

ORIGINAL ARTICLE

The Effect of Eradication Treatment of *Helicobacter Pylori* on the Clinical Outcome of Patients with Pityriasis Versicolor

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ABSTRACT

Key words:

Pityriasis Versicolor,
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pylori stool Ag.

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Background: Although Pityriasis Versicolor (PVC) occurs in healthy individuals, numerous factors predispose to PVC. *Helicobacter Pylori* (HP) was found to be related to some dermatological disorders as vitiligo, atopic dermatitis, chronic spontaneous urticaria, and lichen planus. **Objective:** To evaluate the frequency of HP in patients with PVC and the effectiveness of HP eradication treatment on the clinical outcome of PVC. **Methodology:** A cross-sectional study was conducted on two hundred and sixteen patients who were subjected to history taking, dermatological examination, Wood's lamp, direct microscopic examination of skin scraping with KOH 10%, and HP stool Ag test. Fifty-seven patients with PVC were positive for HP by stool Ag test and were randomly divided into 3 equal groups (n=19), group A included patients treated for PVC only, group B included patients treated for HP only, and Group C included patients treated for both PVC & HP. Follow-up was done after 1 month for all groups clinically and by Wood's lamp to detect clearance of lesions. **Results:** HP stool Ag test was positive in about one-quarter (26.4%) of PVC patients. Complete disappearance of PVC was recorded in the majority of cases in Group A (89.5%), compared to 52.6% of those in Group C. while in Group B, none of the cases improved clinically. **Conclusion:** About one-quarter of PVC patients were positive for HP. The use of HP eradication treatment alone did not affect PVC improvement, while there was significant improvement in PVC with both combined treatment and the treatment of PV alone groups.

INTRODUCTION

Pityriasis versicolor (PVC) is a superficial fungal infection of skin. It is caused by *Malassezia*, a dimorphic lipophilic fungus, also named *Pityrosporum*. It is a component of normal skin flora. To date, 14 species of *Malassezia* have been identified. The main specie isolated in PVC is *Malassezia furfur*. It is clinically presented by hyperpigmented or hypopigmented, round to oval macules, and patches typically affect the trunk, neck, upper arms, and face ¹. Hyperhidrosis, seborrhea, sebum chemical constitution, and hereditary factors play important roles in PVC etiology ².

For the effective management of PVC by oral antifungal therapy, the regimens are itraconazole 200 mg daily for 7 days or fluconazole 300 mg weekly for 2 weeks ³.

Antifungal therapy eliminates the fungus, with good prognosis, though, untreated PVC can persist for years. The recurrence rate is high (up to 80%) ⁴. *Helicobacter pylori* (HP) is a gram-negative, microaerophilic spiral

rod-shaped bacteria that lives just beneath the antral gastric mucosa, on the surface of epithelial cells ⁵. *Helicobacter pylori* is the most common chronic bacterial infection of human beings. It causes some of the most prevalent gastroduodenal diseases as peptic ulcer, gastric cancer, and B-cell gastric lymphoma. In addition, it has been associated with other extra digestive conditions as cardiovascular, immunological, or skin diseases as vitiligo, atopic dermatitis, chronic spontaneous urticaria, and lichen planus ⁶.

H. pylori induce systemic inflammation that plays an important role in the pathogenesis of dermatologic diseases by dysregulation of cell-mediated and cytotoxic mechanisms in the microenvironment of the skin, which can provide the basis for pityriasis versicolor (PVC) infection in *H. pylori*-infected patients. *H. pylori* VacA protein affects T & B-lymphocytes, and macrophages which leads to decrease in IL-2 production and suppression of IL-2-mediated T-lymphocyte proliferation. This suggests that *H. pylori* active infection can decrease the proinflammatory cytokines which leads to immunosuppression ^{7,8}.

Eradication of HP infection was reported to be effective in patients with psoriasis, chronic urticaria, alopecia areata, and Henoch-Schonlein purpura⁹. *Kutlu et al.*¹⁰ found that positivity of UBT, HP IgG, and dyspepsia were higher significantly in PVC patients than in control group. Therefore, HP eradication treatment could be used in PVC patients with dyspepsia and especially patients with PVC resistant to traditional treatments¹⁰.

Study Objectives are to evaluate the frequency of HP in patients with PVC and assess the effectiveness of HP eradication treatment on clinical outcome of PVC.

METHODOLOGY

This study was conducted in the Dermatology Outpatient Clinic of Mansoura University Hospitals, and the Medical Microbiology and Immunology department in Mansoura Faculty of Medicine, Egypt, in the period from January 2022 to December 2023. The study consisted of 2 parts, *part 1* was an observational descriptive cross-sectional study and *part 2* was a randomized clinical trial for 3 different treatment groups.

In part 1 of the study, 216 patients clinically and mycologically diagnosed with PVC were subjected to detailed history taking including age, sex, occupation, marital status, onset, course, duration of PVC, associated GIT symptoms, history of previous infection and PVC treatment, and history of previous HP investigations and treatment. The dermatological examination was done for disease evaluation and description of the site, and color of lesions. The investigations for diagnosis of pityriasis versicolor included Wood's lamp where the PVC lesions may show yellow fluorescence.

The mycological investigations included direct microscopic examination of scraping of the skin lesion by a sterile No. 15 scalpel blade for confirmation, skin scraping was clarified using KOH 10%. Positive samples showed clusters of yeast cells and short tangled pseudo-hyphae with the characteristic appearance of "spaghetti and meatballs" (**Figure 1**). Only patients with confirmed PVC by both clinical and mycological examination were included in this study.

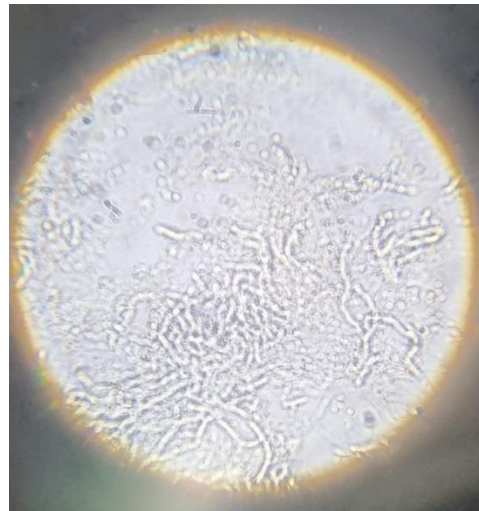


Fig 1: Direct microscopic examination of scales using KOH 10% showing rounded spores and short thick hyphae (spaghetti and meatballs appearance).

The investigation for diagnosis of *H. pylori* included HP stool Ag test using one-step HP Ag test kits (InTec products, INC), a rapid sandwich solid phase immunochromatographic assay. Stool samples were collected from PVC patients, and an aliquot of diluted stool sample was added to the sample well of the test cassette. The test was used to obtain a visual, qualitative result.

In *part 2* of the study, HP-positive PVC patients were randomly divided into 3 equal groups (n=19), group A included patients with PVC treatment only; Fluconazole 150 mg weekly for 4 weeks; group B included patients with HP treatment only, Amoxicillin 1 gm twice daily clarithromycin 500 mg twice daily and omeprazole 20 mg twice daily for 14 days and group C included patients with Both PVC & HP treatments. Follow-up was done after 1 month for all groups by clinical examination and Wood's lamp to detect clearance of lesions and to evaluate the effectiveness of different treatment regimens.

Way of randomization: block randomization was created using <https://www.sealedenvelope.com/>, and then sealed envelopes were used for each treatment option.

Double blinding: Patients and statistical analyst were blinded for the treatment type.

Sample size: A convenience sample was used based on voluntary participation in the study.

Ethical Consideration:

Informed verbal consent was obtained from each participant sharing in this study. Approval of the managers in the health care facility in which the study was obtained. Confidentiality and personal privacy of patients were respected throughout the study. The collected data was used for scientific purposes only. The study protocol was submitted for Institutional Research Board (IRB) approval. Code number: MS.21.04.1456.

Statistical analysis:

Statistical package for social science (SPSS-20) (SPSS Inc., Chicago, IL, USA) is used for statistical analysis. Data is expressed as mean \pm SD (continuous variables), Non normally distributed data are summarized by median, minimum & maximum. Categorical variables are summarized as frequency & percentages. Chi-square test was used to compare categorical variables in different groups. The level of statistical significance is less than 0.05.

RESULTS

A total of 216 clinically and mycologically diagnosed patients with PVC infection were recruited. Nearly half of them belonged to the 15 to 30 years old group (47.7%) while 40.3% were >30 years old. About 45.8% were males and 54.2% were females. One-third of them were students (33.3%), 25% were housewives and 15.3% worked in executive jobs (**Table 1**). Regarding the onset of the disease, 63% of cases had gradual onset, while acute onset was identified in only (37%) of them. The disease course was progressive in most studied patients (82.9%), compared to only 17.1% who had a stationary course. The median duration of the illness was 2 weeks; ranging from one to 16 weeks. Most patients (72%) were presented with multiple regions of affection and 26.4% had a single region affected. The most common region was the neck (60.2%) followed by the back (48.6%), then the arms (41.2%). (**Table 2**). Hyperpigmented lesions were recorded in 44.9% of cases, while hypopigmented lesions were detected in 38.9% (**Figures 2 & 3**).

Table 1: Demographic characteristics of studied PVC patients (n=216)

Variables	Frequency	Percentages
Age in years		
<15	26	12
15-30	103	47.7
>30	87	40.3
Sex		
Male	99	45.8
Female	117	54.2
Marital status		
Single	91	42.1
Married	117	54.2
Divorced or Widow	8	3.7
Occupation		
Professional jobs*	17	7.9
Executive jobs**	16	15.3
Service workers (Farmers-fishermen)	27	12.5
Sales jobs	13	6
Craft repair jobs	17	7.9
Students	72	33.3
Housewives	54	25

*Professional jobs (health care worker, teacher, lawyer) executive jobs** (office workers).

Table 2: Clinical presentation of studied PVC patients (n=216)

Variables	Frequency	Percentages
Onset		
Acute	80	37
Gradual	136	63
Course		
Progressive	179	82.9
Stationary	37	17.1
Duration in weeks		
Median (min-max)	2 (1-16)	
Number of regions		
1	57	26.4
2-3	133	61.6
≥4	23	10.6
Distribution of skin lesion		
Face	55	25.5
Neck	130	60.2
Arms	89	41.2
Trunk	81	37.5
Back	105	48.6
Colour of the skin lesion		
Hypo-pigmented	84	38.9
Hyper-pigmented	97	44.9
Pinkish	11	5.1
Mixed	24	11.1



Fig 2: Hypopigmented pityriasis versicolor



Fig 3: Hyperpigmented pityriasis versicolor

According to the HP stool Ag test, about one-quarter (26.3%) of PVC patients had positive results. More than one-third of PVC patients complained of associated abdominal pain (38.4%), while 29.2% had a sense of bloating, 9.7% were previously tested for HP, and 6.5% had previous HP treatment (**Table 3**).

Table 3: Associated GIT symptoms & HP infection in PVC patients (n=216)

Variables	Frequency	Percentage
Associated GI symptoms		
Abdominal pain	83	38.4
Sense bloating	63	29.2
Nausea	18	8.3
Vomiting	8	3.7
Loss of appetite	14	6.5
Weight loss	3	1.4
Previous HP investigation		
Yes	21	9.7
No	195	90.3
Treatment history for HP		
Yes	14	6.5
No	202	93.5
HP stool ag test		
Positive	57	26.4
Negative	159	73.61

There was a statistically significant difference in the clinical outcome among the three treatment groups examined clinically and by Wood's lamp ($p>0.05$). Complete disappearance of PVC was recorded in the

majority (89.5%) of cases in Group A, compared to more than half (52.6%) of those in Group C. While in Group B, none of the patients showed complete or partial disappearance (**Table 4**)

Table 4: Comparison of clinical outcome among different treatment groups

	Group A Anti-fungal treatment only (n=19)	Group B HP treatment only (n=19)	Group C Combined therapy (n=19)	Test of significance P value
Clinical examination				
Complete disappearance	17(89.5)	0(0)	10(52.6)	$\chi^2=66.4$ $P<0.001^*$
Partial disappearance	2(10.5)	0(0)	9(47.4)	
No disappearance (not improved)	0(0)	19(100)	0(0)	
Total improved	19 (100)	0 (0)	19 (100)	FET P1 undefined P2<0.0001* P3<0.0001*
Woods lamp				
Negative	19(100)	0(0)	16(84.2)	$\chi^2=46.3$ $P<0.001^*$
Positive	0(0)	19(100)	3(15.8)	

χ^2 : chi-square test. *Statistically significant. P1: statistical significance between A &C, P2: statistical significance between B &C. P3: statistical significance between A &B.

Table 5 shows that a higher rate of improvement of PVC was observed in the age group 15-30, female patients, treatment groups A, and C, less than one-month duration of PVC lesion, and patients with no

previous history of PVC. However, there was no significant difference between improved & non-improved PVC patients regarding different factors ($P>0.05$).

Table 5: Factors associated with clinical improvement among studied PVC patients

	Improved n=38	Not improved n=19	P value
Age in years			
<15	4(10.5)	3(15.8)	0.6
15-30	18(47.4)	10(52.6)	
>30 years	16(42.1)	6(31.6)	
Gender			
Male	14(36.8)	9(47.4)	0.4
female	24(63.2)	10(52.6)	
Treatment group			
Group A	19(50)	0(0)	1.00
Group B	0(0)	19(100)	
Group C	19(50)	0(0)	
Duration of PVC in months			
<1 month	26(68.4)	13(68.4)	1.00
1-2 months	6(15.8)	3(15.8)	
>2 months	6(15.8)	3(15.8)	
Past history of similar condition			
No	21(55.3)	14(73.3)	0.1
Yes	17(44.7)	5(26.3)	

χ^2 : chi square test

DISCUSSION

Most cases of PVC occur in healthy individuals. Though, several factors predispose to the development of PVC. These include hot, humid environments, genetic predisposition, immunosuppression, corticosteroid usage, malnutrition, application of oily preparations, and Cushing disease. *Malassezia* is part of the natural skin flora, making it hard to treat with an increased risk of relapse^{11,12}. *Helicobacter pylori* is present in gastric and duodenal mucosa. It causes dyspepsia and can cause gastric cancer¹³. *H. pylori* was found related to some skin diseases as vitiligo, atopic dermatitis, chronic spontaneous urticaria, and lichen planus^{14,15}.

Although some studies detected an association between autoimmune skin disease and HP infection, there are other few studies on HP infection and infectious skin diseases. A study in 2020 reported a statistically significant association between HP infection and PVC, proposing HP infection as a factor in the etiology of PVC, although this has not been confirmed by other studies and the control population were telogen effluvium (TE) patients and was not clearly matched in the demographic data¹⁶.

The current study aimed to evaluate the percent distribution of HP in Egyptian patients with PVC. Additionally, effectiveness of HP eradication on clinical course of PVC was evaluated. To the best of our knowledge, this was the first study to assess the effect of HP treatment on the clinical outcome of PVC, while previous studies have assessed the association between

HP and PVC only. *Helicobacter pylori*-positive PVC patients were divided into three subgroups; group A who received anti-fungal treatment only, group B who received HP treatment only, and Group C who received combined therapy.

This study demonstrated that the age group from 15 to 30 years old was the most commonly affected (47.7%) while 40.3% were more than 30 years old. These results coincide with other studies¹⁷⁻¹⁹. Likewise, Ismail *et al.*,²⁰ have demonstrated that the most frequently affected participants were in the "20-40 years of age" group. This is explained by the role of sebum and hormones in young adults. At puberty, increased sebum production results from increased activity of pilosebaceous glands, thus providing a lipid-rich environment that enhances the growth of *Malassezia* species. The activity of sebaceous glands decreases starting after the 3rd decade of life, that explains why older age groups are less susceptible to PVC¹⁷.

In the current study, PVC was more predominant in female patients (54.2%) than in male patients (45.8%). In accordance with our study, ME & DJ²¹ reported that their study patients were predominately females. This may be due to more awareness of females of their skin condition. However, in other studies, males had a higher rate of PVC than females^{17,20}. This might be due to higher awareness of females about their appearance.

Regarding the occupational distribution of PVC patients; our study demonstrated that 33.3% of PVC patients were students, and 25% were housewives. Similarly, Ghosh *et al.*,²² have demonstrated that students constituted most of the patients (29.09%),

followed by housewives (20%) and manual laborers (15.46%). That can be explained by higher activity of housewives and students with more sweat and sebum production which is considered a media favorable for *Malassezia* species.

Regarding disease characteristics, in this study, 63% of cases had gradual onset, while acute onset was identified in only 37% of them. The disease course was progressive in more than four-fifths (82.9%) of cases and only 17.1% had a stationary course. The average duration of PVC was 2 weeks; ranging from one to 16 weeks. Ghosh *et al.*,²² found that most of the patients (54.55%) had a duration of PVC ranging from two weeks to 2 years, while PVC of more than 10 years' duration was very rare (0.91%).

In the present study, PVC patients with hyperpigmented lesions (44.9%) were more than patients with hypopigmented lesions (39.8%), while mixed and pinkish lesions were found in 11.1% and 5.1% of patients respectively. Many previous studies have demonstrated that hypopigmented PVC was more common than hyperpigmented PVC^{23,24, 22, 25 & 26}. It was reported that hyperpigmented PVC is more common in fair-skinned patients, while hypopigmented PVC is more common in dark-skinned individuals²⁷. During metabolism, Azelaic acid is produced by *Malassezia*, it has a cytotoxic effect on the melanocytes and the process of melanogenesis, and that leads to hypopigmentation²⁸. The reported variation in the morphology and appearance of PVC lesions can be explained by the climate differences and variations in the skin color of different populations¹⁷.

In the present work, the most common sites of affection were the neck (60.2%) followed by the back (48.6%), and then the arms (41.2%) of cases. Most patients (72%) presented with multiple regions of affection compared to (26.4%) with only a single region. Another study demonstrated that the most frequently affected sites are the neck, trunk, and proximal extremities²⁹. Also, Ismail *et al.*,²⁰ have displayed that the most commonly affected site was the back followed by the neck and chest. Likewise, Singla *et al.*,²⁶ have displayed that; the back, chest, and shoulders were affected in (31.8%), (19.4%), and (07.0%) PVC patients, respectively.

About one quarter (26.3%) of the 216 total cases of PVC patients in this study were positive for HP by stool Ag test. 38.4% of cases complained of associated abdominal pain, 29.2% had an associated sense of bloating, 9.7% were previously tested for HP, and 6.5% had previous HP treatment. Another study found that prevalence of HP infection among the countries of the Middle East and North Africa region varies widely ranging from 7–50% in young children and going up to 36.8–94% in adults³⁰. While Abdelmonem *et al.*³¹ found that the prevalence rate of HP in Egypt was 52%. Another study conducted among Egyptian school

children aged 6–15 years, the overall prevalence of HP was 72%³². To our knowledge, one study tested HP prevalence in PVC patients, and it was 66.6%¹⁰. The prevalence of HP in PVC patients in the present study was lower than that reported in previous studies, different testing methods for HP can be one reason, e.g., urea breath test (UBT), molecular detection of *cagA* gene, and Hp IgG. A standardized detection method is required for comparison.

Kutlu *et al.*,¹⁰ reported significantly high rates of HP positivity, and serum HP IgG in PVC patients compared to TE patients ($P < 0.05$). In addition, dyspepsia was higher in PVC patients than in TE group. That finding suggests that active HP infection, that can be detected by UBT, can decrease the proinflammatory cytokines leading to immunosuppression. The discrepancies between the current study and Kutlu study may be because; the control population with TE was not demographically matched¹⁰. Also, geographical changes between both studies and the absence of PVC negative control group in this study may have role in the discrepancy between both results.

Regarding the clinical outcome of PVC among the three treatment groups (Group A: anti-fungal treatment, Group B: HP treatment, Group C: combination), the complete disappearance of PVC was recorded in the majority (89.5%) of cases in Group A, compared to more than half (52.6%) of those in Group C. While Group B., none of the cases had improved. To our knowledge, this was the first study to test the effect of HP eradication treatment on the clinical outcome of PVC. The study showed that there was no significant effect of anti-HP treatment on clinical outcome of PVC. It was suggested that anti-HP treatment can be useful in treating PVC with active HP infection, that can be tested by UBT. In this study, testing for HP was conducted using the stool Ag only, which can be a limitation in this study.

CONCLUSIONS

The current study concluded that HP eradication treatment seemed to have no significant effect on the clinical outcome of PVC.

Limitations: Despite the promising results of this study, it was a single-center study with a small sample size which has been considered as the main limitation. In addition, a single testing method for HP was conducted, which does not necessarily detect active HP infection.

Recommendations: Additional multi-center studies, with a larger number of patients, are required to confirm the actual relationship between HP and PVC and study the effectiveness of HP treatment among PVC patients. Future research is recommended to study the relation between active HP infection and PVC, and the effect of

HP eradication in PVC patients with active HP infection.

Declarations: Ethics Approval and Consent to Participate Mansoura University's Faculty of Medicine's Ethical Committee gave its approval for the study and the patient's participation. Ethics of Humanity was given the all-clear by the Mansoura University Faculty of Medicine's Ethics Committee.

Conflict of interest: The investigators declare no conflict of interest.

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