DOI: 10.7860/JCDR/2014/10350.4853

Original Article

Biochemistry Section

Assessment of BMI, Serum Leptin Levels and Lipid Profile in Patients with Skin Tags

SADAF IDRIS[1], S. SUNITHA.[2]

ABSTRACT

Background: Skin tags (ST) are benign lesions composed of loose fibrous tissue, associated with obesity and atherogenic profile. Thus help in the follow up by considering ST as a useful cutaneous sign for the risk factor of atherosclerosis.

Aim: To evaluate the association of skin tags with BMI, serum leptin and lipid profile.

Materials and Methods: The study was carried out in 40 cases with ST and 40 age and gender matched controls. Subjects on oral contraceptives and systemic drugs especially lipid lowering agents, pregnant women, cases with medical history of endocrine disease, acute infection, erythroderma and psoriasis, cases with a drug history of isotretinoin use in last six months were excluded from the study. Blood samples were collected. Serum lipids and serum leptin were estimated.

Result: The acrochordons group showed significantly higher values of BMI, total cholesterol (TC) and TC/HDL ratio. 60% of the patients with ST were overweight and 10% were obese. There was no statistical significant difference in leptin levels between the groups. Leptin showed a positive significant correlation with BMI in the acrochordons group.

Conclusion: All the above derangements confirm that ST is cutaneous findings frequently associated with obesity and dyslipidemia. Thus follow-up of these patients with regard to the development of diseases associated with atherosclerosis may be beneficial.

Keywords: Dyslipidemia, Hyperleptinemia, Obesity, Skin tags

INTRODUCTION

ST are flesh coloured to dark brown, pin head sized to larger, benign lesions composed of loose fibrous tissue occurring mainly on the neck, eyelids, axillae and major flexures as a soft round, smooth or irregular surfaced, sessile or pedunculated protrusions. They are also called as soft fibromas or acrochordons or fibroadipomas or fibroepithelial polyps. Histologically the stroma has a loose fibrous connective tissue with dilated blood vessels resembling the papillary dermis, with reduced or absent nerve tissue, without any appendages [1,2].

The prevalence of ST in India is about 0.7% [3]. The lesions are more common in women at menopause or later [1]. About 60% of the individuals acquire them by the age of 69 [4].

Skin tags have received little attention in the dermatological literature as they have been regarded as being of little consequence [5]. But recently reports suggest that the presence of ST is associated with diabetes mellitus, obesity and atherogenic lipid profile [6-9]. The 1st report describing the association of ST with atherogenic lipid profile was by M.A. Crook [6]. ST have also been associated with friction, HPV, acromegaly, crohns disease, aging, organ transplant, colonic polyps, pregnancy, increased mast cell counts and increased oestrogen and androgen receptors [10].

The mechanism of formation of ST is due to the presence of leptin receptors residing in epidermis and dermis [11,12]. Leptin is a 167 amino acid protein with molecular weight 16kDa, a product of obese gene (ob), produced mainly by the adipocytes [13]. It is also expressed in the stomach, the placenta and the mammary gland [14]. Leptin levels are directly proportional to the fat mass [13]. It is involved in the regulation of appetite and energy expenditure via hypothalamic mediated effects [15]. It is also involved in carbohydrate and lipid metabolism [16]. Serum leptin levels are increased in obesity, being strongly associated with fat mass [17] and BMI [18]. Hyperleptinemia is more pronounced in obese individuals as leptin is mainly present in free form in these individuals but present in bound form in lean individuals [19]. This indicates that obesity is a leptin resistant state in most obese individuals rather than it being a condition of defective ob gene [14,17]. Leptin binds to the leptin receptors present in the skin and stimulates the growth and proliferation of epidermal and dermal cells [20,21]. It also has a mitogenic effect on keratinocytes which is demonstrated during healing by in vivo studies [11]. The role of leptin has also been reported in carcinogenesis, linking obesity to cancer [22]. It is therefore considered as a new growth factor [20,23].

MATERIALS AND METHODS

Study Design and Population

The present study represents a case-control study. The study was carried out in 40 cases, above 18 y of age, with 3 or more ST and 40 age and gender matched controls without ST who attended the outpatient department. The institutional ethical committee approved the study protocol. Informed consent was obtained from all the participants. Exclusion criteria were patients on oral contraceptives and systemic drugs especially lipid lowering agents, pregnant women, medical history of endocrine disease (Cushing syndrome, acromegaly, pheochromocytoma, hyperthyroidism, glucagonoma), acute infection, erythroderma and/or psoriasis, cases with drug history of isotretinoin use in last six months. Approximately, about 110 patients were seen and based on the criteria 30 were excluded and a sample of 80 was selected. Out of which 40 participants had skin tags.

METHODS

Informed consent was taken from patients and controls. A pre-structured proforma was used to collect the data. Baseline data including age, gender, BMI (kg/m^2), detailed medical history, clinical examinations. After a 12 h fasting period, a venous blood sample was taken in the early morning from all subjects for detection of fasting serum total cholesterol, serum triglycerides, HDL-C, LDL-C and serum leptin. Serum VLDL-C was calculated using the formula, VLDL=TG/5. TC/ HDL and LDL/HDL ratio were determined.

Gender	Cases		Controls		Total
	n	%	n	%	
Male	27	34%	29	36%	56
Female	13	16%	11	14%	24
Total	40	50%	40	50%	80

[Table/Fig-1]: Frequency of ST according to gender in the study sample

	Case Mean ± SD	control mean ± SD	p-value
BMI	26.43 ± 3.21	24.02 ± 2.83	0.001*
TC	204.75 ± 61.28	164.50 ± 32.22	0.001*
TG	189.03 ± 91.15	168.73 ± 94.16	0.124
LDL	127.70 ± 54.60	116.13 ± 33.32	0.402
VLDL	37.38 ± 18.23	33.53 ± 18.80	0.137
HDL	38.80 ± 10.39	37.80 ± 11.94	0.509
TC/HDL	5.46 ± 1.92	4.76 ± 1.92	0.019*
LDL/HDL	3.41 ± 1.73	3.26 ± 1.16	0.874
LEPTIN	28.61 ± 32.49	19.16 ± 22.69	0.106

[Table/Fig-2]: Comparison of biochemical results of study subjects
** Statistically significant*

BMI	Controls		Cases		Total
	n	%	n	%	
<18.5 Underweight	0	0	0	0	0
18.5–24.9 Healthy	24	60	12	30	36
25.0–29.9 Overweight	16	40	24	60	40
30.0–34.9 Obesity	0	0	4	10	4
Total	40	100%	40	100%	80

[Table/Fig-3]: Sample distribution according BMI

STATISTICAL ANALYSIS

Null Hypothesis: There is no significant difference in the mean value of parameter between the two groups i.e. mean 1= mean 2

Alternate Hypothesis: There is a significant difference in the mean value of parameter between two groups i.e. mean 1≠ mean 2

Level of Significance: α=0.05

Statistical test used: t- test and Mann-Whitney test were both used

Decision Criterion: If p<0.05, we reject the null hypothesis and accept the alternate hypothesis.

RESULTS

Among the total sample of 80, 13 females (16%) and 27 males (34%) were carriers of ST. [Table/Fig-1]. The age ranged from 30 to 75 y and the maximum numbers of cases were in the age group of 40-49 y but the mean of age between the cases (50.33 ± 9.94) and controls (49.98 ± 10.87) was not statistically significant.

The mean BMI of the case and controls groups were 26.43 ± 3.21 and 24.02 ± 2.83, respectively, which was found to be statistically significant (p=0.001) [Table/Fig-2]. 60% of cases are in the overweight group (BMI 25-29.9 kg/m^2) and 10% were obese (BMI >30 kg/m^2) [Table/Fig-3].

The mean TC levels in the cases and controls were 204.75 ± 61.28 and 164.50 ± 32.22 respectively, which was found to be statistically significant (p=0.001). The mean TC/HDL ratio in the cases and controls were 5.46 ± 1.92 and 4.76 ± 1.92, respectively, which was found to be statistically significant (p=0.019) There was no significant difference between the case and control group with respect to TG, HDL-C, LDL –C, VLDL-C and LDL/HDL ratio [Table/Fig-2].

Higher mean Leptin was recorded in cases compared to controls but the difference in mean Leptin between the two groups is not statistically significant (p>0.05) [Table/Fig-2]. A significant positive correlation between leptin levels and BMI (ρ=0.313, p=0.049) in cases, though not in controls. (ρ=0.143, p>0.05).

DISCUSSION

ST are proliferations histologically characterized by a papillomatous pattern in epidermis and loose connective tissue, and have been suggested to be associated with obesity and various endocrinal disorders. ST is a part of the aging process and it is natural to find more tags in older subjects [7]. It has been shown in our study that maximum numbers of cases are in the age group of 40-49y. There was a male preponderance in this study (34% male and 16% females) but a significant gender difference could not be found. Studies by Thappa DM [24], Agarwal JK et al., [25], Kahana M et al., [26], Margolis J et al., [27] and Banik R et al., [28] showed that males were affected more than females.

Obesity and dyslipidemia are commonly associated with a recognised risk for the development of Metabolic Syndrome (MS). MS is a complex of factors which include raised blood pressure, elevated glucose, cholesterol and TG levels and low HDL-C [29]. ST commonly develops in individuals with obesity and their prevalence correlated positively with the severity of the obesity [7,30]. In our study, we found that the BMI values in the cases were significantly higher than in the control group.

There have been reports in the literature about the relationship between ST and atherogenic lipid profiles. Crook detailed four patients with multiple ST who had increased serum TG and decreased serum HDL-C levels. Thus, suggesting that ST might indicate an abnormal lipid profile and increase cardiovascular risk. Hyperlipidemia and obesity accompanied ST in 45.8% and 70.8% of the subjects, respectively, in a study by Demir [31]. Erdogan et al., found serum TC levels higher in the ST group than the control group. Thus, suggesting that ST may not be innocent tumoral proliferations. Serum TC and LDL-C levels were higher in the ST group than the control group in a study by Gorpelioglu et al., [23]. Tamega et al., [32] reported higher serum TG levels in the ST group than the control group. Our study showed that the mean TC levels and TC/HDL-C ratio were significantly higher in the cases than those in the control group which was consistent with Erdogan et al.,. This study did not show a statistically significant difference between cases and controls regarding TG, HDL-C, LDL-C, VLDL-C levels and LDLC/ HDL-C ratio which was consistent with study by Erdogan et al.

The study also evaluated the relationship between ST and serum leptin. In this study there was a positive correlation between leptin and BMI in cases with ST and this was consistent with studies by R Sari et al., [7], El Safoury O et al., [10].

How leptin plays a role in the development of the ST is not known. However, there are some studies that might be helpful in the etiopathogenesis of ST Frank et al.,[20], investigated the proliferative effect of leptin on the cutaneous keratinocytes in rodents. They demonstrated that leptin markedly improved re-epithelialization of excisional wounds in obese mice and accelerated normal wound healing conditions in wild type mice. Thus suggesting that delayed wound healing in obese mice is due to impaired re epithelialization in the absence of the growth factor leptin during cutaneous repair. A direct proliferative effect of leptin on mouse and human keratinocytes was showed by Goren et al.,[12]. Stallmeyer et al., [11], showed the importance of leptin as a mitogenic factor in skin repair and also topically administered leptin improved re-epithelialization. They investigated the regulation of leptin system during normal repair in healthy animals and found that highly proliferative keratinocytes of the wound margin epithelia strongly expressed the functional leptin receptor subtype.

In this study, when we investigated the relationship between serum leptin levels in subjects with ST and healthy controls, no statistical significant difference was found between both the study groups. This was consistent with the study by Gorpelioglu et al., [23] who showed that there is positive correlation only between ST and atherogenic lipid profile and not with leptin.

There have also been a few reports in the literature where some researchers have hypothesized that ST may be a marker for insulin resistance [3,6,7,26,27,33]. As our study revealed no significant difference in leptin levels with ST and controls, we speculate that insulin resistance is the culprit linking obesity and ST development.

Our study implicates the utility of BMI and serum lipid profile in subjects with ST at presentation, for evaluating risk of atherosclerosis and CVD, which would be helpful for an early medical intervention.

REFERENCES

[1] Burns T, Breathnach S, Cox N, Griffith CE. Rook's Textbook of Dermatology. 7th edition volume 2. Wiley - Blackwell publishing, 2010. 36.42.
[2] Lowell G, Stephen K, Barbara G, Amy P, David L, Klaus W. Fitzpatrick's Dermatology in General Medicine. 6th edition volume 2. McGraw-hill, 2007. p. 993.
[3] Sudy E, Urbina F, Maliq M, Sir T. Screening of glucose/insulin metabolic alterations in men with multiple skin tags on the neck. *J German Society Dermatol.* 2008;6:852-55.
[4] James WD, Berger T, Elston D. Andrews` Disease of the Skin: Clinical Dermatology. 10th edition. *Elsevier Health Sciences.* 2011. p. 610-11.
[5] Weedon D. Weedon's Skin Pathology: Expert Consult. *Elsevier Health Sciences,* 2009. p. 762-63.
[6] Crook MA. Skin tags and atherogenic lipid profile. *J Clin Path*. 2000;53:873-74.
[7] Sari R, Akman A, Alpsoy E, Balchi MK. The metabolic profile in patients with skin tags. *Clin Exp Med.* 2010;10:193-97.
[8] El Safoury OS, Abdel Hay RM, Fawzy MH, Kadry D, Amin IM, Abu Zeid OM, et al. Skin tags, leptin, metabolic syndrome and change in the life style. *Ind J Dermatol Venereal Leprol.* 2011;77:577-601.
[9] E Erkek, Kisa U, Bagci Y, Sezikli H. Leptin resistance and genetic predisposition as potential mechanism in the development of skin tags. *Hong Kong J Dermatol Venerol*. 2011;19:108-114.
[10] El Safoury O,Fawzi M, Abdel Hay RM, Hassan AS, Maawadawi Z. Increased tissue leptin hormone level and mast cell count in skin tags : A possible role of adipoimmune in the growth of benign skin growths. *Indian J Dermatol Venerol Leprol*. 2010;76:538-42.
[11] Stallmeyer B, Kampfer H, Podda M, Kaufmann R, Pfelschifter J, Frank S. A novel keratinocyte mitogen: Regulation of leptin and its functional receptors in skin repair. *J Invest Dermatol.* 2001;117:98-105.
[12] Goren I, Pfelschifter J, Frank S. Determination of leptin signaling pathways in human and murine keratinocyes. *Biochem Biophys Rea Commun.* 2003;303:1080–85.
[13] Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse gene and its human analogue. *Nature.* 1994;372:425-32.
[14] Mantzoros CS. The role of leptin in human obesity and disease: a review of current evidence. *Ann Intern Med.* 1999;130:671-80.
[15] Morton GJ, Schwartz MW. Leptin and the central nervous system control of glucose metabolism. *Physiol Rev.* 2011;91:389-411.
[16] G Sweeney. Leptin signaling. *Cellular Signaling.* 2002;14:655-63.
[17] Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. Serum immunoreactive – leptin concentrations in normal weight and obese humans. *New Engl J Med.* 1996;334:292-95.
[18] Wauter M, Considine RV, Vangaal LF. Human leptin- from adipocyte hormone to an endocrine mediator. *Eur J Endocrinol*. 2000;143:293-311.
[19] Meier U, Gressner M. Endocrine regulation of energy metabolism: Review of pathobiochemical and clinical chemical aspects of leptin, ghrelin, adiponection, and resistin. *Clinical Chemistry.* 2004;50(9):1511-25.
[20] Frank S, Stallmeyer B, Kampfer H, Kolb N, Pfeilschifer J. Leptin enhances wound re epthilization and constitutes a direct function of leptin in skin repair. *J Clin Invest.* 2000;106:501–09.
[21] Rahmouni K, Morgan DA, Morgan GM, Mark AL, Haynes WG. Role of selective leptin resistance in diet induced obesity hypertension. *Diabetes.* 2005;54:2012-18.
[22] Alexe DM, Petridou E. Leptin and cancer. In: Castracane VD, Henson MC, editor. Leptin. *Springer US:* 2007. p. 1-17
[23] Gorpelioglu C, Erdal E, Ardicoglu Yetal. Serum leptin, atherogenic lipids and glucose levels in patients with skin tags. *Indian J Dermatol.* 2009;54(1):20-22.
[24] Thappa DM. Skin tags as markers of diabetes mellitus: an epidemiological study in india. *J Dermatol.* 1995;22:729-31.
[25] Agarwal JK, Nigam PK. Acrocordon: A cutaneous sign of carbohydrate intolerance. *Australas J Dermatol.* 1987;28:132-33.
[26] Kahana M,Grossman E, Feinstein A, Ronnen M, Cohen M, Millet MS. Skin tags: a cutaneous marker for diabetes mellitus. *Acta Derm Venereol.* 1987;67:175-77.
[27] Margolis J, Margolis L. Skin tags – a frequent sign of diabetes mellitus. *N Eng J Med.* 1976;294:1184.
[28] Banik R, Lubach D. Skin tags: localization and frequencies according to sex and age. *Dermatologica.* 1987;174:180-83.
[29] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood Institute; american heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. *Circulation.* 2009;120:1640-45.
[30] Gracia Hidalgo L, Orozco-Topete R, Gonzalez-Barranco J, et al. Dermatoses in 156 obese adults. *Obes Res.* 1999;7:299-302.
[31] Demir S, Demir Y: Acrochordon and impaired carbohydrate metabolism. *Acta Diabetol.* 2002;39:57–59.
[32] Tamega Ade A, Aranha AM, Guiotoku MM, et al. Association between skin tags and insulin resistance. *An Bras Dermatol*. 2010;85:25-31.
[33] Beltowski J, Wojcicka G, Jamroz A. Leptin decreases plasma paraoxonase 1 (PON1) activity and induces oxidative stress: the possible novel mechanism for proatherogenic effect of chronic hyperleptinemia. *Atherosclerosis.* 2003;170:21-29.

PARTICULARS OF CONTRIBUTORS:
1. Tutor, Department of Biochemistry, Kempegowda Institute of Medical Sciences, Bangalore, India.
2. Associate Professor, Department of Biochemistry, Kempegowda Institute of Medical Sciences, Bangalore, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Sadaf Idris,
#337 16th A Main 4th T block Jayanagar Bangalore-560041, India.
Phone : 9916772063, E-mail : risshaidris@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jun 16, 2014**
Date of Peer Review: **Jul 17, 2014**
Date of Acceptance: **Aug 13, 2014**
Date of Publishing: **Sep 20, 2014**