Med & Health Jun 2023; 18(1): 21-31 https://doi.org/10.17576/MH.2023.1801.04

ORIGINAL ARTICLE

Retrospective Review of Management of Diabetic Retinopathy in Pregnant Diabetics at Hospital Universiti Kebangsaan Malaysia

NOOR ANIAH A[1,2], NOR AZLIN MI[3], AINAL ADLIN N[2], PRAAJEETH NAIR R[2], DIANA L[2], JAMALUDDIN S[2], ISMAIL A[4], BASTION MLC[2]

[1]Department of Ophthalmology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia
[2]Department of Ophthalmology, [3]Department of Community Health & Quality, [4]Department of Obstetrics & Gynaecology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia

ABSTRAK

Retinopati diabetes (DR) boleh berkembang ketika wanita diabetes hamil. Situasi ini adalah jelas bahawa kes diabetes semakin meningkat di seluruh dunia dan bahayanya adalah menakutkan. Kes retrospektif dengan 168 kehamilan dikesan dari senarai pendaftaran Klinik Antenatal Endokrin, Jabatan Obstetrik dan Ginekologi, Pusat Perubatan Universiti Kebangsaan Malaysia dari jangka masa 2016 hingga 2019. Daripada 138 pesakit diabetes yang hamil, 97 rekod (70.3%) didapati hanya mempunyai satu tindakan susulan dengan rekod oftalmologi yang tidak lengkap atau ingkar. Hanya 41 rekod pesakit diabetes yang hamil (29.7%) mempunyai dua tinjauan oftalmologi. Perkembangan DR dicatat dalam 7 pesakit diabetes yang hamil dengan memberikan kadar 17.0%. Satu mata dari seorang pesakit berkembang dari DR non-proliferatif ringan menjadi DR proliferatif (PDR) yang mengancam penglihatan. Semasa membandingkan kumpulan progresor dengan bukan progresor, tidak ada perbezaan yang signifikan secara statistik untuk faktor risiko (umur, jantina, etnik, jenis diabetes, tempoh diabetes, tahap HbA1c, hipertensi, kehadiran makulopati, faktor risiko diabetes dan janin penemuan ultrasound). Kadar tindak balas berulang untuk retinopati semasa kehamilan pada pesakit diabetes adalah sekitar 30%. Kajian ini menunjukkan tidak ada faktor risiko untuk perkembangan DR.

Kata kunci: diabetes, mengandung, retinopati diabetes

Address for correspondence and reprint requests: Mae-Lynn Catherine Bastion. Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-9145 5981 Email: mae-lynn@ppukm.ukm.edu.my

ABSTRACTS

Diabetic retinopathy (DR) may progress when diabetic women pregnant. It is clear that DR cases are increasing around the world and the danger is alarming. This is a retrospective case with 168 pregnant patients which were traced from the registry held by Endocrine Antenatal Clinic, Department of Obstetrics and Gynaecology, Universiti Kebangsaan Malaysia Medical Centre from 2016 to 2019. Of the 138 pregnancies in pre-existing diabetics, 97 records (70.3%) were found to have only one follow-up with incomplete ophthalmology records or defaulters. Only 41 pregnancy records (29.7%) completed with at least two ophthalmology reviews during the pregnancy. Progression of DR was noted in seven of these pregnancies, giving a rate of 17.0%. One eye of one patient progressed from mild non-proliferative DR to sight-threatening proliferative DR (PDR). When comparing the group of progressors with non-progressors, there was no statistically significant difference for risk factors (age, gender, ethnicity, type of diabetes, duration of diabetes, HbA1c level, hypertension, presence of maculopathy, risk factors for diabetes and fetal ultrasound findings). The rate of repeated follow-up for retinopathy during pregnancy in diabetics is about 30%. This study suggested that no risk factors were identified for DR progression.

Keywords: diabetic, diabetic retinopathy, pregnant

INTRODUCTION

Diabetes mellitus (DM) is a rising problem all over the world with many known micro and macrovascular complications including those affecting the eye. According to the International Diabetes Federation, there were 285 million adults diagnosed with DM in 2010 and this number is expected to increase to 439 million adults in 2030 (Cho et al. 2018). Apart from the increase in numbers of diabetic individuals, it is also alarming to discover a trend for type 2 DM to occur in younger individuals which the mean of affected age decreases from 52 to 46 years in the United States from 1988 to 2000 (Koopman et al. 2005). Of those afflicted with DM, there is a small but significant group of diabetics that should warrant more attention, the pregnant diabetic women. The increase in prevalence of type 1 DM worldwide, combined with diabetic women choosing to delay childbearing to later in life, has increased the number of pregnant women with pre-existing type 1 and type 2 DM, respectively (You & Henneberg 2016). Pregnancy increases the risk of DR progression in 50-70% of young expectant mothers (Mallika et al. 2010). It is clear that a mother with visual impairment seriously affects her ability to perform her crucial role towards her new born, family and society; therefore visual impairment should be prevented at all

costs.

In the United Kingdom, there is an increasing number of women receiving adequate retinal examination during pregnancy following the establishment of a well-organised antenatal care program. However, there is still a significant proportion of pregnant women who continue to experience deterioration in retinopathy and this implies the need for closer follow-up. However, recommendations for this follow-up is lacking (Diabetic Retinopathy Guidelines 2012)

Management of DM has changed a lot in the last 10 years with the development of new oral hypoglycaemic agents (OHA) such as dipeptidyl peptidase 4 (DPP4) inhibitors and sodium-glucose cotransporter 2 (SGLT2) inhibitors (Wajid et al. 2019; Kapoor & Thomas 2017). Despite the number of available OHA, diet and lifestyle modification should be attempted in early cases of type 2 DM. Management of DR has also changed. For instance, anti-vascular endothelial growth factor agents (anti-VEGF) are the mainstay of treatment for clinically significant diabetic macular edema (CSME) and an option for proliferative diabetic retinopathy (PDR). However, this will be contraindicated in pregnancy especially early pregnancy, as there were reported cases of abortion and preeclampsia after receiving intravitreal anti-VEGF (Polizzi & Mahjan 2015).

In Malaysia, the only available guideline with reference to screening DR in pregnant diabetics is the Clinical Practice Guidelines (CPG): Screening of DR (Ministry of Health Malaysia 2017). The guideline states pregnant diabetics should have DR screening every three months (every trimester) for no DR or mild DR. If moderate or worse non-proliferative DR (NPDR) is present, then the patient must see an ophthalmologist. However, data is lacking on the management of patients with higher DR levels or patients with risk factors such as hypertension or poor glycaemic control. The Malaysian CPG 2011 for pregnant diabetics management, recommends that women with DM who are planning for pregnancy should have eye examination prior to conception and are counselled on the risk of development and progression of DR (Ministry of Health Malaysia 2017). This is due to the changes in metabolic status in pregnancy may worsen DR. On the other hand, DR screening is usually not needed in gestational DM (GDM), an abnormal glucose intolerance first detected during pregnancy, unless GDM is diagnosed as early as in the first trimester, then DR screening should be carried out like in pre-existing DM.

The review of literature suggests there is a dearth of conclusive evidence for management of DR in type 2 DM in pregnancy especially in Malaysia (Ministry of Health Malaysia 2017). Moreover, there is variability on management of patients with type 1 or 2 DM in pregnancy who have worse grades of retinopathy. Therefore, our study aims to determine the current management of DR in pregnant type 1 and type 2 DM patients who attended the specialist clinics in Universiti Kebangsaan Malaysia Medical

Centre (UKMMC) in terms of rate of progression of DR and visual acuity.

MATERIALS AND METHODS

This was a single centre, retrospective review of case files. Ethics approval from the Medical Research and Ethics Committee of UKMMC (Project no FF-2019-457) was first obtained. Next, a list of patients who had attended the Obstetrics and Gynaecology (O&G) Combined Endocrinology Clinic, UKMMC @ Hospital Tuanku Mukhriz in Kuala Lumpur, Malaysia from 1st January 2016 to 31st May 2019 was obtained from the O&G Department, UKM. The study was conducted in accordance with the Declaration of Helsinki and Malaysian Guidelines for Good Clinical Practice (GCP) from July 2019 until March 2020. All case files were requested from the Department of Records and Statistics, UKMMC. Inclusion criteria was all patients with known DM who was pregnant and attended the O&G Combined Clinic, according to a database kept by the Department of O&G. Cases with less than two ophthalmology follow-up records during the pregnancy or eye examinations were not conducted in UKMMC were excluded. Confidentiality was maintained with data and analysis kept by the principal investigator only.

The files were examined for the demographic data at onset of pregnancy. This demographic data included age, gender, ethnicity, type of diabetes including duration and medication, blood pressure, body mass index (BMI), glycosylated haemoglobin (HbA1c) levels (pre pregnancy and during pregnancy) and obstetrics history, which included foetal outcomes, namely foetal ultrasound findings and infant details following delivery. Ophthalmology history notes were examined for visual acuity, fundus clinical findings including diabetic and DR staging at each antenatal visit. Other investigations, if applicable, such as optical coherence tomography (OCT) of macula, angiography and B-scan ultrasonography were also sought, and the results were recorded. Ocular treatment details, if performed, including pan-retinal and macular photocoagulation or intravitreal anti-VEGF injections, were also noted.

The raw data was entered by the investigators into Microsoft Excel Worksheet and statistical data analysis for demographic data and risk factors were performed using statistical package for Social Science, version 22.0 (SPSS, Inc. Chicago III USA).

RESULTS

A total of 168 pregnancies were noted in the database. All patients' records were requested through the Department of Records and Statistics, UKMMC. Records that could not be traced through the record tracing service were traced to their last location at the clinic or ward. Two of the files could not be traced despite these efforts. OAfter that, the records were examined for suitability to be included into the study. From the 166 records that were traced, 29 were excluded as the patients were gestational diabetics or thyroid patients.

Of the 139 pregnancies in pre-existing diabetics, 97 records were found to have only one follow-up with incomplete ophthalmology records or defaulters. Only 42 pregnancy records (30.2%) in 139 women were complete with at least two ophthalmology reviews during the pregnancy. Progression of DR was noted in seven pregnant women giving a rate of 17.0%. All of these seven were type 2 DM. Figure 1 showed the workflow of the study.

Table 1 showed the comparison of the demographic data between the progressor and non-progressors. Only information which was available was used in the analyses. There was no statistically significant difference between the two groups. In the risk factor comparison, previous gestational diabetes comes close to be a protective factor, but failed to reach statistical significance.

Table 2 illustrated the stages of DR of the non-progressors in each trimester. At this point of the study, it was noted the small number of samples with complete data. Table 3 showed the detailed profiles of each of the seven pregnancies in which DR progressed. Four out of seven of them had DR progression during their early pregnancy but three of them progressed during their late pregnancy. When comparing the demographical data of the defaulters with the non-defaulters in Table 4, no significant factors were found.

DISCUSSION

A more recent study by Makwana et al. (2018) found 8% overall prevalence rate of DR progression for pregnant type 1 and type 2 diabetics in India while reporting an overall prevalence of 10-27%. This was similar to our study in which progression rate of DR was seen to be 17% of our patients with at least two follow-ups.

A recent review on this subject had shown several interesting findings as well as unearthed several questions.

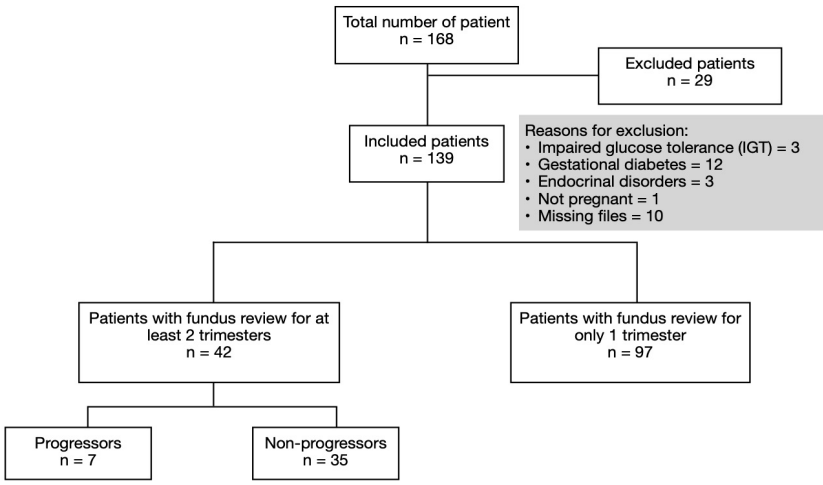

Figure 1: Study flow chart.

Table 1: Demographic data of the cases, between the progressor group and non-progressors . Values were presented as mean or n(%) where appropriate.

	Progressor (n=7)	Non-progressor (n=35)	p-value
Age	33.71	34.51	*0.74
Ethnicity			
Malay	6%	28%	*0.52
Chinese	0%	4%	
Indian	0%	3%	
Others	1%	0%	
Gravida	2.14	2.66	**0.55
Parity	0.71	1.11	**0.51
Type of DM			
Type-1 DM	0%	2%	*0.52
Type-2 DM	7%	33%	
Duration of DM (years)	5.58	5	**0.51
HbA1C level	6.61	6.64	**0.36
Hypertensive, n(%)	4 (57)	10 (29)	*0.14
Maculopathy Progressor, n(%)			
Yes	2%	0%	*0.01
No	5%	35%	
Diabetic nephropathy, n(%)	4(57)	10 (29)	*0.14
Risk Factors for DM			
BMI>27 kg/m2, n(%)	6 (86)	29 (82)	*0.85
Previous GDM, n(%)	0	13 (37)	*0.05
First-degree relative with DM, n(%)	6 (86)	30 (88)	*1
Steroid use, n(%)	0	2 (6)	*0.72
PCOS, n(%)	0	1 (3)	
History of macrosomia, n(%)	0	4 (11)	
Fetal Ultrasound Findings			
Normal US, n(%)	4 (57)	25 (71)	*0.56
Abnormal US, n(%)	3 (43)	9 (26)	

*Chi-Square, **Mann-Whitney U test

Ramussen et al. (2010) investigated the progression of DR in pregnant women with type 2 DM. The risk of progression of DR during pregnancy was generally regarded to be similar for type 1 and type 2 diabetic patients. However, there are more Type 2 diabetics than Type 1. So the number of pregnant women with Type 2 diabetes will be more. Despite DR prevalence rate of 18%,

Table 2: Fundus findings on non-progressors according to the stages of pregnancy.

	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR
First Trimester	16	4	1	0	0
Second Trimester	34	2	2	2	1
Third Trimester	27	1	3	0	2

DR=diabetic retinopathy; PDR=proliferative diabetic retinopathy; NPDR= non-proliferative diabetic retinopathy

Table 3: Detailed case review of the 7 patients who had progression of DR during their pregnancy

Patient no	Age during pregnancy (years)	Gestation during first review	Risk factors for progression	Stage of DR at first review, visual acuity	Stage of DR at last review during pregnancy, visual acuity	OCT of macula if done	Treatment instituted
1	34	1 week	Long duration of DM; 9 years	No DR OU 6/6, N6	Mild NPDR OU 6/6, N6	No OCT	Observation
2	35	23 weeks	Pregnancy-induced hypertension	Severe NPDR OD 6/12 (ph 6/12), N6 OS 6/9 (ph 6/9), N6	PDR OD 6/6, N6 OS 6/9 (ph 6/9), N6	No OCT	Observation
3	26	9 weeks	Poor sugar control, pre-eclampsia	Moderate NPDR OD 6/36 (ph 6/18), N6 OS 6/36 (ph 6/12), N6	Severe NPDR OD 6/36 (ph 6/12), N6 OS 6/36 (ph 6/12), N6	No OCT	Observation
4	33	24 weeks	Nil	No DR VA not available	Mild NPDR OD 6/18 (ph 6/9), N6 OS 6/18 (ph 6/9), N8	OCT at 30 weeks CRT OD 240 µm OD 232 µm	Observation
5	36	6 weeks	Long duration of DM; 7 years	Mild NPDR OU 6/6, N6	Moderate NPDR OU 6/6, N6	No OCT	Observation
6	38	5 weeks	Poor sugar control, pre-eclampsia, long duration of DM; 8 years	Mild NPDR OU 6/12 (ph 6/9), N6	PDR OD 6/18 (ph 6/9), N6 OS 6/24 (ph 6/12), N6	No OCT	PRP
7	34	26 weeks	Long duration of DM; 7 years, pre-eclampsia	No DR OU 6/6, N6	Moderate NPDR with DME OD 6/9 (ph 6/9), N6 OS 6/9 (ph 6/6), N6	OCT at 32 weeks CRT OD 361 µm OS 317 µm	Observation

DR=diabetic retinopathy; NPDR= non-proliferative diabetic retinopathy; PDR=proliferative diabetic retinopathy; OU= oculus uterque (both eyes); OCT= optical coherence tomography; OD= oculus dexter (right eye); OS= oculus sinister (left eye) ; PRP= pan retinal photocoagulation; CRT= central retinal thickness

Table 4: Demographics of defaulters versus non-defaulters. Values were presented as mean or n(%) where appropriate.

	Defaulters (n = 91)	Non-defaulter (n = 48)	*p-value
Age	33.91	34.12	0.76
Ethnicity			
Malay	73%	38%	0.54
Chinese	9%	5%	
Indian	6%	5%	
Others	3%	0%	
Gravida	3.04	2.77	0.41
Parity	1.32	1.33	0.97
Type of DM			
Type-1 DM	6%	2%	0.59
Type-2 DM	85%	46%	
Duration of DM (years)	4.31	4.71	0.51

* Mann-Whitney U test

only 60% of pregnant women with type 2 DM had performed the two eye examinations during their pregnancy. This was played out similarly in our study, whereby less than 30% of the patients in our list were checked twice during their pregnancy. This could be due to their lack of awareness of the importance of eye check-up for pregnant diabetics and how diabetes affects vision. Another possibility was the inconvenience of patients having to go to the Ophthalmology Clinic which was located at another part and floor of the hospital.This situation further exacerbated the persistence of patients in attending follow-up as their vision even in the presence of PDR, were more often than not, still normal.

In another study in Japan, the prevalence of DR in pregnant women with type 2 DM was as high as 28% (Omori et al. 1994). The objective of this study was to document the prevalence and progression of DR in an unselected population of pregnant women with type 2 DM using a standardised photo screening technique. The interesting findings of our review was that all the progressors during pregnancy were type 2 DM. None of the seven patients who progressed were type 1. On the other hand, in this series, only two of the pregnancies were in type 1 DM which contradicts our expectation where majority will be of type 1 DM as they were usually of younger age group and in their child-bearing age. This could be explained by the fact that the age of onset for type 2 DM was younger, as young as 19 years old (Wilmot & Idris 2014). In our study, there was no significant difference found for type of DM and photo screening was not used.

The present study found that in an unselected population of pregnant women with type 2 DM with DR diagnosed in early pregnancy, retinopathy progressed 14% among these pregnant women. Although the progression was mainly mild, but sight-threatening DR was seen in one woman with poor pre-pregnancy

glycaemic control and low compliance to treatment. Sight-threatening DR include severe NPDR, PDR and CSME (Sapkota et al. 2019). A similar report was made by Bastion et al. (2005) which described the rapid progression from no DR to florid proliferative DR in a 35-year-old pregnant diabetic with poorly controlled hypertension. In our more recent series, there were 19% with mild NPDR; none with PDR at the beginning.

In early pregnancy, most women had no or mild retinal changes, which is comparable to previous reports on women with type 1 DM with similar duration of diabetes. Risk of progression of DR in women with type 2 DM in the current study were likely to be lower than in women with type 1 DM.

Progression of DR during pregnancy was mainly due to poor glycaemic control, long duration of diabetes, severity of DR at baseline, rapid decline in HbA1c in early pregnancy, associated hypertension and increased retinal blood flow (Chew et al. 1995; Chan et al. 2004; Vestgaard et al. 2010). However, in our study, the progressors and non-progressors group, had no statistically significant associations with duration of diabetes, baseline HbA1C level and hypertension.

More recently, a study by Egan et al. (2015) reported that progression were seen among pregnant women who had been diabetic for more than 15 years. In contrast, we noted that the patients who progressed in our study had diabetes for less than 15 years. We would also like to highlight that one of the progressors developed rapid progression from mild NPDR to PDR throughout her pregnancy while her poor sugar control, pre-eclampsia as well as long duration of DM may have contributed to this condition (Table 3). Therefore, we recommended that pregnant women with long-standing DM, associated hypertension in pregnancy and worse baseline DR to be monitored closely during pregnancy to avoid sight-threatening complications. Furthermore, optimising glycaemic control before pregnancy among type 1 DM women had been proven to reduce the tendency of progression compared to the women who did not optimise their glycaemic control prior to pregnancy (Alexopoulos et al. 2019; Diabetes Control and Complications Trial Research Group 2000).

Despite a low risk of progression of retinopathy, sight-threatening deterioration did occur in pregnant women with type 2 DM. In our study, four out of seven women developed sight-threatening DR or CSME and they all had diabetes for more than five years. Type 2 DM patients are usually diagnosed at a relatively shorter duration prior to their pregnancies, therefore, their diabetes clinic visits, pregnancy planning and DR screening are less frequent which might contribute to the remarkable progression of DR (Ramussen et al. 2010).

Pregnancy-associated hypertension were also among the risk factors that led to progression of DR during pregnancy (Vestgaard et al. 2010). However, in our study there was no significant association found with these risk factors, this could be due to

the fact that our sample size was too small. Other factors such as diabetic nephropathy were associated with risk of progression, however, we observed, 65% of those who had diabetic nephropathy were not among the progressors.

In our small series, 70% of pregnant diabetics did not have a complete ophthalmology follow-up during their pregnancy, only 30% had at least two fundus review. To our surprise, a study by Hampshire et al. (2013) that looked at the attendance at a pre-pregnancy care program and adequate retinal assessment in the subsequent pregnancy demonstrated 70% of women with pregestational diabetes had incomplete follow-up as well. This type of data and information has never been collected in Malaysian context. Similarly, their findings also had no association with the number of gravida or parity. This is most likely due to their lack of awareness on the sight-threatening complications of diabetes (Buari & Dian 2017).

In our case series, there was no association between DR progression with age. Another study by Vestgaard et al. (2010) found that among women with type 1 DM and good glycaemic control before and during pregnancy, the progression of DR occurred in up to 27%. Maternal age was also lower in women with progression of DR (Table 2) (Hampshire et al. 2013).

However, none of these factors were found to be significantly associated in our case series. This could be due to good control of diabetes and hypertension in those who were compliant and attended their eye examinations.

The limitations of this study included the small percentage that could be examined at two time points or more in this study. This could have resulted in bias towards patients who were generally more compliant to therapy overall, whether to their risk factor control or ophthalmology advice. The small sample size also reduces the power of the study.

Nevertheless, this study presents valuable local data for our population. It also highlights the need for better referral system from the Antenatal clinic to the ophthalmology department which can incorporate contact tracing and more convenient appointment arrangements. This will hopefully improve the compliance with the suggested referral. Pamphlet can be disseminated to patients about progression of DR in pregnant diabetics to improve the attendance.

CONCLUSION

The rate of repeat follow-up for retinopathy in pregnant women with diabetes was about 30%. Among those with complete follow-up, it was noted that there was 17% of progression rate of DR. However, no risk factors were identified for this progression and this may be due to small sample size in our study.

REFERENCES

Alexopoulos, A.S., Blair, R., Peters, A.L. 2019. Management of preexisting diabetes in pregnancy: a review. *JAMA* **321**(18): 1811-9.

Bastion, M.L., Barkeh, H., Muhaya, M. 2005. Accelerated diabetic retinopathy in pregnancy-a real and present danger. *Med J Malaysia* **60**(4):

502-4.

Buari, N.H., Dian, N.I. 2017. The association of awareness and knowledge of diabetic retinopathy with age and residential area in Selangor. *Environ Proc J* **2**(6): 125

Chan, W.C., Lim, L.T., Quinn, M.J., Knox, F.A., McCance, D., Best, R.M. 2004. Management and outcome of sight-threatening diabetic retinopathy in pregnancy. *Eye* **18**(8): 826-32.

Chew, E.Y., Mills, J.L., Metzger, B.E., Remaley, N.A., Jovanovic-Peterson, l., Knopp, R.H., Conley, M., Rand, L., Simpson, J.L., Holmes, L.B., Aarons, J.H. 1995. Metabolic control and progression of retinopathy. The Diabetes in Early Pregnancy Study. National Institute of Child Health and Human Development Diabetes in Early Pregnancy Study. *Diabetes Care* **18**(5): 631-7.

Cho, N.H., Shaw, J.E., Karuranga, S., Huang, Y., da Rocha Fernandes, J.D., Ohlrogge, A.W., Malanda, B. 2018. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract* **138:** 271-81.

Diabetes Control and Complications Trial research Group. 2000. Effect of pregnancy on microvascular complications in the diabetes control and complications trial. The Diabetes Control and Complications Trial Research Group. *Diabetes Care* **23**(8): 1084-91.

Diabetic Retinopathy Guidelines. 2012. The Royal College of Ophthalmologists. https://www.rcophth.ac.uk/wp-content/uploads/2021/08/2012-SCI-267-Diabetic-Retinopathy-Guidelines-December-2012.pdf

Egan, A.M., McVicker, L., Heerey, A., Carmody, L., Harney, F., Dunne, F.P. 2015. Diabetic retinopathy in pregnancy: A population-based study of women with pregestational diabetes. *J Diabetes Res* **2015**: 310239.

Hampshire, R., Wharton, H., Leigh, R., Wright, A., Dodson, P. 2013. Screening for diabetic retinopathy in pregnancy using photographic review clinics. *Diabet Med* **30**(4): 475-7.

Kapoor, N., Thomas, N. 2017. Oral antidiabetic agents: Recently available novel oral antidiabetic agents in India: A clinical review. *Curr Med Issues* **15**(3): 169.

Koopman, R.J., Maninous, A.G., Diaz, V.A., Geesy, M.E. 2005. Changes in age at diagnosis or type 2 diabetes mellitus in the United States, 1988 to 2000. *Ann Fam Med* **3**(1): 60-3.

Makwana, T., Takkar, B., Venkatesh, P., Sharma, J.B., Gupta, Y., Chawla, R., Vohra, R., Kriplani, A., Tandon, N. 2018. Prevalence, progression, and outcomes of diabetic retinopathy during pregnancy in Indian scenario. *Indian J Ophthalmol* **66**(4): 541-6.

Mallika, P., Tan, A., SA, T.A., Alwi, S.S., Intan, G. 2010. Diabetic retinopathy and the effect of pregnancy. *Malays Fam Physician* **5**(1): 2-5.

Ministry of Health Malaysia. 2017. *Clinical Practice Guidelines: Management of Diabetes in Pregnancy.* Putrajaya.

Omori, Y., Minei, S., Testuo, T., Nemoto, K., Shimizu, M., Sanaka, M. 1994. Current status of pregnancy in diabetic women. A comparison of pregnancy in IDDM and NIDDM mothers. *Diabetes Res Clin Pract* **24** Suppl: S273-8.

Polizzi, S., Mahjan, V.B. 2015. Intravitreal anti-vegf injections in pregnancy: case series and review of literature. *J Ocul Pharmacol Ther* **31**(10): 605-10.

Ramussen, K.L., Laugesen, C.S., Ringholm, L., Vestgaard, M., Damm, P., Mathiesen, E.R. 2010. Progression of diabetic retinopathy during pregnancy in women with type 2 diabetes. *Diabetologia* **53**(6): 1076-83.

Sapkota, R., Chen, Z., Zheng, D., Pardhan, S. 2019. The profile of sight-threatening diabetic retinopathy in patients attending a specialist eye clinic in Hangzhou, China. *BMJ Open Ophthalmol* **4**(1): e000236.

Vestgaard, M., Ringholm, L., Laugesen, C.S., Ramussen, K.L., Damn, P., Mathiesen, E.R. 2010. Pregnancy-induced sight-threatening diabetic retinopathy in women with Type 1 diabetes. *Diabet Med* **27**(4): 431-5.

Wajid, S., Menaka, M., Ahmed, F., Samreen, S. 2019. A literature review on oral hypoglycemic drugs – mechanistic aspects. *Asian J Pharm Clin Res* **12**(11): 5-10.

Wilmot, E., Idris, I. 2014. Early onset type 2 diabetes: Risk factors, clinical impact and management. *Ther Adv Chronic Dis* **5**(6): 234-4.

You, W.P., Henneberg, M. 2016. Type 1 diabetes prevalence increasing globally and regionally: The role of natural selection and life expectancy at birth. *BMJ Open Diabetes Res Care* **4**(1): e000161.

Received: 19 Feb 2021
Accepted: 15 Sept 2022