FREQUENCY OF UNRECOGNISED DIABETIC RETINOPATHY AND NEPHROPATHY IN PATIENTS PRESENTING WITH DIABETIC FOOT ULCERS

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ABSTRACT

Objective: To determine the frequency of unrecognised diabetic retinopathy and nephropathy in patients presenting with diabetic foot ulcers.

Methodology: This cross sectional study was conducted from November 2019 to May 2020. All patients presenting with diabetic foot ulcers were included in the study. Diabetic retinopathy was assessed by direct ophthalmoscopy followed by digital retinal camera imaging and diabetic nephropathy was assessed by measuring 24 hours quantitative urinary proteins. Data was analysed with SPSS and presented in tables and graphs.

Results: Among 104 patients, 72 (69.2%) were male. Mean age for both genders was 53.29 ± 10.15 years (range: 33-75). Ninety eight (94.23%) had type 2 diabetes mellitus (T2DM) and 6 (5.76%) were having Type 1 diabetes mellitus (T1DM). The mean body mass index (BMI) was 26.98 ± 5.21 kg/m2 (range: 18.6-42.4) with mean duration of diabetes of 11.45 ± 5.08 years (range: 2-25). The mean HbA1C was 11.13 ± 2.19% (range: 6.6 to 17.5). Ninety two (88.46%) had unrecognised diabetic retinopathy and 46 (44.23%) had unrecognised diabetic nephropathy. Forty four (42.30%) had both unrecognised diabetic nephropathy and retinopathy.

Conclusion: High percentage of unrecognised diabetic retinopathy and nephropathy was found in the patients who presented with diabetic foot ulcers.

Key Words: Diabetes mellitus, Diabetic foot ulcer, Diabetic retinopathy, Diabetic nephropathy, Diabetic neuropathy

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INTRODUCTION

Diabetes Mellitus (DM) is one of the commonest non-communicable diseases, particularly in developing countries. According to World Health Organization's (WHO) estimates (2016), 422 million and international Diabetes Federation's (IDF) report (2019), around 463 million adults are living with DM[1,2]. The prevalence of DM is increasing very rapidly. An international survey of IDF carried out in 2019 suggests that the prevalence of DM will increase from 463 million in 2019 to 578 million in 2030, and 700 million in 2050[2].

In Pakistan, around 20 million people are living with DM with a prevalence of 16.98%[3]. The two national diabetes surveys done in Pakistan, first in 1994-1998 and second in 2016-2017, there has been marked increase in the prevalence of DM from 11.47% to 26.3%[4-6]. Currently, Pakistan is 6th in the list of top 10 countries having highest number of individuals with DM, on the top being China followed by India (2nd) and United States of America (3rd). According to an estimate, Pakistan will exceed United States of America by 2045 in the prevalence of DM[2]. Around 8.5 million patients with DM remain undiagnosed, which accounts for 43.8% of the patients with DM[2]. Around 159,000 patients died in Pakistan in 2019, which is the highest number of mortality due to complications of diabetes among the Middle East and North African countries[2].

Uncontrolled DM can have macrovascular and microvascular complications with high morbidity and mortality[7]. The Microvascular complications include diabetic retinopathy (DR), diabetic nephropathy (DN) and diabetic foot ulcer (DFU). Diabetic retinopathy is one of the leading causes of blindness in the working age group. It has a high global prevalence reaching up to 35% in the people with diabetes and around 12% have

vision threatening DR. According to estimates, 93 million adults are living with DR[2, 8-10]. It has grave outcomes on the life of the patients despite of the fact that it can be prevented or treated with better outcomes if screened and diagnosed early. DN effects one third of the people having DM leading to chronic kidney disease (CKD)[11]. In United Kingdom and United States, 25% and 36% people with DM have CKD, respectively[12,13]. Worldwide, around 80% end stage renal disease (ESRD) cases are either due to DM or hypertension or both[13].

Diabetic peripheral neuropathy compromises the protective sensation of the limbs specifically the foot leading to DFU. DFU is one of the major causes of morbidity which leads to highest number of hospital admissions among the chronic complications of DM[14,15]. Around 2 % of the people with DM have DFU annually and about 1 % end up with some degree of amputation in their life span[2,16]. The global prevalence of DFU is 6.3% while in Pakistan it ranges from 4% to 10%[17,18].

As a standard of care, all patients with Type II diabetes mellitus (T2DM) should be assessed for diabetic neuropathy, retinopathy and nephropathy at the time of diagnosis followed by annual screening and for patients with Type I diabetes mellitus (T1DM), screening should be done 5 years after the diagnosis and annually thereafter[19].

Majority of our patients with DM do not follow screening protocols and seek medical attention only when they have developed overt complications which are mostly irreversible, difficult to treat and pose greater financial, social and psychological burden to the patients. The purpose of this study was to evaluate the burden and status of unrecognised DR and DN in patients having DFU, so that they can be managed in the initial stages in order to decrease the progression of and maintain the patient's quality of life. It will also increase the awareness regarding timely screening of microvascular complications in patients with DM.

METHODOLOGY

This cross sectional study was conducted on 104 patients in the department of diabetes, endocrinology and metabolic diseases, Hayatabad Medical Complex Peshawar, from November 2019 to May 2020. This study was approved by the institutional research and ethics committee. A written informed consent was obtained from all the patients enrolled in our study. After taking detailed history and physical examination, all the relevant information was recorded on a pre-designed questionnaire. Patients' records were assessed for glycemic status and any previous workup done regarding diabetic complications. Using non-probability consecutive sampling technique, the patients having HbA1c of more than 6.5 % with diabetic foot ulcer and having no previously identified diabetic retinopathy or nephropathy, were included in the study. All critically ill patients having acute kidney injury, hyperosmolar hyperglycemic syndrome, diabetic ketoacidosis, stroke, myocardial infarction and urinary tract infection were excluded from the study. Patients having type 1 DM of less than 5 years duration were also not included in the study. All the baseline investigations were sent including complete blood picture, renal function tests, HbA1c, fasting blood sugar, urinalysis and 24 hours urine for total protein and albumin (Roche Cobas C501 Chemistry Analyzer). Fundus examination was performed by direct ophthalmoscopy at the bedside followed by digital retinal camera (Canon CR-1 Digital Retinal Camera) imaging for confirmation of the findings. Diabetic retinopathy was considered in patients having one or more of the findings such as micro-aneurysm, soft exudates, hard exudates, dot and blot haemorrhage, neovascularization, vitreous or pre-retinal haemorrhage while all those patients were labelled as having diabetic nephropathy with urine positive for proteins followed by 24 hours urinary total proteins more than 500 mg/dl or 24 hours urinary albumin more than 300 mg/dl.

Data was stored and analysed by the SPSS version 19.0. All the results were presented in tables and bar charts accordingly.

RESULTS

Total 104 patients comprised of 72 (69.2%) males and 32 (30.76%) females. The means with standard deviations for age, BMI, duration of diabetes and HbA1c are shown in table I and figure 1. Ninety two (88.46%) had unrecognised DR and 46 (44.23%) had unrecognised DN. Forty Four (42.30%) had both unrecognised DR and DN. Forty Four (95.65%) out of 46 patients having DN also had DR. Four (66.6%) out of 6 patients with T1DM had both unrecognised DR and DN. All the patients had established diabetic neuropathy with DFU ranging from grade I to grade IV (Wagner's classification)[20]. Frequencies of DR and DN were analysed in each grade of DFU. (Table 2)

Patients were categorised according to glycemic control on the basis of HbA1c as; good control (HbA1c ≤ 7%), fair control (HbA1c 7.1-9 %) and poor control (HbA1c ≥ 9.1)[21]. Microvascular complications were analyzed in each category for both frequencies and severities. (Table 3 and 4)

Regarding awareness and screening of microvascular complication of DM, among those having DR, around 54.34 % were aware about the retinal complications of the DM and 15.21% were assessed for DR during their disease span. Similarly among those having DN, around 69.56% were aware about the renal complications of DM but no one was properly assessed for DN and re-

garding foot complications of DM, around 55.76% were informed about foot complication of DM and only 3.84% were assessed for the high risk foot before developing ulcer.

DISCUSSION

The current study provided valuable information regarding the burden of unrecognised DR and DN in pa-

Figure 1: Gender wise frequnecies of diabetic retinopathy, diabetic nephropathy and both. (males n=72, females n=32)

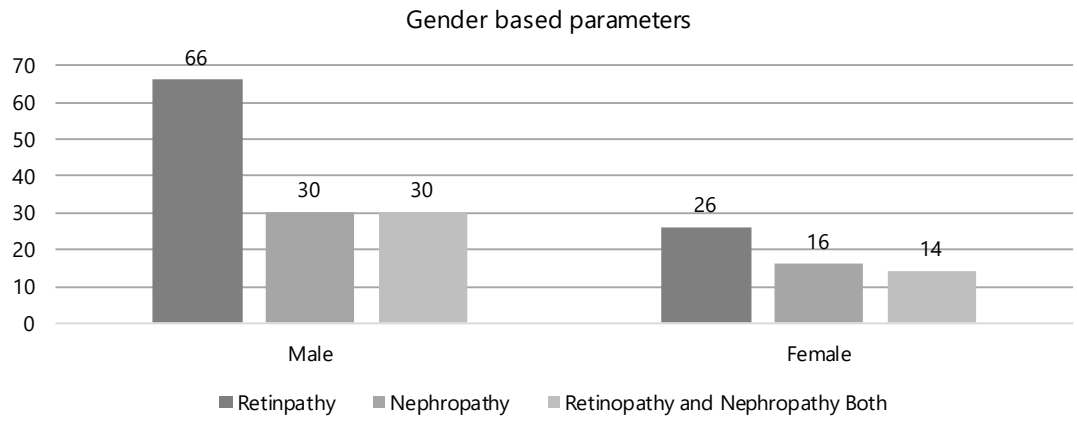

Table 1: Correlation of clinical variables with the established microvascular complications. (P Value > 0.05)

Variables	Overall (n=104)	Retinopathy (n=92/104)	Nephropathy (n=46/104)	Nephropathy And Retinopathy Both (n=44/104)
Age (years)	53.29 ± 10.15	53.38 ± 9.75	50.04 ± 9.58	49.95 ± 9.8
Duration of diabetes (Years)	11.45 ± 5.08	11.84 ± 5.05	11.43 ± 4.2	11.50 ± 4.3
Body mass index (kg/m^2)	26.98 ± 5.2	27.14 ± 5.44	28 ± 6.54	28.21 ± 6.62
HbA1c (%)	11.13 ± 2.19	11.15 ± 2.24	11.9 ± 2.22	11.82 ± 2.24

Table 2: Frequencies of different grades of diabetic foot ulcers in relation to established microvascular complications. (P Value > 0.05)

diabetic foot ulcer (grades)	Frequency (n=104)	Retinopathy (n=92)	Nephropathy (n=46)	Retinopathy and nephropathy both (n=44)
Grade I	8 (7.7%)	8 (8.61%)	6 (13.04%)	6 (13.63%)
Grade II	24 (23.1%)	22 (23.91%)	10 (21.73%)	10 (22.72%)
Grade III	52 (50%)	46 (50%)	20 (43.47%)	20 (45.45%)
Grade IV	20 (19.2%)	16 (17.39%)	10 (21.73%)	08 (18.18%)

Table 3: HbA1c and frequency of microvascular complication. (P Value > 0.05)

HbA1C (%)	Frequency (n=104)	Retinopathy (n=92)	Nephropathy (n=46)	Retinopathy and Nephropathy Both (n=44)
≤ 7	2 (1.92%)	2 (4.34%)	Nil	Nil
7.1-9	16 (15.38%)	14 (15.21%)	4 (8.69%)	4 (9.09%)
≥9.1	86 (82.69%)	76 (82.6%)	42 (91.3%)	40 (90.9%)

Table 4: HbA1C and severity of diabetic retinopathy and diabetic nephropathy (P Value > 0.05)

HbA1C	Retinopathy (n=92) Non proliferative & proliferative		Nephropathy (n=46) 24 hours urinary total proteins (mg/24hours)		
	NPDR	PDR	501-1000	1001-2000	≥ 2001
≤ 7	2 (2.17%)	Nil	Nil	Nil	Nil
7.1-9	12 (13.04%)	2 (2.17%)	2 (4.34%)	Nil	2 (4.34%)
≥9.1	68 (73.91%)	8 (8.6%)	16 (34.7%)	12 (26.08%)	14 (30.43%)
Total	82 (89.1%)	10 (10.8%)	18 (39.1%)	12(26.08%)	16 (34.7%)

tients presented with DFU by showing that more than 85% patients had unrecognised DR and more than 40% had unrecognised DN. It also showed the high prevalence (>95%) of unrecognised DR in patients having both DN and DFU. Our study also highlighted the issue of lack of education and screening of microvascular complications of DM in the studied patients.

A study conducted in Singapore showed that out of 2376 patients with DM, around 800 (33.9%) had DR, of which 671 (83.3%) were unrecognised previously[22]. These findings were quite near to those found in the present study, i.e. around 88.43% had DR, which was not known previously because of lack of screening. Similarly, another study conducted in US, showed that 27 (25%) out 108 inpatients had unrecognised DR and 15 (88.2%) out of 17 patients having DFU had DR[23]. Regarding prevalence of DR, a study was conducted in our region which showed 51% of the patients having DM had DR both identified and unidentified[24]. Reason for increased prevalence in present study could be due to the fact that only those were included who had DFU (established microvascular complication), which increases the chances of other microvascular complications to develop including DR and/or DN[23].

In a study done in Peshawar, the prevalence of DR and DN was 55% and 58% in patients who presented with DFU, respectively[25]. The prevalence of DN in the current study was 44.23%, the reason behind less prevalence in our study group could be due to the fact that we had included only those patients not previously diagnosed as having DN. Similarly there was difference in DR prevalence as well. In our study it was 88.43% compared to 55% in the above mentioned study, the reason could be that our studied population had increase mean age, HbA1c and duration of DM.

A study conducted in Korea showed that around 40.5% and 36.3% were screened for DN and DR respectively. Around 25.1 % were screened for both DN and DR. These percentages were further lower in the rural population and the major factors leading to less screening were lack of awareness, education and socioeconomic status[26]. In the current study, we had lower percentage of the previously screened patients as most of the patients belonged to rural areas, lower socioeconomic status and were less educated.

Regarding awareness of the microvascular complications of DM, it was found that 54.34%, 44.23% and 55.76% were aware about the retinal, renal and foot complications of DM, respectively but they weren't screened as per protocol because of the above mentioned reasons. They came to the health facility just because of foot ulcer, which can be easily identified and warrant treatment, whereas retinopathy and nephropathy are even more severe complications but they were missed because of lack of regular assessment and not identified by the patient until very late. In the present study, 10.8% had proliferative diabetic retinopathy which needed urgent referral to the ophthalmologist for the management. Similarly, around 34.7% had proteinuria of more than 2 gm per 24 hours which needed urgent nephrologist consultation. Lack of proper assessment of neuropathy and education regarding foot care ended up in the foot ulcerations in the studied population.

LIMITATIONS

This study has the weakness of a cross-sectional design where definitive conclusion between the associations and correlations is difficult to obtain. Large scale multi-centre studies are needed at different health facility levels as patients present late in the course of their illness to the tertiary care hospital.

CONCLUSION

Frequency of unrecognised diabetic retinopathy and diabetic nephropathy is quite high in patients who present with diabetic foot ulcers in our setup.

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CONTRIBUTORS

SEM conceived the idea, wrote initial manuscript, collected data and finalized the draft. TG and ZU helped correction of the proposal, literature search, data collection, interpretation and overall supervision of the project. SK, AN and AA provided technical support, helped in data interpretation and provided expert guidance where needed. All authors contributed significantly to the submitted manuscript.