International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

The Prevalence of Hypocalcaemia and Streptococcal Infection in Psoriasis Vulgaris

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Keywords: Psoriasis Vulgaris, Streptococcal Infection, Hypocalcaemia

1. Introduction

Psoriasis is a common, chronic, disfiguring, inflammatory and proliferative condition of the skin in which both genetic and environmental influences have a critical role[1].

Psoriasis can be classified as morphological variants and on location of the lesions. Morphological variants are Chronic stable plaque psoriasis, guttate psoriasis, pustular psoriasis, erythrodermic psoriasis and psoriatic arthritis[2] . Based on location they are classified into scalp psoriasis, palmoplantar psoriasis, inverse psoriasis and nail psoriasis. Out of the different clinical presentations of psoriasis, psoriasis vulgaris is the commonest variant, which is also known as chronic stable plaque psoriasis. The most characteristic lesions consist of red, scaly, sharply demarcated, indurated plaques present particularly over the extensor surfaces and scalp. The disease is enormously variable in duration, with periodicity of flares and extent[2].

Psoriasis is a chronic, meaning lifelong, condition because there is currently no cure. Controlling the signs and symptoms typically requires lifelong therapy[3] and treatment depends on the severity and type of psoriasis[4-5].

The incidence of psoriasis is universal in occurrence [6]. Psoriasis occurs almost equally in males and females[7]. Recent studies show that there may be an ethnic link. It seems that psoriasis is most common in Caucasians and slightly less common in African Americans. In India the the prevalence of psoriasis is approximately between 0. 5 to 1. 5%[8] .

The exact aetiology and pathogenesis of psoriasis is not yet known. Various studies have concluded that it is a multifactorial disorder where multiple genes are involved which are likely to interact with each other as well as with environmental trigger factors[9] . Studies have shown a genetic predisposition to psoriasis while many environmental factors, infection, metabolic factors, sunlight, stress, various drugs, trauma, smoking seems to play an important role in initiation and exacerbation of psoriasis. Psoriasis at the site of injury is well known (Koebner phenomenon), while HIV infection and alcoholism seems to exacerbate the existing disease [2].

Streptococcal infection is strongly associated with acute guttate psoriasis and there is strong evidence to suggest that they may be important in chronic stable plaque psoriasis also[10-13]. Acute episodes of guttate psoriasis is much more common in individuals with family history of plaque psoriasis[14] . One-third of cases of guttate psoriasis progress to the chronic plaque form[15] . Besides guttate psoriasis and chronic stable plaque psoriasis share strong HLA associations, particularly with HLA-Cw6[10-13] .

Hypocalcaemia has been reported to occur in severe forms of psoriasis, particularly generalized pustular psoriasis and it may be a predictor of poor outcome [16-22]. The relationship between generalized pustular psoriasis and psoriasis vulgaris is clear because patients may have phases of ordinary psoriasis before or after generalized pustular form. Family data are similar to those found in psoriasis vulgaris. It can precipitate generalized pustular psoriasis in susceptible persons and has been reported to resolve when treated with oral calcium, vitamin D or its analogues[23-25]. Even in laboratory findings plasma albumin, zinc and calcium levels may be abnormally low[16-17] . Generalized pustular psoriasis of pregnancy which many authors consider as a separate entity while some authors don't, also has hypocalcaemia in laboratory findings[18, 22] .

We did this study to find out if streptococcal infection and hypocalcaemia is prevalent in psoriasis vulgaris as not many studies were done in the past about this topic and from literature it is evident that both these factors play an important role in the precipitation and exacerbation of psoriasis vulgaris.

2. Aims and Objectives

1) To study the prevalence of streptococcal infection in psoriasis vulgaris.
2) To study the prevalence of hypocalcaemia in psoriasis vulgaris.

Research Hypothesis

1) Streptococcal infection could be present in psoriasis vulgaris.
2) Hypocalcaemia could be present in psoriasis vulgaris.

Patients and Methods

Study involves - Humans
No: of groups - One

Inclusion Criteria

- All newly diagnosed untreated cases of psoriasis vulgaris.
- All cases presenting with a relapse of psoriasis vulgaris.

Exclusion Criteria

- Clinical variants of psoriasis other than psoriasis vulgaris
- Patient with any systemic disease or malignancy in the past or present.
- Any patient on antibiotic therapy or calcium supplementation at the time of consultation.
- Women who have attained menopause.

Period of study and sample size:

The study was conducted for one year from December 2007 to November 2008 on all psoriatic patients who came to the Dermatology O. P. D of M. G. M. C & R. I, who fullfilled the above mentioned inclusion criteria.

Parameters Studied

- ASO titre
- Throat swab
- Serum calcium
- Serum albumin

3. Brief Procedure

The demographic details of all patients included in the study were recorded along with the data regarding the disease. If the patient was presenting for the first time with psoriasis vulgaris (as a new case), the duration of the presenting complaints was recorded and if it was recurring, it was mentioned only as relapse. Percentage of body surface area involved was recorded using Psoriasis area severity index (PASI) score at the time of their first visit. The study was approved by the bioethic committee of Mahatma Gandhi Medical College and Research Institute and all participants who gave written informed consent was enrolled in our study.

Initially all participants were examined, their past medical history obtained and all those who fitted into our inclusion criteria, ASO titre and throat swab culture, serum calcium and serum albumin levels were done on their first visit.

Two sterile throat swabs were taken and immediately inoculated in blood agar, maconkey agar and chocolate agar. One of the swabs was gram stained. Incubation was done with 5-10% Carbondioxide and identification was done by colony morphology, gram smear and bacitracin sensitivity.

A streptococcal antibody test, namely antistreptolysin O (ASO) was also done as elevated or rising antistreptococcal antibody titers provide reliable confirmation of a recent streptococcal infection.

Either a positive culture for streptococci or an ASO titre of greater than 200iu/ml (upper limit of normal, 200 IU/mL) in patients, were considered as positive results for streptococcal infection.

Patients with serum calcium level of less than 8. 62mg/dl were considered to have hypocalcaemia. It was found out by calcium arsenazo method using calcium arsenazo reagent (Normal range 8. 62-10. 22mg/dl). Serum albumin level was also found out as low serum albumin levels could itself cause hypocalcaemia. It was found out using albumin bromocresol green method using bromocresol green reagent (Normal range 3. 5-5. 2g/dl).

Pateints found to have streptococcal infection were treated with appropriate antibiotics and patients with hypocalcaemia were given calcium supplementation. With the help of the data collected the prevalence of streptococcal infection and hypocalcaemia in psoriasis vulgaris were determined and expressed in terms of percentage.

4. Results

The results obtained were as follows:

Total sample size was fifty five. Male subjects numbered 34 while female subjects were 21.

The mean age of the patients was 39. 9years (range 8-70). Patients were widely distributed over various age groups and the majority of patients were in the age group of 31-40 years accounting to 23 in number (41. 81%), while 41-50 years comprised the second largest group accounting to 17 in number (30. 9%).

38 patients were above the age of 35 years (69. 1%).

(The age distribution is shown in Bar diagram-Fig. No. 1)

29 cases were newly diagnosed cases of psoriasis while 26 cases were relapses. (The age distribution of all the newly diagnosed cases is shown in Bar diagram-Fig. No. 2).

The mean PASI score of the patient's was17. 02 (range 2. 1-56. 2).

Total number of patients found to have streptococcal infection were 12 (21. 82%).

The number of patients in whom we were able to culture β-haemolytic streptococci were 9 (16. 36%) .

Total number of patients who had a high titer of ASO reactivity (more than 200 IU/ml) were 10 (18. 18%).

7 patients (12. 73%) had both throat swab culture positive & high ASO titer while 2 patients (3. 64%) had only throat swab culture positive and 3 patients (5. 45%) had only high ASO titer. (The age distribution and number of patients having streptococcal infection is shown in Bar diagram-Fig. No. 3)

A total of 28 (50. 91%) patients were found to have hypocalcaemia. (normal serum calcium level is 8. 62-10. 22 mg/dl in adults)

20 patients (36. 36%) had hypocalcaemia with normal serum albumin levels. (Normal serum albumin level is 3. 5-5. 2g/dl in adults)

8 patients (14.55%) had both hypocalcaemia and hypoalbuminemia.

The total number of patients with hypoalbuminemia were 8 (14. 55%) while none of the patients had only hypoalbuminemia with normal serum calcium.

In 28. 57%, which accounts to 8 out of 28 hypocalcaemic patients, low serum albumin levels were noted. (The age distribution and number of patients having hypocalcaemia is shown in Bar diagram-Fig. No. 4) Interestingly 7 patients (12. 72%) had both hypocalcaemia and streptococcal infection while 22 patients (40%) had either streptococcal infection or hypocalcaemia.

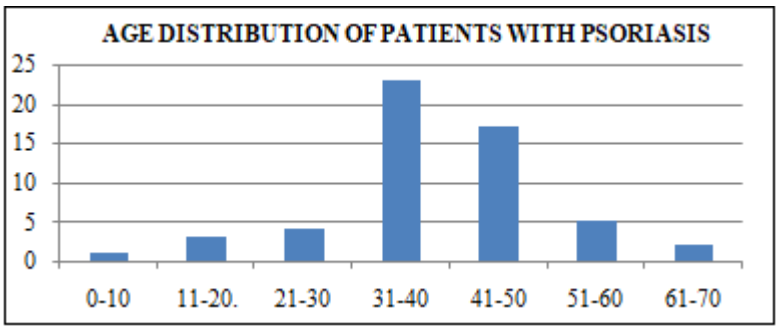


Figure 1

X axis indicates the age group distribution of patients
Y axis the number of patients.
Age group of 31-40 had the maximum number of patients (23 in number)

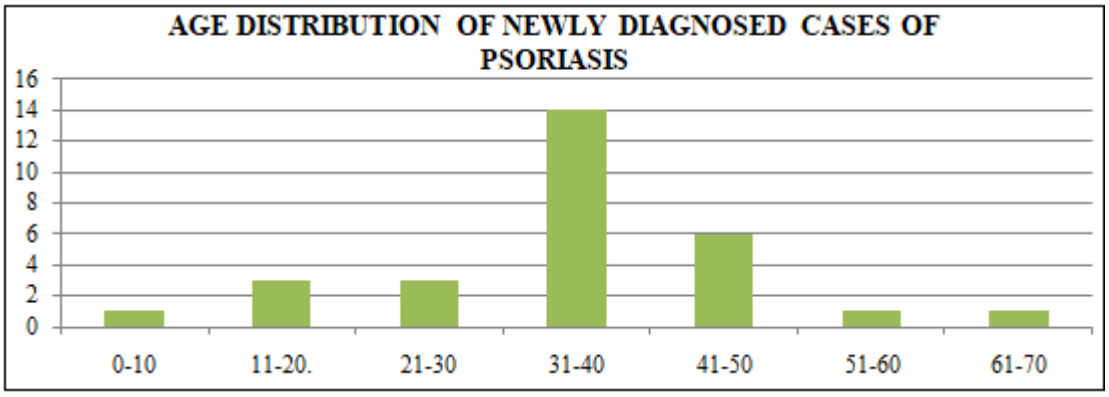


Figure 2

X axis indicates the age group distribution of all newly diagnosed cases of psoriasis
Y axis indicates the number of patients.
Age group of 31-40 had maximum number of patients (14 in number)

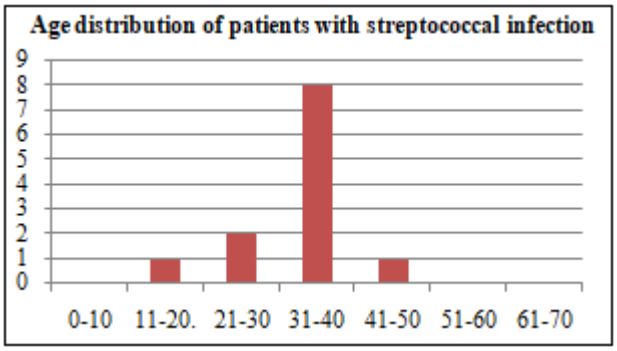


Figure 3

X axis indicates the age group distribution of patients
Y axis indicates the number of patients
The age group of 31-40 had the maximum number of patients (8 in number)

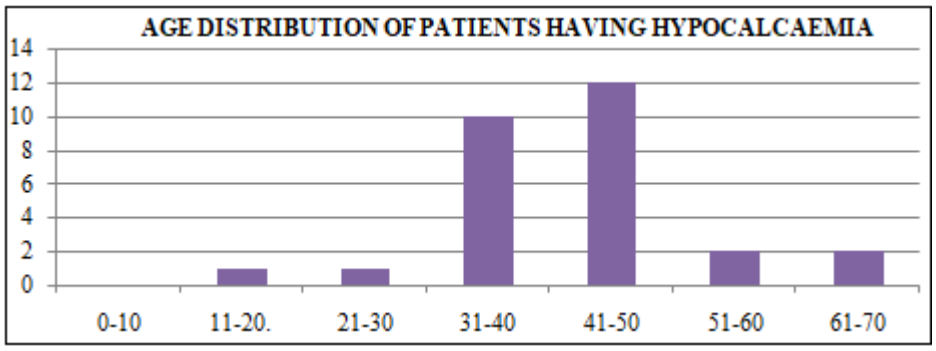
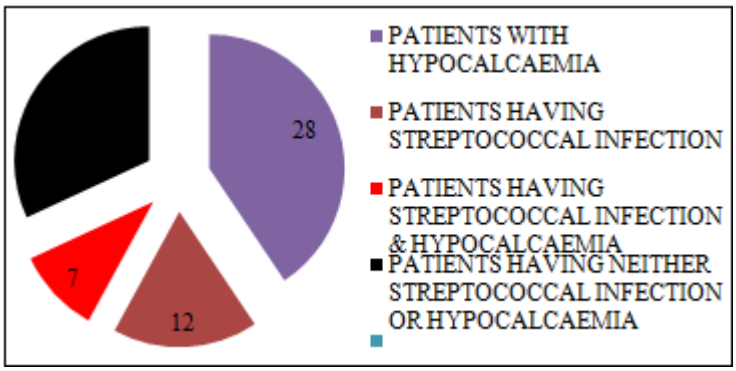


Figure 4

X axis indicates the age group distribution of patients
Y axis indicates the number of patients
The age group of 41-50 had the maximum number of patients (12 in number)



An Exploded Pie Diagram- Figure 5

Result of our study
8 patients had hypocalcaemia
12 patients had streptococcal infection
7 patients had streptococcal infection and hypocalcaemia
22 patients had either streptococcal infection or hypocalcaemia

5. Discussion

This is to our knowledge the first prevalence study on streptococcal infection and hypocalcaemia in psoriasis vulgaris, conducted in India. Very few studies have been done regarding this topic internationally too.

Fifty five patients were investigated in our study. We had included all newly diagnosed cases of psoriasis vulgaris or relapse of psoriasis vulgaris and excluded other clinical variants of psoriasis. Patient with any systemic disease or malignancy in the past or present were also excluded from our study, along with woman who had attained menopause and patients on any antibiotic therapy or calcium supplementation at the time of consultation as it would have hindered with our results.

The age group of the involved subjects showed that majority of our patients were above 35 years of age (38 patients which was 69. 1%). The age group of 31-40 had the maximum amount of patients accounting to 23 in number. (The age distribution is shown in Bar diagram-Fig. No. 1)

The youngest patient in our study was 8 years old and the oldest was 70 years old. The mean age of our patient was 39. 9 years and the mean PASI score was 17. 02.

In a similar study done by Gudjonsson et al[13, 39], the mean age of patients was 46. 7 years (range 5-82). Our study and Gudjonsson et al [13, 39], had similarity in the fact that patients who had psoriasis were more in the age group above 35 years. Our study showed almost 70% of our patients were above 35 years of age while their study had about 80% patients above 35 years of age. The PASI score varied drastically at the time recruitment of the patients into our study and their study.

In another similar study conducted by Mallbris et al[40], the age of onset ranged from 14-84 years with the mean age of 44 for plaque psoriasis. This matched more with our data. The mean PASI score in his study at the time of recruitment of patients was 3. 7 which was again very different from our mean PASI score.

In a study conducted in United Kingdom by Nevitt et al[104], the mean age of onset was 33 years, while in a large study reported in China, the average age of onset was 36years[33] .

A study conducted in North India by Kaur et al [105] reported the mean age of onset was higher for males than females (37 vs 29 years). In another study done by Bedi et al [106] in Delhi and surrounding areas, which was done over a span of 5 years and 530 patients, he reported 60% patients had an onset of psoriasis before the age of 30 and 86% before the age of 40.

In another large study done by Gelfand et al [107] in United Kingdom on 114521 subjects with psoriasis, he reported that

psoriasis peaks in young adults and gradually increases aged 30 to 69 and then significantly declines.

The average mean age of patients in our study was similar to various studies mentioned above. Gender difference was also quite apparent. In some studies the subjects were mostly men while in others there was female predominace. In the study done by Mallbris et al[40], there was a female predominance (54%:46%). In the study conducted by Bedi et al[106] there was a male predominace (2. 4:1). In the study conducted by Gelfand et al [107], he reported that the prevalence of psoriasis increases more rapidly in female patients compared to male patients in the age group less than 20 years and thereafter the prevalence is similar by sex as the population ages.

In our study we had male predominance (34:21 which is 62%:38%). In the 29 newly diagnosed cases of psoriasis, 14 of them belonged to the age group of 31-40 in which 8 of them were males while 6 of them were females. The age group of 41-50 had 6 new cases of psoriasis and this included 3males and 3 females. (The age distribution is shown in Bar diagram-Fig. No. 2).

Since there is no evidence that the disease is phenotypically different between sexes and various studies have shown various results depending on the sampling techniques used, psoriasis is considered to affect both males and females equally [26-38]. The fact that the state where my study was done has a male predominace over females in the general population could be the reason why such a result was found. Since our study includes two parameters, we have discussed both of them separately.

Prevalence of Streptococcal infection:
Throat cultures are the conventional method for establishing the diagnosis of streptococcal infection. In an untreated patient with streptococcal pharyngitis, a properly obtained throat swab vigorously swabbing both tonsils and posterior pharynx, when cultured is almost always positive. Unfortunately, the culture does not reliably distinguish between acute streptococcal infections and streptococcal carriers with concomitant viral infections. Acute pharyngitis is more frequently caused by viruses than by bacteria, and adenovirus infections frequently give rise to exudative pharyngitis and thus may closely mimic streptococcal sore throat. Furthermore, influenza and parainfluenza viruses may also simulate streptococcal pharyngitis. Since we wanted to find out the prevalence of streptococcal infection in psoriasis vulgaris we also did a streptococcal antibody test, namely antistreptolysin O (ASO) as an elevated or rising antistreptococcal antibody titers provide reliable confirmation of a recent streptococcal infection. Elevated titers may persist for several weeks to a few months and may rise and fall more rapidly too.

Gudjonsson et al[13, 39] in his study isolated 19 positive throat swab cultures for β-haemolytic streptococci from 208 patients, which was 9. 1%. Mallbris et al[40] isolated 31 positive throat swab cultures for β-haemolytic streptococcus pyogenus from 439 patients (7%).

Telfer et al[10] isolated Streptococcus pyogenes from 19 (17%) of all 111 patients (9 of 34[26%] with acute guttate psoriasis, four of 30[13%] with guttate exacerbations of chronic psoriasis, and five of 37[14%] patients with chronic psoriasis). Studies done by Gudjonsson et al [13] and Mallbris et al[40] did not do any streptococcal antibody test for evidence of recent streptococcal infection unlike our study while Telfer et al[10] found Serologic evidence of recent streptococcal infection was present in 19 of 33 (58%) patients with acute guttate psoriasis compared with 7 of 27 (26%) patients with guttate exacerbations of chronic psoriasis and 1 of 12 (8%) patients with chronic psoriasis.

In a study done by Tervaert et al[11], they had 20-30% positive throat cultures for β-haemolytic streptococci, while 25-30% had raised antistreptolysin O titres.

In our study which had 55 cases, 12 of them (21. 82%) were found to have streptococcal infection. This included patients who had positive throat swab culture or high and reactive ASO titer (more than 200 IU/ml). The number of patients in whom we were able to culture beta haemolytic streptococci were 9 (16. 36%) and the total number of patients who had a high ASO reactive titer were 10 (18. 18%). 7 patients (12. 73%) had both throat swab culture positive & high ASO reactive titer while 2 patients (3. 64%) had only throat swab culture positive and 3 patients (5. 45%) had only high ASO reactive titer. Majority of our patients (8 of them [67%]) having streptococcal infection belonged to the age group of 31-40, 8patients . (The age distribution and number of patients having streptococcal infection is shown in Bar diagram-Fig. No. 3).

Our study had almost similar percentage of positive throat swab isolation of β-haemolytic streptococcus pyogenus in chronic plague psoriasis to the study conducted by Telfer et al [10] [16% and 14%].

This could also be due to the fact that the study conducted by Telfer et al [10] and our study had both small sample size while Gudjonsson et al [13] and Mallbris et al[40] had larger sample size.

All bacterial strains isolated from the patients were β-haemolytic streptococcus pyogenus in our study as well as all the above mentioned other studies.

Our study also found out that streptococcal infection could be prevalent in psoriasis vulgaris, similar to the various literature reviewed al [41-88] and the studies with which we had compared our study. It still remains unclear exactly how streptococcal infection influences psoriasis however increased frequency of throat infections in patients with psoriasis especially with streptococcus pyogenus suggests that these individuals may have an abnormal defence mechanism confined to their tonsils as there is no evidence that they have increased susceptibility to streptococcal infections elsewhere.

From the results we got, we concluded that we agree with the research hypothesis that streptococcal infection is prevalent in psoriasis vulgaris as out of the 55 cases studied, 12 of them (21. 82%) were found to have streptococcal

infection which is in terms of percentage and number significant.

We suggest a course of specific antibiotics against streptococci in all patients having psoriasis especially in patients with a history of sore throat irrespective of whether it's a fresh case of relapse. Our study suffered due to the small sample size, as we excluded patient with any systemic disease or malignancy in the past or present and women who have attained menopause.

Prevalence of hypocalcaemia

Hypocalcaemia had been reported in several cases of chronic plaque psoriasis in the past as explained in my review of literature, however very few studies had been undertaken to find out their prevalence in chronic stable plaque psoriasis [103-110]. No similar study has been conducted in India and only one study has been reported from Tabriz university of Medical sciences, Iran by Herizchih et al[96], where the role of serum calcium in the exacerbation of psoriasis has been studied and patients have been evaluated for hypocalcaemia and hypoalbuminemia.

From the literature reviewed it has been reported that hypocalcaemia could be one of the exacerbating factors in psoriasis, along with other factors like stress, drugs, infections, etc [89-102].

The earliest literature regarding suggesting that hypocalcaemia can precipitate psoriasis was reported way back in 1963 by Vickers & Sneddon [94] and by Montgomery in 1964 [24] . Both of them were case reports based on observation on few of their patients.

In a study conducted in India by Verma et al[108], 132 cases of psoriasis were studied. They represented 0. 8% of the patients seen in Medical College Hospital, Rohtak. 122 cases were between the ages of 2 - 40 years. Ratio of males to females was 4:1. Hypercalcaemia was seen in 13 cases (10%)and hypocalcaemia in 20cases (15%).

In another study of 300 patients having psoriasis by Mehta et al[109], hypercalcaemia was noted in60 cases (20%)while only 10 cases (3. 33%) showed hypocalcaemia. The maximum incidence of 260 cases (86. 67) was seen in the age group of 11-50 years.

In a study conducted by Anuja et al[110] on 39 patients having psoriatic arthropathy, Arthritis followed the onset of skin or nail lesions in 29 patients (74. 36%). The serum calcium levels was markedly reduced (< 8. 4mg%) in 16 patients and moderately (8. 5-9mg%) in another 9 patients. Thus, 25 (64. 1%) of the arthropathic patients had hypocalcemia and 29 of the 39 patients were suffering from psoriasis vulgaris before they developed psoriatic arthropathy.

Herizchih et al[96], studied 98 patients with psoriasis. 36 of them (37. 2%) were hypocalcaemic and 23 of them (65% of hypocalcaemic patients) had low serum albumin. None of them were hypercalcaemic.

In our study 55 patients were investigated and 28 of them were found to have hypocalcaemia (50.91%). Out of this 20 patients (36.36%) had hypocalcaemia with normal serum albumin levels while in 8 (14.55%) of them hypoalbuminemia and hypocalcaemia were noted. Only 8 of them (14. 55%) had hypoalbuminemia and none of them had only hypoalbuminemia with normal serum calcium levels. Hypercalcaemia was not noted in any of the patients. So 8 out of our 28 patients (28. 57%) having hypocalcaemia had hypoalbuminemia.

The age group of 41-50 had maximum number of patients having hypocalcaemia (12 patients [42. 85%]), while 31-40 years of age formed the second largest group having patients with hypocalcaemia (10 patients [35.71%]). In our study also 85. 45% of patients belonged to the age group of 10-50 years. (The age distribution and number of patients having hypocalcaemia is shown in Bar diagram-Fig. No. 4)

The number of patients we found having hypocalcaemia were much higher than any other studies mentioned above and hypoalbuminemia was noted less often than the study by Herizchih et al[96].

Even though our sample size was small, a significant number of patients was found to have hypocalcaemia (28 patients [51%]) in which 20 of them (36. 36%) had hypocalcaemia with normal hypoalbumnemia. This was unlike previous studies were hypocalcaemia caused by hypoalbuminemia was not ruled out.

We conclude that hypocalcaemia is present in psoriasis vulgaris as it was clearly evident from our study, justifying our research hypothesis. Hypocalcaemia has to be considered an important factor in aggravation of psoriasis, even in chronic stable plaque psoriasis and perhaps also play an important role in precipitation of psoriasis vulgaris.

We suggest further studies in similar lines with a bigger sample size and to investigate all patients with psoriasis for hypocalcaemia. If they are found to be hypocalcaemic, they should be treated accordingly and followed up to see if their condition improved on correction of hypocalcaemia. We also suggest all patients with psoriasis vulgaris to take calcium supplementation.

Our studies suffered due to small sample size, which was predominantly due to exclusion of patients with systemic diseases which we felt may give us false positive results.

Another interesting observation in our study was that 7 (12. 72%) of our patients had both hypocalcaemia and streptococcal infection while 22 (40%) of our patients had either streptoccal infection or hypocalcaemia. (The results have been represented as an exploded pie diagram. Fig. No. 5)

6. The limitations of our study include

1) Small sample size.
2) Exclusion criteria which were common for the study regarding the prevalence of streptococcal infection and hypocalcaemia.
3) Our patients were not compared with another set of subjects as control.

7. Summary

This study titled 'Streptococcal infection and hypocalcaemia in psoriasis vulgaris' was done in the Department of Dermatology, Venereology and Leprology of Mahatma Gandhi Medical College and Research Institute.

We studied the prevalence of streptococcal infection and hypocalcaemia in 55 patients with psoriasis vulgaris who satisfied our inclusion criteria over a period of 1 year. After obtaining written consent from these patients, a throat swab was cultured for streptococcal infection and blood tested to check for a reactive high ASO titer. Serum calcium and serum albumin levels were also found out.

12 (21. 82%) of our patients had streptococcal infection while 28 (50. 91%)of our patients had hypocalcaemia. We were able to isolate 9 (16. 36%) positive throat swab culture with beta- hemolytic streptococcus pyogenus while 10 (18. 18%) patients had a rective high ASO titer.

Out of the 28 patients having hypocalcaemia, 8 (14. 55%) of them had hypoalbuminemia which was 28. 57% of the patients with hypocalcaemia.

20 (36. 36%) of them had hypocalcaemia with normal serum albumin levels. 7 (12. 72%)of our patients had both hypocalcaemia and streptococcal infection while 22 (40%)of our patients had neither of these.

We conclude that both streptococcal infection and hypocalcaemia is prevalent in psoriasis vulgaris and that early treatment of streptococcal sore throat and calcium supplementation may be beneficial for patients with psoriasis vulgaris. We suggest a course of specific antibiotics against streptococci in all patients having psoriasis especially in patients with a history of sore throat irrespective of whether it's a fresh case of relapse. Patients having psoriasis vulgaris should be investigated for hypocalcaemia and if found to have it should be corrected as this might lead to the improvement of psoriasis.

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