INTERNATIONAL JOURNAL OF APPLIED BIOLOGY AND PHARMACEUTICAL TECHNOLOGY

Volume: 2: Issue-3: July-Sept -2011 IJABPT *ISSN 0976-4550*

PREVALENCE OF SCLERODERMA IN NORTH INDIAN POPULATION: DIABETICS VERSUS NON- DIABETICS

[1]Sonney Singh Kapoor, [2]Anterpreet Kaur Arora and [3]Jyotika Kalsy

[1]Department of Pediatrics. [2]Department of Anatomy. Sri Guru ram das institute of medical sciences and research, vallah, sri amritsar.

[3]Department of Dermatology, Venerology and Leprosy. Govt Medical College, Amritsar

ABSTRACT: Diabetes mellitus is a common condition which frequently has skin manifestations. The attachment of glucose to protein may result in a profound effect on structure and function of that protein, and account for clinical manifestations of the disease. It has been suggested that increased crosslinking of collagen in diabetic patients is responsible for the fact that their skin is generally thicker than that of non-diabetics. The present study was undertaken to assess the incidence and to compare the incidence of waxy skin and scleroderma in diabetics and non diabetics. The study was done on 250 patients who attended the skin camp held in a village of Punjab. This study was conducted by specialists of Dermatology and Medicine. Thorough general physical examination and the dermatological examination were done in each case. All the cases of scleroderma and waxy skin were noted and compared between diabetics and non diabetic patients.

Keywords: Scleroderma, cutaneous manifestations, diabetic complications, collagen disorders.

INTRODUCTION

It is hardly surprising that diabetes mellitus also involves the skin. Nearly one third of diabetic patients have cutaneous manifestations. [1]

A broad spectrum of cutaneous disorders may be encountered in patients with both type I and type 2 diabetes mellitus. On occasion, these dermatologic findings may precede any clinical or biochemical evidence for diabetes. An estimated 30% of patients with diabetes develop skin manifestations during the course of their chronic illness. Although the mechanism for much diabetes associated skin conditions remains unknown, the pathogenesis of others is linked to abnormal carbohydrate metabolism. [2]Several skin conditions are specific to diabetes, but most of them also occur in the non-diabetic population. [3]

It was concluded by Mackool et al [4] that the amount of glucose in whole skin is greater than can be attributed to distribution in extracellular fluid. The ratio of glucose/gm skin to glucose /gm blood is increased in diabetic skin, suggesting that the insulin regulates intracellular deposition of glucose in the skin. According to Freinkel and Freinkel [5] who studied 100 hospital based patients with diabetes mellitus, 14% had Scleroedema Diabeticorum. He also concluded that the duration of Scleroedema also correlated with the duration of diabetes. These findings highlight the relatively common occurrence of this skin condition which goes often unrecognised in people with diabetes.

Thickening of skin of the hand is a common occurrence, with a range of manifestation from simple pebbling of the knuckles to the diabetic hand syndrome. The diabetic hand syndrome consists of thickened skin over the dorsum of the digits and limited joint mobility, especially of the interphalangeal joints. [6] [7] [8]

The diabetic hand syndrome consists of thickened skin over the dorsum of the digits and limited joint mobility, especially of interphalangeal joints. The earliest description of this phenomenon was apparently the observation that insulin dependent diabetes was occasionally complicated by painful stiff hands. [9] At least 30% of diabetic patients have hand skin thickening, and some have demonstrable involvement of the dorsum of the feet. Clinical clues which suggest such a thickening include difficulty in tenting the skin, pebbled or rough skin on the knuckles or periungual region [6] and decreased skin wrinkling following immersion in water. [10] Biopsy specimens of involved skin show pronounced thickening of periarticular rather than articular collagen, which may be due to non-enzymatic glycosylation of collagen.

MATERIAL AND METHODS

This study was conducted by specialists of Dermatology and Medicine in a camp held in a village of Punjab in 250 patients. The patients were equally divided into two groups of 125 patients each (Group A and Group B).Group A: consisted of 125 diabetics in the age group of 30-60 years. Group B: consisted of 125 non-diabetic control patients in the age group of 30-60 years. The diabetics were diagnosed as per the revised criteria of glucose tolerance given by Alvin (2001). [11] Routine investigations were done in each case in both the groups. Certain special investigations to confirm the diagnosis were carried out where required Fundoscopic examination was done.The incidence of scleroderma dibeticorum and waxy skin in diabetic group, non- diabetic control group were assessed separately and then the incidence of scleroderma and waxy skin were compared in the two groups to know whether diabetes mellitus had any association with diseases of skin(Table-1 and2).

OBSERVATIONS

The incidence of waxy skin was 45 (36.0%) cases in diabetic group and 22 (17.6%) cases in non-diabetic group. The difference was statistically significant. The incidence of scleroedema dibeticorum was 3 (2.4%) cases each in diabetic group and 0% in non-diabetic group and in all the above conditions the difference was statistically non-significant. (Table I).

In our study the incidence of skin changes was 45 (36.0%) cases in diabetic group and 22 (17.6%) cases in non diabetic group. (Table 1)The difference was statistically significant. In the diabetic group out of 45 cases there were 18 cases with skin thick over dorsum of hands especially fingers, 13 cases with pebbling of skin over knuckles, 12 cases with waxy skin and 2 cases with skin thick over both dorsum of hands and feet. (Figure 3) (Table 2) Except for one case all the above cases had age more than 40 years with family history of diabetes positive. In non diabetic group out of 22 cases, 1 case had skin thick over dorsum of hands especially over fingers. 9 cases had pebbling of skin over knuckles and 12 cases had waxy skin. (Table 2)Majority of the above cases had family history of diabetes positive and age more than 40 years. We have recorded three cases of scleroedema diabeticorum in diabetic group only, the incidence being 3 (2.4%). (Table 1) In 125 cases 85 females (68.0%) and 40 (32.0%) were diabetic. (Table 3).

TABLE 1 : PREVALENCE OF SCLERODERMA DIABETICORUM AND WAXY SKIN IN DIABETICS AND NON- DIABETICS

Manifestation	Group A(Diabetic) n=125		Group B(Non-Diabetic) n=125		X^2	p value
	No	%	No	%		
WAXY SKIN	45	36.0	22	17.6	4.24	<0.05
SCLERODERMA DIABETICORUM	3	2.4	0	0	0.80	>0.05

TABLE 2: COMPARISON OF PERCENTAGE OF MANIFESTATIONS IN DIABETICS AND NON DIABETICS

Diabetics Versus Non Diabetics	Manifestations							
	Thick skin over dorsum of hands		Pebbling over knuckles		Waxy Skin		Thick Skin over both dorsum of hands and feet	
	Cases	%age	Cases	%age	Cases	%age	Cases	%age
Diabetics n= 45	18	40.0	13	28.9	12	26.7	2	4.5
Diabetics n= 22	1	4.5	9	41	11	50.0	1	4.5

TABLE 3: DIABETIC CASES ACCORDING TO SEX

Sex	No. of Cases	%age
Female	85	68.0
Male	40	32.0
Total	125	100

DISCUSSION

Persons with diabetes tend to have thicker skin than their non-diabetic counterparts. There are three aspects to this observation. Firstly, diabetics in general have a clinically inapparent but measurable increase in skin thickness unassociated with symptoms and which go unnoticed by patients and physicians. Using pulsed ultrasound, it can be demonstrated that diabetics have thicker forearm skin than their age and sex matched non diabetic counterparts**.** [12] Second is clinically apparent thickening of skin involving the fingers and hands ranging from pebbled skin of knuckles to diabetic hand syndrome. The diabetic hand syndrome (Waxy skin) consists of thickened skin over the dorsum of digits and limited joint mobility, especially of the interphalangeal joints. [13]Third is an infrequent syndrome of diabetic scleroedema in which the patient develops markedly thickened dennis on the upper back. Thickening of the skin on the backs of the hands may occur in as many as 20% to 30% of persons with diabetes. [14]

Scleroedema adultorum

Scleroedema adultorum of diabetes is a syndrome characterized by a marked increase in dermal thickness posteriorly on back (Figure-1) and upper neck in middle aged, overweight, poorly controlled type II diabetic subjects. It is not recognised as being related to digital sclerosis and we found no correlation by ultrasound measurements of back skin and hand skin thickness (Figur-2). It has a reported prevalence of 2.5% in patients with type II diabetes**.** [15]

Figure 1 : Sleoderma Diabeticorum

Figure 2: Thickened Skin over Dorsum of Hands

Figure 3: Thickened Skin over Dorsum of Feet

Histologically one finds a thickened dermis with large collagen bundles that are separated by wide, clear spaces. There may be increased number of mast cells. [16] Scleroedema adultorum a well-defined entity has been recognised a cutaneous manifestation of diabetes. In contrast to the identical changes occuring after infection scleroedema associated with diabetes may not remit even after long periods of time. Diabetic scleroedema occurs mainly in obese diabetic individuals with evidence of vascular complications. [17]**.** An excellent review of literature [18]also concluded that Scleroedema Diabeticorum is a diffuse, nonpitting induration of the skin characteristically occurring on the upper back, neck and shoulders in 2.5% of diabetics resulting in the limitation of movement·[19] [4] It has also suggested,

A) Scleroedema of Buschke, which occurs at any age and undergoes spontaneous resolution in 8-18 months.

B) Scleroedema diutinum, which does not follow acute infection, tends to chronicity and is often associated with diabetes mellitus [15] Male diabetics are more affected than female (ratio 4: 1). Generally the diabetes is long standing and patients are obese, exhibiting high frequency of Diabetic Retinopathy, neuropathy, hypertension and Ischemic heart disease. [3]

The incidence of limited joint mobility ranged from 8-50%. The variations of incidence are probably explainable by differences in age groups, duration of diabetes in the studies and lack of standardized testing. Rosenbloom and Frais described three adolescent patients with the syndrome of long-standing diabetes mellitus, restricted joint mobility, thick tight waxy skin, growth impairment, and maturational delay. Rosenbloom et al later reported in a study of 309 mostly juvenile diabetics that 30 percent had joint limitation and one third of these had thick tight, waxy skin that the examiner could not tent, mostly involving the dorsum of the hands. This work has been confirmed by other authors and these observations have been extended to patients with type II diabetes mellitus. [7] The skin becomes thickened, with a waxy appearance, in about one third of patients (Figure-1 and 2). Such a skin resembles sclerodermic skin; however, the absence of other signs (Raynaud's phenomenon, ulcerations, nail calcinosis, and visceral organ involvement) clearly rules systemic scleroderma out. Histologically, dermal collagen thickening and elastic fiber reduction are observed. [20] The presence of diabetes mellitus is generally associated with measurably thickened skin. Using pulsed ultrasound, it can be demonstrated that diabetics have thicker forearm skin than their age and sex-matched non-diabetic counterparts. Contrary to the pattern in non-diabetics, skin thickness may increase with age (apparently associated with increased duration of diabetes.) Most studies have used the upper extremity skin in evaluating skin thickness, and it may not be a valid conclusion that diabetic skin is thickened at other sites.

Some researchers have also demonstrated an increased skin thickness on the dorsum of the feet, but not the back, suggesting that increased skin thickness is not necessarily universal in diabetes. It appears to be a safe observation that patients with diabetes mellitus have thicker skin on their extremities. These terms are synonyms denoting one and the same skin disorder. In European literature, the term scleroderma-like syndrome (SLS) is preferred, whereas the terms reduced joint mobility and waxy skin syndrome prevail in American literature. [20]

To evaluate the frequency of SLS and its association with other diabetes-related pathology in diabetic population among Jewish and Arab patients, 153 IDDM patients and 45 healthy age- and gender-matched controls were studied. While no diabetes-related pathology was found in the controls, SLS was detected in 47% of all patients (skin, 31.4%; arthropathy, 37.9%; both, 22%), Independent of age, SLS directly correlated with diabetes duration ($p < 0.01$) One or more features of systemic diabetic involvement were present in 22% of patients with SLS, compared to only 7.2% in patients without SLS ($p < 0.009$). When patients were analyzed according to ethnicity, the frequency of skin involvement and neuropathy were found to be higher among Arab patients, particularly males ($p < 0.002$ and $p < 0.005$, respectively), and detection of one was significantly associated with the presence of the other ($p < 0.001$). In conclusion, their results suggest that SLS was the most common diabetic complication among Jewish and Arab IDDM patients. [21] In a study, total of 142 patients (68%) had at least one cutaneous disorder, and 81 patients (38%) had skin lesions considered to be associated with diabetes. The most prevalent cutaneous manifestation was xerosis, found in 22% of type 1 diabetic patients. In control subjects, the ichthyosiform changes affected only 3% of the children and adolescents. The difference was highly significant ($P < 0.01$). Thyroid-stimulating hormone levels were normal in all patients with diabetic hand (scleroderma-like changes and/or limited joint mobility). [22]

The prevalence of scleroderma spectrum disorders (including systemic sclerosis [SSC] meeting the American Rheumatism Association criteria and the less typical disorders meeting only the study criteria) was determined in a random sample of 6,998 subjects from the general population of South Carolina. The results suggested that the prevalence of these disorders might range from 67 to 265 per 100,000, which was 4.9 to 19.2 times higher than previously reported for definite SSC. The ratio of nondefinite cases to definite cases of SSC (those meeting American Rheumatism Association criteria) was 2.5. Most of the nondefinite cases were unrecognized prior to the study, which suggests the need for improved early diagnosis of scleroderma spectrum disorders. Brief histories of the 7 patients with scleroderma spectrum disorders were reported. [23]

In another study, diabetic hand, a variety of sclerodermoid lesions in diabetic patients, was seen in only 2.3% of our patients but was strongly related to diabetes duration ($P < 0.001$). In young patients with type 1 diabetes with three-times-longer disease duration, the prevalence of scleroderma-like changes of the hand was 39%. [24]. This finding was in variance with the study of Cole et al (1983) where the prevalence of scleroedema was 3% in patients with NIDDM.

SUMMARY AND CONCLUSION

Among the disorders of collagen most common was waxy skin observed in 36% of cases which was statistically significant when compared with non diabetic group. We even had one case each of necrobiosis lipoidica diabeticorum, granuloma annul are and scleroedema diabeticorum.

From the foregoing account it became clear that the skin is involved in diabetics quite often. The manifestations are numerous and many a times they can serve as diagnostic markers for the underlying undetected diabetes. So whenever patients present with multiple manifestations their diabetic status should be checked and controlled, or if they are obese and have positive family history of diabetes mellitus, a high index of suspicion should be kept regarding their diabetic status. In this way diabetes can be detected quite early and early intervention can prevent morbidity from this deadly disease. Sports physicians and patients with diabetes should be aware of these manifestations, so that optimal physiotherapy programmes can be devised that do not exacerbate existing complaints and encourage continuing physical activity in this group.

REFERENCES

1. Norman RA, Chakrabarty A, Phillips TJ. Cutaneous Manifestations of Diabetes Diagnosis of Aging Skin Diseases. 2008: 253- 263.
2. Mahajan S, Koranne RV, Sharma SK. Cutaneous manifestation of diabetes mellitus. Indian J Dermatol Venereol Leprol. 2003; 69(2):105-8.
3. Braverman, Braverman IM. Cutaneous Manifestations of Diabetes Mellitus. Medical Clinics of North America 1971; 55 (4): 1019-1029.
4. Mackool BT, Lowitt MH, Dover JS. Skin manifestations of diabetes mellitus in Kahn C.R., Weir G.C.,eds. Joslin's diabetes mellitus. Thirteenth Ed, B.I.Waverly pvt.Ltd. New Delhi 1996: 900-911.
5. Freinkel RK and Freinkel N. Cutaneous Manifestations of Endocrine Disorders in Dermatology in General Medicine, 3rd Ed. Editors: Fitzpatrick TB, Eisen AZ, Wolff K, Freeberg IM, Austen KF. McGraw-Hill Information Services Company, New York. 1987; 2: 2063-2081.
6. Sattar MA, Diab S, Sugathan TN, Sivanandasingham P, Fenech FF. Diabet Med. 1988; 5 (5): 465-8.
7. Huntley A. M.D. Dermatology Online Journal. 1995; Vol. 1, (2): http://dermatology.cdlib.org/DOJvol1num2/diabetes/dmreview.html. Accessed on 12.05.11.
8. Wyatt L H, Ferrance R J. The musculoskeletal effects of diabetes mellitus. J Can Chiropr Assoc. 2006; 50(1): 43–50.
9. Lundbaek K. Stiff hands in long term diabetes. Acta Med Scand. 1957; 158: 447-51.
10. Clark CV, Pentland B, Erwing DJ, Clark BF. Decreased skin wrinkling in diabetes mellitus. Diabetes Care 1984; 7: 224-227.
11. Cole GW, Headley J, Skowsky R. Scleroedema diabeticorum. A common and distinct cutaneous manifestation of diabetes mellitus. Diabetes Care. 1983; 6: 189-92.
12. Cohen BA, Wheeler Jr CE, Briggaman RA. Scleroedema adultorum of Buschke and diabetes mellitus. Arch Dermatol 1970; 101: 27-35.
13. Freinkel Ruth K. Diabetes Mellitus in Dermatology in General Medicine 5th edition, Editors: Fitzpatrick TB, Eisen AZ, Wolff K, f Freeberg 1M, Austen KF. McGraw-Hill Information Services Company, New York, 1999; 2: 1969-1975.
14. Krishna K and Kavita K. Skin manifestations of Diabetes Mellitus. Dermatology update. 2000; 18:28-34.
15. Binkley GW. Dermopathy in the diabetic syndrome. Arch Dermatol. 1965; 92: 625- 634.
16. Alvin C. Powers. Diabetes mellitus. In: Harrison's Principle of Internal Medicine. Braunwald, Fausi, Kasper, hausell, Longo, Jameson. 15th ed. McGraw Hill Publications, U.S.A. 2001; 2109-2137.
17. Collier A, Mathews AM, Kellett MA, Clarke BF, Hunter JA. Change in skin thickness associated with cheiroarthropathy in Insulin dependent diabetes mellitus. Br Med J 1986; 292: 936.
18. Brik R, Berant M, Vardi P. The scleroderma like syndrome of insulin dependent diabetes mellitus. Diab Metab Rev. 1991; 7: 121-128.

19. Fitzcharles MA, Duley S, Wade RW. Limitation of joint mobility in adult non insulin dependent diabetic patients. Ann Rheum Dis. 1984; 43: 251-7.

20. Renar P, Lipozencic J. Diabetes mellitus and skin. 1998; http://www.idb.hr/diabetologia/98no2-2.html. Accessed on 12.05.11.

21. Brik R, Berant M, Sprecher E, Yarnitsky D, Ganaym Z, Vardi P. Ethnicity and prevalence of scleroderma-like syndrome: a study of Arab and Jewish Israeli insulin-dependent diabetic children. J Diabetes Complications. 1997; 11(6): 323-7. http://www.ncbi.nlm.nih.gov/pubmed/9365872. Accessed on 12.05.11

22. Miloš D, Pavlović, Milenković T, Dinić M, Mišović M, Daković D.The Prevalence of Cutaneous Manifestations in Young Patients With Type 1 Diabetes. Diabetes Care. 2007; vol. 30(8), http://care.diabetesjournals.org/content/30/8/1964.full. Accessed on 12.05.11.

23. Hildegard R. Maricq, Martin C. Weinrich, J E. Keil, EA. Smith, F E. Harper, A I. Nussbaum. Prevalence of scleroderma spectrum disorders in the general population of South Carolina. Journal of arthritis and rheumatic disease. 2005; Vol 32 (8): 998 – 1006. http://www3.interscience.wiley.com/journal/112208643/abstract?CRETRY=1&SRETRY=0. Accessed on 12.05.11.

24. Smith L L, Burnet J D, McNeil. Musculoskeletal manifestations of diabetes mellitus. Br J Sports Med. 2003; 37:30-35. http://bjsportmed.com/content/37/1/30.full, Accessed on 12.05.11.