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Original Article

Serum levels of homocystiene, vitamin B_{12} and folic acid in Indian patients with psoriasis: results of a pilot study

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ABSTRACT

Introduction: Hyperhomocystienemia has emerged an independent risk factor for cardiovascular diseases with an implication for cardiovascular morbidity in psoriasis patients. Both vitamin B_{12} and folic acid influence homocystiene metabolism as cofactors. **Aim:** To study the serum levels of homocystiene, vitamin B_{12} and folic acid in patients with chronic plaque psoriasis and age matched controls. **Methods:** 55 males aged 22-66 years with chronic plaque psoriasis of 6 months to 20 years and 55 healthy male controls aged 20-65 years were studied. **Results:** Body surface area involvement was <10% in 38 (69%), between 10-20% in 10 (18.2%) and >20% in 7 (12.8%) patients, respectively. The PASI was <6 in 41 (74.5%), 6-12 in 10 (18.2%) and >12 in 4 (7.3%) patients, respectively. The serum homocystiene levels of >12 μmol/L were higher than normal (5-12 μmol/L) in all patients and 11 (22%) controls and the difference was statistically significant. The serum vitamin B_{12} levels of <150 to 513pg/ml were on the lower side of the normal (174-878pg/ml) in all patients. The serum folic acid levels varied between 5.65 and >24ng/ml and elevated levels of 17.83 to >24ng/ml (normal 3-17 ng/ml) were noted in 17 (30.9%) patients. Except for elevated serum homocystiene in 11 (22%) controls, other biochemical parameters were within normal range. **Conclusions:** Implications of hyperhomocystienemia for cardiovascular comorbidities in psoriasis patients and whether supplementing vitamin B_{12} and folic acid will prevent comorbidities by normalizing homocystiene metabolism needs evaluation by large well designed studies.

Key words: Hyperhomocystienemia; Psoriasis comorbidities; Psoriasis

INTRODUCTION

Psoriasis is a common inflammatory dermatosis with epidermal hyperproliferation in the basal layer. Both genetic and environmental influences (trauma, infection, drugs, alcohol, smoking, metabolic factors, psychological stress) are considered important in its pathogenesis. The disease has a significant impact on health related quality of life because of lifelong chronicity, extent of severity, periodicity of flares, and more importantly, from associated comorbidities. Elevated plasma homocystiene has been widely studied as an independent risk factor for atherosclerotic disease involving the coronary, peripheral, and cerebral circulations that may result in early death from myocardial infarction, pulmonary embolism or stroke [1,2]. Psoriasis patients reportedly have significantly higher plasma homocysteine levels corresponding with severity of disease than control subjects [3]. They also demonstrate significantly lower levels of vitamin B_{12}, folate, and tissue plasminogen activator than controls. Reduced plasma folate and vitamin B_{12} levels in psoriasis patients have been attributed to their increased utilization in the skin, reduced absorption from the gut, or as an adverse effect of systemic medications like methotrexate (folate

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antagonist) [3,4]. Deficiencies in vitamin B_{12} and folate have been associated with increased levels of plasma homocystiene, and supplementation is shown to decrease plasma homocystiene levels [1,3]. It is possible that higher levels of plasma homocysteine perhaps contribute to the increased risk for cardiovascular morbidity observed in patients with psoriasis [5]. We studied serum levels of homocystiene, vitamin B_{12} and folic acid in Indian patients with psoriasis and age matched controls.

MATERIAL AND METHODS

Serum levels of homocystiene, vitamin B_{12} and folic acid were studied in 55 consecutive adult males having chronic plaque psoriasis for at least 6 months after written/informed consent during Jan-Dec 2012. The study was approved by the Institutional Protocol Review Board and Institutional Ethics Committee (Rgn no ECR/490/Inst/HP/2013). Patients were instructed to stop taking alcohol, coffee or any topical/systemic treatment for 1 week, 2 weeks and 4 weeks, respectively, and consumption of animal protein 24 h prior to blood sampling. Only topical emollients and oral anti-histaminics were allowed. Patients having palmoplantar psoriasis, psoriatic arthritis, systemic diseases (thyroid, hepatic or renal disease, hematologic disorders diabetes mellitus, coronary heart disease, stroke, peripheral vascular disease, systemic lupus erythematosus), on antifolate medications (anticonvulsants, penicillin, levodopa, cyclosporine, isoniazide), or drugs that cause hyperhomocystienemia (phenytoin, carbamazapine, theophylline, oral contraceptives, azathioprine, thiazide diuretics, metformin), were excluded from the study. Patients with history of substance (opium) abuse and current smokers were also excluded. A detailed demographic profile, medical history and clinical details of psoriasis were recorded. Body Surface Area (BSA) involvement was calculated as per 'Rule of Nines' and the Psoriasis Area-and-Severity Index (PASI) score was determined as suggested originally by Fredriksson and Pettersson [6]. Fifty-five age-matched males with minor dermatoses (scabies, dermatophytoses) were enrolled from the outpatient clinic after informed written consent as controls for serum sampling in a similar manner.

Venous blood (5ml) samples were collected after overnight fasting between 8.00 and 10.00 AM for complete blood count including platelets, fasting blood glucose, urea, creatinine, bilirubin, serum glutamic oxaloacetic transaminase and serum glutamic pyruvate transaminase, alkaline phosphatase and thyroid functions tests. Quantitative estimation for serum homocystiene vitamin B_{12} and folic acid levels was performed in institutional biochemistry laboratory by standard chemiluminescence enzyme immunoassay (CLIA) method [7] and as per manufacturer protocol using Immulite® ready to use *in-vitro* kits purchased from Siemens Healthcare, Diagnostic Products Ltd, United Kingdom. Results were analyzed using unpaired student's *t*-test and standard deviation for mean. A '*p*' value <0.05 calculated at 5% level (95% confidence limits) was considered statistically significant.

Ethics

This study was performed on human subjects; thus, all patients were aware of the presence of the study and they were fully informed about study parameters.

RESULTS

These 55 male patients aged between 22 and 66 years had 25 (45.5%) patients between 22 and 40 years and comprised the majority. Twenty-three (41.8%) patients were aged 41 - 60 years, and 7 (12.7%) patients were >60 years of age. They had psoriasis for 6 months to 20 years at the time of visit. In 20 (36.4%) patients, the psoriasis was present for >5 years while 35(63.6%) patients had the disease for <5 years. Body surface area involvement was <10% in 38 (69%), 10-20% in 10 (18.2%) and >20% in 7 (12.8%) patients, respectively. PASI score was <6 in 41 (70%), 6-12 in 10 (18.2%) patients and >12 in 4 (7.3%) patients, respectively. The controls comprised 55 males aged between 20-65 years.

Biochemical Parameters

None of the patients or controls showed any alteration in routine hemogram, serum biochemistry or thyroid function tests. Other studied biochemical parameters of 55 patients and 55 controls are tabulated (Table 1). Elevated homocystiene levels (normal 5-12 μmol/L) in the range of 12.8 to >50 μmol/L (mean 31.49 ± 9.99 μmol/L) were seen in all patients while in controls the values ranged between 5.1 and 22.3 μmol/L (mean 9.99 ±3.71 μmol/L). The difference was statistically significant when compared with controls. However, the elevated serum homocystiene levels did not vary with BSA/PASI score (Figs. 1a,b,c and 2a,b). The vitamin B_{12}

levels in patients ranged from <150 to 502 pg/ml (mean 230.74 ± 64.09 pg/ml) and were on the lower side of the normal range (174-878 pg/ml). Serum vitamin B_{12} measuring between <150 and 156 pg/ml were lower than normal in 6 (10.9%) patients and controls each. Mean serum folic acid levels in all the patients were 14.42 ± 5.21 ng/ml and ranged from 5.65 to >24 ng/ml (normal 3-17 ng/ml). The mean value of serum folic acid levels of >17ng/ml (17.83 - >24ng/ml) in 17 (30.9%) patients was above the normal range. The mean value of serum folic acid levels of controls was 13.51±4.64 ng/ml (range 5.9-25ng/ml). Overall, except for slightly elevated serum homocystiene levels (12.1-24 μmol/L) in 11 (22%) controls, all parameters were within normal range and the difference was not statistically significant (Table 2).

DISCUSSION

High plasma homocystiene is considered an independent risk factor for coronary artery disease, stroke, peripheral vascular disease and possibly Alzheimer's disease especially in patients with homocystienuria [8]. A non-linear and inverse association between plasma homocystiene concentration, vitamin B_{12} and plasma folate concentration has been well documented and attributable to either deficient absorption or excessive utilization of folic acid, vitamins B_6 and B_{12} [3]. All the 55 (100%) patients in our study had high serum homocystiene levels (mean 31.49 ±9.99 μmol/L, range 12.8 - >50 μmol/L) as compared to the controls (mean 9.99 ± 3.71 μmol/L, range 5.1-22.3 μmol/L) and the difference was statistically significant (p <0.05). The levels of serum vitamin B_{12} were at the lower levels (mean 217.7±46.22 pg/ml, range 150-310 pg/ml) of the normal in 26 (86.6%) patients while in 6 (10.9%) patients the values were lower (<174 pg/ml) than the normal.

Table 1: Biochemical parameters of patients and controls

Range	Patients (%) n=55	Controls (%) n=55
Serum homocystiene levels (μmol/L), normal 5-12 μmol/L		
0-12	0	44 (80)
12.1-24	12 (21.8)	11 (20)
24.1-36	27 (49.1)	0
36.1-48	12 (21.8)	0
>48	04 (7.3)	0
Serum vitamin B12 levels (pg/ml), normal 174-878 pg/ml		
1-173	6 (10.9)	6 (10.9)
173.1-275	38 (69.1)	38 (69.1)
275.1-374	9 (16.4)	7 (12.7)
374.1-474	2 (3.6)	4 (7.3)
Serum folic acid levels (ng/ml), normal 1.9-25 ng/ml		
3-10	14 (25.5)	15 (27.3)
10.1-17	24 (43.6)	33 (60)
>17	17 (30.9)	7 (12.7)

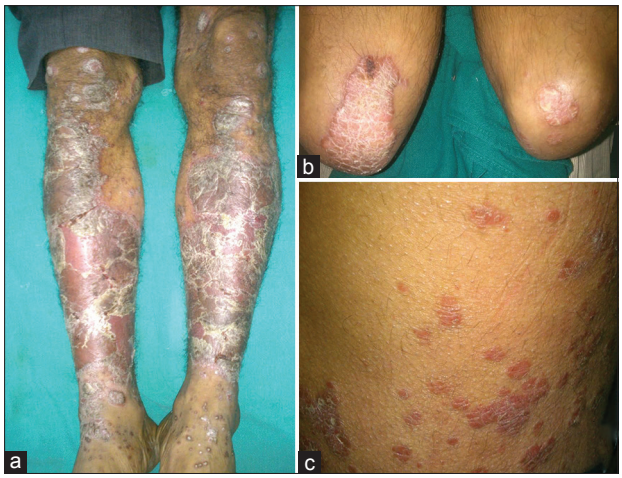

Figure 1: (a) A patient of psoriasis with BSA-30% and PASI 8.4 had Serum homocystiene 25.6μmol/L, Serum vitamin B_{12} 156pg/ml, and Serum folic acid 15.9ng/ml. (b and c) This patient had BSA-10%, and PASI 4.9, and Serum homocystiene 36 μmol/L, Serum vitamin B12 <150 pg/ml, and Serum folic acid 7.7ng/ml.

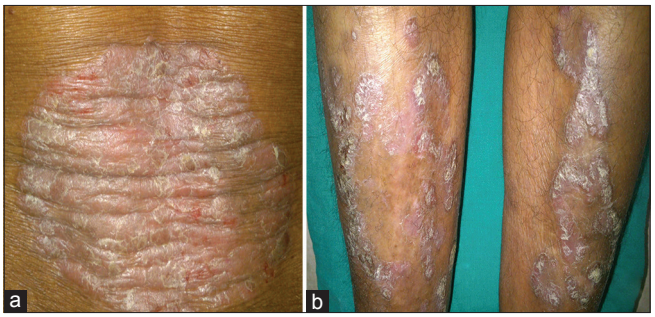

Figure 2: (a) A patient of psoriasis with BSA-5% and PASI 4 had Serum homocystiene >50 μmol/L, Serum vitamin B_{12} <150 pg/ml, and Serum folic acid >24ng/ml. (b) This patient had BSA-3% and PASI 4.1, and Serum homocystiene >50μmol/L, Serum vitamin B_{12} 156pg/ml, and Serum folic acid >24ng/ml.

Table 2: Significance of the results

	Serum homocystiene (N=5-12 μmol/L)		Serum vitamin B_{12} (N=174-878 pg/ml)		Serum folic acid (N=3-17 ng/ml)	
	Patients	Controls	Patients	Controls	Patients	Controls
Range	12.8- >50	5.1-22.3	150-502	150-513	5.65- >24	5.9-25
Mean	31.49±9.99	9.99±3.71	230.74±64.09	235.1±77.63	14.42±5.21	13.51±4.64
p value	<0.00001		0.357		0.166	
	Significant		Not significant		Not significant	

Note: p value<0.05 was considered statistically significant

The difference was not statistically significant when compared with controls. Serum folic acid levels varied between 5.65 and >24 ng/ml (mean 14.42±5.21 ng/ml) and 5.9 and 25 (mean 13.51±4.64 ng/ml) in all the patients and controls, respectively, and were within normal range. Brazzeli et al [9] also made similar observations in a cohort of 98 patients with chronic plaque psoriasis and 98 healthy controls. They observed significantly higher prevalence of hyperhomocystienemia and low serum vitamin B_{12} levels in psoriasis patients as compared to healthy controls but not for serum folic acid. In a similar study, Malerba et al [3] noted higher plasma homocystiene levels and lower folic acid levels in 40 chronic plaque psoriasis patients without known risk factors for acquired homocystienemia than 30 age-matched controls. Although the plasma homocystiene levels in patients with psoriasis also correlated directly with disease severity and inversely with folic acid levels, no abnormalities were detected in plasma vitamin B_6 and B_{12} levels. In a similar study by Cakmak et al [10] serum homocystiene levels inversely correlated with serum folic acid levels but not with serum vitamin B_{12} both in 70 patients with psoriasis and healthy controls. However, authors did not find any difference between their serum levels in patients and controls. Trends towards low serum folic acid and hyperhomocystienemia in patients with psoriasis were also observed by Tobin et al [11] but they did not study serum vitamin B_{12} in their patients. Our observations of hyperhomocystienemia, serum vitamin B_{12} at lower end of the normal and variable serum folic acid levels in all patients are suggestive of some significance of hyperhomocystienemia and low serum vitamin B_{12} and folic acid levels. However, a possibility of avoiding non-vegetarian food altogether by these patients subsequent to development of their disease leading to serum vitamin B_{12} at lower end of the normal range cannot be ruled out entirely. Hyperhomocystienemia in patients with psoriasis as in our 100% patients has been documented previously [3,9-11]. Contrarily, Uslu et al [12] in a recent study of 50 patients with psoriasis and 48 healthy controls found no statistically significant differences between the patients and the control group in terms of age, sex, body mass index (BMI), plasma homocystiene folic acid, and vitamin B_{12}. They attributed this variation to the differences in the genetic pool of the studied Turkish population.

CONCLUSIONS

Hyperhomocystienemia, lower than normal levels of vitamin B_{12} and variable serum folic acid levels in all our patients suggests their possible dysregulation in psoriasis patients. Implications of hyperhomocystienemia for cardiovascular comorbidities in psoriasis patients and whether supplementing vitamin B_{12} and folic acid will prevent comorbidities by normalizing homocystiene metabolism needs further evaluation by large well designed studies in different ethnicities.

Statement of Human and Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statement of Informed Consent

Informed consent was obtained from all patients for being included in the study.

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