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Original Research Article

Estimation of serum levels of Parathyroid hormone, Vitamin D, Calcium and Phosphorus to study their association with age, gender, disease duration, and severity of chronic plaque psoriasis: Results of a case control study

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ABSTRACT

Background: Psoriasis is a chronic inflammatory disease characterized by rapid turnover of epidermal keratinocytes; presenting clinically as erythema, induration, and scaling Parathyroid hormone (PTH) is secreted by parathyroid glands and its elevated levels may be seen in psoriasis and several other disorders of keratinization. PTH/PTH-related peptide receptors are present in dermal fibroblasts & regulate proliferation and maturation of fibroblasts and keratinocytes. Release of PTH is under the feedback regulation of serum Ca2+, Vit.D_3 and PO_4.

Objectives: To assess the Parathyroid hormone levels in patients of Psoriasis along with Vitamin D, Serum Calcium and Serum Phosphorus levels.

Materials and Methods: Out of the 50 cases aged between 18 and 91 years majority of patients i.e 22 (44%) were in the age group of 18-40 years followed by 20 (40%) patients in 41-60 years age group. Eight (16%) patients were above >60 years. 32 (64%) patients who had psoriasis for less than ≤60 months while 18 (36%) patients had psoriasis for more than >60 months Serum PTH (normal 10–65pg/ml), Vitamin D(normal 20-50(ng/ml), calcium (normal 9-11mg/dl and phosphorus (normal 2.5-4.5mg/dl) levels were measured after overnight fasting.

Results: A total of 50 psoriasis patients along with 50 non-psoriatic age and sex matched controls were recruited for the study. There were 28 males and 22 females in the patient group aged between 18 and 91 years (mean±SD 43.52±16.23 years). The mean age of controls was 47.12±16.29 years with 19(38%) subjects in 18-40 years age group and 21(42%) in 41-60 years age group. Amongst the cases, there were 10(20%) patients who had abnormal PTH levels (six had elevated levels of PTH and four patients with low PTH levels) while 40(80%) had normal levels (mean±SD 47.97±25.46 pg/ml).

Conclusion: The interpretation of our observation remains complex and any conclusion for the significance of these biochemical abnormalities remain conjectural. Moreover, association of psoriasis with abnormal biochemical parameters remains debatable in view of limited number of studies whether abnormal biochemical parameters can serve as markers of severity and their correction can lead to improvement in the disease needs confirmation with more well designed experimental and prospective clinical studies.

1. Introduction

Psoriasis' is a hyperproliferative skin disease which is characterized by microscopic (histological) and corresponding macroscopic (clinical) skin alterations

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in the form of well defined erythematous, indurated papulo-plaques with micaceous (silvery white mica like) scales particularly over the extensor surfaces and the scalp.[1] It is a well known fact that psoriasis worsens in life stages accompanied by hormonal disturbances (puberty and menopause) and during pregnancy. Even though the sex hormones and prolactin have a major role in psoriasis pathogenicity, there are a lot of other hormones which can influence psoriasis and its clinical manifestations i.e. glucocorticoids, epinephrine, thyroid hormones, parathyroid hormone and insulin.[2]

The sensitive process of calcium and phosphate homeostasis in the blood is maintained primarily by an adequately functioning parathyroid gland. The parathyroid gland secretes parathyroid hormone (PTH), in response to low calcium levels in the blood. PTH is a polypeptide that is synthesized and cleaved into an active form within the parathyroid gland.

PTH facilitates the synthesis of active vitamin D, calcitriol (1,25-dihydroxycholecalciferol, or vitamin D3) in the kidneys. In conjunction with calcitriol, PTH regulates calcium and phosphate.[3] A few studies have demonstrated an elevation of serum PTH levels in diseases like psoriasis and other diseases of keratinization of unknown etiology. Also in some cases, generalized pustular psoriasis has been associated with hypocalcemia and hypoparathyroidism.[4]

Vitamin D3 has multiple functions in the skin as it inhibits proliferation and promotes the differentiation of keratinocytes, modulates the humoral and cellular immune system and also participates in the hair cycle. These actions are due to the binding of vitamin D3 in their receptors present in keratinocytes. 25-hydroxy vitamin D is converted into its active form 1,25-hydroxy vitamin D3 by the kidneys under the influence of parathyroid hormone. The importance of vitamin D3 in psoriasis can be demonstrated by a good therapeutic response to vitamin D3 analogues (deltanoids) which are used topically in the treatment of this disease. Studies have shown that vitamin D can act on the immune system by inhibiting important cytokines for Th1 and Th17 differentiation that are one of the most important pathways in the pathophysiology of psoriasis.[5,6]

Therefore, in view of the paucity of data on correlation between psoriasis and above mentioned biochemical parameters, we intended to carry out this study to assess the levels of Parathyroid hormone along with serum Calcium, Phosphorus and Vitamin D3 in patients of Psoriasis.

2. Materials and Methods

This case control study was conducted from June 2021 to May 2022 after approval from Institutional Ethics Committee & consent was obtained from each patient

2.1. Inclusion criteria

All patients >18 years of age and having chronic plaque psoriasis for at least 6 months.

2.2. Exclusion criteria

1. Known case of Hypo-parathyroidism or Hyper-parathyroidism.
2. Pregnancy & Lactation.
3. Patients having Chronic Kidney Disease.
4. Patients on drugs affecting the parathyroid metabolism.
5. Post Thyroidectomy patients.
6. Patient having sepsis.
7. Patients having deranged RFT's, LFT's, TFT's.

The demographic profile & clinical history of the psoriatic patients was recorded. Equal number of healthy, age- and sex-matched controls were taken. Severity of psoriasis was defined as mild, moderate or severe as shown in the table

Table 1: PASI grading

Severity	Psoriasis area severity index
Mild	<6
Moderate	6-12
Severe	>12

3. Results

A total of 50 psoriasis patients along with 50 non-psoriatic age and sex matched controls were recruited for the study. 32 (64%) patients who had psoriasis for less than ≤60 months while 18 (36%) patients had psoriasis for more than >60 months.

Table 2: Age and gender distribution

		Case	Control	P Value
Age Group (Years)	18-40	22	19	0.792
	41-60	20	21	
	>60	8	10	
Mean age		43.52±16.23	47.12±16.29	
Sex	Female	22	27	0.212
	Male	28	23	

Amongst the cases, there were 10(20%) patients who had abnormal PTH levels (six had elevated levels of PTH and four patients with low PTH levels) while 40(80%) had normal levels (mean±SD 47.97±25.46 pg/ml). Amongst the controls, none had the abnormal parathyroid hormone levels (mean±SD 26.74±11.12 pg/ml. The mean PTH levels in relation to BSA were 47.22±20.13 in mild disease (≤10% BSA), 51.37±46.72 in moderate disease (>10-20% BSA) and 47.65±20.59 in patients with severe disease (>20%

Table 3: BSA & PASI distribution

		n =50 (%)
Total Duration (months)	≤60 months	32 (64%)
	>60 months	18 (36%)
Severity (BSA)	Mild (≤10%)	32(64%)
	Moderate (>10-20%)	8(16%)
	Severe (>20%)	10(20%)
Severity (PASI score)	Mild (≤6)	37 (74%)
	Moderate (>6-12)	9 (18%)
	Severe (>12)	4 (8%)

of BSA). The mean PTH levels in relation to PASI were 46.55±21.04 in score of ≤6, 52.1±40.77 in >6-12 score and 51.85±27.39 in patients with a score of >12. There was no statistically significant difference in mean PTH levels in relation BSA & PASI.

Amongst the cases, there were 10 (20%) patients who had abnormal calcium levels while 40 (80%) had normal levels (mean±SD 9.31±0.72 mg/dl). Amongst the controls, 39(78%) had abnormal calcium levels (mean±SD 8.3±0.88 mg/dl). There was significant difference between the groups in terms of calcium levels (p value <0.001). The mean calcium levels were 9.25±0.68, 9.23±0.88 and 9.59±0.73 mg/dl in ≤10%, >10-20% and >20% BSA involved respectively with no statistically significant difference (p value of 0.419).

Although, no statistically significant difference was observed in mean calcium levels in relation to PASI severity grading however, the calcium levels were increasing (though in normal range) in relation to PASI score with values as 9.2±0.68, 9.53±0.86 and 9.82±0.59 mg/dl in mild , moderate & severe disease respectively.

There were 22 (44%) patients amongst the cases who had abnormal vitamin D3 levels (mean±SD 23.93±16.28 ng/ml) while amongst the controls, 20(40%) patients had abnormal vitamin D3 levels (mean±SD 28.36±15.53 ng/ml). There was no statistically significant difference between the groups in terms of vitamin D3 levels (p value =0.420). No statistically significant difference was observed in mean vitamin D3 levels in relation to PASI severity grading & BSA involvement with p value of 0.771.

20 (40%) patients amongst the cases and 32 (64%) patients amongst the controls had abnormal phosphorus levels with statistically difference between both the groups (p value= 0.014). The mean phosphorus levels were significantly higher in the controls (4.6±2.4 mg/dl) than that in cases (3.5±0.61 mg/dl) with a p value of 0.003.

However, No statistically significant difference was observed in mean levels of phosphorus in relation to BSA involvement and PASI (p value 0.586).

Table 4: Distribution of mean parameters among cases and controls

.	Case	Control	p value
PTH	47.97±25.46	26.74±11.12	<0.001
Ca^{2+}	9.31±0.72	8.3±0.88	<0.001
Vit D_3	23.93±16.28	28.36±15.53	0.168
PO_4	3.5±0.61	4.6±2.4	0.003

4. Discussion

The study comprised 28 males and 22 females (M:F 1.27:1) with majority 22 (44%) patients, being ≤ 40 years of age and 20 (40%) patients were aged from 40 -60 years. Only 8 (16%) patients were aged ≥60 years. Thirty two patients (64%) had the disease for less than 5 years (60months) while eighteen (36%) were suffering from psoriasis for more than 5 years. These features were conforming to the established clinico-epidemiological profile of psoriasis; having a bimodal age of onset, presenting before the age of 40 years (peak at 16-22 years) approximately in 75% patients and another peak at 55-60 years of age without any predilection for gender with a characteristic chronic relapsing and remitting course.[7] In our study, 32 (64%) patients were having ≤10% BSA and 10(20%) with >20% BSA involvement and PASI score of ≤6 was observed in 37(74%) cases while only 4(8%) had a PASI score of >12.

It is a known fact that hormones can influence psoriasis and its clinical manifestations i.e. glucocorticoids, epinephrine, thyroid hormones, parathyroid hormone and others. Furthermore, abnormalities in the serum levels of calcium, phosphorus and vitamin D3 in association with psoriasis has also been mentioned in the literature.[2] The increased serum levels of PTH in some patients with disorders of keratinization has been described in the past.[8] The studies have documented that a combination of different factors (low vitamin D levels, loss of calcium through the skin and therapy with retinoids) may stimulate secretion of PTH and hence the exacerbation of the disease.[9,10] Researchers in the past have demonstrated that hypocalcaemia triggers psoriasis and in post parathyroidectomy patients with hypocalcemia, psoriasis intensification have been suggested as a manifestation of hypoparathyroidism.[8] The importance of vitamin D3 in psoriasis can be demonstrated by a good therapeutic response to vitamin D analogues used topically in the treatment of the disease.[11] Recent studies have shown that vitamin D3 can act on the immune system by inhibiting important cytokines for Th1 and Th17 differentiation which are the key pathways implicated in the pathophysiology.[12] In the present study, ten cases were found to have abnormal levels of PTH and a positive correlation was found between values of PTH & serum calcium. We detected increased mean serum PTH levels in psoriasis patients (47.97±25.46 pg/ml) as compared with the control group (26.74±11.12

pg/ml). Similar results were obtained by Regana MS et al[13] in which they observed mean PTH levels of 42.3±1.8 pg/ml in psoriasis cases and 23.4±9 pg/ml in controls. However, Martinez-Lopez A et al[14] did not find significant difference between the mean PTH levels in cases and in controls (47.00±18.45 pg/ml and 46.52±15.28 pg/ml respectively). Out of the ten cases, six had elevated levels of PTH along with deficiency in either serum Ca2, PO4 or Vit D3 levels, which was consistent with a similar study by Regana MS et al.[13] Exacerbation of psoriasis has been reported with hypo and hyper-parathyroidism in the literature.[13,15] However none of our patients with abnormal PTH levels had severe disease. Abnormal PTH levels in disorders of keratinization is attributed to decreased levels of vitamin D3 and loss of calcium through skin shedding in patients with extensive disease.[9] The mean PTH levels in relation to PASI were 46.55±21.04 pg/ml in PASI score of ≤6, 52.1±40.77 pg/ml in >6-12 PASI score and 51.85±27.39 pg/ml in patients with a PASI score of >12 and showed positive correlation with PASI but the relation was statistically insignificant (p value 0.896). Based on our findings, we suggest that elevation of serum PTH levels may reflect disease activity but no definite conclusions can be drawn.

Psoriasis per se has been found to be aggravated with the decrease in the serum calcium levels. This is because the calcium has an important role in the regulation of keratinocytes and cell adhesion molecules which can be damaged by hypocalcemia.[16] We found 10 patients and 39 controls with abnormal calcium levels with mean serum values of cases being 9.31±0.72 mg/dl and controls being 8.3±0.88 mg/dl with p value <0.001. Ramteke P et al[17] observed the mean serum calcium levels among cases was 8.64±1.59 mg/dl while among controls it was higher (9.69±0.59 mg/dl) with statistically significant difference. Qadim et al[18] and carried out a similar study where they compared 98 psoriasis cases with 100 controls and the prevalence of hypocalcemia was 37.2% in the cases compared to 9% among the controls. Morimoto S et al[19] observed serum calcium levels was similar in both the groups (9.1±0.4mg /dl among psoriatic patients and 9.3±0.4 mg/dl among controls). Though hypocalcemia is a well known triggering factor for psoriasis,[16] no such correlation was found between the disease severity and calcium levels in our study.

Vitamin D3 is known to regulate keratinocyte growth and differentiation by acting on VDR as it influences the immune functions of dendritic cells and T lymphocytes, which play a key role in the pathogenesis of psoriasis.[20,21] Vitamin D3 deficiency is ubiquitous in epidemic proportions all over the Indian subcontinent, with a approximate prevalence of 70%-100% in the general population[22]. Likewise, in our study 40% of the controls had vitamin D deficiency in comparison to 44% of the psoriatic cases. We observed that mean vitamin D3 level in cases was lower than that of controls with values as 23.93±16.28 ng/ml and 28.36±15.53 ng/ml respectively. We also observed a high prevalence of vitamin D3 deficiency among patients with psoriasis in our study. However, we did not observe significant difference in mean vitamin D3 levels in relation to PASI severity grading & BSA involvement (p value 0.771).

Phosphate is found in ATP, cAMP, many proteins, and other vital compounds in the body. Phosphorylation and dephosphorylation of proteins are involved in the regulation of cell function. Calcium and phosphate metabolism are closely regulated as many stimuli that increases calcium absorption including 1,25-dihydrocholecalciferol also increases phosphorus absorption. Serum calcium and phosphorus levels are inversely related to each other.[23] In a study by Ramteke P et al,[17] the mean serum phosphorus level among psoriatic cases was found to be higher (4.57 ± 1.03 mg/dl) than controls (3.92±0.79 mg/dl). In another study by Morimoto S et al[19] they observed serum phosphorus levels to be similar in both the groups (3.8±0.4 mg /dl among psoriatic patients and 3.7± 0.4 mg/dl among healthy controls). In our study we observed the mean phosphorus levels were significantly higher in the control group (4.6±2.4 mg/dl) than in cases (3.5±0.61 mg/dl). The exact mechanism behind this finding is not known however there is an inverse relationship between calcium and phosphorus which may conclude our results.

On running a linear correlation test of PASI with these 4 biochemical parameters, we observed a weak association of PASI with PTH, Ca2, Vit D3 and PO4 levels with correlation co-efficient values of .019, .290, .044, .046 respectively. Thus the interpretation of our observation remains complex and any conclusion for the significance of these biochemical abnormalities remain conjectural. Moreover, association of psoriasis with abnormal biochemical parameters remains debatable in view of limited number of studies whether abnormal biochemical parameters can serve as markers of severity and their correction can lead to improvement in the disease needs confirmation with more well designed experimental and prospective clinical studies.

5. Conclusion

The interpretation of our observation remains complex and any conclusion for the significance of these biochemical abnormalities remain conjectural. Moreover, association of psoriasis with abnormal biochemical parameters remains debatable in view of limited number of studies whether abnormal biochemical parameters can serve as markers of severity and their correction can lead to improvement in the disease needs confirmation with more well designed experimental and prospective clinical studies.

6. Source of Funding

None.

7. Conflict of Interest

None.

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