Review Article

SAARC Academy of Ophthalmology – Tailoring Clinical Standards for Diabetic Retinopathy Care to Available Resources

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ABSTRACT

The South Asian Association for Regional Cooperation (SAARC) is a geopolitical union of 8 member states of South Asia, one of the rapidly transforming regions in the world. It houses 25% of the world population, with a similar rise in at-risk population for diabetes and its complications. Diabetic retinopathy (DR), is one of the major causes of blindness and visual impairment. Despite the region's dramatic demographic and economic transformation, its healthcare system is nascent enough to achieve the over-reaching recommendations by developed countries. Our review helps in tailoring the clinical care to the available resources, focusing on an integrated approach for timely detection and management of sight-threatening diabetic retinopathy (STDR). Our study also recommends urgent measures to be taken to implement diabetes registers by all care providers and take the responsibility of ensuring that patients with STDR are referred for treatment. This tailored framework helps in the screening and treatment of those with STDR in resource-constrained settings, thereby decreasing the health and economic burden in all SAARC countries.

Key words: Diabetic retinopathy, SAARC, Sight threatening diabetic retinopathy, South Asia.

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INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of visual impairment and blindness. The rising prevalence of type 2 diabetes has not spared any country. By 2025, more than 80% of people with type 2 diabetes are expected to be from low and middle-income countries. (King et al, 1998) Evidence from population-based surveys from the eight South Asian Association for Regional Cooperation (SAARC) countries (Afghanistan, Bangladesh, Bhutan, India, The Maldives, Nepal, Pakistan, and Sri Lanka) show that the rates of diabetes are higher than the WHO record of 3.5% for developing countries in 2000. (White & Rafique, 2002) With increasing diabetes, the prevalence of DR will also increase unless DR care pathways improve. Although the International Council of Ophthalmology (ICO) guidelines provide overarching recommendations on evidence-based DR care pathways, many of the SAARC countries do not have the basic requirements to implement these pathways. In this paper, we gathered local evidence from all eight countries to share best practice in order to work our way to the clinical standards followed in developed countries.

Epidemiology of Diabetic Retinopathy in SAARC countries

Table 1 shows the prevalence of DR based on population-based surveys in SAARC countries

Table 1: Epidemiology of Diabetic Retinopathy in SAARC countries.

Country	*DM disease burden (20–79 years)			Author	Year	Number of subjects	Type of study	Prevalence of diabetes	Prevalence of †DR	Prevalence of §DME	Prevalence of ¶STDR
	Estimated in 2019	Projected in 2045	% Increase								
Bangladesh	8.4 million	14.9 million	77.38	Akhter A et al	2013	836	Population -based	-	5.40%	-	-
				Biswas T et al	2016	51252	Scoping review	7.40%	-	-	-
Bhutan	46 000	88 000	91.3	IDF	2019		-	10.30%	-	-	-
India	77.0 million	134.2 million	74.28	Raman R et al	2014	13079	Population -based	10.10%	10.30%	-	3.80%
Maldives	22 800	48 500	112.71	Thoufeeq et al	2018	3100	Population -based	-	3.10%	-	-
Nepal	0.69 million	1.59 million	130.43	Raba Thapa et al	2018	1860	Population -based	9%	23.80%	4.20%	9.50%
Sri Lanka	1.23 million	1.54 million	25.2	Katulanda P et al	2014	5000	Community based	12.00%	27.40%	5.30%	5.30%
Afghanistan	-	-	-	Abdianwall MH et al	2015	1281	Population -based	-	1.40%	-	-

*DM - Diabetes Mellitus; †DR - Diabetic Retinopathy; §DME - Diabetic macular edema; ¶STDR - Sight threatening diabetic retinopathy.

(Akhter et al, 2013; Biswas et al, 2016; IDF, 2019; Raman et al, 2014; Thoufeeq et al, 2018; Thapa et al, 2018; Katulanda P et al, 2014; Abdianwall & Doğan, 2018). Table 1 shows that there is a lack of prevalence data from some of the member countries. Although it is estimated that more than one-third of those with diabetes worldwide have DR, the prevalence of DR in SAARC countries is estimated to be approximately 15-20%. However, the proportion of STDR is 5-10% and mirrors the prevalence in Western population. (IDF, 2019) Moreover, Leasher et al, reported that DR related moderate/severe visual impairment in ≥ 50 years age group was highest in South Asia (0.5%). DR related blindness in ≥ 50 years age group was 0.1% in these regions. (Leasher et al, 2016)

It is encouraging to note that there is a decline in high-income countries, that has been attributed to concerted public health prevention efforts including improved glycemic and blood pressure control, and early detection and treatment of STDR through systematic DR screening programs (Klein R & Klein BE, 2010). However, there is very limited data on incidence of DR from SAARC countries. To witness a decline in incidence and prevalence of STDR in SAARC countries, there is an urgent need to strengthen the health system to ensure that primary care can manage diabetes and monitor for complications such as DR. Currently, DR management is not a priority in SAARC countries as the fight against communicable diseases and maternal & infantile mortality rates supersede prevention strategies. Table 2 highlights the paucity of DR

Table 2: Diabetic Retinopathy services in SAARC countries.

Parameter	Bangladesh	Bhutan	India	Maldives	Nepal	Srilanka	Pakistan	Afghanistan
National guidelines on *DR	No	No	Yes	No	Yes	Yes	No	No
*DR screening at †PHC level	No	Limited	No	No	Limited	Yes	Yes	No
Govt support for *DR screening	Yes, National Eye Care (NEC)	Yes	Yes, through the AIOS	Government will fund if requested	Yes, but limited	Yes available	Yes available	No
*DR screening, part of national program	Yes	Yes,	Yes	No	Yes	No	No	No
Data maintenance	Paper type	Paper type	Electronic &paper	Paper	Electronic & paper	Paper	Electronic & paper	Paper
Ophthalmologists trained in *DR	Yes, medical & surgical	Severe deficiency	Yes, medical & surgical	Medical retina alone, not surgical	Yes, medical & surgical	Yes, medical & surgical	Yes, medical & surgical	Yes, medical alone
Laser facility	Yes, at THC	at §THC	Yes, at SHC and THC	Yes	Yes, at THC	Yes	Yes, at THC	Yes, at THC
Injection facility	Yes, at THC	at §THC	Yes, at THC	Yes	Yes, At THC	Yes	Yes, At THC	Yes, at THC
Country-based registry for *DR	No	Available	No	No	No	No	No	No

*DR - Diabetic Retinopathy; †PHC - Primary health centre; ‡SHC - Secondary health centre; §THC - Tertiary health centre.

care. While guidelines and clinical standards assume a well-established public health system is in place in each country, SAARC countries have fundamental deficiencies that make many aspects of the guidelines superfluous. For example, there is no national or regional register of people with diabetes in many of the SAARC countries while some have established but incomplete national non-communicable disease (NCD) registries. There is very minimal input from the government to establish systematic DR screening and funding for this complex pathway is limited with very few trained ophthalmologists to deliver treatments such as retinal laser, intravitreal injections or vitreo-retinal surgeries. These interventions are all unaffordable especially as healthcare is an out-of-pocket expense for most people living in SAARC countries. In addition, public primary care systems are in their infancy. Retinal screening for DR using retinal cameras is recommended for all people with diabetes but these cameras are also costly. Public awareness of diabetes-related blindness is limited. Therefore, all the SAARC countries are still practicing opportunistic or targeted screening. Late presentation of DR as irreversible advanced eye disease is common and inequity in treatment provision is significant due to the high cost of treatment and lack of access to retinal experts.

Strategies to improve Diabetic Retinopathy care tailored to local resources

- Blood sugar level: DR screening should be done for all people with known diabetes on treatment, a single record of random blood sugar (RBS) of ≥ 200 mg/dl (≥ 11.1 mmol/l), or glycated hemoglobin (HbA1C) ≥ 6.5% (48mmmol/l).
- DR screening: It should be provided by every healthcare provider including primary care doctors, diabetologists and ophthalmologists. If the primary care doctors are not qualified to do DR screening, they must refer the patients to the eye care professionals. Importance of DR screening should be made aware of in the general population.
- Co-existing complications: People with other macro/micro vascular complications of diabetes such as diabetic kidney disease, peripheral neuropathy and cardiovascular disease are at increased risk of developing STDR.
- NCD registers: All SAARC countries should ensure that their NCD registers are comprehensive and updated. Diabetes registry should be maintained in all healthcare centers, including primary health centers and tertiary medical institutions.
- Support facilities: Pharmacies/ medical shops and laboratories are important sources , legislation to maintain and update diabetes registers before supply of medications will be a rapid method of maintaining national diabetes registers.
- Patient diary: Patients should be encouraged

Table 3: Recommended eye examination schedule for patients with diabetes.

Type of diabetes	First retinal examination	Follow up
Type 1 diabetes	Within 5 years after the onset of diabetes	At least annually
Type 2 diabetes	At the time of diagnosis	At least annually
Pregnant women		
With pre-existing type 1 or type 2 diabetes	Prior to conception and in the first trimester	Every trimester and 6 weeks postpartum as indicated by the degree of retinopathy (every 3-12 months for no retinopathy or moderate non-proliferative diabetic retinopathy (NPDR), or every 1-3 months for severe NPDR)
Confirmed to have gestational diabetes	Do not require an eye examination during pregnancy, and do not appear to be at increased risk for developing diabetic retinopathy during pregnancy	

to keep their own diary of DR screening until systematic screening from a diabetes register with recall facilities is established.

- Dilated fundoscopy: All people with diabetes should have a dilated eye examination at least once a year. The screening and follow-up guidelines for people with varying severities of DR and their management is provided in Table 3. Patients with STDR should be promptly referred to an ophthalmologist.
- No fundus view: Patients visiting ophthalmologists for cataract surgery with no view of fundus, should have fundus examination for assessment of DR should be performed during the immediate post-operative review.

Management of STDR by ophthalmologists

STDR is defined as proliferative retinopathy and / or DME. FFA and OCT are sensitive investigative tools used for diagnosis of STDR.

Treatment for DME

An ophthalmologist treating DME should have facilities for FFA and OCT. Treatment options differ based on location and associated morbidities. FFA differentiates the presence of proliferative retinopathy where OCT is the mainstay in the treatment of DME.

DME classification based on OCT

Based on OCT, DME involving the central subfield zone of the ETDRS grid is termed

center-involving DME (CI-DME) involving central 1 mm of ETDRS grid on OCT and non-center-involving DME (NCI-DME) is defined as retinal thickening beyond and not involving the central 1 mm.

Management of non-center involving macular edema (NCI-DME)

i. NCI-DME with good vision (6/6-6/9) can be observed with three monthly follow-ups. (Raman & Bhende, 2015).

ii. NCI-DME with vision worse than 6/9 attributed to DME may be treated with a macular laser. (Raman & Bhende, 2015) - Focal Laser can be done to leaking MA.

One should avoid treatment of nerve fiber layer retinal hemorrhage (flame or splinter hemorrhage) and blot hemorrhage >125 μm in size.

iii. Predominantly NCI-DME (circinate exudates) after intravitreal anti-VEGF injections or laser with plaque of hard exudate and normal foveal contour.

- Patients should be evaluated for control of systemic conditions such as hypertension and dyslipidemia; Any treatment may aggravate sub foveal deposits and patients should be warned of this adverse effect. (Srinivas et al, 2020)

vi. CI-DME converting to NCI-DME after intravitreal injections should be treated with laser according to ETDRS treatment guidelines. Observation with close follow up is an option. Treatment has to be tailored depending on patients' ability to follow- up and logistics.

Management of center involving macular edema (CI-DME)

i. Treatment naïve CI-DME:

Anti-VEGF therapy is the first line of treatment for all CI-DME without traction. (Aiello et al, 2011) The DRCR protocol for CI-DME starts with monthly injections for 4 to 6 months initially. The patient is followed monthly, visual acuity and OCT is documented. The management is as follows:

1. OCT and/or vision shows improvement: continue the treatment with anti-VEGF agents.

2. OCT shows progressive improvement but vision not improving: continue anti-VEGF but consider to evaluate for concomitant ischemia.

3. Vision improving but no OCT improvement: continue the treatment with anti-VEGF agents or macular laser can be applied.

4. Stopping anti-VEGF injections: Further treatment with anti-VEGFs is deferred when vision has improved to 6/6 and OCT has become normal or when 'No further improvement' is noted on OCT,

which is defined as <10% decrease in central subfield thickness or no change in visual acuity since the most recent injection.

5. Once injections are stopped, close monitoring (at least every 3 months) with either an as needed or a 'treat and extend' treatment approach should be done.

6. Retreatment should be considered if there is reappearance of significant edema.

7. Switching to other agents is recommended in patients with progressive worsening of vision over three consecutive visits in the presence of active DME.

8. Switching to intravitreal steroids can be considered in patients with difficulty to maintain frequent follow up, pseudophakic patients who have reached a plateau, persistent edema and needing cataract surgery, occurrence of vascular event while on an anti-VEGF agent. (Regillo et al, 2017)

9. Additional laser to treat persistent edema considered after 4-6 injections may also be considered in eyes with persistent CSME with visible microaneurysms.

10. Good control of systemic factors and follow-up based on time of last injection is mandatory.

Treatment of PDR

In SAARC countries, PRP should be recommended for all eyes with any evidence of PDR and should not be restricted to only high-risk characteristics as the risk of disease progression due to lack of follow-up is high. Impending or recent cataract surgery or pregnancy may increase the risk of progression and may influence the decision to perform PRP in severe NPDR too. Additional PRP with anti-VEGF therapy should be considered in the following situations:

- Failure of the neovascularization to regress despite repeated PRP sessions.
- New areas of neovascularization/ Vitreous haemorrhage.

For patients who have concurrent CI-DME, combined anti-VEGF therapy and PRP at the first treatment session should be considered.

Management of PDR with DME

Naïve PDR with DME without evidence of traction should be treated with PRP along with anti-VEGF. In presence of a vitreous haemorrhage, where the view of the retina is compromised, a B-scan should be done to rule out traction at the macula. PRP should be done to cover the visible peripheral retina. In presence of extramacular traction, PRP should be done 2DD away from the traction and DME treated as standard protocol. In the presence of vision-threatening traction, a vitrectomy is indicated in addition to PRP.

Typical indications for vitrectomy include the following:

- Non-clearing vitreous haemorrhage.
- Tractional retinal detachment threatening the macula.
- Combined rhegmatogenous and tractional retinal detachment.
- Dense pre-macular sub-hyaloid hemorrhage.

Neovascular glaucoma secondary to PDR

Neovascular glaucoma (NGV) is an advanced eye disease which occurs secondary to PDR. This glaucoma is often refractory to medical management. The primary goal in the management of the NVG is making the hypoxic retina anoxic by laser/cryo application. (Putera et al, 2020) The next role is anti-VEGF combined with Glaucoma drainage devices, which is often used to control refractory glaucoma. Careful control of systemic parameters is essential to achieve favorable outcomes.

Conclusion

An investment to increase public awareness of the need to regularly screen and treat STDR is critical in countries where primary care is under-developed and diabetes care is not integrated. Patients, if made aware of diabetes-related blindness, will take their own initiative to have their eye examined. Family physicians should have adequate knowledge of DR and the current international classification systems of DR and DME to follow recommendations for adequate screening schedules and referral, including urgency of referral to the specialized ophthalmologist.

It is recommended that urgent measures are taken to implement diabetes registers by all health care providers and take the responsibility of ensuring that the patient is screened for STDR or referred for screening. Data collection on DR screening and its outcome is critical to ensure and monitor the rate of visual impairment due to STDR in SAARC countries. Feedback on the outcome of STDR treatment for patients identified from the DR screening program should be mandated so that the screening to treatment loop is completed.

India is the most advanced in terms of vitreo-retinal training and other SAARC countries may utilize these training opportunities and resolve the training needs to increase capability. There is a need to increase capacity to deliver laser treatment throughout SAARC centers. Many patients are treated sub-optimally with these agents because of lack of compliance and incurred costs. Therefore, patients having these therapies should also be treated at least with macular laser so that they do not suffer from irreversible visual loss due to incomplete anti-VEGF therapy.

This tailored approach gives a framework for screening and treating STDR in SAARC countries based on available resources.

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