Inflammatory Allergic Immune Response in Scabies Pyoderma

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Abstract: Scabies is a highly pruritic disorder induced by an immune allergic response to infestation of the skin by the mite sarcoptes scabiei that burrows in the stratum corneum of the skin. Scabies persists despite the availability of topical insecticides because the disease is transmitted before it is diagnosed and treated and significant resistance to insecticides has developed. The aim of this study was to investigate immunobiochemical response of the host's inflammatory/immune response to scabies during infestation in schoolchildren at rural areas. The number of eosinophil, neutrophil, serum IgE and serum interleukin (IL)-5 were assessed in 21 patients with 20 healthy control subjects. In the present study significantly higher number of eosinophil (11.90 ± 2.0 %vs. 4.12 ± 1.75 %; p<0.001) and highly significant elevation in neutrophil (%) in the scabies group compared to the healthy controls (39.9 ± 5.2%vs. 23.5 ± 2.0%, p<0.001). There was a highly significant elevation in serum IgE in the scabies group compared to the healthy normal controls (150 ± 58 IU/ml vs. 36.7 ± 18.0 U/ml p<0.001). As regards serum IL-5, there was a highly significant elevation in Interleukin-5 in the scabies group compared to the healthy normal controls (44.0 ± 15.3 ug/l vs. 12 ± 3.6 ug/l p<0.001).The results of this study suggest that there is a potent inflammatory immune response during the infestation of sarcopties scabiei. In conclusion, scabies is a dangerous disease affecting the immune system and should be treated once discovered to prevent the hazards of being epidemics.

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Key Words: Scabies; Eosinophil; IgEl; Interleukin (IL)-5; risk factors of scabies; epidemics.

1. Introduction

Scabies is a common parasitic infestation of global proportion. Worldwide, an estimated 300 million cases occur annually [15]. The arthropod *Sarcoptes scabiei* var *hominis* causes an intensely pruritic and highly contagious skin infestation which affects males and females of all socioeconomic status and ethnic groups [14]. Scabies infestation has been reported for more than 2500 years. Aristotle discussed "lice in the flesh," which resulted in vesicles, and Celsus recommended sulfur mixed with liquid pitch as a remedy for the disease [10]. However, the disease was first ascribed to the mite by Giovan Cosimo Bonomo in 1687. It was the first human disease recognized to be caused by a specific pathogen.

Mode of Transmission

Transmission of scabies is predominantly through direct skin-to-skin contact, and for this reason, scabies has been considered a sexually transmitted disease. Those at high risk include men who have sex with men and men with sexual contacts [15]. A person infested with mites can spread scabies even if he or she is asymptomatic. There may be a prolonged interval (up to 10 wk) between the primary infestation, when the patient becomes contagious, and the onset of clinical manifestations. It is less frequently transmitted by indirect contact through fomites such as infested bedding or clothing. However, the greater the number of parasites on a person, as in crusted scabies, the more likely that indirect contact will transmit the disease [14].

The *S scabiei* var *hominis* mite that infests humans is female and can be seen with the naked eye (0.3-0.4 mm long). The male is about half this size. The mite has 4 pairs of legs. It does not penetrate deeper than the outer layer of the epidermis (Figure 1). Mites are unable to fly or jump. They crawl at a rate of 2.5 cm/min. While the mite's life cycle occurs completely on its host, they are able to live on bedding, clothes, or other surfaces at room temperature for 2-3 days, while remaining capable of infestation and burrowing. At temperatures below 20°C, *S scabiei* are immobile, although they can survive such temperatures for extended periods [16].

Life cycle:

The scabies mite is an obligate parasite and completes its entire life cycle on humans. Other variants of the scabies mite can cause infestation in other mammals such as dogs, cats, pigs, and horses, and these variants can irritate human skin as well. However, they are unable to reproduce in humans and only cause a transient dermatitis. Eggs incubate and hatch in 3-4 days (90% of the hatched mites die).

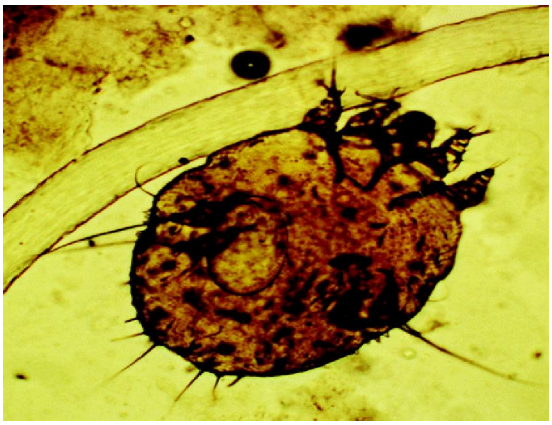

FIG. 1. Female scabies mite with egg, taken from skin scraping [16].

Larvae (3 pairs of legs) migrate to the skin surface and burrow into the intact stratum corneum to make short burrows, called molting pouches (3-4 d). Larvae molt into larger nymphs and then into adults. Mating takes place once, and the female is fertile for the rest of her life (1-2 mo), and the male dies soon after mating. She makes a serpentine burrow using proteolytic enzymes to dissolve the stratum corneum of the epidermis, laying eggs in the process, and she continues to lengthen her burrow and lay eggs for the rest of her life (1-2 mo). Transmission of impregnated females from person-to-person through direct or indirect skin contact. The time required to induce immunity in primary infestations probably accounts for the latent period of 4 weeks of asymptomatic infestation. In reinfestation, the sensitized individual may develop a rapid reaction (within hours). The resultant skin eruption, and its associated intense pruritus, is the hallmark of classic scabies [14].

Frequency:

International

While many accounts of the epidemiology of scabies suggest that epidemics or pandemics occur in 30-year cycles, this may be an oversimplification of its incidence. These accounts coincided with the major wars of the 20th century. Because it is not a reportable disease, and data are based on variable notification, the incidence of scabies is difficult to ascertain. Although epidemics have been reported (1919-1925, 1936-1949, 1964-1979), it is clearly an endemic disease in many tropical and subtropical regions. Scabies is 1 of the 6 major epidermal parasitic skin diseases (EPSD) that is prevalent in resource-poor populations. Prevalence rates are extremely high in aboriginal tribes in Australia, Africa, South America [10], and other developing regions of the world. Incidence in parts of Central America and South America and in one Indian village approach 100%. In parts of Bangladesh, the number of children with "the itch" exceeds the number with diarrheal and respiratory diseases combined [14]. In 2009 retrospective study of 30,078 children in India, scabies was found to be the second most common skin disease in all age groups of children, and the third most common skin disease in infants [4].

Worldwide, the prevalence of scabies has been estimated at 300 million cases annually [5]. In the United States and in other developed regions around the world, scabies occurs in epidemics in nursing homes, hospitals, long-term care facilities, and other institutions. It is seen frequently in the homeless populations but occurs episodically in other populations as well. No recent published data are available on its incidence in the United States. Studies conducted in Brazil [6&7] identified major risk factors for scabies in an impoverished rural community. The risk factors were young age, presence of many children in the household, illiteracy, low family income, poor housing, sharing clothes, and towels, and irregular use of showers.

Mortality/Morbidity:

Hundreds to millions of mites infest the host individual, who is usually immunocompromised, child, elderly, or physically or mentally disabled and impaired. Crusted scabies can be easily confused with severe dermatitis or psoriasis because widespread, crusted lesions appear with thick, hyperkeratotic scales over the elbows, knees, palms, and soles. The diagnosis of crusted scabies should be considered when suspected dermatitis or suspected psoriasis do not respond to usual treatments. Serum immunoglobulin E (IgE) IgG immunoglobulins, and neutrophil levels are extremely high in these patients, yet the immune reaction does not seem to be protective. Cell-mediated immunity in classic scabies demonstrates a predominantly CD4 T-cell infiltrate in the skin [10 & 16]. It has been suggested that bullous scabies could develop after long persistency of the parasites leading to a specific immune response with activation of T-helper type-2 cells leading to high levels of the cytokine interleukin 5 and subsequent eosinophilia. Secretion of proteolytic enzymes near the basal membrane zone might explain the development of intra-epidermal, often suprabasal blisters. In a patient with a positive biopsy and immunofluorescence result, the scabies infestation may have triggered a flare of the underlying autoimmune disease [3].

As a result, it is hypothesized that scabies

may exist in a great population of rural Beni-Suef, Egypt. The aim of this study was to discover and measure the inflammatory markers in infested patients compared to controlled group hoping a new future for a neglected disease to be treated.

2. Subjects and Methods

The consent of the parents of schoolchildren in rural areas of Beni-Suef, Egypt was taken. The schools of these children were built inside the village near the animals. History taking especially itching and scratching, more than the surface of the skin, and good questionnaire with thorough examination of skin were done. Twenty-one patients with age range 6-7 years of age with totally irritated skin due to scabies infestation (crusted type) were selected from whom were compaining severe itching. We have known about their low socio-economical conditions, big family size, malnutriton, and bad hygiene in dirty culture (we searched about skin rash at hand, between fingers, wrist, elbow, lower abdominal, genital or scrotum with severe itching specially at night, infected skin regions- from scratching).

The diagnosis of scabies is relatively easy for the physicians. A physical examination revealed the tell tale characteristics of scabies, and a skin scraping from a burrow can reveal the presence of the actual mite, although in most cases the skin scraping isn't necessary. To confirm diagnosis [13] superficial scraping was done and examination, under a low-power microscope, of material that has been expressed from a burrow revealed the mite, ova, or mite feces by the entomology specialist. The diagnosed subjects (21 out of 34) were compared with 20 control subjects from urban areas with completely normal skin.

All subjects were asked about the asthmatic symptoms and the requirement of rescue medication to be excluded. Analysis of both stool and urine was done also to exclude the other parasitic causes.

By using Sysmex cell counter, we took a blood sample to measure:

The white blood corpuscle count including both the eosinophil and neutrophil.

Eosinophil count was performed using Wright's stain [12]. (a specially prepared mixture of methylene blue and eosin in methanol, used in staining blood smears). Five hundred non-squamous cells were counted in Wright's-stained slides and the results were expressed as percentage of the non-squamous counts.

- Serum immunoglobulin IgE was measured (IU/ml) by immuno-nephelometric assay; Dade Behring Marburg GmbH/ Germany
- Interleukin (IL)-5 was measured (µg/ml) by quantitative 'sandwich' enzyme-linked immunosorbent assay using IL-5 kit (Sigma chemical Co., St. Louis, USA) according to the manufacturer's instructions

Prevention and Control of scabies

Human scabies is caused by an infestation of the skin by the human itch mite (Sarcoptes scabiei var. hominis). The microscopic scabies mite burrows into the upper layer of the skin where it lives and lays its eggs. The most common symptoms of scabies are intense itching and a pimple-like skin rash. The scabies mite usually is spread by direct, prolonged, skin-to-skin contact with a person who has scabies. [1].When a person is infested with scabies mites the first time, symptoms may not appear for up to two months after being infested. However, an infested person can transmit scabies, even if they do not have symptoms. Scabies usually is passed by direct, prolonged skin-to-skin contact with an infested person. However, a person with crusted (Norwegian) scabies can spread the infestation by brief skin-to-skin contact or by exposure to bedding, clothing, or even furniture that he/she has used. [11, 4].

Scabies is prevented by avoiding direct skin-to-skin contact with an infested person or with items such as clothing or bedding used by an infested person. Scabies treatment usually is recommended for members of the same household, particularly for those who have had prolonged skin-to-skin contact. All household members and other potentially exposed persons should be treated at the same time as the infested person to prevent possible reexposure and reinfestation. Bedding and clothing worn or used next to the skin anytime during the 3 days before treatment should be machine washed and dried using the hot water and hot dryer cycles or be dry-cleaned. Items that cannot be dry-cleaned or laundered can be disinfested by storing in a closed plastic bag for several days to a week. Scabies mites generally do not survive more than 2 to 3 days away from human skin. Children and adults usually can return to child care, school, or work the day after treatment. . [4].

A scabies prevention program involves:

The infection control practitioner should be responsible for (1) identification of contacts of symptomatic case(s), (2) prevention of transmission, (3) treatment of symptomatic cases, (4) treatment of contacts, (5) post-treatment assessment and (6) assessment of treatment failures. [4]. All levels of the health care team. The program should include an assessment of the skin, hair and nail beds of all new admissions as soon as possible following arrival. Pruritus, rashes and skin lesions should be documented and brought to the attention of the

nursing supervisor and the attending physician for further follow-up.

Essential elements of a successful scabies prevention program include: 1. Written policies and procedures for prevention and control of nosocomial scabies; 2. Health care workers who are trained to be suspicious of scabies in themselves or their patients if unexplained rash or pruritus occurs in themselves or their patients, and to report such occurrences to their supervisors; 3. A policy to screen newly admitted patients for scabies during the initial assessment (especially if transferred from another healthcare facility) and any suspect patient will immediately be placed on contact isolation until examined for scabies; 4. A policy that all new employees (especially employees who work at more than one facility) will be screened for scabies as part of pre-employment screening; 5. Access to and use as needed of the diagnostic skills of a consultant experienced in recognizing scabies to evaluate difficult or unusual cases or response to treatment;6. Assurance of adequate support from hospital administration, medical staff, infection control, employee health and line staff for appropriate evaluation and treatment of employees, in-house patients and exposed discharged patients should an outbreak of nosocomial scabies occur [20].

Statistical Analysis:

Results are expressed as mean ± standard deviation (SD). Data were collected coded and analyzed using SPSS software version 15 under windows XP.

3. Results:

Our study was done on 41 primary schoolchildren from Beni-Suef, Egypt in rural and urban areas, which were divided into two groups: Scabies group (9M/12F) and the healthy control group (10M/10F), both were matched in age and sex. Scabies group was proved to be of low socioeconomical conditions and ignore good hygienic measures in opposite to the control group as shown in table 1.

Table 1. Subjects' Clinical Characteristics

	Scabies group (n = 21) From rural areas	**Healthy control group (n = 20) From urban areas**
Age (years)	6 ± 0.7	6 ±.0.5
Sex,(male : female)	9 : 12	10 : 10
Socioeconomical conditions (Nutrition)	Bad	Good
Hygienic measures	Bad	Good
Skin morphology	Deep scratches	Normal intact skin

Table 2: Descriptive statistics of the different studied variables in the studied groups

Variables	**Scabies group (n = 21)**	**Healthy control group (n =20)**	***P* value**
Eosinophil (%)	11.90 ± 2.0	4.12 ± 1.75	0.001
Neutrophil (%)	39.9 ± 5.2%	23.5 ± 2.0	0.001
Serum IgE (IU/ml)	150 ± 58	36.7 ± 18.0	0.001
Interleukin-5 (μg/l)	44.0 ± 15.3	12 ± 3.6	0.001

P<0.001 is highly significant

As table 2 illustrates, there was a highly significant elevation in Eosinophil (%) in the scabies group compared to the healthy controls (11.90 ± 2.0 %vs. 4.12 ± 1.75 %, p<0.001). There was also a highly significant elevation in Neutrophil (%) in the scabies group compared to the healthy controls (39.9 ± 5.2%vs. 23.5 ± 2.0%, p<0.001). There was a highly significant elevation in serum IgE in the scabies group compared to the healthy normal controls (150 ± 58 IU/ml vs. 36.7 ± 18.0 U/ml p<0.001). As regardes IL-5, there was a highly significant elevation in Interleukin-5 in the scabies group compared to the healthy controls (44.0 ± 15.3 ug/l vs. 12 ± 3.6 ug/l p<0.001).

4. Discussion:

Scabies is a worldwide disease and a major public health problem in many developing countries, related primarily to poverty and overcrowding. Scabies is more prevalent in children and young adults. Scabies is more common in women than in men, which agreed with our results, and more common in winter than summer [4]. Scabies is very easy to misdiagnose because early subtle cases may look like small pimples or mosquito bites. Over a few weeks, however, mistakes like this become evident as patients feel worse and worse with symptoms they can't ignore.

Scabies is a neglected worldwide health problem. In the U.S., it occurs frequently in the general population and in institutions such as daycare centers and nursing homes. The prevalence is nearly 100% in infants and >50% in older children and women in some populations in the world. Scabies persists despite the availability of topical insecticides because the disease is transmitted before it is diagnosed and treated and significant resistance to insecticides has developed. The first time a person becomes infested with scabies the inflammatory/immune reaction in the skin is delayed for 4-8 weeks and there are no symptoms. The delay in the symptoms suggests that these mites may produce substances that can initially inhibit the host response. Previous studies have shown that mite extracts modulate the cytokine expression of keratinocytes, fibroblasts, monocytes, dendritic cells and lymphocytes. It appears that skin endothelial cells may play a key role in this delay of symptoms. A previous infestation with S. scabiei induces protective immunity. The mechanisms responsible for the delayed primary response and the protective immunity from a previous infestation are not understood [5 &16].

Classic scabies is primarily a nuisance. However, it can indirectly lead to long-term morbidity. The main symptoms of scabies are due to immune reaction to burrowed mites and their products (e.g. faeces, saliva or eggs. Scabies and other parasitic skin diseases can lead to long-term colonization of skin lesions by group A streptococci. Several studies have demonstrated a correlation between poststreptococcal glomerulonephritis (PSGN) and scabies. In remote Aboriginal communities in Australia where scabies is endemic, the repeated infestations and secondary streptococcal infections appear to be related to the extremely high levels of renal failure and rheumatic heart disease observed in the communities. While the microbiology of secondary bacterial infection in scabies lesions probably changes based on geographic location, one study demonstrated that the predominant aerobic and facultative bacteria recovered from lesions were *Staphylococcus aureus,* group A streptococci, and *Pseudomonas aeruginosa.* Multiple anaerobes were recovered as well, suggesting polymicrobial colonization of lesions [9]. Other complications of scabies include impetigo, furunculosis, and cellulitis. The staphylococci or streptococci in the lesions can lead to pyelonephritis, poststreptococcal glomerulonephritis, abscesses, pyogenic pneumonia, sepsis, and death [8]. Chronic inflammation is recognized as the major characteristic of eosinophil seems to play a key role. IL-5 is associated with eosinophilic inflammation. IL-5 is important in the terminal differentiation of eosinophils, in promoting eosinophil survival, and in priming and activating eosinophils [2].

Our patients group showed strong proliferative responses (peripheral blood mononuclear cells) to the scabies antigens, most of patients were crusted scabies which showed increased secretion of the Th2 cytokines interleukin 5 (IL-5). These data confirm that a non-protective allergic response occurs in the crusted disease form and demonstrate that clinical severity is associated with differences in the type and magnitude of the antibody and cellular responses to scabies proteins, in response to the active cysteine protease [17].

The modern concept of personal hygiene not only includes the prevention of diseases by cross-infection, but also the avoidance and removal of dirt which disturb the immune system [1].

Conclusion and recommendations:

Scabies can spread between schoolchildren, especially in rural ares, through close personal contact (relatives, schoolchildren, and crowded communities). Scabies should be treated once discovered to prevent the hazards of being epidemics. The most important factor to limitate the outbreak seems to be the prophylaxis of people who are in contact with the patients like friends, teachers, family members and car-drivers. The most exposed patients seemed to be those with diminished independence, diabetes, post-streptococcal and malnutrition. Consultation with a dermatologist or an infectious disease specialist may be required for severe, refractory scabies or for disseminated scabies in patients who are immunocompromised. Infested children must be treated cauciously with simple prophylactic treatment to close contacts.

The long term goal is to develop a better understanding of the host parasite relationship that will lead to development of novel strategies for the control/prevention and treatment of this disease. Determination of mite secretions and extracts and

testing isolated molecules for immunomodulating activity in several skin and blood cell types should be studied.

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