Prevalence of diabetic retinopathy in Pakistan: A systematic review

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ABSTRACT
Objectives: Primary aim was to review the literature on the prevalence of diabetic retinopathy (DR) and vision threatening diabetic retinopathy (VTDR) in Pakistan.

Methods: A search of the bibliographic databases (Medline, Pubmed, and Google scholar) was conducted from 1990 to March 2017. Articles about prevalence of DR and VTDR in Pakistan were retrieved and scrutinized. The studies satisfying the inclusion/exclusion criteria were considered for detail review.

Results: Forty one articles on prevalence of DR were traced out. Exclusion and inclusion criteria were met in 29 studies. In selected studies (29), pooled Prevalence of DR was found to be 28.78% with a variation of 10.6% to 91.3%. Out of 29 studies, DR was classified in 19 studies. Pooled Prevalence of VTDR in these 19 studies was found to be 28.2% (variation of 4% to 46.3%) of patient with retinopathy and 8.6% of all diabetics.

Conclusion: A great variation in the values of DR and VTDR was observed in this study. Researchers suggest a community based study with uniform methodology to find out a comparable value of prevalence of DR and VTDR in all provinces of Pakistan.

KEYWORDS: Diabetic Retinopathy, Prevalence, Vision Threatening Diabetic Retinopathy.

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INTRODUCTION

Second national survey on prevalence of blindness in 2004 showed cataract, glaucoma, and corneal disease as common causes of blindness. Posterior segment diseases were responsible for 9.5% as compared to 5.4% in first national survey in 1990. Diabetic retinopathy related blindness (DRB) was not considered in 1990 survey; but in second survey DRB was recorded as < 0.5% amongst the causes of posterior segment disease. Diabetes is increasing and so will be its chronic complications. Studies by King et al Wild et al and Shaw et al have shown that diabetes mellitus is likely to double between 2000 and 2030 mostly in developing countries. In 2010, of an estimated 285 million people worldwide with diabetes, over one-third had signs of DR, and one fourth of these were afflicted with vision-threatening diabetic retinopathy (VTDR), defined as severe non-proliferative DR, proliferative DR (PDR) and diabetic macular edema (DME).
There are sufficient studies from countries with large population like China and India to show the threat from diabetes and its complications and these countries have National plans to prevent the problems of diabetes. Pakistan with more than 200 million (recent census) is expected to have large number of diabetic patients with DR with no plan to combat the consequences. We are lacking in conclusive data highlighting problem of diabetes and DR to generate enough advocacy of the policy makers to plan a “National program” to address diabetes related blindness. In a review article by Hakeem R et al prevalence of diabetes has been quoted as 7.6% to 11%. In a recent press release by Baqai Institute of Diabetology and Endocrinology (BIDE), prevalence of diabetes in Pakistan is 26%. Very little work has been done on DR and VTDR. Values quoted in literature are between 10.6% and 91.34% for DR. Prevalence of VTDR has been quoted between 4% and 46%.

In the present article, Researchers intended to study the screening modalities used in Pakistan, heterogeneity in results and its reasons, flaws in the classifications used for DR and find out pooled statistics for DR and VTDR.

This study was designed to review the articles since 1990 to March 2017 on the prevalence/frequency of DR and VTDR in Pakistan. This data will be helpful for advocacy of the policy makers to consider planning regarding “National program on diabetes related blindness”.

**METHODS**

**Appraisal of Study Methodology:** This study was approved by “Research Ethical Committee (REC) of Isra Post-graduate Institute of Ophthalmology, Karachi. There were no conflicts among reviewers.

**Research Design and Methods:** A systematic literature review was conducted to identify all population-based and hospital-based studies done in Pakistan during 1990 – March 2017.

**Exclusion Criteria:** The articles were excluded on basis of nationality (Non Pakistani), duplication, incompleteness, irrelevance and ambiguity of data.

**Inclusion Criteria:** Articles and abstracts electronically accessible with DR/VTDR as keyword. All studies having Hospital and/or population-based data for DR/STDR in English language were included.

**Data extraction:** Articles were retrieved from Medline, Pub Med and Google scholar by putting search key words, “diabetic retinopathy”, frequency/prevalence and “Pakistan”.

The identified studies were reviewed for authors, study design, duration & place of study, sample size, tools used to detect DR, and scales used to classify DR.

A total of 41 articles were traced in which 35 were full articles and 6 abstracts. Out of these studies, 29 studies fulfilled the inclusion criteria in which 25 were full text articles, 3 abstracts and one thesis. All the studies were published in national journals except one which was published in Turkish journal. 

*All the selected articles were reviewed by following criteria:*

**Setting of the retinal screening:** Retinal Screening for DR/VTDR was either Hospital based where retinal screening was done in diabetic patients attending a secondary/tertiary centers (Hospital based) for any health problem or community based where screening was done in the community.

**Tools used for retinal screening:** The tools used for screening of DR were direct Ophthalmoscopy, indirect ophthalmoscopy, Slit-lamp bio-microscopy with 90D fundus lens in dilated pupil or digital photography with Non-Mydriatic fundus camera (NMFC). In Non-Mydriatic fundus camera, the screening was done through un-dilated pupil taking one 45° retinal image with center to the macula of each eye. Fluorescence Fundus Angiography (FFA) and Optical Coherence Tomography (OCT) were done in selected cases.

**Human resource involved in retinal screening:** Screening of retina for retinopathy was mostly done by retina trained ophthalmologist, general ophthalmologist, optometrist, family/general physician and diabetologist.

**Classification or Grading of DR:** Classifications used were either “Modified Airlie House / EDTRS classification” or “International Clinical Disease Severity Scale for DR”. Former classification is based on stereo photographs of seven fields and is used as a research tool rather than clinical use. Common classification in use is “International Clinical Disease Severity Scale for DR”3. It does not require specialized examinations such as optical coherence tomography or fluorescein angiography. In this classification, five stages are recognized. (TableA)

Diabetic macular edema (DME) is separately described. It is classified as mild, moderate and severe depending on the distance of the exudates and thickening from the center of the fovea. DME can be present alone or in association with any stage of retinopathy. PDR and macular edema are considered “Vision threatening DR (VTDR) whereas mild, moderate and severe non proliferating diabetic retinopathy without macular...
edema considered is considered as Non-Vision Threatening DR (NVTDR).

**Data Analysis:** Statistical Package for Social Sciences Version 20.0 (SPSS Software, Chicago, USA) was used to analyze the data. Frequencies and percentages were calculated for quantitative variable. Pooled Prevalence of DR from 29 studies reported in Table-I. Classification of DR was reported in Table-II. Box plot showed for different Province with respect to prevalence of DR.

**RESULTS**

Total studies on prevalence of DR/VTDR published between 1990 and March 2017, were 41. Studies fulfilling all criteria for review were 29. All these studies were from three provinces, Sindh, Punjab and KPK. No study was reported from Baluchistan or Northern areas. All the studies excluding one were reported in 8 different national journals. One study was published outside Pakistan in Turk J Med Sci.
Table-I: Patients with Prevalence of Diabetes Mellitus & Prevalence of Diabetes Retinopathy (DR) in Pakistan.

| Study# | Title                                                                 | Author                  | Journal/Year | Type of Study                                      | Sample Size | Tools used to Detect DR                      | Frequency of DR (%) | Grading Scale | Types of DR Found       |
|--------|-----------------------------------------------------------------------|-------------------------|---------------|---------------------------------------------------|-------------|-----------------------------------------------|---------------------|---------------|-------------------------|
| 1      | Prevalence of DR in Pakistani Subjects A Pilot Study                  | Akhtar et al.           | JPMA/1991      | x                                                 | 3000        | Slit Lamp & Top Con Fundus Camera             | 780 (26%)           | x             | NPDR = 617 PDR = 163   |
| 2      | Presentation of Diabetic Retinopathy                                  | Naeem et al.            | JPMI/2003      | Retrospective cross sectional analysis            | 100         | Bio Microscope Indirect Ophthalm & Direct Ophth | 38 (38%)            | x             | NPDR = 28 PDR = 10     |
| 3      | Prevalence of Microvascular Complications Among Diabetic Patients     | Shafiq et al.           | PJMS/2004      | x                                                 | 573         | Direct Ophthalmoscope                        | 102 (55%)           | x             |                         |
| 4      | Prevalence of DR Among Individuals Screened Positive For Diabetes in Five Community Based Eye Camps In Northern Karachi Pakistan | Jamal et al.            | J Ayub Med College Abbottabad/2006 | x | 160 | 90-dioptre Slit lamp Topcon Fundus Camera | 17 (10.6%)            | x             | Mild NPDR =6 (35.3%) Moderate NPDR = 5(29.4%) Severe NPDR =2 (11.8%) PDR =1 (59%) Maculopathy 3 |
| 5      | Screening for DR: A Comparative Study b/w Hospital & Community Based Screening b/w Paying & Non-paying Patients | Tayyab et al.           | J Ayub Med College Abbottabad/2007 | Comparative study | 8227 | 90 D lens on slit-lamp & indirect Ophth. | 1834 (22.29%)            | x             |                         |
| 6      | Frequency of Retinopathy In Newly Diagnosed T2DM Patients            | Shahid et al.           | JPMA/2008      | Cross sectional                                   | 130         | LogMar, Refraction, Biometry, Undilated fundus exam, Slit lamp, Digital photography | 101 (15.3%)            | x             |X                        |
| 7      | Prevalence of DR & Influence Factors Among Newly Diagnosed Diabetics in Rural & Urban Areas of Pakistan, Data Analysis from the Pakistan National Blindness & Visual Impairment Survey 2003 | Aurangzeb et al.        | PJMS/2008      | Survey                                            | 660         | NPDR =18 PDR = 2 Maculopathy 4               |                      |               |                         |
| 8      | Patterns of Retinopathy Among Diabetic Patients At Tertiary Care Hospital Jamshoro Hyderabad | Ghauri et al.           | Medical Channel/2010 | Descriptive (Case Series Comp-arative) | 100         | NPDR = 48 (96%) PDR = 2 (4%)                |                      |               |                         |
| 9      | Frequency of DR in Patients After 10 Years of Diagnosis of T2DM      | Mumtaz et al.           | Ayub Med College Abbottabad/2010 | x | 200 | Used 90 Di-opter lens Indirect Ophth. | 460 (27.43%)            | x             | NPDR = 334 (72.61%) PDR = 96 (20.87%) NPDR+CSME = 10 (2.17%) PDR+CSME = 12 (2.61%) Adv. PDR = 8 (1.74%) |
| 10     | Prevalence of T2DM & DR, The Gadap Study                             | Pir et al.              | JCPSP/2010      | Descriptive                                        | 1677        |                                           |                      |               |                         |
| No. | Study Title                                                                                                                                                    | Authors          | Journal/J.                                      | Sample Size | Methods                                                                 | Prevalence | DR Types                          | Other Information                                      |
|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|------------------------------------------------|-------------|-------------------------------------------------------------------------|------------|-----------------------------------|---------------------------------------------------------|
| 11  | Prevalence of Retinopathy & Its Associated Factors in T2DM Patients Visiting Hospitals & Diabetic Clinics in Faisalabad Pakistan                               | Hassan et al.    | Pakistan J. Zool/2010                           | x 500       | x                                                                       | 207 (41.4%) | x                                 | X                                                       |
| 12  | The Prevalence of DR in Faisalabad, Pakistan A Population Based Study                                                                                       | Fatma et al.     | TU BIT AK/2011                                  | x 1524      | x                                                                       | 183 (12%)  | x                                 | NPDR = 106 (7%) PDR = 77 (5%)                          |
| 13  | Frequency & Types of DR in Type II Diabetes, A Hospital Based Study                                                                                         | Mehtab et al.    | JUMHS/2011                                      | 244         | Descriptive case series                                                | 44 (100%)  | x                                 | EDRS Mild NPDR = 61 Moderate - Severe NPDR = 17 PDR = 22 |
| 14  | Frequency of DR in Hypertensive Diabetic Patients in Tertiary Care Hospital of Peshawar, Pk.                                                                  | Shafique et al.   | J Ayub Med College Abbottabad/2011              | 200         | Cross sectional                                                       | 102 (51%)  | x                                 | X                                                       |
| 15  | Study of DR in Patients Admitted to A Tertiary Care Hospital For Non Ophthalmological Reasons                                                               | Shafqat-ullah et al. | Gomal Journal of Medical Sciences/2012   | 462         | 90D with the help of slit lamp binocular microscope                    | 422 (91.34%) | x                                 | Background DR = 188 Pre-proliferative DR = 172 Proliferative DR = 62 |
| 16  | Frequency of DR in a Tertiary Care Hospital Using Digital Retinal Imaging Technology                                                                         | Aziz et. al.     | JPMI/2012                                       | 2123        | Descriptive study                                                      | 680 (32.03%) | x                                 | International Clinical DR Disease Severity Scale         |
| 17  | Frequency, Severity & Risk Indicators Of Retinopathy In Patients With Diabetes Screened By Fundus Photographs, A Study From Primary Health Care                  | Saleh et al.     | PJMS/2013                                       | 10768       | Observational                                                         | 2661 (24.27%) | x                                 | T1DM Mild NPDR = 59% Moderate NPDR =03% Severe NPDR =01% PDR = 05% CSME+NPDR = 31% CSME+PDR = 03% 01% Advanced DR = 02% 01% |
| 18  | Risk Factors of Retinopathy in T2DM At A Tertiary Care Hospital, Bahawalpur Pakistan                                                                         | Sadiq et al.     | PJMS/2013                                       | 300         | Cross sectional descriptive                                            | 74 (23.9%) | x                                 | X                                                       |
| 19  | To determine the prevalence of DR in Karachi                                                                                                               | Safila et al.    | Journal of Scientific and Innovative Research/2014 | 150         | Population based cross sectional survey                               | 71 (47.33%) | EDRS                              | X                                                       |
| 20  | Diabetic Retinopathies & Their Associated Factors, A Study In Tertiary Care Hospital in Karachi Pk. (Monograph)                                                  | Tahir et al.     | Thesis, Department Community Med., Univ. of Oslo/2014 | 1167        | Retrospective cross sectional analysis                                 | 853 (73.1%) | ETDRS & Airline House             | Mild NPDR = 395 Moderate NPDR = 321 Severe NPDR = 45 PDR = 92 |
| 21  | Sight Threatening DR in T2DM                                                                                                                                  | Memon et al.     | Pak Journal Ophthalmology/2014                  | 200         | x                                                                       | 134 (67%)  | EDRS                              | NPDR = 72 PDR = 62                                     |
| No. | Title                                                                 | Authors             | Journal                          | Study Type          | Size | Method                          | Cases | Prevalence | Guidelines/Practice                                                                 | Findings                                                                 |
|-----|-----------------------------------------------------------------------|---------------------|----------------------------------|---------------------|------|---------------------------------|-------|------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| 22  | Frequency And Patterns Of Eye Diseases In Retina Clinic Of A Tertiary Care Hospital In Karachi | Aimal et al.       | Pak Journal of Ophthalmology/2014 | Case study method   | 3615 | 20 D and 90 D lenses binocular indirect ophthalmoscope | 1440  | 39.83%     | x                                                                                   | Bilateral NPDR = 624 (43.3%), NPDR+PDR = 216 (15%), NPDR+ADED = 192 (13.3%), Bilateral ADED = 96 (6.6%), PDR+ADED = 120 (8.3%) |
| 23  | Prevalence of DR Among T2DM Patients in Pakistan – Vision Registry    | Mehreen et al.      | Pakistan Journal of Ophthalmology/2014 | Descriptive cross sectional | 202  | Ophthalmoscope                  | 115   | 56.9%      | The Guidelines of Good Epidemiology Practice                                       | Hemorrhages n=70, Cotton Wool Spots n=21, Neovascularization n=15, Hard Exudates n=67 |
| 24  | Frequency of Diabetic Retinopathy and Microalbuminuria in Newly Diagnosed Type II Diabetes Mellitus patients and their association with each other | Khurram et al.      | PJMHS/2014                       | Descriptive case series study | 157  | Fundoscopy                      | 34    | 21.66%     | x                                                                                   |                                                                                                                         |
| 25  | Frequency of DR in Karachi, A Hospital Based Study                    | Saba et al.         | Journal of the Dow University of Health Sciences Karachi/2015 | Cross sectional descriptive | 570  | Top Con PS-61E Slit lamp Bio Microscope | 315   | 55.3%      | International Clinical DR Disease Severity Scale                                   | Mild NPDR = 231, Moderate NPDR = 33, Severe NPDR = 11, PDR = 40 |
| 26  | Frequency of Diabetic Retinopathy in Type II Diabetics presenting at DHQ Hospital Sahiwal | Khalid et al.       | PJMHS/2015                       | Cross sectional study | 340  | Slit-lamp and 90-D hand held, indirect funduscopy | 57    | 17%        | ETDRS                                                                                | NPDR = 50 (87.72%), PDR = 07 (12.28%) |
| 27  | Diabetic Retinopathy; Prevalence, among patients attending the free Eye camps for cataract surgery in Southern Punjab, Pakistan | Rasheed et al.      | TPMJ/2016                        | Cross sectional study | 759  | Direct/indirect ophthalmoscope and slit-lamp, 90-dioptre lens bio-microscope | 93    | 15%        | ETDRS                                                                                | NPDR = 87 (93.5%), PDR = 06 (6.5%) |
| 28  | Diabetes Retinopathy Frequency at Level of HbA1c greater than 6.5%     | Waseem et al.       | Professional Med. J./2017         | Descriptive case study | 130  | Fundoscopy                      | 31    | 23.85%     | International Clinical DR Disease Severity Scale                                   | NPDR = 23 (74.2%), PDR = 08 (25.8%) |
| 29  | Prevalence of Retinopathy Detected by Fundoscopy among Newly Diagnosed Type 2 Diabetic Patients Visiting a Local Hospital in Lahore | Tasnim et al.       | PJZ/2017                          | Cross sectional study | 200  | Fundoscopy                      | 66    | 33%        | Retinopathy Disease Severity Scale                                                  | PPDR = 14 (7%), PDR = 12 (6%) |
| 30  | Total                                                                 |                     |                                  |                     | 38,438 | 11,064 (28.78%)                 |       |            |                                                                                       |                                                                                                                         |
Majority (24 out of 29) studies were done in hospital setting, four studies (Study # 4, 8, 10 & 17) were community based and only one study (Study # 5) was mixed. The methodology of every study was dissimilar in terms of inclusion/exclusion criteria, tools for DR detection.

Tools used for screening: Non-Mydriatic fundus camera was used in one study (Study #17) and Mydriatic fundus camera was used in 3 studies (Study # 1, 4, 7). Findings in these 4 studies were confirmed with bio-microscopy. Direct Ophthalmoscopy alone was used in 7 studies (Study # 2, 3, 5, 10, 19, 26, & 27). In remaining 18 studies retinal screening was done by slit lamp bio microscopy using fundus lens. Human Resource involved: Personnel involved in screening were ophthalmologist. In one study only (study #17) optometrist used NMFC for screening of DR and referred the DR cases to the retina trained ophthalmologist for grading and intervention.

Macular edema was mentioned only in four studies (Study # 4, 8, 10, and 17). In all of 29 studies a total of 38438 diabetics were screened for diabetic retinopathy (DR). Pooled prevalence of DR was found to be 11064 (28.78%) (With 95% confidence interval [C.I] 29.55 - 47.73) having a huge variation of 91.3% to 10.6%. (Table-I). Amongst 19 studies where DR was classified into VTDR and NVTDR, pooled Prevalence of VTDR was found to be 28.2% (variation 4% to 46.3%) of all DR and 8.6% of all diabetics. (Table-II) When the prevalence of DR was compared between Provinces a large variation in values was found in KPK studies, however in Sindh and Punjab less variation in the data was noted. It was also seen that median line of Punjab was showing less prevalence whereas KPK was showing biggest median in terms of prevalence. (Fig.3)

**DISCUSSION**

Pooled prevalence of DR in Pakistan in this study was found to be 28.78% in all diabetics and that of VTDR was 28.2% of all DR and 8.6% of all diabetics (Table 2). DR varies between 10.6% and 91.34%. VTDR varies between 4% and 46%. Huge variations of DR and VTDR in published articles reflect similar values quoted in various national seminars and workshops. This study has explored the reason for inconsistent results. The probable reason of variation in the published articles were sampling criteria, sample
size, duration of study, type of study, methods to detect DR and expertise of the person (ophthalmologist/optometrist). Sample size of at least 12 studies were ≤ than 200. When standard error of proportion was calculated, it was found to be 0.085. This is far too little to prove generalization of results of these review articles for the population. Variation of age group was also not taken into account in many studies. Low frequency can partly be due to failure of detection of DR in early stages especially in cases of diabetic macular edema. Out of 29 studies, macular edema has been mentioned in 4 studies only. Second reason is presence of lens changes masking the fundus. Third reason is the ability of the screener. The effectiveness of different screening modalities has been widely investigated. UK studies show sensitivity levels for the detection of sight-threatening diabetic retinopathy of 41%- 67% for general practitioners, 48%-82% for optometrists, 65% for ophthalmologists, and 27%-67% for Diabetologist and hospital physicians using direct Ophthalmoscopy.4 The reasons of high prevalence of diabetic retinopathy in some studies could be the area of screening. Screening in a community with lack of awareness, inaccessible and unaffordable eye care service, and lack of knowledge about diabetes and its complications may result in pooling of DR and high frequency. KAP study about diabetics and DR in Gaddap town showed that overall knowledge of diabetes in sample population of (n=527) was 35.23% amongst whom only 7.4 percent respondents considered Diabetic retinopathy as cause of blindness.5 With all gaps, the values of DR 28.78% (with 95% confidence interval [CI] 29.55 – 47.73) and VTDR high enough to be of significant national public health problem needing urgent attention of policy makers, executives and health care providers.

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Note: Some of the studies included had used the word frequency along with prevalence as well.

CONCLUSION: This study provides approximate prevalence estimate of DR and VTDR (PDR, DME) using data from available published studies, mostly hospital based from all over Pakistan. Although published estimates for DR and VTDR varies widely, this study provides an approx. estimates for DR and VTDR high enough to be of significant national public health problem needing urgent attention of policy makers, executives and health care providers.

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