

Clinical and microbiological pattern of intertrigo

A B Wickramanayake¹, L S M Sigera², P I Jayasekera³, G Patabendige⁴, J K W Akarawita⁵

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Abstract

Background: Intertrigo is a common disorder affecting many flexural areas of the body with significant morbidity.

Objectives: To determine the clinical pattern of intertrigo. To determine bacterial and fungal pathogens associated with intertrigo. To assess the antibacterial and antifungal sensitivity pattern of the responsible organisms.

Methods: A total number of 230 patients with intertrigo attending dermatology unit were included in the study after ethical clearance. Laboratory investigations were done to identify the etiologic agent and their sensitivity pattern.

Results: Majority of patients (75%) belonged to 20-60 years of age. Male to female ratio was 1.15:1. Remarkable proportion (52%) presented with the involvement of more than one intertriginous area. The most common site involved was toe web space (63%) in particular 4th toe web space. Of all positive bacterial cultures 45% revealed *Staphylococcus aureus* (MSSA+MRSA) followed by CNSA (Coagulase negative *Staphylococcal aureus*), diptheroids and pseudomonas. The majority of MSSA (Methicillin sensitive *Staphylococcus aureus*) isolates (91%) were sensitive to cloxacillin and MRSA (Methicillin resistant *Staphylococcus aureus*) to teicoplanin (85%). CNSA isolates showed considerable proportion of sensitivity to vancomycin (37%) and majority of diptheroids isolates were sensitive to penicillin (87%). All isolates (100%) of pseudomonas were sensitive to gentamicin. Of all positive fungal cultures, candida species constituted the majority (35%) followed by fusarium species (33%) and dermatophytes (30%). Overall fusarium species shows high value of MIC₅₀ and MIC₉₀ for itraconazole, fluconazole and ketoconazole. Fluconazole showed very high MIC₅₀ and MIC₉₀ (256 ug/ml) for dermatophytes and fusarium species whereas itraconazole and ketoconazole showed lower MIC for these fungi.

Conclusion: Intertrigo can affect various intertriginous areas, among which toe web space is the most common region involved. Intertrigo can be caused by a variety of organisms: *Staphylococcus aureus* and candida species constituted the majority of cases. Majority of MSSA sensitive to cloxacillin and MRSA to teicoplanin. MIC of itraconazole, fluconazole and ketoconazole are high in fusarium species comparing to candida and dermatophytes. However, itraconazole and ketoconazole had lower MIC than dermatophytes and fusarium comparing to fluconazole.

Introduction

Intertrigo, or intertriginous dermatitis, may be defined as inflammation resulting from moisture trapped in skin folds subjected to friction¹. It is a common skin condition and can affect many areas of the body such as axilla, submammary, retroauricular, groin, perineum, intergluteal and interdigital spaces¹. Among all these variants interdigital intertrigo (including toe or finger webs) is the commonest variant².

Intertrigo may be symptomatic as a painful, exudative, macerated, erosive, inflammatory process which is sometimes malodorous or asymptomatic incidental finding³. It can result in significant morbidity and mortality with serious systemic infections. Studies have shown that 60% of cellulitis of the legs are associated with toe web intertrigo⁴.

Intertrigo can be infected with fungi and bacteria, as compromised skin facilitates the entry of microorganisms¹. Following is a list of commonest fungal species associated with intertrigo;

Candida species: *C.albicans*, *C.tropicalis*, *C.parapsilosis*, *C.glabrata*, *C.guilliermondii*³.

Dermatophytes species: *Trichophyton rubrum*, *T.mentagrophytes*, *T.tonsurans* and *Epidermophyton floccosum*⁵.

Fusarium species: *Fusarium solani*⁶.

Bacteria that are commonly associated with intertrigo are coagulase-negative *staphylococci*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Corynebacterium minutissimum*^{1,2,6}.

In addition group A β -hemolytic *Streptococcus*, *Escherchia coli*, *Proteus mirabilis*, *Enterococcus faecalis*, *Klebsiella* spp and *Acinetobacter baumannii* also isolated from intertrigo^{6,7}.

Studies related to microbiological aspects of intertrigo are lacking in Sri Lanka even though this condition is commonly seen in Sri Lankan clinical setup.

¹Senior Registrar in Dermatology, National Hospital of Sri Lanka, Colombo, ²Senior Registrar in Clinical Mycology, Department of Mycology, Medical Research Institute of Sri Lanka, ³Consultant Clinical Mycologist, Department of Mycology, Medical Research Institute of Sri Lanka, ⁴Consultant Clinical Microbiologist, Department of Microbiology, National Hospital Sri Lanka, Colombo, ⁵Consultant Dermatologist, National Hospital of Sri Lanka, Colombo.

Objectives

1. To determine the clinical pattern of intertrigo.
2. To determine the bacterial and fungal pathogens associated with intertrigo.
3. To assess the antibacterial and antifungal sensitivity pattern of the responsible organisms in intertrigo.

Methodology

Study design: Descriptive cross-sectional study.

Study setting: Dermatology Unit, National Hospital, Colombo, Sri Lanka.

Sample selection: Patients who attended or were referred to the Dermatology Unit, National Hospital of Sri Lanka (Colombo) with intertrigo were recruited into this study after obtaining informed written consent, starting from July 2016. All patients referred to this Unit were at or above the age of 13 years.

Patients who were already on treatment were kept free of topical antifungal drugs and antibiotics for 2 weeks and oral antifungal drugs and antibiotics for 4 weeks before recruiting into the study.

Data were collected according to a preformed questionnaire and patients were subjected to following; Bacteriological studies: This was carried out in Microbiology Department, National Hospital, Sri Lanka and consist of three components.

- I. Gram staining: Lesions were cleaned with sterile normal saline and cotton swabs were taken from the lesions. Smears were prepared and stained with gram stain. This was examined under microscope using oil immersion.
- II. Bacterial culture: The culture media was blood agar plate, MacConkey's agar plate and chocolate agar plate. The swabs were inoculated on these media and incubated for 24 hours at 37°C. The blood agar and chocolate agar were incubated in 5-10% carbon dioxide. The MacConkey's agar plate was incubated aerobically. The processing was carried out using standard operation procedures in the Laboratory Manual by Sri Lanka College of Microbiologists (SLCM). Bacterial cultures were considered as negative if there is no growth for 48 hours.
- III. Antibiotic sensitivity: All the bacteria that were isolated were tested for commonly using antibiotic sensitivity according to Clinical Laboratory Standard Institute (CLSI) guidelines.

Specifically in this study antibiotic sensitivity pattern of CNSA and diphtheroids were assessed as they are culprit pathogens in intertrigo by overgrowing on macerated area^{1,2,7}.

Mycological studies: This was carried out at the Department of Mycology, Medical Research Institute (MRI) Colombo and consist of three components.

- I. Skin scraping for direct microscopy using 10% potassium hydroxide (KOH) test: The lesions were cleaned with sterile normal saline swab and allowed to dry. Scrapings were collected using a blunt scalpel and put on a clean glass slide to which 1 to 2 drops of 10% KOH were added. It was covered with a cover slip and kept for few minutes. Then the slide was examined microscopically for yeast cells, fungal filaments and fungal spores.
- II. Fungal culture: Part of the scraping was inoculated in Sabouraud's dextrose agar (incorporated with antibiotics and chemicals to inhibit environmental fungi) and incubated at 26°C for 2 weeks. Species identification was done by doing biochemical testing and morphological identification.
- III. Antifungal sensitivity testing: All the fungi that was isolated, was tested for following commonly using antifungal drugs according to Clinical Laboratory Standard Institute (CLSI) guidelines. Antifungal drugs that were tested include itraconazole, fluconazole and ketoconazole. The results were indicated as minimal inhibitory concentration (MIC) using Enz MIC Tm strips.

For patients who had an involvement of more than one intertriginous area, bacteriological and mycological studies were done from each area separately.

Results

A total of 230 patients with intertrigo were included in the study. Their age ranged from 13 to 89 years, with mean age of 47 (± 16) years, median age 48 years and most frequent age of presentation was 42 years. Seventy five percent (n=173) of patients were between 20 to 60 years.

Among them, 123 (53%) were males and 107 (47%) were females. Male to female ratio 1.15:1.

Considering the presentation, 157 (68%) patients presented directly due to intertrigo, on the other hand in 106 (32%) patients, this was an incidental finding(indirect presentation). One hundred and twenty-four patients (54%) presented with 1st episode,

whereas 106 (46%) presented with recurrent episode. Eight patients had a history of recurrence more than 3 times.

Distribution of intertrigo, 135 (58%) patients had 1 site involvement followed by 45 (20%) with two site involvement and 50 (22%) had more than two site involvements. Patients with multiple site involvement each and every site analyzed separately.

From total, commonest affected site was toe webs (n=146, 63%) followed by groin (n=94, 41%), axillary (n=38, 17%), gluteal cleft (n=36, 16%), sub-mammary

(n=35, 15%), finger webs (n=23, 10%), retro-auricular (n=9, 4%), suprapubic fold (n=7, 3%) and other areas (n=4, 1.7%) such as hand creases, abdominal folds, LRT scar and intermammary area.

In 146 patients with toe web intertrigo, both feet affected in 89 (61%) patients and the commonest affected toe web was 4th toe web (n=127, 87%). In 23 patients with hand intertrigo, one hand affected in 14 (61%) and it was mainly right hand (n=10). The commonest finger web affected was 3rd finger web, which affected in 22 (96%) patients.

Area wise distributions and microbiological assessment

Table 1. Area wise gender distribution

	<i>Toe webs</i>	<i>Groin</i>	<i>Axilla</i>	<i>Gluteal cleft</i>	<i>Submammary</i>	<i>Finger webs</i>	<i>Retroauricular</i>	<i>Suprapubic fold</i>
Male	93	45	10	14	01	10	07	-
Female	53	49	28	22	34	13	02	7
Total	146	94	38	36	35	23	09	7

Table 2. Area wise bacteriological assessment

	<i>Toe webs</i>	<i>Groin</i>	<i>Axilla</i>	<i>Gluteal cleft</i>	<i>Submammary</i>	<i>Finger webs</i>	<i>Retroauricular</i>	<i>Suprapubic fold</i>
Gram Stain								
GPC	51	26	06	03	06	05	-	01
GPR	18	04	-	-	-	-	-	-
GNC	03	-	-	01	-	-	-	-
GNR	30	6	01	05	-	-	-	01
Bacterial Culture								
CNSA	20	11	02	01	02	01	01	01
MSSA	12	23	05	08	10	02	02	02
MRSA	07	04	03	-	02	03	-	-
Diphtheroids	27	05	01	01	01	-	-	01
Pseudomonas	10	-	-	-	-	-	01	-
Coliforms	03	-	-	-	-	-	-	-
Total of culture positivity	79 (54%)	43 (46%)	11 (29%)	10 (28%)	15 (43%)	06 (26%)	04 (44%)	04 (57%)

Table 3. Area wise mycological assessment

	<i>Toe webs</i>	<i>Groin</i>	<i>Axilla</i>	<i>Gluteal cleft</i>	<i>Submammary</i>	<i>Finger webs</i>	<i>Retroauricular</i>	<i>Suprapubic fold</i>
Direct smear								
Yeast	24	08	01	03	02	-	01	-
Filaments	59	26	09	06	05	09	-	-
Pseudohyphae	03	01	-	-	01	-	-	-
Spores	01	07	03	01	01	-	-	-
Fungal culture								
<i>C.albicans</i>	17	-	-	-	01	07	-	-
<i>C.parapsilosis</i>	10	03	01	-	02	-	-	-
<i>C.tropicalis</i>	01	01	-	-	-	-	-	-
<i>C.glabrata</i>	-	01	-	-	-	-	-	-
<i>T.mentagrophytes</i>	02	14	04	02	03	-	-	-
<i>T.rubrum</i>	-	04	01	-	-	-	-	-
<i>E.flocossum</i>	-	04	-	-	-	-	-	-
Trichosporon species	02	-	-	-	-	-	-	-
Fusarium species	35	01	01	01	-	03	-	-
Exophiala species	-	-	-	-	01	-	-	-
Total of culture positivity	67 (46%)	28 (30%)	07 (18%)	05 (14%)	09 (26%)	10 (43%)	- -	- -

Antibiotic sensitivity pattern

As an overall, bacterial culture positivity noted in 190. The commonest organism isolated from bacterial culture was MSSA (n=66, 35%) followed by CNSA (n=49, 26%), diptheroids (n=39, 21%), MRSA (n=20, 10%), pseudomonas species (n=13, 6.5%) and coliform species (n=03, 1.5%).

Table 4.1. Antibiotic sensitivity pattern (S-Sensitive, R-Resistance)

	<i>Ciprofloxacin</i>		<i>Erythromycin</i>		<i>Vancomycin</i>		<i>Cloxacillin</i>		<i>Fucidic acid</i>		<i>Clindamycin</i>		<i>Tetraplanin</i>		<i>Penicillin</i>		<i>Clotrimazole</i>		<i>Chloramphenicol</i>	
	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R
MSSA (n=66)	24	17	27	27	38	01	60	00	34	14	53	06	36	01	-	-	25	02	-	-
CNSA (n=49)	10	08	01	13	18	-	08	07	06	11	08	06	15	-	-	-	05	06	-	-
Diphtheroids (n=39)	-	01	-	01	30	-	-	-	10	02	-	-	01	-	34	03	-	-	25	04-
MRSA (n=20)	02	10	-	16	16	-	-	20	12	08	13	06	17	-	-	-	02	04	-	-

Table 4.2. Antibiotic sensitivity pattern (S-Sensitive, R-Resistance)

	<i>Ciprofloxacin</i>		<i>Ceftazidime</i>		<i>Amikacin</i>		<i>Gentamycin</i>		<i>Meropenem</i>		<i>Imipenem</i>		<i>Cefpime</i>		<i>Cefuroxime</i>		<i>Ticarcillin</i>		<i>Co-amoxiclav</i>	
	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R
<i>Pseudomonas</i> species (n=13)	10	01	07	03	07	-	13	-	01	01	06	-	05	-	-	-	04	-	-	-
Coliform species (n=03)	-	01	01	-	01	-	-	01	01	01	01	01	-	01	01	-	-	-	01	-

Antifungal sensitivity pattern

As an overall, fungal culture positivity noted in 126. Among them, commonest species isolated was *Candida* species (n=44, 35%) followed by *Fusarium* species (n=41, 33%), Dermatophytes (n=38, 30%), *Trichosporon* species (n=2, 1.3%) and *Exophiala* species (n=1, 0.7%) Figure 1.

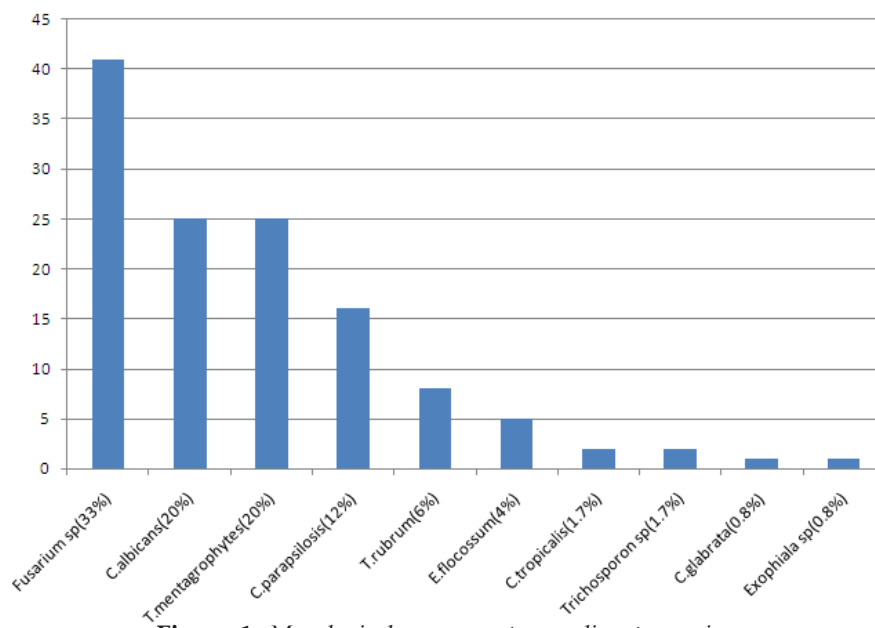


Figure 1. Mycological assessment according to species.

Antifungal sensitivity pattern

Minimal inhibitory concentration (MIC) was measured in microgram per milliliters (ug/ml). MIC₅₀ and MIC₉₀ were calculated for itraconazole, fluconazole and ketoconazole Table 5.

Table 5. Antibiotic sensitivity pattern (S-Sensitive, R-Resistance)

	Itraconazole		Fluconazole		Ketoconazole	
	MIC ₅₀	MIC ₉₀	MIC ₅₀	MIC ₉₀	MIC ₅₀	MIC ₉₀
Candida species	0.047	0.094	0.125	0.38	0.125	0.38
Dermatophytes	0.032	0.38	256	256	0.25	32
Fusarium species	32	32	256	256	32	32

Discussion

According to our findings, majority (75%) of patients presented between 20 to 60 years. This finding is compatible with the finding of Krishna *et al*² (21 to 60 years). Mean age of presentation (47 years) is also compatible with the finding of Ahamed *et al*⁸. Keita *et al*⁹ concluded intertrigo can affect any age group which tally with the overall age range in this study of 13 to 89 years.

A slight male preponderance was noted which is contrary to S. Krishna *et al*² which showed a male to female ratio of 1:3. However Ahamed *et al*⁸ showed

higher preponderance in males in toe web intertrigo (56.7%) which is compatible with our finding of male:female ratio of 1.8:1. The toe webs being the commonest site affected in our study, this explains the overall male preponderance probably secondary to occlusive shoes in men. Area wise distribution is almost the same with the exception of female preponderance in axillary, sub mammary and supra-pubic flexural areas. This may be due to anatomical variations.

In our study 58% presented with the involvement of one site followed by 20% and 15% of two sites and

three site involvements. Majority had the involvement of toe webs (63%) followed by groin and other areas. This is concordance with Krishna *et al*² in which toe web is the commonest site affected.

In toe web intertrigo, bilateral feet involvement and common involvement of 4th toe web is very well tallied with findings of Ahamad *et al*⁸ and Hassab *et al*³. This is probably secondary to anatomical occlusive nature of 4th toe web. In finger webs, common occurrence in 3rd finger web is well described in Adams *et al*¹⁰. Predominant involvement of right hand can be elucidated by the right hand dominance in the majority which leads to increased exposure such as to water as well as increased sweating with exertion of the dominant hand.

According to our study, the commonest bacterial organisms isolated were MSSA (35%), CNSA (26%), diptheroids (21%), MRSA (10%), pseudomonas species (6.5%) and coliforms (1.5%). In Ahamad *et al*⁹ commonest organisms isolated was *Staphylococcus aureus* which accounted for (83.4%). In our finding same, nevertheless both MSSA and MRSA accounted for only 45%. Even though, CNSA is a skin commensal, it acts as a pathogen by overgrowing in macerated intertriginous areas. Here, CNSA was isolated in 26% which approximate with finding of Karaka *et al*⁵ which isolated CNSA in 20%. *Corynebacterium minutissimum* is a diptheroid bacillus which causing toe web intertrigo due to its keratolytic properties and may coexist with a dermatophyte infection, particularly in the toe webs¹¹. Unfortunately, in our set up we don't have the facilities to isolate *C. minutissimum* separately; however, diptheroids can be isolated which includes *C. minutissimum*. We have isolated 21% diptheroids as an overall and it is the commonest bacteria isolated in toe webs which was 34% (n=27) of all positive cultures (n=79). Pseudomonas species were isolated in 6.5% in overall and 13% in toe webs. This is compatible with the finding of Ahamad *et al*⁸ which isolated 10% of pseudomonas in toe webs. Many studies concluded previous prolonged antibiotics and antifungal therapy can predispose to gram negative bacterial intertrigo^{7,12}.

Considering the antibiotic sensitivity pattern of organisms, high proportion of MSSA (91%) isolates were sensitive to cloxacillin in concordance with the finding of Hanumanthappa *et al*¹³ study conducted in Karnataka which showed almost similar sensitive proportion 92.9%. In addition, they demonstrated equal sensitive proportion in both MSSA and MRSA to vancomycin. Contrary to this, in our study more MRSA (80%) showed sensitivity to vancomycin (80%) than MSSA (58%). Same time, in our study high

proportion of MSSA showed sensitivity to clindamycin (80%) than MRSA (65%), though highest proportion of MRSA were sensitive to teicoplanin (85%). Even though CNSA isolates were more sensitive to vancomycin, considerable proportions were resistant to erythromycin (27%) and fucidic acid (22%), this may be secondary to high rate of administration of macrolide group antibiotics for respiratory tract infections and topical application of fucidic acid for infected eczema and superficial skin infections. Diptheroids sensitive proportion to penicillin (87%) chloramphenicol (64%) and lesser extent to fucidic (26%) and this is useful in treating this infection either with oral or topical antibiotics.

According to our findings, highest proportion of pseudomonas species was sensitive against gentamycin (100%) and ciprofloxacin (77%). However, study of Yadav *et al*¹⁴ South Chhattisgarh in India demonstrated 53% and 51% of sensitive proportion of pseudomonas species to above two antibiotics and highly sensitive ratio in meropenem and imipenem (91%). This different pattern may be due to differences in local antibiotic policies with the consequent development of resistance. However, sensitive proportion to ceftazidime of 54% is compatible with the finding of Yadav *et al*¹⁴.

In this study the predominant fungal species isolated was candida species (35%) which is comparable but was relatively lower occurrence than the findings in Krishna *et al*² and Ahamad *et al*⁸ which showed 51.33% and 60% respectively. Isolation of dermatophyte species in 30% is consistent with the study of Ahamad *et al*⁸ which demonstrated 31% of dermatophytes. Fascinatingly, fusarium species were isolated in 33% in our study.

Fusarium onychomycosis is well recorded in Sri Lanka¹⁵, on the other hand records related to fusarium intertrigo are lacking in Sri Lanka as well as in international literature except few case reports¹⁶. Thus, this necessitates the more elaborated studies on this aspect. According to Ranawaka *et al*¹⁷, Fusarium toe nail infection is a difficult challenge in eradication with a prolonged therapeutic reservoir in nails for 11 months therefore need at least 1 year follow up to confirm the complete cure. This may be also applicable for the intertrigo especially toe webs and may explain the chronic nature of this disease in our set up with recurrence. However, to confirm this assumption more elaborated and comprehensive studies are needed.

Considering, antifungal sensitivity filamentous species such as fusarium followed by dermatophytes

showed high MIC values comparing to the yeast like candida. On the other hand, MIC of fluconazole for dermatophyte and fusarium is markedly higher comparative to itraconazole and ketoconazole. Higher MIC values for fluconazole have also been reported by some authors previously¹⁸ and indicating higher chances of treatment failure when treated with this drug. Itraconazole and ketoconazole had lower MIC for of dermatophytes and fusarium comparing to fluconazole which indicates that these drugs could be the better option for successful treatment of these infections than fluconazole. Many studies on dermatophytes have reported similar findings with itraconazole and ketoconazole¹⁸. According to these results among these three Azoles, itraconazole is a better choice for successful treatment of dermatophytes, fusarium and candida infection.

Overall MIC of itraconazole, fluconazole and ketoconazole are high in fusarium species comparing to other fungi which may indicate difficult eradication, prolong treatment and treatment resistance. However, this necessitates further elaborated studies.

Conclusion

Intertrigo is a disease predominantly affecting the age group of 20-60 years, with a slight male preponderance. It can be an incidental finding and can have recurrent episodes. It can involve multiple sites at same time, however the commonest site affected was toe webs with a predilection to 4th toe web space followed by groins. Common bacterial organisms causing intertrigo are *Staphylococcus aureus* (MSSA+MRSA) followed by CNSA, diptheroids and pseudomonas species. The majority of MSSA isolates are sensitive to cloxacillin, MRSA to teicoplanin, CNSA to vancomycin, diptheroids to penicillin and pseudomonas to gentamicin. Common fungi result in intertrigo are *Candida* species followed by fusarium species and dermatophytes. Among *Candida* species *C.albicans* is the commonest organism and among dermatophytes, *T.mentagrophytes* is the commonest organism. MIC of itraconazole, fluconazole and ketoconazole are high in fusarium species comparing to candida and dermatophytes. However, itraconazole and ketoconazole had lower MIC than dermatophytes and fusarium comparing to fluconazole.

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