

## Frequency and Pattern of Cutaneous Manifestations in Type 2 Diabetes Mellitus at Northern Institute of Medical Sciences Abbottabad

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**Abstract:** Skin lesions are common in type 2 diabetic patients and sometimes the only manifestation of the disease. Its association with micro-vascular complications of diabetes has been reported. This study was conducted to find out frequency and pattern of cutaneous manifestations in type 2 diabetes in our setup. It was a hospital-based descriptive study conducted at Medicine Department of Northern Institute of Medical Sciences (NIMS) Abbottabad from September 2009 to January 2010. In this study, 105 type 2 diabetic patients of both sexes were included and examined by a consultant dermatologist for skin lesions strongly related to diabetes, skin infections, skin lesions related to diabetic complications and to anti-diabetic therapy. From all patients, history of skin diseases, pattern of cutaneous manifestations, duration of type 2 diabetes and type of treatment received-whether oral anti-hyperglycemic agents or insulin or combined treatment, were noted in detail. Smear, culture and biopsy of the skin lesions have been undertaken for definite diagnosis. Weight, height, blood pressure and BMI were also noted. Fasting and post-prandial blood sugar and HbA<sub>1c</sub> were measured in all patients. The mean age of the study population was 55±11 years; 60 (57.14%) were female and 45 (42.85%) male with M to F ratio of 1:1.33. Mean duration of diabetes was 12±7 years and mean HbA<sub>1c</sub> was 7.8±1.6%. The overall prevalence of cutaneous lesions in our study was 65%. Infections were the major cutaneous manifestations occurring in (63.8%) of our patients with fungal infections being dominant in (39.04%) patients, followed by bacterial infections in (21.90%). The second most common cutaneous manifestation associated with diabetes was pruritus occurring in 42 (40%) patients. Diabetic foot was the most common cutaneous manifestation associated with diabetic complications and was seen in (18.1%) of our cases. Cutaneous manifestations related to anti-diabetic therapy were least common detected only in (4.75%) patients. Majority (65%) of patients had more than one skin lesion. Hypertension (46.6%) and retinopathy (11.4%) were the most common systemic complications in type 2 diabetic patients associated with cutaneous manifestations. This study concludes that majority of type 2 diabetic patients with cutaneous manifestations were obese and females having un-controlled disease. Furthermore, infections were the most common skin lesions while hypertension and retinopathy were the most common systemic complications of diabetes. Hence there is definite need of health education to promote proper skin care and tight glycemic control in type 2 diabetics.

**Key words:** Cutaneous manifestations • Frequency • Infections • Insulin • Oral anti-hyperglycemic agents • Type 2 diabetes mellitus

### INTRODUCTION

Diabetes Mellitus (DM) is a worldwide problem and the most common endocrine disorder. Its prevalence is increasing in the present scenario of a sedentary lifestyle in the general population.

Worldwide, prevalence of type 2 diabetes mellitus has been estimated to rise from 150 million to 225 million by

the end of 2010 and to as many as 300 million by 2025 [1, 2]. In Pakistan 6.9 million people are affected by type 2 diabetes mellitus with International Diabetes Federation (IDF) estimating that it will grow to 11.5 million by 2025 unless preventive measures are taken to control the disease [3]. The hyperglycemia resulting from impaired secretion or function of insulin can lead to metabolic, vascular, neurological and immunological abnormalities.

Affected organs include the cardiovascular, renal and nervous systems, eyes and the skin [4]. Skin is particularly important in diabetics because it essentially did get involved in one way or the other [5]. The cutaneous manifestations of diabetes mellitus are well known and considered as common in 30-71% of diabetic patients [6, 7]. The skin is affected by both the acute metabolic derangements and chronic degenerative complications of diabetes. Although the mechanism for many diabetes associated skin conditions remains unknown, the pathogenesis is linked either ; to abnormal carbohydrate metabolism, other altered metabolic pathways, atherosclerosis, micro-angiopathy, neuronal degeneration and impaired host mechanisms [8]. or dys-regulation of glucose, insulin and lipids lead directly to physical signs in skin of diabetic patients and chronically elevated blood glucose lead to non-enzymatic glycosylation (NEG) of cutaneous proteins, which eventually leads to irreversible advanced glycosylation end-products (AGEs) [9].

The cutaneous manifestations of diabetes mellitus can be classified into four categories; Skin diseases with weak or strong association with diabetes (e.g Necrobiosis lipoidica, diabetic dermopathy, yellow skin, eruptive xanthomas, oral leukoplakia, lichen planus, acanthosis nigricans) ; Infections (such as fungal, bacterial, viral) ; Cutaneous manifestations due to diabetic complications (such as micro-angiopathy, macro-angiopathy and neuropathy); and Skin lesions due to anti-diabetic medications (e.g sulphonylurea) [10].

In most studies, skin lesions have been described in both types of diabetes mellitus. However, there is little information about the prevalence of skin lesions in type 2 diabetic patients [10, 11]. Although type 2 diabetes mellitus is very common in Pakistan, systemic surveys for cutaneous manifestations in type 2 diabetic patients are lacking. Hence this study has been conducted in order to explore this problem in our own setup.

## PATIENTS AND METHODS

This hospital-based descriptive study was conducted at outpatient as well as Diabetic Clinic in Medicine Department of Northern Institute of Medical Sciences (NIMS) Abbottabad.

NIMS is a private medical college situated in Abbottabad of District Hazara in North West Frontier Province (NWFP) of Pakistan. It has attached 450 beds teaching hospital which cover both urban as well as rural population of Hazara division. The hospital has all facilities of a tertiary care institute in our setup.

During this study, one hundred and five (105) consecutive type 2 diabetic patients of both sexes having skin lesions were enrolled as the subject material from September 2009 to January 2010. The protocol for this study has been approved by the Ethical Committee of Institute's research board and an informed written consent obtained from all subjects.

We included all type 2 diabetic patients (according to American Diabetic Association criteria; Fasting blood sugar = 126mg/dl for two times) who were over forty years old, no obvious signs and symptoms of insulin deficiency and duration of diabetes more than ten years. On the other hand, patients with duration of diabetes less than ten years, type 1 diabetes mellitus, diabetic nephropathy, gestational diabetes, past history of cutaneous diseases and those with major systemic illnesses were excluded from this study.

Data of all type 2 diabetic subjects was collected on a pre-designed proforma. This includes age, sex, cutaneous complaints (e.g; site, duration, pattern, progression and treatment modalities for skin lesions), involvement of nails, toe-web, soles of feet, mouth and vagina (in female patients). Other important parameters noted in the history were duration of type 2 diabetes, control of their diabetic status and type of treatment received-whether on oral anti-hyperglycemic agents or insulin therapy or combined treatment. Any history of previous drug therapy must be obtained. A detailed general physical as well as systemic and local dermatological examinations were undertaken. All cutaneous lesions noted were again re-examined by a consultant dermatologist. All patients were assessed for blood pressure, weight, height and body-mass index (BMI). A detailed fundus examination of all patients had done by an Ophthalmologist. The neurological assessment was undertaken using Michigan neuropathy screening instrument [12].

Laboratory analysis in all patients include, complete hemogram, fasting and post-prandial blood glucose estimations, urine examination, lipid profile, liver and renal function tests, 24-hours urinary protein excretion and Electro-cardiogram (ECG). Control of diabetic status was assessed by glycosylated hemoglobin (HbA<sub>1c</sub>) estimation (controlled = 7.0% and uncontrolled = 7.0%). Specimens of nail scraping, high vaginal and oral swabs have been collected for culture and smear examination. Relevant microbiological and histopathological examinations of skin lesions were carried out to confirm the diagnosis wherever necessary. The data was processed on computer software SPSS 10.

During this study, patients with diabetic foot and carbuncles (boil) were admitted in the ward for pus culture and sensitivity and given surgical wound care. They were also kept for tight glycemic control with insulin and broad spectrum antibiotics.

## RESULTS

One hundred and five (105) type 2 diabetic patients having cutaneous manifestations were included in this study. The age of the patients ranged from 40-80 years (mean age  $55 \pm 11$  years), 60 (57.14%) were female and 45 (42.85%) male with M to F ratio of 1:1.33. The mean duration of diabetes was  $12 \pm 7$  years (duration ranges from 10-25 years) and mean fasting and post-prandial blood sugars were  $170 \pm 15$  mg/dl and  $253 \pm 17$  mg/dl respectively.

The mean BMI was  $27 \pm 4$  kg/m<sup>2</sup>. The mean HbA<sub>1c</sub> level was  $7.8 \pm 1.6\%$  suggesting that cutaneous manifestations are closely associated with uncontrolled long standing diabetes mellitus. Oral anti-hyperglycemic agents were used by 60 (57.14%) patients, while insulin therapy by 15 (14.28%) and combined treatment taken by 30 (28.57%) patients. This demographic profile has been shown in Table 1. The overall prevalence of cutaneous manifestations in type 2 diabetic patients in our study was 65%. Of the 105 patients, 85 (81%) were known diabetics having skin lesions and 20 (19%) diagnosed diabetes after cutaneous manifestations.

The total number of cutaneous lesions was 255 and majority (65%) had more than one skin lesion. The cutaneous manifestations were more prevalent in females (57%), obese and over-weight diabetics having longer duration of the disease. Only about 5% of cutaneous lesions appeared within one year of diabetes diagnosis, while majority more than ten years of diagnosis after the disease. The frequency and pattern of various cutaneous manifestations in type 2 diabetic patients is shown in the Table 2.

Among the cutaneous manifestations related to diabetes; pruritus was the most common in 42 (40%) patients, followed by acanthosis nigricans in 16 (15.2%), diabetic thick skin in the form of finger pebbles in 11 (10.5%) and 10 (9.5%) with cutaneous xanthomas.

Of the ten patients with xanthomas, five had an eruptive variant and in addition with hypertriglyceridemia. Cutaneous infections constituted the commonest manifestation observed in 63.8% of our

Table 1: Demographic profile of type 2 diabetic patients.

1	Total Number of Patients	105
2.	Mean Age ( $\pm$ SD)	$55 \pm 11$ years
3.	Family History of Diabetes (%)	72%
4.	Mean Duration of Diabetes ( $\pm$ SD)	$12 \pm 7$ years
5.	Type of treatment received(%)	
	Oral therapy (alone)	60
	Insulin (alone)	15
	Combination therapy	30
6.	BMI (Normal 20-25kg/m <sup>2</sup> )	$27 \pm 4$ kg/m <sup>2</sup>
7.	Mean Fasting Blood Sugar ( $\pm$ SD)	
	(Normal range 70-110mg/dl)	$170 \pm 15$ mg/dl
8.	Mean Postprandial Blood Sugar ( $\pm$ SD)	
	(Normal range 120-180mg/dl)	$253 \pm 17$ mg/dl
9.	Mean Serum Cholesterol ( $\pm$ SD)	
	(Normal Range 150-200mg/dl)	$210 \pm 12$ mg/dl
10.	Mean Glycosylated hemoglobin ( $\pm$ SD)	
	(Normal Range <7%)	$7.8 \pm 1.6\%$

patients, while skin lesions related to diabetic complications and to anti-diabetic therapy have occurred in 37.2% and 4.75% respectively. Among the cutaneous infections, most common were fungal infections (39.04%) followed by bacterial (21.90%) and viral infections (2.85%).

Among the fungal infections, onychomycosis was commonest followed by vulvo-vaginal and intertrigo candidiasis and were caused mainly by tinea unguium (22.4%), candida albicans (18%) respectively.

The tinea pedis was less common in our study (7.5%). The common bacteria isolated from cutaneous lesions were, staphylococcus aureus (12%) and pseudomonas aeruginosa (12%) followed by streptococcus pyogenes (6%) and proteus mirabilis (4.5%). The most common bacterial lesions were cellulitis, carbuncles and folliculitis. The viral infections were least common in our study detected in only (2.85%) of patients. This has been shown in Table 3. Among cutaneous manifestations related to diabetic complications, diabetic foot was the most common present in (18.1%) patients followed by hyperhidrosis in (10.5%) and diabetic neuropathy in (8.6%). The cutaneous manifestations related to anti-diabetic therapy were least common detected in (4.75%) of our patients. They were skin reactions related to sulphonylurea therapy (2.85%), insulin lipo-atrophy (0.95%) and insulin lipo-hypertrophy (0.95%). These results are shown in detail in Table 2.

**Relation with Glycemic Control:** Out of 105 patients with cutaneous manifestations, 74(70.5%) had un-controlled and 31 (29.52%) controlled glycosylated hemoglobin (HbA<sub>1c</sub>) levels.

Table 2: Frequency and Pattern of Cutaneous Manifestations in Type 2 diabetic patients

Cutaneous Manifestations	No. of Patients	Percentage
A) Cutaneous Manifestations Related to Diabetes		
1. Pruritus	42	40%
2. Acanthosis nigricans	16	15.2%
3. Diabetic Thick Skin	11	10.5%
4. Cutaneous Xanthomas	10	9.5%
5. Diabetic Dermopathy	6	5.7%
6. Skin tags	6	5.7%
7. Rubeosis faciei	6	5.7%
8. Diabetic bullae	5	4.7%
9. Lichen planus	5	4.7%
10. Granuloma annulare	5	4.7%
11. Diabetic xerosis	4	3.8%
12. Vitiligo	3	2.8%
13. Acquired perforating dermatoses	2	1.9%
14. Necrobiosis lipoidica	1	0.95%
Total	122	
B) Cutaneous Manifestations Related to Infections		
Fungal	41	39.04%
Bacterial	23	21.90%
Viral	3	2.85%
Total	67	
C) Cutaneous Manifestations Related to Diabetic Complications		
Diabetic foot	19	18.1%
Hyperhidrosis	11	10.5%
Diabetic neuropathy	09	8.6%
Total	39	
D) Cutaneous Manifestations Related to Anti-Diabetic Therapy		
Sulphonylurea-related skin lesions	3	2.85%
Insulin lipo-atrophy	1	0.95%
Insulin lipo-hypertrophy	1	0.95%
Total	5	

Table 3: Isolated Micro-Organisms from Cutaneous Infections among Type 2 Diabetic Patients.

Type of Infections	No. of Patients	Percentage
A) Fungal Infections		
1. Tinea unguium	15	22.4%
2. Candida albicans	12	18%
3. Tinea pedis	5	7.5%
Tinea Corporis	3	4.5%
5. Tinea Cruris	3	4.5%
6. Tinea versicolor	2	3.0%
7. Tinea Barbae	1	1.5%
Sub-total	41	61.4%
B) Bacterial Infections		
1. Staphylococcus aureus	08	12.0%
2. Pseudomonas aeruginosa	08	12.0%
Streptococcus pyogenes	04	6.0%
Protein mirabilis	03	4.5%
Sub-total	23	34.5%
C) Viral Infections		
1. Herpes zoster	02	3.0%
2. Herpes simplex	01	1.5%
Sub-total	03	4.5%

Table 4: Frequency of systemic diabetic complications Associated with cutaneous manifestations (n=105)

Name of Complications	No. of patients	Percentage
Hypertension	49	46.6%
Retinopathy	12	11.4%
Nephropathy	11	10.5%
Coronary artery disease	10	9.5%
Peripheral Neuropathy	4	3.8%
Peripheral vascular disease	3	2.8%
Total	89	84.8%

**Association with Systemic Diabetic Complications:**

Table 4 has delineated the systemic complications of type 2 diabetes with cutaneous manifestations. Hypertension was the most common systemic complication in type 2 diabetes with cutaneous manifestation and has seen in 49 (46.6%) of our patients. Likewise retinopathy, nephropathy and coronary artery disease were less common and have seen in 12(11.4%), 11(10.5%) and 10(9.5%) of our patients respectively. Peripheral neuropathy and peripheral vascular disease were least common systemic complications associated with cutaneous manifestations. Many of our patients had more than one underlying systemic complication.

**DISCUSSION**

Diabetes mellitus is a chronic disease of metabolic dys-regulation involving the abnormal metabolism of glucose. Nearly all patients with diabetes eventually develop cutaneous manifestations of the disease. Cutaneous signs of the disease are extremely valuable to the clinician.

Our study showed female predominance, as reported by Mahajan, *et al* [8] and Romano, *et al* [13]. Cutaneous manifestation in majority of our patients have appeared in fifth and sixth decades of life, an observation also noted by other researchers [8,13,14]. The relative increased frequency of cutaneous manifestations with age in diabetic patients may be attributed merely to long duration of the disease. This study showed that the frequency of cutaneous lesions in type 2 diabetics is about 65%, which is compatible with the results of other studies ranging from 49-84% [7,8,10,11,13,14]. In present study, majority of patients were female (57%), obese and over-weight diabetics having longstanding disease. The correlation of cutaneous manifestations with obesity status showed statistically significant difference ( $p < 0.05$ ), as reported by Yosipovitch, *et al* [7]. It has also been significantly correlated with duration of diabetes

( $p < 0.05$ ) and similar association was reported by Dogra, *et al* [15]. As the duration of diabetes increases, there is non-enzymatic glycosylation of dermal collagens and muco-polysaccharides leading to various cutaneous manifestations.

Among the cutaneous manifestations, skin infections comprised the largest group affecting (63.8%) of our patients, which is closer to previous reports [8,13,14,16]. However, Sasmaz, *et al* [10] has reported only (31%) of patients with cutaneous infections. The difference in prevalence of cutaneous infections from various studies can be explained by differences in blood sugar level, hygiene, socio-economic and health status in the studied population. The incidence of cutaneous infections was more in un-controlled diabetics because of hyperglycemia and defects in polymorphonuclear leukocyte functions. Fungal infections formed the largest group (39.04%) with onychomycosis being commonest (22.4%) in our patients, which is quite similar to studies of Baloch, *et al* [17] and Gupta, *et al* [18]. According to Dogra, *et al* [15], high incidence of onychomycosis in type 2 diabetics was probably due to older age and impaired peripheral circulation. *Candida albicans*, causing vulvo-vaginal and intertrigo candidiasis was second common fungal infection seen in (18%) of our patients and quite closer to studies by Baloch, *et al* [17]. The bacterial infections were seen less frequently (21.90%) in our study. This is in contrast to the results of previous studies conducted by Khoharo KH [19] and Najdawi F [20], who found bacterial infections in (50%) and (62.5%) respectively. Therefore, strict control of blood glucose and proper skin care can prevent cutaneous infections in diabetics.

Pruritus was another most common cutaneous manifestation related to type 2 diabetes and observed in (40%) of our patients. Similar results have been reported by Khoharo KH [19] in their studies. However generalized itching, after excluding skin infections, dryness of skin and abnormal sweating, may be more likely to longstanding type 2 diabetes. Acanthosis nigricans was present in (15.2%) of our cases and quite closer to results of other studies by Naheed T, *et al* [21]. Cutaneous xanthomas have been demonstrated in (9.5%) of our patients. This is again close to the results of study by Naheed T, *et al* [21] who found xanthomas in (8.8%) of their patients. About (50%) of eruptive xanthomas in our study were often associated with hyper-triglyceridemia. These findings can be related to high prevalence of insulin resistance and obesity in our study. Diabetic thick skin in the form of finger pebbles was noted in (10.5%) of patients. This is in contrast to studies by Khoharo KH

[19] who discovered thick skin in (50%) of their patients. Diabetic dermopathy also known as shin-spots is usually asymptomatic and found in (5.7%) of our patients. It often falls within the range of previous reports of 3.5-9.37% [8, 14]. However, diabetic dermopathy is an uncommon finding in this study, as compared to Sasmaz S [10] and Khoharo KH [19] studies. Necrobiosis lipoidica was least common cutaneous manifestation (0.95%) in our study and similar to that reported by Nigam and Pande [14]. Dermatoses associated with an increased incidence of diabetes like vitiligo, lichen planus and acquired perforating dermatoses less frequently detected in the present study, have been reported previously [6].

Diabetic foot has emerged as another common cutaneous complication of type 2 diabetes and found in (18.1%) of our patients. This is quite similar to studies by Miller F [22], who reported the prevalence of diabetic foot ulcer in (15-20%) of their patients. According to him, diabetic foot ulcer can be either ischemic or neuropathic. Furthermore, all type 2 diabetic patients with foot ulcer should be evaluated for micro-vascular complications of the disease. Therefore, diabetics with foot ulcer should have tight glycemic control and education on proper feet care. Although cutaneous manifestations related to anti-diabetic therapy were seen in only (4.75%) of our patients. Skin lesions have been demonstrated more frequently in patients kept on sulphonylurea drugs than on insulin therapy, which could be either due to poor metabolic control. Insulin related lipo-atrophy and lipo-hypertrophy were observed in (0.95%) of patients each, which is in contrast to study by Tariq M [23], who found it's prevalence in (2.4%) of their patients. This difference might be due to inadequate education of patients regarding technique of insulin injections.

Most of the patients with cutaneous manifestations had un-controlled diabetes, as found by Yosipovitch, *et al* [7], which increases the risk of micro-angiopathy and related sequelae. In present study, majority (84.8%) of our patients with cutaneous manifestations had systemic complications like hypertension, retinopathy, nephropathy and coronary artery disease, which is closer to reported by Mahajan, *et al* [8]. Hypertension (46.6%) followed by retinopathy (11.4%) were the commonest systemic complications in our study associated with cutaneous manifestations and these results have been consistent with previous report of Mahajan, *et al* [8]. Hence, it has been confirmed that cutaneous manifestations strongly correlate with systemic complications of diabetes.

## CONCLUSION

From above discussion, we concluded that majority of type 2 diabetics with cutaneous manifestations were obese and females having un-controlled disease. Among dermatoses associated with type 2 diabetes; cutaneous infections were commonest followed by pruritus, diabetic foot ulcers and acanthosis nigricans, while hypertension followed by retinopathy were commonest systemic complications of the disease.

Since skin involvement in type 2 diabetes is fairly common phenomenon and whenever such patients present with multiple cutaneous manifestations, their diabetic status should be checked and controlled. Furthermore, poor glycemic control often increases the susceptibility to cutaneous infections. The recognition of such findings is the key to management plan. Hence, there is definite need of health education to promote proper skin care and tight glycemic control in type 2 diabetics. All general practitioners and related specialist should identify these disorders and refer them to dermatologists and diabetologists for further evaluation.

## ACKNOWLEDGEMENT

The authors wish to thank Mr. Zohaib Ahmed Khan for his contribution in typing of this article.

## REFERENCES

1. Wild, H., G. Roglic, A. Green, R. Sicree and H. King, 2004. Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. *Diabetes Care*, 27: 1047-53.
2. Zimmet, P., 2003. The burden of type 2 diabetes: are we doing enough? *Diabetes Metab.* 29: (4Pt2):689-18.
3. International, Diabetes Federation. *World Diabetes Atlas 2006*. 3<sup>rd</sup> edition. Brussels Belgium: IDF 2006. [www.idf.org](http://www.idf.org)
4. Jennifer, L. and E. John, 2003. *Diabetes mellitus*. In: Irvin M.F. Arthur, Z. Klaus, W. Austen, K.F. Goldsmith, L.A. Katz SI, editors. *Dermatology in General Medicine*, 6<sup>th</sup> (ed). Mc Graw Hill. Medical Publishing Division: New York. pp: 1651-61.
5. Dogra, S. and B. Kumar, 2003. Epidemiology of fungal infections, a study from Northern India. *Pediatr. Dermatol.*, pp: 20-470.
6. Paron, N.G. and P.W. Lambert, 2000. Cutaneous manifestations of diabetes mellitus. *Prim. Care*, 27: 371-383.

7. Yosipovitch, G., E. Hodak, P. Vardi, I. Shrager, M. Karp, E. Sprecher and M. David, 1998. The prevalence of cutaneous manifestations in IDDM patients and their association with diabetes risk factors and microvascular complications. *Diabetes. Care*, 21: 506-509.
8. Mahajan, S., R.V. Koranne and S.K. Sharma, 2003. Cutaneous manifestations of diabetes mellitus. *Indian J. Dermatol. Venerol. Leprol.*, 69: 105-8.
9. Goldin, A., J.A. Beckman, A.M. Schmidt and M.A. Creager, 2006. Advanced glycation end products: sparking the development of diabetic vascular injury. *Circulat.*, 114(6): 597-605.
10. Sasmaz, S., M.A. Buy Ukbese, Cetin A. Kaya, M. Celik and O. Arican, 2005. The prevalence of skin disorders in type-2 diabetic patients. *Int. J. Dermatol.*, pp: 133-6.
11. Wahid, Z. and A. Kanjee, 1998. Cutaneous manifestations of diabetes mellitus. *J. Pak. Med. Assoc.*, 48(10): 304-5.
12. Mogtaderi, A., A. Bakhshipour and H. Rashidi, 2006. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. *Clin Neurol. Neurosurg*, 108: 477-81.
13. Romano, G., G. Moretti, Di A. Benedetto, C. Giofre, Di E. Cesare, G. Russo, *et al.* 1998. Skin lesions in diabetes mellitus: Prevalence and clinical correlation. *Diabetes Res. Clin. Pract.*, 39: 101-6.
14. Nigam, P.K. and S. Pande, 2003. Pattern of dermatoses in Diabetes. *Indian J. Dermatol. Venerol. Leprol.*, 69: 83-5.
15. Dogra, S., B. Kumar, A. Bhansali and A. Chakrabarty, 2002. Epidemiology of onychomycosis in patients with diabetes mellitus in India. *Int J. Dermatol.*, 41: 647-51.
16. Talat, N., A. Nabeel, A. Naeen, *et al.* 2002. Skin manifestations among diabetic patients admitted in a general medical ward for various other medical problems. *Pak. J. Sci.*, 18: 291-6.
17. Baloch, H.G., M.N. Memon, R.B. Devrajani, P. Iqbal, K.N. Thebo, *et al.* 2008. Cutaneous manifestations of type 2 diabetes mellitus. *J. Liaquat. Univer. Med. Heal. Sci.*, May-Aug. 7(2): 67-70.
18. Gupta, A.K., N. Konnikov, P. MacDonald, P. Rich, N.W. Rodger, M.W. Edmonds, *et al.* 1998. Prevalence and epidemiology of toenail onychomycosis in diabetic subjects: a multicentre survey. *Br. J. Dermatol.*, 139: 665-71.
19. Khoharo, K.H., S. Ansari and F. Qureshi, 2009. Frequency of Skin Manifestations in 120 type 2 Diabetics Presenting at Tertiary Care hospital. *J. Liaquat. Univer. Med. Heal. Sci.*, 8(1): 12-15.
20. Najdawi, F. and M. Fa'ouri, 2002. Frequency and types of skin disorders and associated diabetes mellitus in elderly Jordanians. *East Mediterr Health. J.*, 8: 574-8.
21. Naheed, T., N. Akbar, N. Akbar, M. Shehzad, S. Jamil and T. Ali, 2002. Skin manifestations amongst diabetic patients admitted in a general medical ward for various other medical problems. *Pak. J. Med. Sci.*, 18(4): 291-6.
22. Miller, F., III. 1998. Management of diabetic foot ulcers. *J. Cut. Med. Surg.*, 3(Suppl 1): 13-7.
23. Tariq, M., B. Arfan and A. Humayun, 2005. Cutaneous manifestations of diabetes mellitus. *J. Pak. Assoc. Dermatol.*, 15: 227-32.