day drug during about two and a half year. Trials random comparing FA implant with maintenance standard (repeated laser or observation) in DME patients does not show evidence of edema in 58 percent the receiving eye implant compared to with 30 percent the receiving eye maintenance standards, and improvements sharpness vision three lines or more more often seen in the test eye (28 percent vs. 15 percent, $p < 0.05$). However, in the implanted eye tool said, 95 percent eye fakia need extraction cataracts, 35 percent experience increased IOP, and 28 percent need procedure filtering. (Ahmad SS, et al., 2017)

Implant fluocinolone acetonide others, which can unraveled in a way life, has developed by Alimera Sciences, and marketed as Iluvien. Iluvien release fatty acids at a level of 0.2 or 0.5 μg per day until three year. Iluvien entered to in eye with needle measuring 25 G, while Retrieve implanted through surgery. (Ahmad SS, et al., 2017) *Fluocinolone Studies Acetonide Macular Edema (FAME)* was performed during 36 month period covering a total of 956 patients with DME. This study consists of from two clinical trials prospective, randomized, controlled, masked double, and separate

multicenter studies were performed For evaluate efficacy and safety of FA (*Fluocinolone Acetonide*) intravitreal dose low (release 0.2 µg / day) and dosage high (0.5 µg / day) (Illuvien) in patients with DME. At 24 months, 28.7 percent from group dose low and 28.6 percent from group dose tall experience 15 letter fix or more, compared with 16.2 percent in the group pseudo (p = 0.002 for both). Analysis beginning at 30 months show repair sharpness 15 letter vision or more than 39.8 percent patients who receive insert dose low. The 36 -month data report presented at the meeting The Association for Vision and Ophthalmology Research 2011 showed that subgroup patient with DME in progress more from three year it seems own ratio greater risk - benefit big than those who experience less DME from three years. At 24 months, 3.7 percent from group dose low, 7.6 percent from group dose high, and 0.5 percent from group pseudo need operation glaucoma incisional. Cataract develop more often in groups care, with around 75 percent from initially phakic patient undergo operation cataracts at 24 months. (Ahmad SS, et al., 2017)

d. Pars Plana Vitrectomy

Vitrectomy introduced first by Machemer in the 1970s as method For take bleeding vitreous. At the time That indication main done vitrectomy is eye with bleeding severe vitreous which is not can is lost spontaneous after 1 year and retinal detachment at the central macula. However with development techniques and instruments, indications vitrectomy become the more wide. (Ahmad SS, et al., 2017)

main purpose surgery vitrectomy in a way specifically for retrainopathy diabetic is get sharpness useful vision. Important goals other is prevent development more advanced neovascular process diabetic so that get success in a way functional and also anatomical in term long. (Hana N, et al., 2023). Pars plana vitrectomy can become choice therapy for ablation posterior hyaloid especially If proven There is posterior hyaloid traction and diffuse diabetic macular edema. Indication vitrectomy in RD with complications : (Hana N, et al., 2023)

1. Bleeding vitreous settle down more from 1 – 6 months
2. Tractional retinal detachment or threaten macula
3. Tractional and rhegmatogenous retinal abalasio
4. Diffuse diabetic macular edema associated with with traction posterior hyaloid
5. Bleeding vitreous repetitive although has PRP is performed
6. Neovascularization anterior segment
7. Bleeding premacular subhyaloid

CONCLUSION

Based on studies literature that has been done, found that underlying pathogenesis and management retinopathy diabetic is : Dysfunction vascular including the disappearance cell pericytes, formation capillary acellular (death) cell endothelium), thickening basement membrane and increased permeability capillary until closing vessels blood that leads to retinal

ischemia-infarction is pathogenesis the occurrence diabetic retinopathy. Management retinopathy diabetic depends heavy lightness Symptoms. Management No only in the form of observation on blood sugar control, hypertension systemic, and hypercholesterolemia, but also given therapy like laser photocoagulation, administration *Anti- Vascular Endothelial Growth Factor (Anti-VEGF)*, intravitreous steroid or IVTA (*Intra Vitreous Triamcinolone Acetonide*), and action pars plana virectomy

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