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TOTAL AND CANDIDA-SPECIFIC IgE IN RECURRENT VAGINAL CANDIDIASIS

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Total and candida specific serum IgE levels were studied in 21 patients who fulfilled the criteria for recurrent vaginal candidiasis, and 45 controls. The candida specific IgE levels were significantly higher in patients with recurrent vaginal candidiasis when compared with the controls. There was no significant difference in the total IgE levels between patients and the controls. IgE is postulated to inhibit the cellular immune response to candida and thereby prevent its eradication. There may be a genetic basis for the increased IgE levels.

Key words : Recurrent vaginal candidiasis, IgE.

Vaginal candidiasis is a common infection in humans.[1-3] In the United States it is the second commonest form of vaginal infection.[4] Predisposing factors like administration of antibiotics,[4] pregnancy[5] and diabetes[6] are thought to increase the risk of vulvo-vaginal candidiasis. Iron deficiency anaemia, as a predisposing cause, has been refuted in several studies.[7]

Although most women who suffer an isolated episode of candidial vaginitis recover readily with antifungal agents, there exists a group of women who suffer from recurrent episodes of vulvo-vaginal candidiasis in whom there appears to be no apparent predisposing factors, and in whom the morbidity is considerable. In some instances this places a heavy stress on marital relations.[8] Hobbs[9] has defined this group of patients with recurrent vaginal candidiasis as having at least three clinical exacerbations within six months or prior history of the disease longer than one year's duration. Perhaps the most widely held hypothesis on the pathogenesis of the recurrent form is that of persistent intestinal carriage of the pathogen. However, this hypothesis has since been refuted by several studies.[11,12] It is therefore conceivable that other factors such as lack of host immunological resistance may play a part. Deficiencies of T-lymphocytes and/or phagocyte function have been reported to be associated with candidial infections.[13] In another study, lymphocytes from patients with candidial vaginitis showed decreased thymidine uptake against candidial antigen although candidial killing tests and skin tests for delayed hypersensitivity against candidial extracts were normal.[9] Since it has been shown in chronic dermatophyte infection that IgE levels were elevated and that IgE may be responsible for perpetuating chronicity,[14] it is possible that a similar mechanism may be present in recurrent vaginal candidiasis. In this study, total and candida specific IgE is measured in a cohort of recurrent vaginal candidiasis patients and compared with controls.

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Materials and Methods

Twenty one patients with chronic vaginal candidiasis attending between July and December 1984 were randomly recruited into the study. Chronic vaginal candidiasis cases were selected if they fulfilled the criteria of Hobbs : (a) 3 clinical exacerbations within the last 6 months; or (b) prior history of disease longer than one year's duration. In both cases, at least one of the attacks was proven by culture and microscopy to be solely due to *Candida albicans* and not to any other pathogenic agent. All cases had symptoms and/or signs of vaginitis at the time of examination. The regular sexual consorts of the patients had no clinical evidence of candi-

diasis. The vaginal swabs were taken from the secretions in the mid-vaginal epithelium. The smears were Gram-stained and examined microscopically for yeasts. The swabs were cultured at 37°C for 48 hours in Trichosel medium(Becton Dickinson & Company, BBL, USA) which is regarded to be as good as Sabouraud's medium for the culture of candidial organisms.[15] The total IgE levels and the *Candida albicans* specific IgE levels were determined in all patients recruited on their initial visit, by Phadezym IgE PRIST and Phadezym RAST techniques respectively (Pharmacia Diagnostics AB, Sweden).

Forty five random controls who were healthy female blood donors and never had any episode suggestive of vaginitis, were similarly tested for total and Candida-specific IgE levels. None of the cases or controls had history of asthma, hay fever, atopic dermatitis or any other obvious cause of raised IgE levels. None had diabetes, endocrinopathy, or contraceptive intake. No patient had taken any antibiotic for at least 2 weeks prior to the study.

The mean values of the total and Candida-specific IgE levels were compared between cases and controls using the two-tailed unpaired t-test.

Results

Among the cases, there was a slight predominance (33.3%) in the 20-29 years age group and a smaller proportion (19.1%) in the above 50 years age group. Controls in general were younger than the cases, with a higher proportion (40%) in the 20-29 years age group and only 8.9% in the above 50 years age group. However, the correlation between age and IgE levels was statistically weak. Hence, IgE levels were compared between cases and controls without statistical adjustment for age.

Total IgE levels were widely scattered in both the groups, the cases and the controls, with a skew to the left (Fig. 1). The mean total IgE concentration in the cases was 0.351 OD units, not significantly higher than a mean value of 0.323 OD obtained in the controls (SE= 0.063, t=0.437, df=64). The distribution of Candida-specific IgE concentrations in the patients and controls was like-wise skewed to the left (Fig. 2). Patients had a higher mean Candida-specific IgE level of 0.066 OD units (SE=0.015 OD units) than that of controls, with a mean of 0.050 OD units (SD=0.019 OD units). The difference in mean Candida-specific IgE levels is highly significant (Two-tailed unpaired t-test : $SE=4.66\times10^{-3}$, df=64, t=34, $0.01> p> p0.001$).

Comments

IgE antibodies are the classical anaphylactic antibodies and mediate most anaphylactic (immediate or Type I) reactions. It is present in normal serum in very small amounts.[16] The serum concentration of IgE is significantly elevated in most patients with allergic diseases such as hay fever,[16] atopic disease,[16] extrinsic asthma[15] and parasitic disorders.[18,19] Hannifin[20] and Hay[21] have reported that up to 50% of patients with chronic dermatophytosis frequently had elevated IgE levels. It appears that IgE can be elevated in a spectrum of allergic disorders particularly those of a chronic nature. In our study, the total IgE levels in recurrent vaginal candidial patients did not differ from normal controls while the candida specific IgE levels were very significantly increased.

Selection of recurrent candidial vaginitis patients on the criteria of Hobbs poses some potential problems. Since the cases were selected from a hospital clinic, they may be biased towards the more chronic intractable cases. However, as selection was random and many women had self referred themselves it is not expected that this should be a significant problem. It is also possible that the patients had sexual partners other than those examined with candidiasis who therefore were a source of reinfection. However, the importance of sexual transmission remains uncertain and no controlled studies have verified the efficacy of treating the partner.[4]

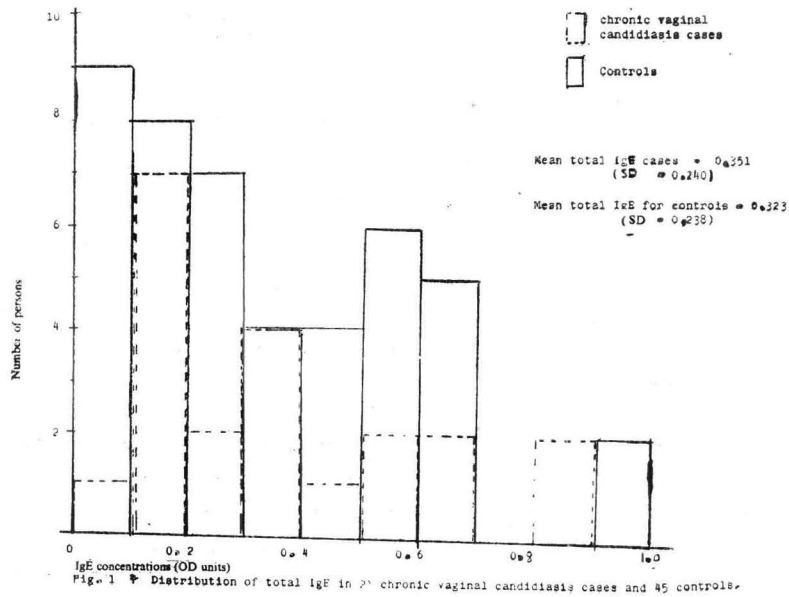

Fig. 1 : Distribution of total IgE in 21 chronic vaginal candidiasis cases and 45 controls.

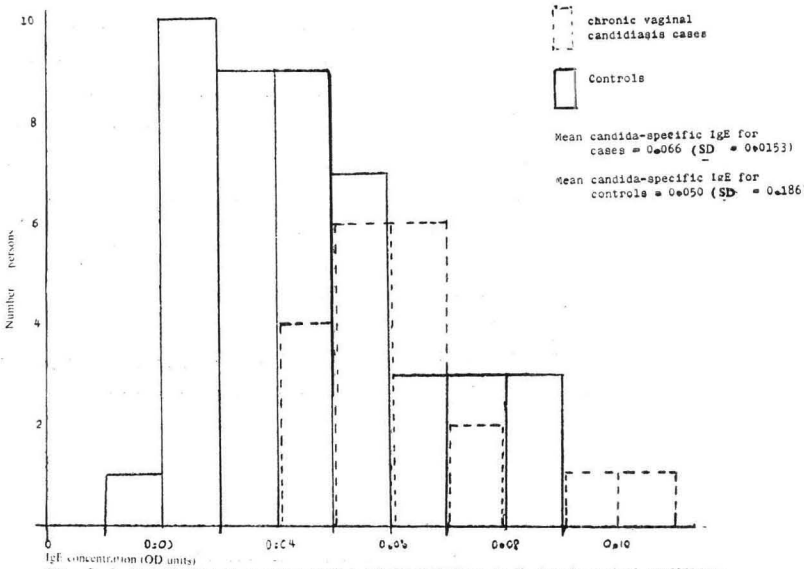

Fig. 2 : Distribution of candida-specific IgE concentration in 21 chronic vaginal candidiasis cases and in 45 controls.

Another potential confounding variable is the difficulty in distinguishing patients relapsing due to inadequate treatment from those reinfected in spite of adequate treatment. This problem was overcome in our study by negative post-treatment smears and cultures one month after clinical cure. Hence, all our patients had adequate treatment for each episode of candidial vaginitis.

The findings of Mathur[22] that the majority of his patients with recurrent vaginal candidiasis had raised total IgE is in contrast to our study. A possible explanation is the fact that Mathur only had three normal controls. Hence, it is most likely that if more normals had been used, most of his patients would fall within the normal range. Like us, Mathur did find increased levels of candida specific IgE in his chronic vaginitis. No attempt was made by him to define this group of patients nor was the use of the absorbance techniques to determine candida specific IgE adequate to rule out non-specific binding.

The question that needs to be addressed is the role of IgE in recurrent vaginal candidiasis. It has been hypothesized in chronic dermatophytosis that the IgE antibody either depletes the available antigen by combining with it or forms complexes that antagonise cell mediated immunity.[23] Consequently, the reduced inflammatory damage to the epidermis decreases the availability of antifungal factors.[25] A similar hypothesis may be used to explain the chronicity of some patients with vaginal candidiasis. IgE-Ag complexes may diminish the immune response by blocking receptors on the surface of the cells involved or inhibit the production of chemical mediators that trigger their activity.[26] Studies by Witkin[27] showed that some women with recurrent vaginal candidiasis respond to infection by producing candida specific suppressor lymphocytes and a soluble factor which block the cellular immune response to candida. IgE antibodies have been demonstrated specifically against *Staphylococcus aureus* and *Candida* in patients with hyper-immunoglobulin E syndrome and recurrent infections.[29] The production of these IgE antibodies may contribute to the increased susceptibility of these patients to infection with these particular organisms. Hyposensitization[28] with extracts of *Candida albicans* has been attempted in 10 women with recurrent vaginal candidiasis, 8 of whom showed improvement. This was done on an open trial and although its results have to be interpreted with caution, it shows that blocking IgE antibodies produce a favourable outcome which would imply a pathogenitic role for this antibody.

It may be argued that since recurrent candidiasis is defined on the basis of an inflammatory response, a correlation between specific IgE and disease could be the result of a protective effect of the antibody.[30] Furthermore, high specific IgE levels have been shown to be present in cervico-vaginal washings of patients with vaginal candidiasis.[22]

The bulk of current evidence appears to favour IgE acting as an inhibitor of the cellular response to candidial infections. This would be consistent with our finding of raised candida specific IgE in patients with recurrent candidial infection. These raised levels could have a genetic basis. Further work is required in this area. Such knowledge will lead to more effective therapy and thereby decrease the associated morbidity substantially.

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