Discussion

There are a number of issues of contention regarding diabetic macular ischemia. For example, what role does macular ischemia play in the development of diabetic macular edema? Diabetic macular edema is generally attributed to a breakdown of the blood-ocular barrier. This vasogenic edema results in extracellular accumulation of serous fluid**(98)**.

Others have proposed cytotoxic edema as an additional causative mechanism for DME. Cytotoxic edema may initially manifest as intracellular edema induced by hyperglycemia or hypoxia**(98)**.

Retinal hypoxia exacerbated by nocturnal hypotension or high altitude may induce macular edema as evidenced by reversibility upon resolution of the aggravating factor**(99)**.

The two proposed types of macular edema may not be mutually exclusive. The same factors (ischemia / hypoxia) that presumably induce intracellular edema by a cytotoxic mechanism may also initiate extracellular vasogenic edema through the induction of VEGF**(100)**.

In eyes with clinically significant macular edema and ischemia, is it safe to treat microaneurysms that line the foveal avascular zone? The ETDRS research group advised against treating microaneurysms bordering capillary dropout near the fovea so as to avoid further capillary closure**(91)**.

This advice appears to have been anecdotal. There is no hard evidence that current focal treatment will exacerbate ischemia. A separate issue is whether the patient might become aware of a scotoma from parafoveal photocoagulation. Further study is needed, but this treatment approach is not proscribed by high-level evidence at this time.

Does the value added by DMI interpretation in clinical care justify the use of fluorescein angiography (FA)? Certainly, the role of FA has decreased with the widespread availability of non-invasive optical coherence tomography (OCT). OCT has proved useful in the management of diabetic macular edema, preretinal membranes and vitreomacular traction syndromes.

Isolated macular ischemia is also identifiable as retinal thinning and loss of retinal structure**(59)**.

The adjunctive use of fluorescein angiography may particularly be helpful in advanced proliferative diabetic retinopathy complicated by macular edema and/or preretinal membranes. In these clinical scenarios the identification of extensive capillary dropout on fluorescein angiography may lead the ophthalmologist away from aggressive treatment aimed at recovery of central vision. However, routine use of fluorescein angiography screening for diabetic macular ischemia appears unnecessary.

What is the role of the choroid in diabetic macular ischemia? Evidence supports recent theories of an ischemic penumbra in diabetic retinopathy, wherein there is preservation of hypoxic retina in a paravascular distribution in the peripheral retina due to the diffusion of oxygen from the larger caliber radial vessels**(42)**.

The persistent release of VEGF from the hypoxic retina may perpetuate the neovascular response in PDR. The release of VEGF also protects retinal capillary endothelial cells from apoptosis and subsequent capillary closure**(35)**.

Similarly, the choroidal circulation may play a role in the development of capillary dropout in diabetic retinopathy. The choroid supplies oxygen to the outer retina up to the inner nuclear layer**(101)**.

Therefore, the neurosensory retina in the FAZ derives its blood supply from the choroid. Conceivably, the choroidal circulation may offer relative protection against ischemic neurosensory apoptosis from diabetic retinopathy. The general preponderance of retinal capillary occlusion in the peripheral retina as opposed to the posterior pole is consistent with the greater choroidal blood flow in the posterior pole compared with the periphery**(102)**.

If choroidal perfusion becomes impaired, the retina might be more susceptible to ischemic damage from retinal capillary basement membrane thickening. Indeed, there is evidence of a relationship between decreased choroidal blood volume and flow in eyes with more advanced diabetic retinopathy**(103)**.

It is interesting to note that choroidal blood flow increases in the macula following panretinal photocoagulation, suggesting a possible secondary beneficial effect on macular perfusion. Pentoxyphylline also improves choroidal blood flow in diabetic retinopathy**(104)**.

Evaluation of the vascular state of the macular is on important part in studying the vascular state of the retina in eyes with diabetic retinopathy. Most of the investigators direct their attention to the vascular hemodynamic pattern of the retina not to the macular microcirculation.

Different methods are used for evaluation of the macular micro circulation, as trypsin digest(112) psychophysical methods (113) around with the confocal scanning laser ophthalmoscope (SLO) (114) , and classic intravenous fluorescein angiography used by Bresnick (55), Mansour(115) and in our study.

Ischemic affecting the nacular has received less attention in the literature likely duo to difficulty in detection and lack of treatment options (116)

Also prevalence data are not available as major reputing studies of diabetic retinopathy are not geard to identify macular ischemic (16).

ischaemic maculopathy ranks low as a cause for blindness in persons with diabetes due to its relative rarity, the condition is important because it is not amenable to treatment, unlike PDR and DME. Most studies consider it merely the macular involvement in the setting of a generalised capillary drop-out and retinal ischaemia, and not a unique entity *perse* .(118)

In the present study macular ischemia was found in 12.2% of the cases, there was no significant sex difference between them, there was a direct proportion (relation) between the prevalence of MI and both retinopathy stage and duration of diabetes, these findings are in agreement with(116) who mentioned that it is not surprising to find the FAZ dimension larger in the diabetic patients compared to the controls and within the diabetic patients as retinopathy stage advances. FAZ enlargement occurs also with the duration of diabetics but not independently of retinopathy stage.

Also Mansour(115) and Sander et al(119) found the same results. Elagouz et al., reported that MI is more common in the severer stages of DR (63.5%) in eyes with more sever DR compared to 36.5% in eyes with less sever DR.

These findings are in agreement with(120) who found that macular ischaemia was more common in severe stages of retinopathy (26.5% in eyes with early proliferative retinopathy and 73.5 % in high-risk retinopathy).

In the current study the outstanding factor is the duration of diabetes, as MI was significantly higher among those with duration more than 10 years of diabetes and also among those on insulin therapy, which indirectly means long duration of diabetes. While no significant difference was found among the age groups of duration more than 10 year.

In the current study there was a statistically significant relation between poorer visual acuity (VA) and ischemia, this agree with (Dawn et al., 2013) (121) who found that DMI is associated with reduced VA in eyes with moderate to severe MI grades but preserved in milder grades.

In the current study, the significant association was found between MI and systemic hypertension while in other studies of (El agoze et al.,) (122) ( Shukola et al., )(123) the association was found between MI and nephropathy. This disagreement between these studies and the present study could be attributed to the method of diagnosis of nephropathy. In the present study, nephropathy was excluded according to patient history while in the other two studies(122), nephropathy was diagnosed on laboratory findings (blood urea, serum creatinine and albuminurea) indicating accurate diagnosis, their observations may attract the attention to consider the elevated systemic blood pressure in diabetic patients with MI is most probably renal hypertension and direct the patients to investigate their renal function before the stage of renal failure.

The association of macular ischemia with nephropathy could possibly be explained on the basis of similar ischemic microangiopathy in the two end-organs. Similar to the retinal capillaries in DR renal glomerular also exhibit basement membrane thickening early in diabetic renal disease, resulting in characteristic modular diffuse and exudative glomerular lesions. The common end point of these renal lesions is glomerular hyalinsation, primarily an ischemic event (123).