Original Article

# Antibiotic Resistance Pattern of *Neisseria gonorrhoeae* in Hospital Kuala Lumpur, Malaysia (2001-2005)

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**Abstract**

**Background** Gonorrhoea is the third most common sexually transmitted infection (after syphilis and non-gonococcal urethritis) seen in patients attending the Genitourinary Medicine (GUM) Clinic in Hospital Kuala Lumpur (HKL). Its association with poor reproductive health outcomes and the increasing prevalence of antimicrobial resistance has made it a major public health concern.

**Objective** To determine the antibiotic resistance pattern of *Neisseria Gonorrhoeae* in patients attending the GUM Clinic in HKL and its comparison with other countries.

**Method** A retrospective study of all patients with *gonorrhoea* (new and recurrent) between 2001-2005. Antimicrobial susceptibility testing by standard disc diffusion method was performed to detect sensitivity to penicillin, tetracycline, kanamycin, ciprofloxacin, spectinomycin, ceftriaxone and cefuroxime.

**Results** A total of 416 positive culture isolates of *N.gonorrhoeae* from 2001-2005 were reviewed. Highest level of resistance was detected to tetracycline (86.8% of 296 isolates). Resistance to penicillin was noted in 64.4% of all isolates. Penicillinase Producing *N.gonorrhoeae* (PPNG) accounted for 62% of cases. Both penicillin and tetracycline showed an increasing resistance trend from 2001-2005. The third commonest antibiotic resistance was to kanamycin (38.3%), followed by ciprofloxacin (10.4%). The resistance to spectinomycin was 1.7%. No resistance was detected to ceftriaxone and cefuroxime. All gonorrhea patients in GUM Clinic, HKL were treated with ceftriaxone, and subsequent cultures on follow-up were negative. We compared our results with the data obtained from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP)[6] and the WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme (GASP)[7].

**Conclusion** Penicillin and tetracycline resistance remain high in Malaysia and other Western Pacific countries. Resistance to ciprofloxacin was however lower in Malaysia compared to other countries. There was no resistance to ceftriaxone and cefuroxime. The current first line antibiotic for treating gonorrhoea in GUM Clinic, HKL is ceftriaxone.

**Keywords** Gonorrhoea, Antibiotic Resistance Pattern

## Introduction

Gonorrhoea is amongst the most common sexually transmitted infections in the world and is caused by gram negative bacterium *Neisseria gonorrhoeae*. It usually infects the mucosal surfaces, causing sexually transmitted urethritis in men and endocervicitis in women. It can also cause anorectal and pharyngeal infections and in neonates, ophthalmic infection is acquired during passage through the birth canal. Complications particularly affect women, and include salpingitis, pelvic inflammatory disease, first trimester abortion and decreased fertility. In men, extension of mucosal infection to contiguous areas may give rise to epididymo-orchitis and thus reduced fertility. In a small proportion of patients, gonococcaemia may occur and result in septic arthritis, endocarditis and meningitis. It is well recognized that gonorrhea, together with genital ulcer disease, are potent amplifiers of the spread of HIV[1]. Rates of HIV transmission in those with gonorrhoea may be as much as 5 times more than in persons without gonorrhoea[1]. Those with gonorrhoea are also more susceptible to acquisition of HIV infection[2].

Gonorrhoea remains a major global disease with an estimated 60 million cases per year globally, making it a major public health concern[3]. About half of these cases occur in the Western Pacific and South East Asia regions[5]. In GUM Clinic, HKL, gonorrhoea accounts for the third most common sexually transmitted infection (after syphilis and non-gonococcal urethritis). In the recent years, incidence of gonorrhoea has also increased in other developed countries, with the highest rates in the socially and economically deprived subpopulations, and in homosexual men[4].

Attempts to treat and control gonorrhoea are compromised by the emergence and spread of antibiotic resistant *Neisseria gonorrhoeae*. There are many surveillance programmes on antibiotic resistance pattern of N.gonorrhoeae such as GRASP (Gonococcal Resistance to Antimicrobial Surveilance Programme), which is based in London, UK and WHO WPR GASP (World Health Organization Western Pacific Region Gonococcal Antimicrobial Surveilance Programme)[5, 6]. Tetracycline resistance is encountered in many countries. Since penicillin resistance emerged in the late 1970's, it has spread to most parts of the world[7]. This is either due to Penicillinase Producing *Neisseria gonorrhoeae* (PPNG) or chromosomally mediated resistance (CMRNG). South East Asian countries are noted to have high PPNG rates[7]. Resistance to quinolones was first observed in the South East Asia and the Western Pacific regions in the 1990's, and have now spread widely within and beyond the Western Pacific Regions[8]. There were also reported cases of altered susceptibility to third generation cephalosporin in the Western Pacific Region[9, 10] and recently these strains have also appeared in centres outside the region. Antibiotic resistance pattern vary between different geographical areas. Therefore, it is important to know the local antibiotic resistance pattern, so that appropriate treatment can be instituted. In HKL, kanamycin was used during the early 1970's and 80's, which was subsequently changed to spectinomycin, followed by ceftriaxone since the early 1990's.

## Objectives

To determine the antibiotic resistance pattern of *N.gonorrhoeae* in patients attending the GUM Clinic, HKL and to compare it with other countries.

**Table 1.** Positive culture isolates of *N.gonorrhoeae*

| YEAR | Number of isolates |
|---|---|
| 2001 | 81 |
| 2002 | 86 |
| 2003 | 72 |
| 2004 | 89 |
| 2005 | 88 |
| TOTAL | 416 |

**Demographics**

Majority of the patients (51.7%) were between the ages of 21-30 years old (Figure 1). 96.6% were males and 3.4% females. The majority of the patients were Malays (63.7%), followed by Indian (23.6%), Chinese (8.9%) and others (3.8%). (Racial distribution of patients attending the GUM Clinic, HKL from 2001-2005 : Malay-44.7%, Indian-25.3% Chinese-18.6% and Others-11.4%).

## Materials and methods

This is a retrospective study of all patients with gonorrhoea (new and recurrent), attending the GUM Clinic, HKL between 2001-2005. Antimicrobial susceptibility testing by standard disc diffusion method was performed to detect resistance to penicillin, tetracycline, kanamycin, ciprofloxacin, spectinomycin, ceftriaxone and cefuroxime. All information was obtained from patients' case notes.

## Results

A total of 416 positive culture isolates of Neisseria gonorrhoeae from 2001-2005 were reviewed. The number of isolates for each year is shown in **Table 1**.

**Figure 1.** Age of patients with gonorrhoea (n=416)

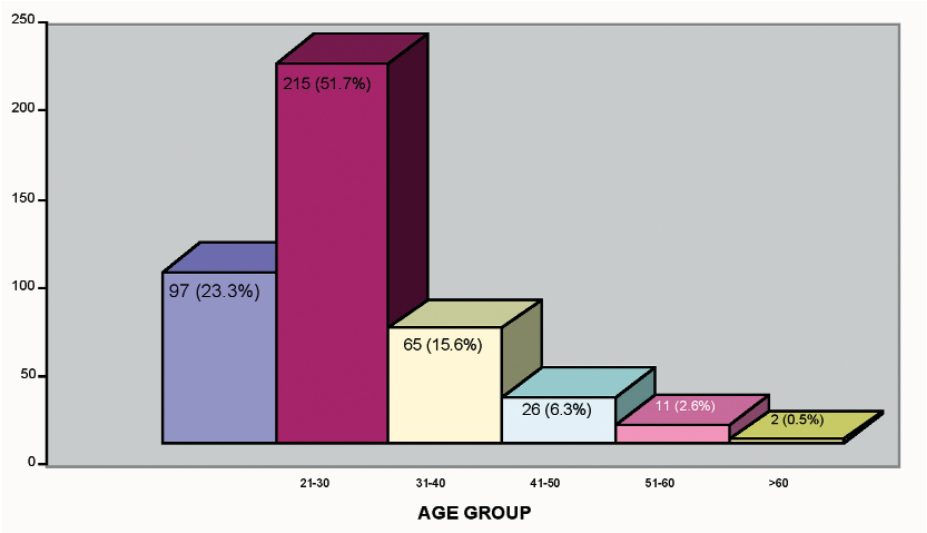

**Table 2.** Summary of antibiotic resistance pattern of *N.gonorrhoeae* (2001-2005)

| Year / Antibiotics | 2001 | 2002 | 2003 | 2004 | 2005 | Overall (2001-05) |
|---|---|---|---|---|---|---|
| Tetracycline | ND | 57.4% (27/47) | 76.4% (55/72) | 100% (89/89) | 97.7% (86/88) | **86.8% (257/296)** |
| Penicillin | 54.3% (44/81) | 65.1% (56/86) | 41.7% (30/72) | 70.8% (63/89) | 85.2% (75/88) | **64.4% (268/416)** |
| PPNG | 49.4% (40/81) | 50% (43/86) | ND | ND | 85.2% (75/88) | **62% (158/255)** |
| CMRNG | 4.9% (4/81) | 15.1% (13/86) | ND | ND | 0% (0/88) | **6.7% (17/255)** |
| Kanamycin | 13.6% (11/81) | 89.7% (35/39) | ND | ND | ND | **38.3% (46/120)** |
| Ciprofloxacin | ND | 8.7% (4/46) | 10.5% (6/57) | 9.0% (8/89) | 12.5% (11/88) | **10.4% (29/280)** |
| Spectinomycin | 1.2% (1/82) | 2.3% (2/86) | 0% (0/9) | ND | ND | **1.7% (3/177)** |
| Cefuroxime | 0% (0/81) | 0% (0/39) | ND | ND | ND | **0% (0/120)** |
| Ceftriaxone | 0% (0/81) | 0% (0/86) | 0% (0/72) | 0% (0/89) | 0% (0/88) | **0% (0/416)** |

ND - Not done

**Figure 2.** Antibiotic resistance pattern of *N.gonorrhoeae* (2001-2005)

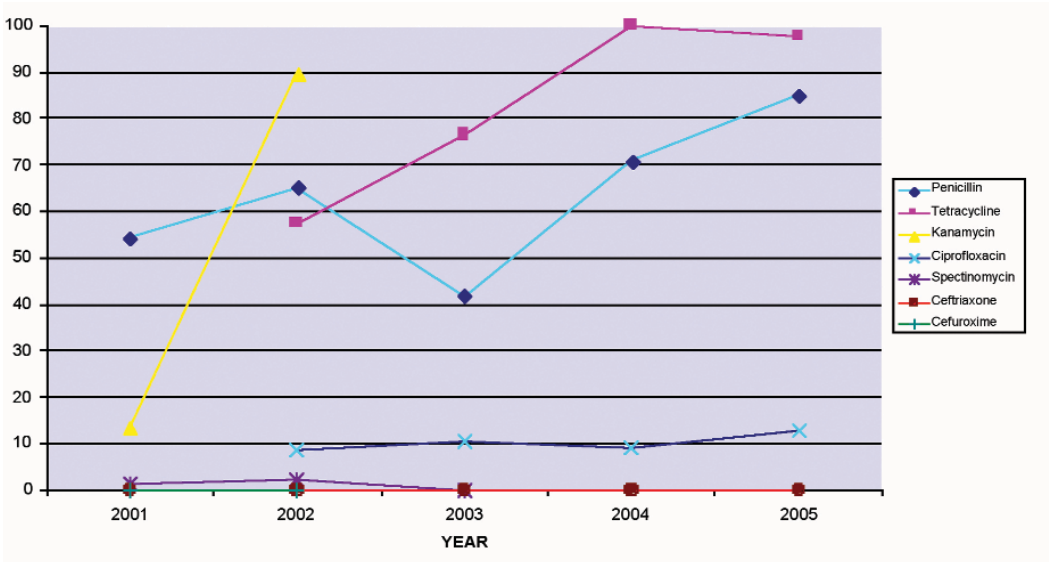

**Figure 3.** Overall antibiotic resistance pattern of *N.gonorrhoeae* (2001-2005)

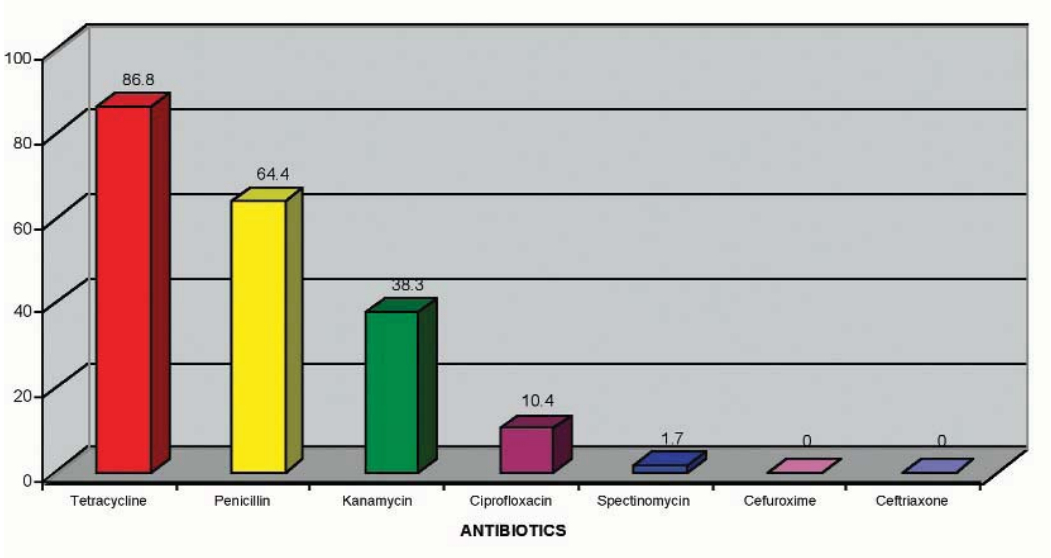


**Figure 4.** Resistance of *N.gonorrhoeae* to Penicillin

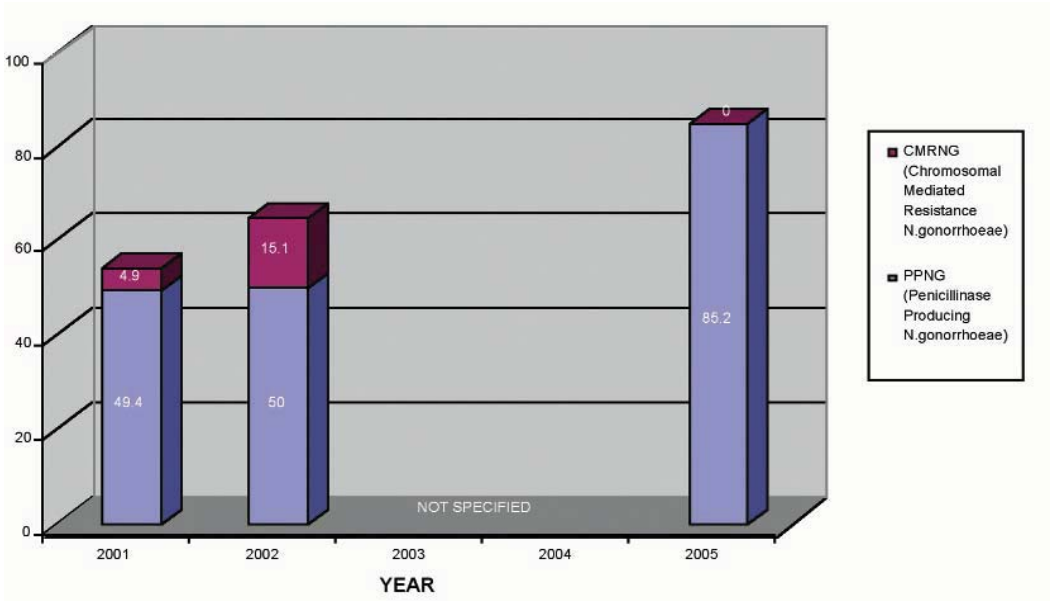

**Table 3.** Comparison of *N.gonorrhoeae* antibiotic resistance pattern in Hospital Kuala Lumpur (HKL) with other countries

| Country / Centre | % Tetracycline Resistant | % Penicillin Resistant | | % Ciprofloxacin Resistant |
|---|---|---|---|---|
| | | Overall | PPNG | |
| **HKL (2001-05)** (n= 416) | **86.8** | **64.4** | **62** | 10.4 |
| Singapore[7] (n= 160) | 71.9 | 50.5 | 48.7 | 56.2 |
| Philippines[7] (n= 175) | 8.0 | 51.4 | 37.1 | 48.5 |
| New Zealand[7] (n= 773) | 17.9 | 5.8 | 3.7 | 20.9 |
| Australia[7] (n= 3,542) | 13.8 | 21.7 | 11.1 | 23.3 |
| China[7] (n= 1,203) | 34.2 | 75.2 | 48.8 | 99.2 |
| England and Wales[6] (n= 1,744) | 44.5 | 11.2 | 5.9 | 14.1 |

[7]The WHO Western Pacific Gonococcal Antimicrobial Surveilance Programme (GASP) 2004
[6]The Gonococcal Resistance to Antimicrobials Surveilance Programme (GRASP) 2004

## Antibiotic resistance pattern of *Neisseria gonorrhoeae*

### 1. Tetracycline

Tetracycline has never been used for treating gonorrhoea in HKL as the resistance is very high. Nevertheless, the resistance pattern is continuously monitored for epidemiological purposes. In 2002, 57.4% of the isolates were resistant to tetracycline and the levels have continued to rise, reaching 100% in 2004 (**Table 2** and **Figure 2**). The overall tetracycline resistance from 2001-2005 is 86.8% **(Figure 3)**.

### 2. Penicillin

Resistance to penicillin also showed an increasing trend from 54.3% in 2001 to 85.2% in 2005 (**Table 2** and **Figure 2**). The overall resistance rate from 2001 to 2005 is 64.4% **(Figure 3)**. This can be due to Penicillinase Producing N.gonorrhoeae (PPNG) or Chromosomal Mediated Resistance *N.gonorrhoeae* (CMRNG) **(Figure 4)**. Of the isolates resistant to penicillin, 62% were PPNG and 6.7% CMRNG.

### 3. Kanamycin

Kanamycin was used for treating gonorrhoea in HKL in the early 1970's and 80's. However, because of increasing resistance since the early 1990's, it is not used anymore. Resistance of *N.gonorrhoeae* to kanamycin was done in 2001 and 2002 only. There was a marked increase in the resistance pattern from 13.6% in 2001 to 89.7% in 2002 (**Table 2** and **Figure 2**). The overall resistance to kanamycin from 2001 to 2005 is 38.3% **(Figure 3)**.

### 4. Ciprofloxacin

Ciprofloxacin is not the first line treatment for gonorrhoea in our clinic. However, it is used by the primary care doctors for treating gonorrhoea due to its accessibility and ease of administration. Susceptibility testing to ciprofloxacin was done since 2002. There was a gradual increase from 8.7% in 2002 to 12.5% in 2005 (**Table 2** and **Figure 2**). The overall resistance rate from 2001-2005 is 10.4% **(Figure 3)**.

### 5. Spectinomycin

Spectinomycin showed a low resistance rate of 1.2% in 2001 and 2.3% in 2002 (**Table 2** and **Figure 2**). The susceptibility testing was discontinued in 2003. The overall resistance to spectinomycin from 2001-2005 is 1.7% **(Figure 3)**.

### 6. Cephalosporins - Cefuroxime and Ceftriaxone

Susceptibilty of N.gonorrhoeae to cefuroxime was tested in 2001 and 2002. None of the isolates were found to be resistant to cefuroxime. Similarly, since 2001 to 2005, none of the *N.gonorrhoeae* isolates were found to be resistant to ceftriaxone (**Table 2, Figure 2** and **Figure 3**). All patients in our clinic were treated with ceftriaxone and subsequent cultures on follow-up were negative.

### 7. Multi-resistant *N.gonorrhoeae*

44.3% of the *N.gonorrhoeae* isolates were found to be resistant to both penicillin and tetracycline. 5.1% of the isolates were resistant to all 3 antibiotics-penicillin, tetracycline and ciprofloxacin.

The summary of *N.gonorrhoeae* antibiotic resistance pattern from 2001 to 2005 is illustrated in **Table 2** and **Figure 2**. The overall (average) antibiotic resistance pattern from 2001-2005 is shown in **Figure 3**.

## Conclusion

Attempts to treat and control gonorrhoea are compromised by the emergence and spread of antibiotic-resistant *N. gonorrhoeae*. WHO expert committee has recommended that treatment regimens be altered once resistance to a particular antibiotic reaches 5 percent.11 Penicillin and tetracycline resistant *N.gonorrhoeae* remain high in Malaysia and other Western Pacific countries and the resistance rate continue to increase. Resistance to ciprofloxacin was however lower in Malaysia compared to other countries. However, the level is gradually increasing and has to be monitored closely. Current first line antibiotic for treating gonorrhoea in GUM Clinic, HKL is ceftriaxone, which has no documented resistance so far.

## Acknowledgement

We would like to convey our special gratitude to Dr Akbal Kaur, Encik Othman Thani and other staff from the Genitourinary Medicine Clinic, HKL for data collection.

## References

1. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. Lancet 1998;351 (Suppl III):5-7.
2. Cohen MS, Hoffman IF, Royce RA et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of transmission of HIV-1. Lancet 1997;349:1868-73.
3. Gerbase AC, Rowley JT, Heyman DHL, Berkley SFB, Piot P. Global prevalence and incidence estimates of selected curable STDs. Sex Transm Inf 1998;74 (suppl 1):S12-S16.
4. Surveillance of antibiotic resistance in Neisseria gonorrhoeae in the WHO Western Pacific Region, 1998. Commun Dis Intell 2000;24:1-4.
5. Tapsall JW. Antibiotic Reistance in Neisseria gonorrhoeae. Clin Infect Dis 2005;41:S263-268.
6. GRASP Steering Group. The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) Year 2004 report. London: Health Protection Agency 2005.
7. The WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic resistance in Neisseria gonorrhoeae in the WHO Western Pacific Region, 2004. Commun Dis Intell 2006;30:129–132.
8. WHO Western Pacific Region Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic susceptibility of Neisseria gonorrhoeae in the WHO Western Pacific Region 1992–4. Genitourin Med 1997;73:355–361.
9. The WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic resistance in Neisseria gonorrhoeae in the WHO Western Pacific Region, 2001. Commun Dis Intell 2002;26:541–545.
10. The WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic resistance in Neisseria gonorrhoeae in the WHO Western Pacific Region, 2000. Commun Dis Intell 2001;25:274-276.
11. Guidelines for the management of sexually transmitted infections WHO/HIV-AIDS. Geneva: World Health Organization; 2001. Report No.WHO/RHR/01.10. Available online. URL:http://www.who.int/docstore/hiv/STIManagemntguidelines /who_hiv_aids_2001.01/
12. Ito M, Deguchi T, Mizutani KS, Yasuda M, Yokoi S, Ito S et al. Emergence and spread of Neisseria gonorrhoeae clinical isolates harbouring mossaic-like structure of penicillin-binding protein 2 in Japan. Antimicrob Agent Chemother 2005;49:137-143.
13. Tapsall JW. Annual Report of the Australian Gonococcal Surveilance Programme, 2004. Commun Dis Intell 2005;29:136-141.
14. Wang SA, Lee MV, O'Connor N, Iverson CJ, Ohye RG, Whiticar PM et al. Multidrug-resistant Neisseria gonorrhoeae with decreased susceptibility to cefixime - Hawaii, 2001. Clin Infect Dis 2003;37:849-852.

Original Article

# A 10-year Retrospective Study on Changing Pattern of Sexually Transmitted Infections in Hospital Kuala Lumpur, Malaysia

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**Abstract**

**Background** Sexually transmitted infections (STIs), and HIV especially, are a major health problem in Malaysia. The emergence of HIV infection has increased the importance of early and effective treatment of STIs as any delay may lead to enhance transmission or acquisition of HIV infection. A proper understanding of the patterns of STIs is necessary for effective planning and control strategies. The present study is designed to determine the changing pattern of STIs in the Genito-urinary Medicine Clinic (GUM), Hospital Kuala Lumpur (HKL).

**Objective** To study the sociodemographic characteristics of patients with STIs attending the GUM Clinic in HKL and to analyze any changes in the pattern of STIs seen between the 2 study periods of 1995-1999 and 2001-2005.

**Method** A retrospective review of case notes of new patients with STIs attending the GUM clinic, HKL was done during two study periods of 1995-1999 (Poster presentation on "Pattern of STDs" at 14th RCD, Asia-Australasia, 26-30 July 2000, KL, Malaysia by HB Gangaram et al) and 2001-2005.

**Results** In 1995-1999, a total of 3150 STI patients were studied. Among them, 2016 (64%) were males and 1134 (36%) were females. In 2001-2005, a total of 2909 STI patients were examined, of which 1862 (64%) were males and 1047 (36%) were female. There was a decrease of 8.3% in the total number of cases seen in 2001-2005 as compared to 1995-1999. The decline was more evident with bacterial STIs which included syphilis, gonorrhoea, NGU and chancroid. Viral STIs which consisted of herpes genitalis, genital warts and HIV showed an increasing trend.

A younger age group (20-39 years old) appeared to be infected with STIs in 2001-2005. Males outnumbered females in the ratio of 1.8:1, which remained unchanged in both the study periods. Based on ethnicity, there was an increase in the percentage of Malays being infected in STIs in the later study period. Syphilis was the commonest STI seen in both the study periods. The second commonest STI seen in 1995-1999 was gonorrhoea and non-gonococcal urethritis (NGU). In 2005, there were 184 patients with syphilis; 64% were heterosexuals; 39.6% homosexuals and 1.6% bisexuals. Majority (82%) were asymptomatic (latent syphilis with positive syphilis serology at presentation. Symptomatic patients with early infectious syphilis constituted 15% (Primary 8%; Secondary 7%). Screening for HIV was positive in 31 (16.8%) patients. HIV infection was noted to be the commonest STI associated with syphilis.

**Conclusion** was an overall decline in the number of patients with STIs attending the GUM clinic, HKL. The decline was more evident with bacterial STIs; viral STIs however showed an increasing trend. Syphilis was still the commonest STI seen in the two study periods although the percentage has declined. Non specific urethritis has superseded gonorrhoea as the second commonest STI. HIV was found to be the commonest STI seen in association with syphilis.

**Keywords** Changing pattern, Sexually transmitted infections, STI

## Introduction

Nearly one million new people are infected with sexually transmitted infections (STIs) every day nationwide. World Health Organization (WHO) estimated that approximately 340 million new cases of the four main curable STIs gonorrhoea, NGU, syphilis and trichomoniasis occur every year[2,13]. STIs are responsible for an enormous burden on morbidity and mortality in many developing countries because of their effects on reproductive and child health and

their role in facilitating the transmission of HIV infection. The emergence of HIV infection has increased the importance of measures aimed at control of STIs. A proper understanding of the patterns of STIs prevailing in different geographic regions of a country is necessary for proper planning and implementation of STI control strategies[4]. It is with this aim that the present study was undertaken.

## Objectives

To study the sociodemographic characteristics of patients with STIs attending the Genitourinary Medicine Clinic (GUM), Hospital Kuala Lumpur and to analyze any changes in the pattern of STIs seen between the 2 study periods of 1995-1999 and 2001-2005.

## Materials and Methods

This is a retrospective review of case notes of new patients with STIs attending the GUM Clinic, HKL during two study periods of 1995-1999 and 2001-2005. The National Statistics figures were obtained from the Department of Public Health, Malaysia.

## Results

This study included a total of 2909 patients in 2001-2005 as compared to 3150 patients in 1995-1999 **(Table 1)**. There was a decrease of 8.3% in the total number of cases seen in 2001-2005.

Majority of the patients (51.7%) were between the ages of 30-49 years old in 1995-1999. In the present study, a younger age group between 20-39 years old appear to be infected with STIs[1,2,3,4,9,10] as shown in **Figure 2**. 64% were males and 34% females in both the study periods. In 1995-1999, Malay comprised the majority of the patients (38%), followed by Indian (22%), Chinese (17%), foreigners (18%) and others (5%). In 2001-2005, there is was increase in the percentage of Malays (47.8%) being infected with STIs, followed by Indian (21.4%), Chinese(18.9%), foreigners (8.0%) and others (3.9%) (refer **Figure 2**). *(Ethnic Distribution of Patients Attending the GUM Clinic, HKL from 2001-2005 : Malay-44.7%, Indian-25.3% Chinese-18.6% and Others-11.4%).*

**Table 1.** Classification of Syphilis in GUM Clinic 2005 (n=184)

| Types of Syphilis | | Number | Percentage % |
|---|---|---|---|
| Primary | | 21 | 11.4 |
| Secondary | | 12 | 6.5 |
| Latent | Early | 39 | 21.2 |
| | Late | 110 | 59.9 |
| Tertiary | | 1(Neurosyphilis) | 0.5 |
| Congenital | | 1 | 0.5 |
| Total | | 184 | 100 |

**Figure 1.** Total number of new patients with STI in GUM Clinic, HKL

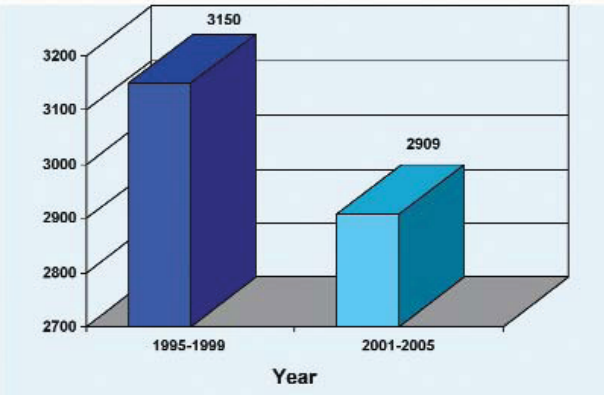



**Figure 2.** Age distribution of new patients with STI

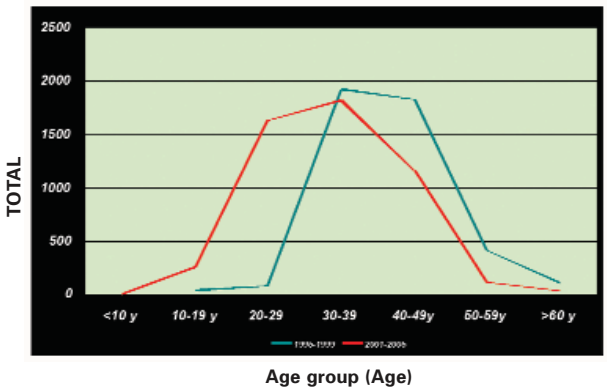


**Figure 3.** Sex distribution of new patients with STI

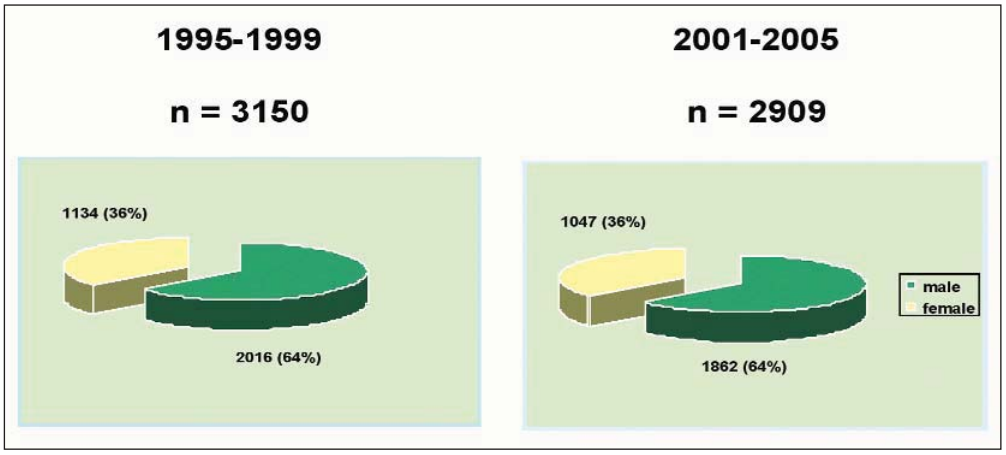
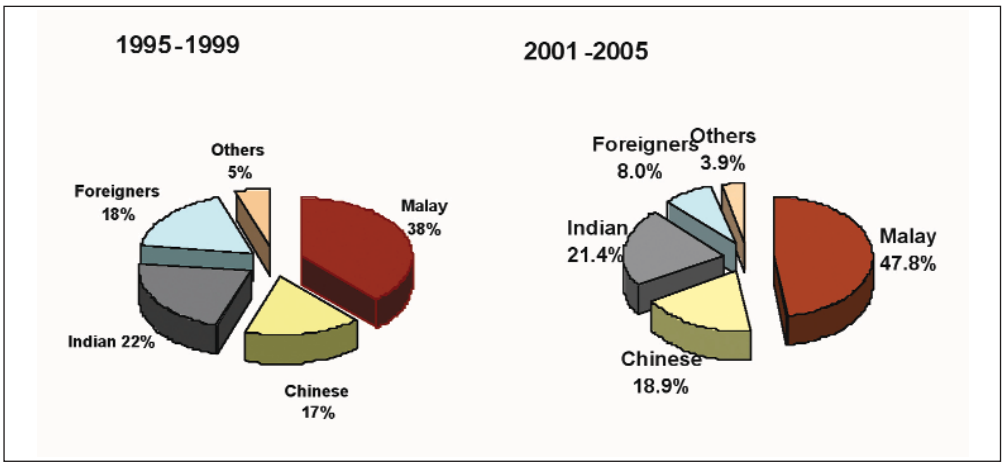



**Figure 4.** Ethnic distribution of new patients with STI




Syphilis was the commonest STI seen in both the study periods although there was a decline from 982 (31.2%) to 702 (24.1%) **(Figure 5)**. In 2005, there were 184 patients. 118 (64.1%) were heterosexual, 73 (39.6%) homosexuals and 3 (1.6%) and 3 (1.6%) bisexuals **(Figure 7)**. Majority (82%) were asymptomatic (latent syphilis with positive syphilis serology at presentation **(Table 1)**. The second commonest STI seen in 1995-1999 was gonorrhoea and non-gonococcal urethritis (NGU) in the present study **(Figure 5)**. Generally, there was an overall decrease in bacterial STI (syphilis, gonorrhoea, NGU and chancroid) with an increase in viral STI (genital warts, genital herpes and HIV)[1,4,8,9] **Figure 6.**

**Figure 5.** Types of STIs between 1995-1999 and 2001-2005

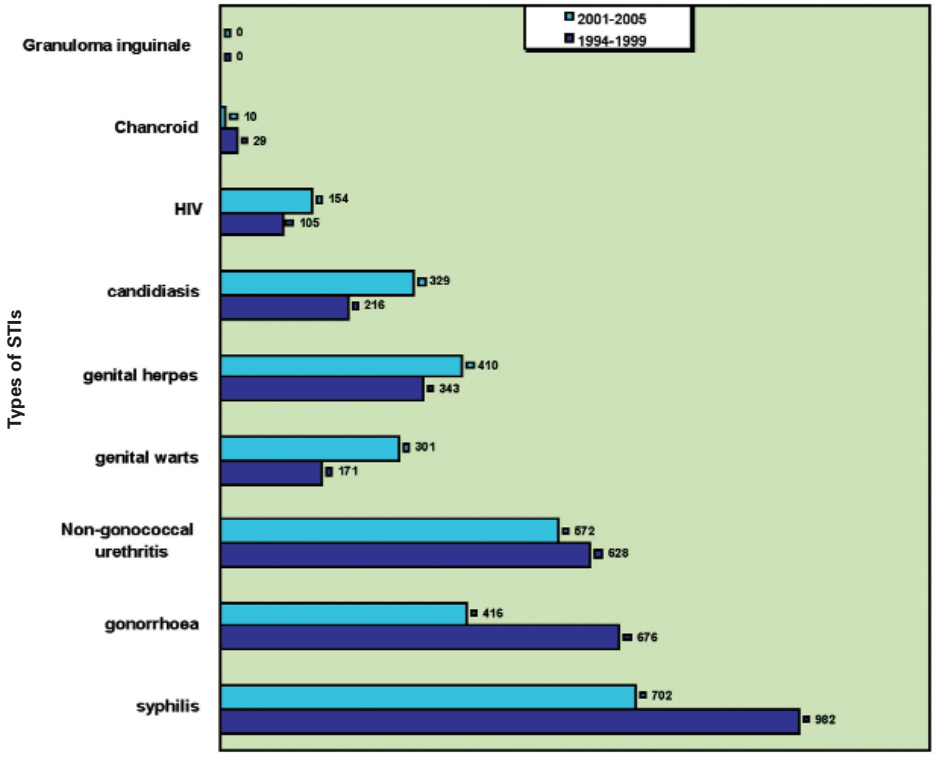



**Figure 6.** Comparison between Bacterial STI and Viral STI

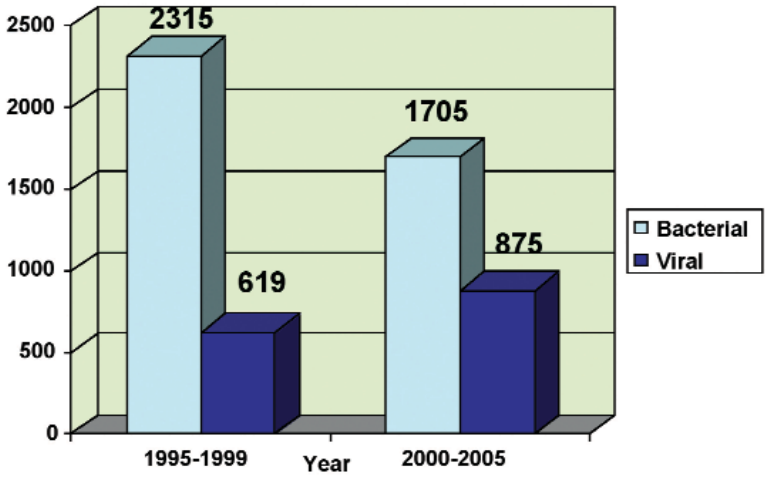
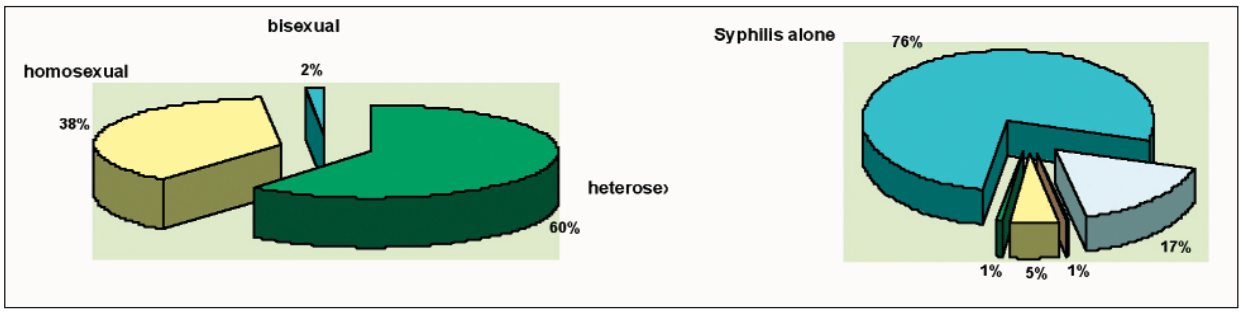
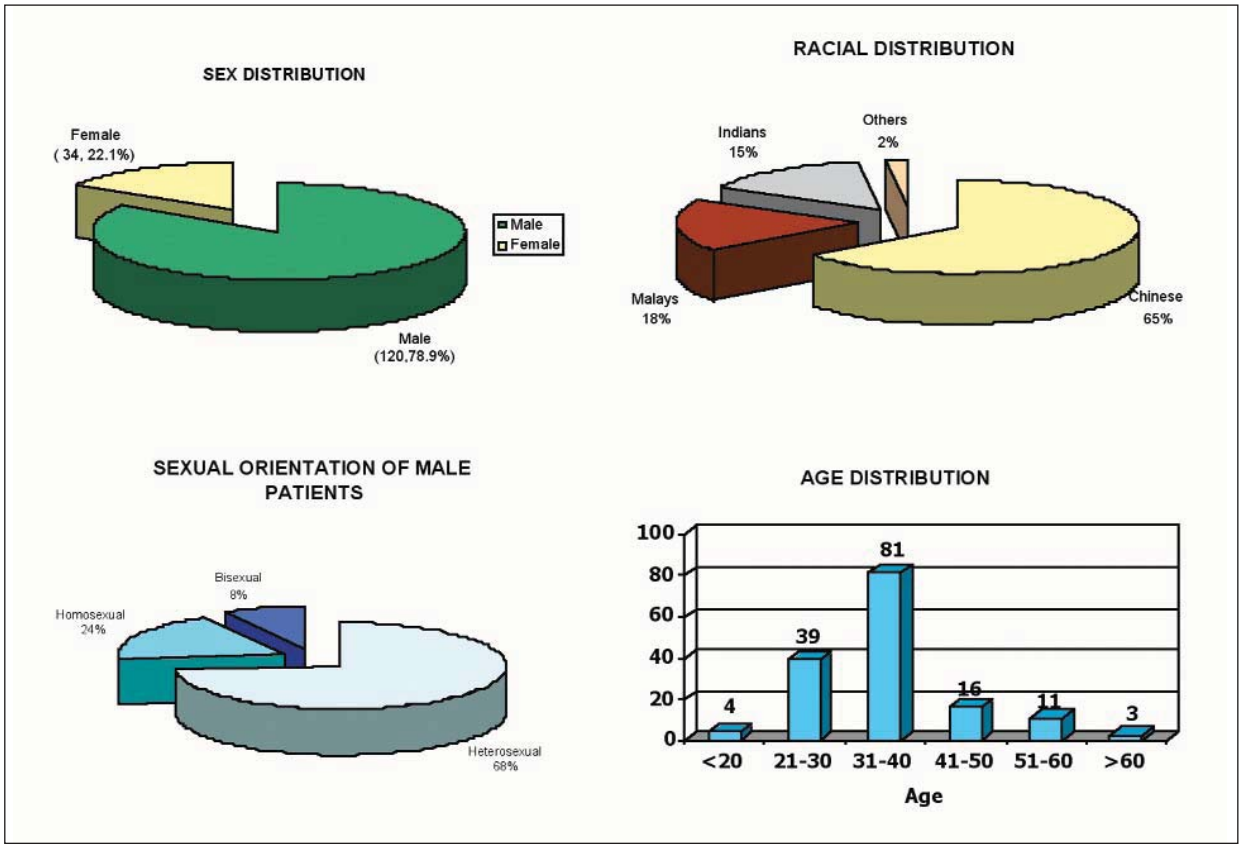


**Figure 7.** Syphilis in GUM Clinic, HKL 2005 (n=184)




HIV seropositivity was 5.3% of all clinic attendes during 2001-2005. Of these 78 % were males and 22% females. 68 % were homosexuals, 24% heterosexuals and 8% bisexuals in HIV male patients. Chinese comprised the majority of patients (65%) followed by Malays (18%), Indian (15%) and others (2%). Majority of patients were in the age group 21-40 years old which is also the most sexually active age group.

**Figure 8.** HIV patients in GUM Clinic, HKL 2001-2005 (n=154)



## Discussion

This study demonstrated an overall decline in the total number of STI cases[1,4,8,9]. The total number of patients with bacterial STIs such as syphilis, chancroid and gonorrhoea also showed a declining trend. However there was an increase in viral STIs like HIV, herpes genitalis and genital warts. This is similar to the findings in other studies. This decline in the number of patients with STIs attending the GUM clinic could be attributed to either a true decline in STIs with the onset of HIV more commonly patients seeking treatment at private general practitioner (GP) clinic, expecting more confidentiality in dealing with these diseases. Awareness and fear of contracting HIV have influenced the risk-taking behaviour of people, thereby reducing the likelihood of being infected with STIs.

In the present study, males outnumbered females by 1.8:1. This pattern of male preponderance is also seen in other studies[1,4,8,9]. Of particular interest, the age group with the highest number of cases has shifted to a younger age[11,14] (20-39 years old ). This is not surprising as the average age for sexual debut nowadays occurs earlier. Factors that could contribute to this include increasing exposure to sex periodicals, advertisements, the theater, radio, television and the internet. This group are at a high risk of being behaviourally more vulnerable to STI acquisition, as they generally have a higher number of sexual partners and more concurrent partnerships and change partners more often than older age groups. Being the economically productive group, there is great loss of workforce due to STI morbidity, measured as disability adjusted life years (DALYS)[1] lost. Although the teenagers were not spared, the percentage of STI cases was not high. Nevertheless the young adults and adolescents should constitute the priority target group in STI control programme.

The disporportionate attendance of Chinese patients could be their preference for seeking treatment from GP clinics as compared to government hospitals/ clinics.

Syphilis is the commonest STI seen in both the study periods although there is a decline. Of the different types, latent syphilis was the most common. The second commonest STI seen in 1995-1999 was gonorrhoea whilst in the present study it was non-gonococcal urethritis (NGU). This pattern change was also seen in most countries. HIV was the commonest STI seen in association with syphilis. Syphilis increases the risk of both transmitting and getting infected with HIV and can be harder to cure and may progress more quickly and severely in people infected with HIV[2]. However, further studies are required to confirm this association.

## Conclusions

There was an overall decline in the total number of patients with STIs attending the GUM Clinic, HKL. The decline was more evident with bacterial STIs; viral STIs however showed an increasing trend. Syphilis was still the commonest STI seen in the two study periods although the percentage has declined. NGU has superseded gonorrhoea as the second commonest STI. HIV was found to be the most common STI seen in association with syphilis.

## Acknowledgement

We would like to convey our special gratitude to Dr Akbal Kaur, Encik Abdul Manaf B. Yusoff and other staff from Genitourinary Medicine Clinic, HKL for data collection.

## References

1. Krishna Ray et al; Changing trends in sexually transmitted infections at a Regional STD Centre in north India; Indian J Med Res 2006;124:559-68-.
2. WHO Europe; Trends in sexually transmitted infections and HIV in the European Region, 1980-2005; technical briefing document 01B/06, Copenhagen, 12 September 2006.
3. Sevgi O. Aral et al; Sexually Transmitted Infections and HIV in the Southern United States: An Overview; Sexually Transmitted Diseases; July (suppl) 2006;33(7):1-5.
4. Narayanan B; A retrospective study of the pattern of sexually transmitted diseases during a ten-year period; IJDVL 2005;71(5):333-7.
5. Kevin A. Fenton et al; Reported Sexually Transmitted Disease Clinic Attendance and Sexually Transmitted Infections in Britain: Prevalence, Risk factors and Proportionate Population Burden; The Journal of Infectious Diseases 2005;191(Suppl 1):127-38.
6. Christopher J. Smith; Social geography of sexually transmitted diseases in China; Asia Pacific Viewpoint; April 2005;46(1):65-80.
7. E.N. Nnoruka and A.C.J.Ezeoke; Evaluation of syphilis in patients with HIV infection in Nigeria; Tropical Medicine and International Health; Jan 2005;10:58-64.
8. Abdul Wahab Al-Fouzan and Nawaf Al- Mutairi; Overview of Incidence of Sexually Transmitted Diseases in Kuwait; Clinics in Dermatology; 2004; 22:509-512.
9. Sharma VK, Khandpur S.; Changing patterns of sexually transmitted infections in India, Natl Medical Journal India; 2004;17(6):310-319.
10. Jaswal AK et al; Changing trends in Sexually transmitted diseases in North Eastern India; IJDVL2002;68(2):65-66.
11. Hiok-Hee Tan, Roy Chan; Sexually transmitted infections in Singapore Youths; National Skin Centre, Singapore 2005.
12. William K.Bosu; Syndromic management of sexually transmitted diseases; Tropical Medicine and International Health ; February 1999:(4);2:114-119.
13. WHO, Office of Information; Sexually transmitted infections increasing- 250 million new infections annually,1990;(152):1-6.
14. Donald WH; The changing pattern of sexually transmitted diseases in adolescents; Practitioner;1979; 222(1329):383-5.
15. Raval RC et al; A study of a changing patterns of sexually transmitted diseases and HIV prevalence during intervals of different years; International Conference AIDS July 7-12, 2002;14: Abstract No. C10895

Original Article

# Allergic Contact Dermatitis in a private practice Dermatology Clinic in Ipoh: A Seven-Year Retrospective Study

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**Abstract**

Patch testing has been accepted as the most important investigative technique of assessing allergic contact dermatitis (ACD) and identifying the contact allergens. The epidemiology of ACD differs in different geographic region as the environmental allergens vary in different populations. In this study 59.8% of the patients had a positive patch test reaction to one or more allergens. The prevalence of ACD was 64.7% in women and 51.4% in men. The commonest causes of ACD were nickel (30.4%), fragrance mix (18.16%) and balsam of Peru (6.73%).

**Keywords** contact dermatitis, prevalence, patch tests

## Introduction

Patch testing has been accepted as the most important investigative technique of assessing allergic contact dermatitis (ACD) and identifying the contact allergens[1] The epidemiology of ACD differs in different geographic region as the environmental allergens vary in different populations. A study done in Hospital Kuala Lumpur using the European standard allergens for the period 1994-1996 showed the top three allergens to be nickel (36%), rubber chemicals (19%) and fragrance mix (17%) while in Singapore nickel (13.9%), fragrance mix (8.4%), flavine (6.3%) and potassium dichromate (6.3%)[2,3]. The prevalence of ACD in 2471 patients patch tested in Singapore was 49.2% in women and 49.8% in men[3]. The epidemiology of ACD in a private practice dermatology clinic has not been well documented. This is an epidemiologic study of ACD of patients attending a private practice dermatology specialist clinic in Ipoh. It also aims to identify the most common contact allergens in this population.

## Materials and methods

All patients seen at the Foong Skin Specialist Clinic between 1999 and 2006 who have had patch tests done were included in the study. The age and sex of the patient were recorded. All were patch tested to the NSC standard battery (Chemotechnique) and additional allergens where indicated. The test allergens were mounted on Scanpore tape. The allergens were removed at 48 hours and reaction recorded 15 minutes after removal. The reactions were recorded again at 96 hours.

Reactions were recorded according to the standard scoring system recommended by International Contact Dermatitis Research Group. NR = nonreactive; +/- = erythema; + = erythema with papules; ++ = palpable erythema, papules and vesicles; +++ = palpable erythema, vesicles, bullae; IR = irritant reactions. Reactions of + and greater were considered positive. The prevalence of ACD (patients with one or more positive reactions) was evaluated.

## Results

During the study period, 317 women and 173 men were patch tested. The age ranged from 6-86 years with a mean of 37.5 years. The prevalence of contact dermatitis was 64.7% (205/317) in women and 51.4% (89/173) in men.

**Table 1** shows the prevalence of positive reaction according to age and sex. Most were in the 20-29 years age group. The rate appeared to increase with age. For those less than 40 years old it was 58.2% (174/299) and more than 40 years 62.8% (120/191).

**Table 2** shows the prevalence of contact dermatitis according to the ethnic group. The rate was not significantly different from the major ethnic groups but was highest in the Chinese followed by Malays and Indians.

**Table 3** shows the prevalence of contact dermatitis to standard allergens according to sex. Nickel (30.4%), fragrance mix (18.16%), Balsam of Peru (6.73%), cobalt (5.31%), potassium dichromate (3.47%), neomycin (3.27%), wool alcohol (3.27%) and parabens (3.27%). were the

**Table 1.** Prevalence of Allergic Contact Dermatitis according to the age group and sex

| Age Group | Female | Male | Total |
|---|---|---|---|
| <20 yr | 18/35 (51.4%) | 9/19 (47.4%) | 27/54 (50%) |
| 20-29 yr | 60/91 (65.9%) | 15/29 (51.7%) | 75/120 (62.5%) |
| 30-39 yr | 51/85 (60%) | 21/40 (52.5%) | 72/125 (57.6%) |
| 40-49 yr | 39/50 (78%) | 12/31 (38.7%) | 51/81 (63%) |
| >49 yr | 37/56 (66.1%) | 32/54 (59.3%) | 69/110 (62.7%) |
| Total | 205/317 (64.7%) | 89/173 (51.4%) | 294/490 (59.8%) |

**Table 2.** Prevalence of Allergic Contact Dermatitis according to ethnic group and sex

| Ethnic Group | Female | Male | Total |
|---|---|---|---|
| Chinese | 165/248 (66.5%) | 72/128 (56.25%) | 237/376 (63%) |
| Malays | 30/46 (65.2%) | 11/28 (39.3%) | 41/74 (55.4%) |
| Indians | 10/19 (52.6%) | 5/12 (41.7%) | 15/31 (48.4%) |
| Others | 0/4 | 1/5 (20%) | 1/9 (11.1%) |
| Total | 205/317 (64.7%) | 89/173 (51.4%) | 294/490 (59.8%) |

**Table 3.** Prevalence of Allergic Contact Dermatitis according to standard battery allergens and sex.

| Allergens | Female n+317 | Male n=173 | Total n=490 |
|---|---|---|---|
| *Metals* | | | |
| Nickel | 115 (36.3%) | 34 (19.3%) | 149 (30.4%) |
| Potassium dichromate | 12 (3.79%) | 5 (28.9%) | 17 (3.47%) |
| Cobalt chloride | 20 (6.31%) | 6 (3.47%) | 26 (5.31%) |
| *Medicaments* | | | |
| Flavine | 3 (0.95%) | 3 (1.73%) | 6 (1.22%) |
| Neomycin | 15 (4.73%) | 1 (0.58%) | 16 (3.27%) |
| Rubber chemicals | | | |
| Thiuram mix | 2 (0.63%) | 2 (1.16%) | 4 (0.82%) |
| Mercapto mix | 1 (0.32%) | 2 (1.16%) | 3 (0.61%) |
| *Preservatives/Fragrances* | | | |
| Fragrance mix | 67 (21.14%) | 22 (12.72%) | 89 (18.16%) |
| Balsam of Peru | 30 (9.46%) | 3 (1.73%) | 33 (6.73%) |
| Wool Alcohol | 12 (3.79%) | 4 (2.31%) | 16 (3.27%) |
| Ethylenediamine | 2 (0.63%) | 1 (0.58%) | 3 (0.61%) |
| Chlorocresol | 3 (0.95%) | 3 (1.73%) | 6 (1.22%) |
| Parabens | 9 (2.84%) | 7 (4.05%) | 16 (3.27%) |
| *Others* | | | |
| Colophony | 8 (2.52%) | 3 (1.73%) | 11 (2.24%) |
| Epoxy resin | 0 | 3 (1.73%) | 3 (0.61%) |
| PPD | 0 | 1 (0.58%) | 1 (0.20%) |

commonest allergens. Nickel allergy was more common in women. Female patients outnumbered the male patients in their allergens for the above except potassium dichromate and parabens where the reverse is true.

## Discussion

Allergic contact dermatitis (ACD) is an important dermatologic disease with considerable morbidity and economic impact. It represents delayed type hypersensitivity to small molecular weight chemicals which acts as haptens. It is caused when contact with a specific allergen elicits a specific immunologic inflammatory response in the allergic individual 24 to 72 hours after re-exposure. Diagnosis of ACD is frequently facilitated or confirmed through the use of patch test procedure.

The prevalence of contact dermatitis to various allergens differs in different population group. Therefore, it is important for dermatologists to be aware of the common allergens and to monitor them in their place of practice. At our dermatology clinic in Ipoh, 59.8% of patients had a positive patch test reaction to one or more allergens. The prevalence was 49.5% in Singapore[3], 55% in Scotland[4] and 60.5% in Spain[5]. In this study the prevalence of ACD and the causative allergens are not much different from existing published epidemiological studies.

It has been found that allergic contact dermatitis was more frequent in women as compared to men[6]. The preponderance in women could be due to the high rate of sensitization to certain allergens such as nickel and fragrances. In our study the prevalence of allergic contact dermatitis was 64.7% (205/317) in women and 51.4% (89/173) in men. The prevalence of ACD was significantly higher in women than in men. (test of significance, p value <0.05) However, Goh in his study found that men and women were equally susceptible to epicutaneous sensitization. In his study the prevalence was 49.2% in women and 49.8% in men[3].

ACD in different ethnic groups has seldom been studied before. The prevalence between black and white Americans appeared to be the same[8]. In our study, Chinese had the highest prevalence rate (63%), while Malays had a prevalence rate of 55.4% and Indians 41.7%.

Nickel allergy (30.4%) was the commonest cause of ACD in our study. It was more common in women (36.3%) than in men (19.3%). The unique ethnic lifestyle has brought about peculiar presentation of nickel allergy as scarf button dermatitis under the chin as a result of the pin worn by Muslim women. The use of costume jewellery and ear piercing are among the common causes of sensitization to nickel.

Fragrance mix (18.16%) was the second commonest contact allergen in this study. The rate appeared to be higher in women (21.14%) than in men (12.72%). Fragrance is present in most perfumes, cosmetics, toiletries and many household products. They are important in our community because they are widely used. Balsam of Peru formed the third commonest contact allergen. Balsam of Peru is a plant product, a balsam derived from the trees of the genus Myroxylan found in Central and South America. It contains a mixture of fragrance constituents such as cinnamic acid, eugenol, benzyl benzoate, benzyl alcohol, vanillin, etc. As such it is a useful marker to detect fragrance allergy. Not surprising, it was higher in women (9.74%) than in men (1.73%).

Other common contact allergens were cobalt (5.31%), potassium dichromate (3.47%), neomycin (3.27%), wool alcohol (3.27%) and parabens (3.27%). In women, co-sensitivity of cobalt and nickel occur commonly due to wearing of costume jewellery. In men, cobalt allergy is often associated with chromate allergy due to occupational cement exposure.

## References


1. Ang P, Ng SK. Chapter editor: "The Principles and Practice of Contact and Occupational Dermatology in the Asia-Pacific Region." Edited by Ng SK and Goh CL. Investigative techniques in Contact Dermatitis." World Scientific 2001.
2. Rohna R. Pattern of contact and photocontact dermatitis at Hospital Kuala Lumpur - a two year study (1994-1996). Paper presented at the Update Contact Allergy Occup Dermatoses, Kuala Lumpur, 6 April 1996.
3. Goh CL. Epidemiology of Contact Allergy in Singapore. Int J Dermatol 1998;27:308-311.
4. Husain SL. Contact Dermatitis in the west of Scotland. Contact Dermatitis 1977;3:327-332.
5. Romaguera, C, Grimalt F. Statistical and comparative study of 4600 patients tested in Barcelona (1973-1977). Contact Dermatitis 1980;6:309-315.
6. Rees JL et al. Sex differences in susceptibility to development of contact hypersensitivity to dinitrochlorobenzene (DNCB) Br J Dermatol 1989; 120:371-374.
7. Hammershoy O. Standard patch test results in 3225 consecutive Danish patients from 1973-1977. Contact Dermatitis 1980; 6:263-268.
8. Leyden JJ, Kligman AM. Allergic contact dermatitis: sex differences. Contact Dermatitis 1977; 3:332-336.

Original Article

# Prevalence of herpes simplex virus infection in patients with genital herpes using the immunofluorescent antibody test

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**Abstract**

**Background** Herpes genitalis (HG) is the commonest cause of sexually transmitted ulcerative disease in the world, including Malaysia[1]. Herpes simplex virus (HSV) type 2 is more frequently implicated than HSV type 1. This pattern has seen some changes in many parts of the world, with increasing HSV type 1 rates[2].

**Objective** The aim of this study was to determine the type of HSV implicated in patients with herpes genitalis at the Genito-Urinary Medicine Clinic, Department of Dermatology, Hospital Kuala Lumpur.

**Methods** A retrospective study was undertaken on 242 patients with a diagnosis of herpes genitalis at the Genito-Urinary Medicine Clinic from January 2000 to December 2004. The study included all cases of genital herpes in patients aged over 12 years. The typing was done by a immunofluorescent - labeled monoclonal antibody technique specific for HSV antigens.

**Results** Majority (76%) were between the ages of 20-49 years. Males outnumbered females by 1.6:1. Younger women (20-29 years old) tend to be more frequently affected than their male counterpart. One fourth (25.7%) of the patients reported having sex with sex workers and less than 1% (0.4%) were sex workers. A significant percentage (30.5%) of married men reported extramarital relationship with sex workers or had a casual or regular partner. Usage of condoms was low at 12%. Clinical diagnosis at presentation was primary herpes genitalis (56%) and recurrent (44%). 162 (67%) out of a total of 242 patients had the herpes immunofluorescent test done. 110 (68%) of those done were negative. Only 34 (21%) of patients with herpes genitalis had a positive immunofluorescent antibody test. Of the 21%, herpes simplex virus type 2 was found in 19 (12%) of patients with herpes genitalis, HSV type 1 in 10 (6%) and HSV types 1 & 2 coinfection in 5 (3%) patients.

**Conclusions** In our study, HSV-2 was still more common causing 57% of the cases seen, HSV-1 29% and HSV-1 and HSV-2 coinfection in 14%. An increased rate of HSV-1 seen could possibly be due to a change in sexual behavior of the patients especially with regards to oro-genital sexual contact.

**Keywords** Genital herpes, Immunofluorescent antibody test, HSV types

## Introduction

Herpes genitalis (HG) is the commonest cause of sexually transmitted ulcerative disease in the world, including Malaysia[1]. It is associated with not only physical but also important psychosocial and economic consequences. Herpes simplex virus (HSV) type 2 is more frequently implicated than type 1. This pattern has however seen some changes in many parts of the world, with HSV type 1 becoming more common than HSV type 2. This is evident in most parts of the world including Australia, Europe and the USA. Some of the reasons postulated included earlier onset of sexual debut, change in sexual behavior especially with regards to oro-genital sexual contact and lower rates of pre-pubertal HSV-1[2].

The aim of this study was to determine the type of HSV implicated in patients with herpes genitalis at the Genito-Urinary Medicine Clinic, Department of Dermatology, Hospital Kuala Lumpur.

## Materials and Methods

A retrospective study was undertaken on 242 patients with a clinical diagnosis of herpes genitalis at the Genito-Urinary Medicine Clinic from January 2000 to December 2004. The study included all clinical cases of genital herpes in patients aged over 12 years. Specimens were collected

from genital lesions with a cotton-tipped swab and smeared onto micro-wells of daflon-coated slides, air-dried, fixed with acetone and stained with ImagenTM HSV-1 or HSV-2 using specific monoclonal antibodies conjugated to FITC in two individual wells, from Dalco Cytomation Co; United Kingdom[3]. This direct immunofluorescent antibody technique (IFAT) read with a fluorescent microscope was utilized for HSV detection as well as typing. This is the routine, cost-effective and rapid detection method for genital HSV in this hospital.

## Results

**Table 1.** Total number of new cases of herpes genitalis by year (n=242)

| YEAR | NUMBER (%) |
|---|---|
| 2000 | 62 (26) |
| 2001 | 49 (20) |
| 2002 | 38 (16) |
| 2003 | 31 (13) |
| 2004 | 62 (25) |
| TOTAL | 242 (100) |

A total of 242 case notes were reviewed

**Table 2.** Source of referral of herpes genitalis (n=242)

| SOURCE OF REFERRAL | NUMBER (%) |
|---|---|
| Self Referred | 52 (21) |
| Out patient department | 44 (18) |
| Other departments in HKL | 33 (14) |
| Other hospitals | 30 (12) |
| General practitioner | 27 (11) |
| Follow-up | 14 (6) |
| Maternal & child health clinic | 2 (1) |
| Others | 40 (17) |
| TOTAL | 242 (100) |

Majority of the patients were self-referred or came from the outpatient department of the hospital

**Table 3.** Occupation of patients with herpes genitalis (n=242)

| OCCUPATION | NUMBER (%) |
|---|---|
| Office worker | 53 (21.9) |
| Unemployed | 34 (14) |
| Housewife | 29 (12) |
| Manual worker | 27 (11.2) |
| Student | 15 (6.2) |
| Salesman | 8 (3.3) |
| Professional | 7 (2.9) |
| Army/police | 5 (2.1) |
| CSW | 1 (0.4) |
| Bus/lorry driver | 1 (0.4) |
| Others | 62 (25.6) |
| TOTAL | 242 (100) |

Majority were office-workers. Only 1% of the patients were commercial sex workers.

**Table 4.** Distribution of herpes genitalis by age & sex (n=242)

| AGE | MALE | FEMALE | TOTAL |
|---|---|---|---|
| 12-19 | 3 (2%) | 4 (4%) | 7 (3%) |
| 20-29 | 23 (15%) | 45 (49%) | 68 (28%) |
| 30-39 | 40 (27%) | 27 (29%) | 67 (28%) |
| 40-49 | 37 (25%) | 11 (12%) | 48 (20%) |
| 50-59 | 31 (21%) | 5 (5%) | 36 (15%) |
| 60 & above | 16 (10%) | 0 | 16 (6%) |
| TOTAL | 150 (62%) | 92 (38%) | 242 (100%) |

Younger women (20-29 years old) tend to suffer more from herpes genitalis than men.

**Table 5.** Risk factors and marital status in patients with herpes genitalis (n=282)

| RISK FACTOR | MARRIED | UNMARRIED | DIVORCED | WIDOW | TOTAL |
|---|---|---|---|---|---|
| SEX WITH SPOUSE | 136 (70%) | 8 (10%) | 0 | 0 | 144 (51%) |
| SEX WITH SEX WORKER | 34 (18%) | 33 (41%) | 3 (60%) | 2 (67%) | 72 (26%) |
| SEX WITH CASUAL PARTNER | 17(8.5%) | 17 (21%) | 1 (40%) | 1 (33%) | 35 (12%) |
| SEX WITH REGULAR PARTNER | 7 (4%) | 21 (26.3%) | 1 (40%) | 0 | 29 (10%) |
| SEX WORKER | 0 | 1 (1%) | 0 | 0 | 1 (0.4%) |
| TOTAL RESPONSES | 194 (69%) | 80 (28%) | 5 (2%) | 3 (1%) | 282 (100%) |

A significant percentage (30.5%) of married men reported extramarital relationship with sex workers or had a casual or regular partner

**Table 6.** Provisional diagnosis at first visit (n=242)

| Type of Herpes genitalis | Male | Female | Total |
|---|---|---|---|
| Primary | 52 | 83 | 135 (56%) |
| Recurrent | 85 | 22 | 107 (44%) |
| Total | 137 | 105 | 242 (100%) |

Provisional diagnosis at first visit was :
Primary herpes genitalis 135 (56%) Recurrent herpes genitalis 107 (44%)

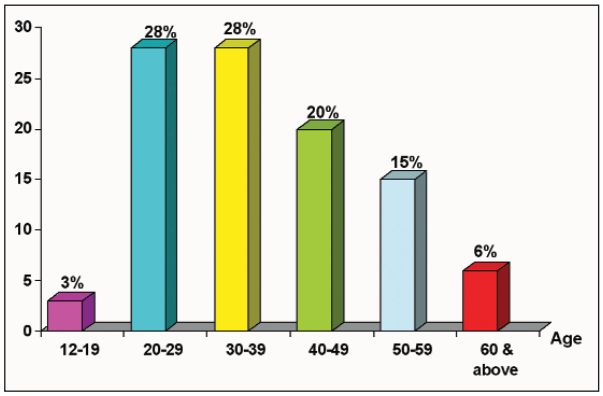
**Table 7.** Correlation of clinical presentation and immunoflourescent test (n=162)

| Clinical type of herpes genitalis | Herpes IMF test | | | | Total |
|---|---|---|---|---|---|
| | Positive | | | Negative | |
| | HSV 1 | HSV 2 | Both HSV 1 & 2 | | |
| Primary herpes genitalis | 3 (30%) | 12 (63%) | 2 (40%) | 70 (64%) | 87 + 12 UT |
| Recurrent herpes genitalis | 7 (70%) | 7 (37%) | 3 (60%) | 40 (36%) | 57 + 6 UT |
| Total | 10 (6%) | 19 (12%) | 5 (3%) | 110 (68%) | 144 + 18 UT = 162 |

UT – HSV test untraceable

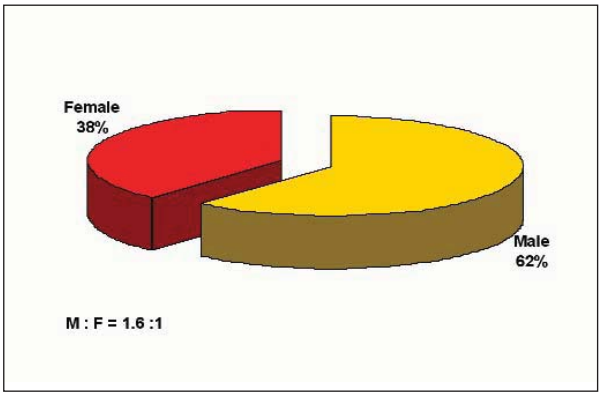
In primary herpes genitalis, HSV type 2 accounted for 70.6% of the positive cases, HSV type 1, 17.6% and HSV types 1 and 2 coinfection in 11.8%. In recurrent herpes genitalis, HSV types 1 and 2 were found to be equally frequent (41.2%) and HSV types 1 and 2 coinfection in 17.6%.

**Figure 1.** Age distribution of patients with herpes genitalis (n=242)



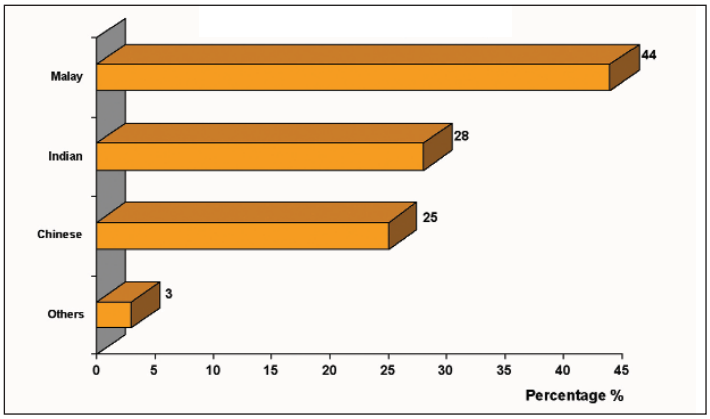

Majority (76%) of the patients were between the ages of 20-49 years

**Figure 2.** Distribution of herpes genitalis by sex (n=242)



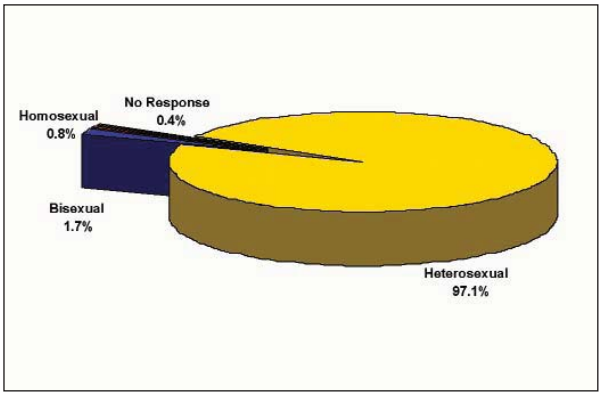

Males outnumbered females by 1.6 :1

**Figure 3.** Racial distribution of patients with herpes genitalis (n=242)



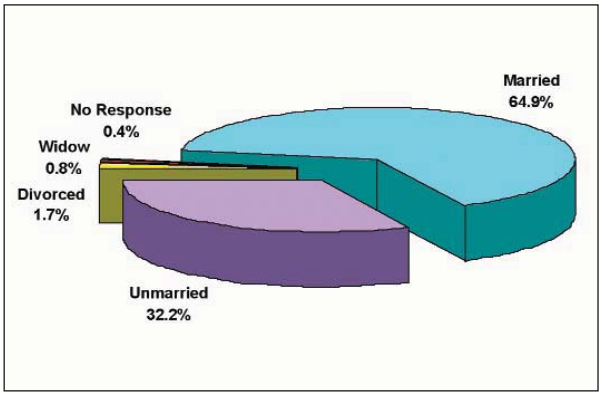

Malays accounted for 44%, Indians 28% and Chinese 25% of the total patients. This probably reflects the normal pattern of clinic attendance

**Figure 4.** Sexual orientation of patients with herpes genitalis (n=242)



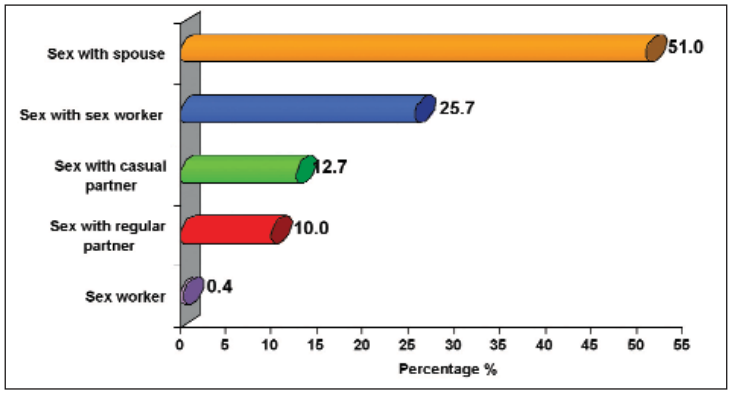

Majority (97%) of the patients were heterosexually orientated

**Figure 5.** Marital status of patients with herpes genitalis (n=242)



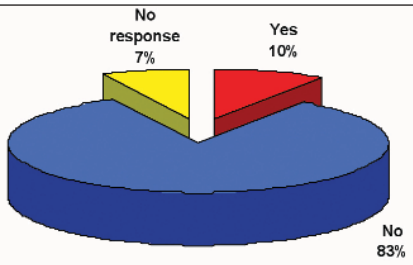

About two thirds (64.9%) of the patients were married

**Figure 6.** Risk factors in patients with herpes genitalis (n=242)




About 1/4 (25.7%) of the patients reported sex with sex workers. Less than 1% (0.4%) of the patients were sex workers

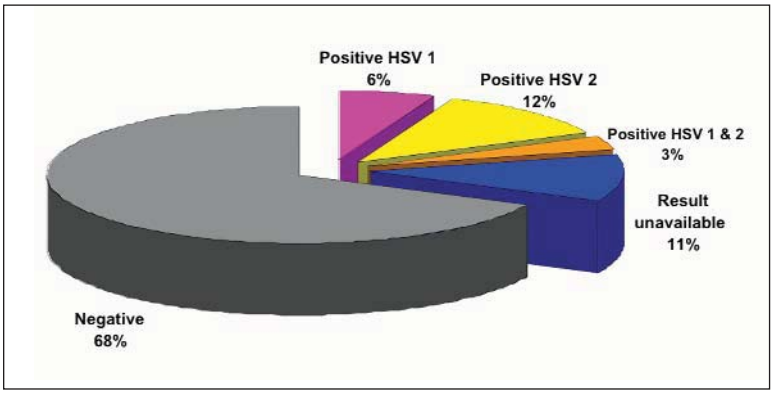
**Figure 7.** Use of condoms by patients with herpes genitalis (n=242)




| Sex | Use of Condoms | Sexual Orientation | | | |
|---|---|---|---|---|---|
| | | Heterosexual | Homosexual | Bisexual | No Response |
| Male | Yes | 17 (7%) | 1 (50%) | 1(25%) | |
| | No | 115 (49%) | 1 (50%) | 3(75%) | |
| | No Response | 12 (5%) | | | |
| Female | Yes | 4 (2%) | | | |
| | No | 81 (34%) | | | 1(100%) |
| | No Response | 6 (3%) | | | |
| | TOTAL | 235 (100%) | 2 (100%) | 4(100%) | 1(100%) |

Condom usage was low (12%)

**Figure 8.** Herpes immunoflourescent test in patients with herpes genitalis (n=162)




162 (67%) patients had the herpes immunofluorescent antibody test done. 110 (68%) of those done were negative. Only 34 (21%) patients with herpes genitalis had a positive immunofluorescent antibody test. Of the 21%, herpes simplex virus type 2 was found in 19 (12%) patients with herpes genitalis, HSV type 1 in 10 (6%) and HSV types 1 & 2 coinfection in 5 (3%) patients. Therefore, the most frequent type of HSV causing herpes genitalis in our study was found to be HSV type 2 (57%), HSV type 1 (29%) and HSV type 1 & 2 coinfection (14%).

## Discussion

Genital herpes is a common lifelong virally transmitted sexually transmitted disease which may cause not only significant physical but also severe psychological and emotional impact on the life of a patient. It almost certainly facilitates HIV acquisition[4] and can cause a life-threatening encephalopathy if transmitted to an infant around birth[5]. It is hence important that we make an accurate diagnosis. It is equally important to determine the infecting viral type in order to assess the natural history, prognosis and clinical management of a patient with genital herpes. The clinical presentation of genital primary HSV-1 and HSV-2 infections is similar. However, their natural history is different. Genital HSV-1 infections are characterized by less asymptomatic shedding, a lower transmission frequency to new patients[6], longer time between recurrences, and lower clinical recurrence rates[7]. Once the primary or non-primary attack has resolved, 88% of untreated patients with HSV-2 genital infection suffer episodes of recurrence at a mean rate of 0.3 and 0.4 recurrences per month, compared to 55% of people infected with HSV-1 with a mean recurrence of 0.09 per month[8].

Recent studies suggest that HSV-1 is becoming more frequent as a cause for genital herpes[2]. The table below compares the prevalence of HSV-1 and 2 in genital herpes in various countries. A striking observation seen in both the Bangkok and Sydney studies was the increase in rates of HSV-1 as a cause of genital herpes. Our HSV-1 rate is similar to the second study done in Sydney.

Prevalence of Herpes simplex virus using immunofluorescence antibody test type (IFAT)

| HSV type | Kuala Lumpur, Malaysia | Bangkok, Thailand* | | Western Sydney, Australia[2]** | |
|---|---|---|---|---|---|
| | 2000-2004 (n=242) | 1994-1996 (n=154)[9] | 1998-2004 (n=1125)[10] | 1979-1988 (n=17,512) | 1989-2003 (n=4359) |
| HSV-1(%) | 29 | 18.7 | 39.0 | 9.8 | 23.3 |
| HSV-2(%) | 57 | 81.3 | 43.1 | 78.8 | 76.7 |
| HSV-1 & 2 (%) | 14 | | 17.9 | | |

*Used viral culture followed by IFAT **Used viral culture followed by IFAT

The sensitivity of the IFAT is about 75%. The specificity however, is higher at 85%. Viral culture, said to be the 'gold standard', is not routinely available in our hospital. Although the PCR assay is available in-house, we did not apply this technique for HSV diagnosis on genital lesions mainly because of the prohibitory cost. Moreover, the genital lesion specimens are collected sporadically, not in batches. The IFAT can be applied to even one clinical sample at a time, is rapid giving results within an hour, if necessary. The benefits of Imagen IFAT technique over viral isolation for reduction of hospitalization and reduction of anti-bacterial use, are well established. The immunofluorescence positive rate for herpes simplex virus in our study was about 21%. Being a retrospective study, some of the reasons for this would include the stage of the disease when the specimen was taken, possibility of inadequate specimen for antigen testing, pretreatment with specific anti-viral agents, and the technique itself.

In conclusion, our study showed that HSV-2 was found in 12% of patients with herpes genitalis, HSV-1 in 6% and HSV-1 & 2 co-infection in 3%. Therefore, the most common type of HSV causing herpes genitalis is HSV-2 (57%), followed by HSV-1 (29%) and HSV-1 & 2 co-infection (14%). The increased rate of HSV-1 is possibly due to a change in sexual behavior of the patients especially with regards to oro-genital sexual contact.

## References


1. S Zainah, M Sinniah, Y M Cheong et al. A microbiological study of genital ulcers in Kuala Lumpur. Med J Malaysia 1991;46:274-282.
2. L J Haddow, B Dave, A Mindel et al. Increase in rates of herpes simplex virus type 1 as a cause of anogenital herpes in western Sydney, Australia, between 1979 and 2003. Sex Transm Infect 2006;82:255-259.
3. Patrick C.Y. Woo, Susan S Chiu, Wing-Wong Seto, Malik Peiris. Cost-effectiveness of rapid diagnosis of viral respiratory tract infections in pediatric patients. J Clin Mivrobiol 1997;35(6):1579-1581.
4. Freeman EE, Weiss HA, Glynn JR, et al. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies. AIDS 2006;20:73-83.
5. Whitley R. Neonatal herpes simplex virus infections. J Med Virol 1993;41(Suppl1):13-21.
6. Kinghorn GR. Limiting the spread of genital herpes. (Review) (39 refs). Scand Infect Dis (suppl.) 1996;100:20-5.
7. Mindel A, Weller IV, Faherty A, Sutherland S, Fiddian AP, Adler MW. Acyclovir in first attacks of genital herpes and prevention of recurrences. Genitouri Med 1986;62:28-32.
8. Corey L. The current trend in genital herpes: progress in prevention. Sex Trans Dis 1994;21:S38-44.
9. Puthavathana P, Kanyok R, Horthongkham N, Roongpisuthipong A.Prevalence of herpes simplex virus infection in patients suspected of genital herpes; and virus typing by type specific fluorescent monoclonal antibodies. J Med Assoc Thai 1998 Apr;81(4):260-4.
10. Bhattarakosol P, Visaprom S, Sangdara A, Mungmee V. Increase of genital HSV-1 and mixed HSV-1 and HSV-2 infection in Bangkok, Thailand. J Med Assoc Thai 2005 Sep;88 Suppl 4:S300-4.

Original Article

# Autoimmune Bullous Diseases in Ipoh, Malaysia: A 5-Year Retrospective Study

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**Abstract**

**Background** Autoimmune bullous diseases (ABD) represent a group of chronic blistering dermatoses in which management is often challenging. Epidemiologic data on these diseases in Malaysia has been limited.

**Objectives** Our purpose was to study the spectrum of the various ABD presented to the Department of Dermatology, Ipoh Hospital, and to determine the clinico-epidemiological pattern of the 2 main ABD, namely pemphigus and bullous pemphigoid.

**Methodology** We performed a retrospective review of records for all patients who were diagnosed with ABD confirmed by histopathology and direct immunofluorescence test in this centre between 2001 and 2005. The data were analyzed with regard to age, sex, ethnicity, subtypes of ABD, treatment provided and outcome.

**Results** There were a total of 79 cases of ABD presented to us during this period. Bullous pemphigoid was observed to be the commonest (60.8%) followed by the pemphigus group (36.7%) with the mean incidence of 0.45/100,000/year and 0.28/100,000/year respectively. 44% of patients were of ethnic Chinese origin. There was an overall female preponderance. The mean age of presentation was 65.5 years for bullous pemphigoid and 55 years for pemphigus group. The mean duration of disease before presentation was 1.6 months for bullous pemphigoid and 6.3 months for pemphigus. Various combinations of immunosuppressive agents were used to treat the patients. 48% of bullous pemphigoid cases were controlled with prednisolone alone while 67.9% of pemphigus group required at least 2 immunosuppressive agents to achieve disease control.

**Conclusion** In our study population, bullous pemphigoid was more frequently seen than pemphigus.

**Keywords** Autoimmune bullous diseases, bullous pemphigoid, pemphigus vulgaris

## Introduction

Autoimmune bullous diseases (ABD) represent a group of chronic blistering dermatoses in which management is often challenging. Broadly, it encompasses the pemphigus group in which 2 major subtypes are recognized, namely, pemphigus vulgaris (PV) and pemphigus foliaceus (PF); and the subepidermal group which includes bullous pemphigoid (BP), dermatitis herpetiformis (DH), linear IgA bullous dermatosis (LABD), lichen planus pemphigoides (LPP), epidermolysis bullosa aquisita (EBA), cicatricial pemphigoid (CP), pemphigoid gestationis (PG) and bullous systemic lupus erythematosus (BSLE). Epidemiologic data on these conditions in Malaysia has been limited. In 1992, a study carried out in a university-based hospital in Malaysia on the epidemiology of ABD showed that pemphigus vulgaris was the commonest ABD encountered followed by bullous pemphigoid, with an incidence of 0.2/100,000/year and 0.12/100,000/year respectively1. The study also showed that Indians were more likely to develop ABD, especially BP, when compared to the other ethnic groups in Malaysia.

We aim to study the spectrum of various ABD presented to the Dermatology Department, Ipoh Hospital, Malaysia and to determine the clinico-epidemiological pattern of the 2 main ABD, namely pemphigus and bullous pemphigoid.

## Materials and Methods

The Department of Dermatology, Ipoh Hospital, is the main referral centre for all dermatological diseases in the state of Perak, Malaysia, with a catchment area of about 2.15 million populations. The ethnic mix of Perak's population between 2001 and 2005 comprised 53% Malay, 31.5% Chinese, 12.8% Indian and 2.7% others. In this retrospective study, the case records of all patients diagnosed to have ABD in Ipoh Hospital between January 2001 and December 2005 were analyzed.

Patients with typical clinical and histopathological findings were included. Diagnosis was further confirmed by direct immunofluorescence (DIF) test from perilesional skin

biopsy. Various clinico-epidemiological characteristics including age, sex, ethnicity, duration of disease, treatment provided and the outcome were analyzed for all cases. Disease was considered controlled when the skin eruptions were minimal while the patients were receiving treatment. Remission was defined as no development of new lesions and patients were able to taper down the immunomodulators. The data findings were analyzed using SPSS statistical analysis for Windows 10.

## Results

Over the 5 year period, 79 patients were diagnosed to have ABD in which 48 (60.8%) had bullous pemphigoid (BP); 29 (36.7%) pemphigus (pemphigus vulgaris (PV) -16, pemphigus foliaceus (PF) -11, pemphigus vegetans (PVG) -1 paraneoplastic pemphigus (PNP) -1); 1 (1.3%) linear IgA bullous dermatosis and 1 (1.3%) lichen planus pemphigoides. The racial distribution for all cases of ABD was as follows: 44% Chinese, 37% Malay and 16% Indian. There was a female preponderance in both BP and pemphigus group with a male to female ratio of 1:1.53 and 1:1.8 respectively. The estimated incidence of BP in the state of Perak, Malaysia was 0.45/100,000/year whereas for the pemphigus group was 0.28/100,000/year. The age of patients at presentation ranged from 15 to 91 years; the mean age of presentation for BP and pemphigus was 65.5 years and 55 years respectively. Patients with BP appeared to present earlier with the mean disease duration before first presentation of 1.6 months (range 0.3 – 12 months) for BP compared to 6.3 months (range 0.3 – 48 months) for the pemphigus group **(Table 1)**.

Among the pemphigus cases, PV was the predominant subtype seen in 16 patients followed by PF in 11 patients, pemphigus vegetans (PVG) in 1 patient and paraneoplastic pemphigus (PNP) in 1 patient. PV appeared to be more common among the Chinese (50%) while PF was more frequently seen among Malays (54.5%). The mean age of presentation was 49.6 years for PV and 65.2 years for PF. The mean duration of disease before presentation was 7.1 months for PV and 6.7 months for PF **(Table 2)**. One patient presented with oral erosions for 4 years to various doctors before the diagnosis of mucous membrane PV was made while another patient with PF took 3 years before presenting to us. Our only patient with PNP was a 65 year old Malay female with non-Hodgkin's lymphoma stage 3B who succumbed to her disease even before treatment was instituted. Majority of the PV patients had both oral erosions and skin lesions while none of the PF patients had mucosal involvement.

Prednisolone was used alone or together with various combinations of immunomodulators to treat the ABD which included azathioprine, dapsone, cyclophosphamide, tetracycline and mycophenolate mofetil **(Table 3)**. Majority of the pemphigus cases (67.9%) required at least 2 immunomodulators to treat while 47.9% of BP cases were controlled with prednisolone alone. The mean duration to achieve disease control was 3.8 months for BP and 13.6 months for pemphigus.

Among the 48 patients with BP, 11 (23%) died but none of the deaths were directly related to their disease. The cause of death was due to other medical problems like cerebrovascular accidents, ischaemic heart disease, complications of diabetes and malignancy. Of the 5 out of 29 patients with pemphigus who died, 1 succumbed to sepsis while the others died of unrelated illnesses. None of the BP patients had active disease at the time of death and were on low dose corticosteroids.

## Discussion

Bullous pemphigoid was the commonest ABD seen at our centre, representing 60.8% of all cases. This is in contrast to the previous study done in Malaysia1 in which pemphigus was more commonly encountered. The incidence rate of 0.45/100,000/year and 0.28/100,000/year respectively for BP and pemphigus is higher than previously thought. However, the true incidence of ABD in this region may be higher than reported in this study as some cases may have been treated and followed up by dermatologists in private practice and hence, not captured in this study. Mild cases of BP with localized disease may have also been treated by primary care physicians and not reaching us. There may also be some referral bias; for example pemphigus confined to the oral mucosa may have been referred to the dentists and CP to the ophthalmologists. Furthermore, some cases could have been treated by traditional/complementary medicine (TCM) practitioners instead as this is not an uncommon practice among Malaysians. This could explain the lower incidence for both BP and pemphigus in this region as compared to the incidence rate of other countries **(Table 4)**.

There was a predilection of ABD for ethnic Chinese which comprised 44% of all cases although they constitute only 31.5% of the Perak population during the study period. The Malays, on the other hand, were less likely to develop ABD while the percentage of Indians affected corresponds to the ethnic distribution of this region. This, again, differed from the result of an earlier study done in this country which showed a predilection of ABD for ethnic Indians1. Although the incidence of ABD in the Malays was relatively lower, it was observed that they were more predisposed to develop PF where they made up of 54.5% of all PF cases in this study **(Table 2)**. The Singapore study noted an over-representation of PF in their Malay population, which constituted 25% of all PF cases studied when compared to their normal ethnic composition, of which the Malays constitute 10%[4].

Although an equal sex predisposition has been reported in the previous Malaysian study[1], we observed a female preponderance in both bullous pemphigoid (M:F = 1:1.53) and pemphigus (M:F = 1:1.8). A similar observation was also seen in Kuwait[2,3]. Singapore reported an equal sex

**Table 1.** Comparison of characteristics between bullous pemphigoid and pemphigus

| Characteristic | Bullous pemphigoid (n=48) | Pemphigus (n=29) |
|---|---|---|
| Incidence (per 100,000/year) | 0.45 | 0.28 |
| Age (years) | 65.5 (15 - 91) | 54.8 (17 - 80) |
| Race (%) | | |
| Malay | 33.3 | 39.3 |
| Chinese | 45.8 | 46.4 |
| Indian | 18.8 | 10.7 |
| Others | 2.1 | 3.6 |
| M:F ratio | 1:1.53 | 1:1.8 |
| Duration to diagnosis (months) | 1.6 (0.3 - 12) | 6.3 (0.3 - 48) |
| Duration to disease control (months) | 3.8 | 13.6 |
| No. of deaths over 5 years | 11 (23%) | 5 (17.2%) |

**Table 2.** Demographic data, treatment and course of disease in patients with pemphigus vulgaris and pemphigus foliaceus

| | Pemphigus vulgaris (n = 16) | Pemphigus foliaceus (n = 11) |
|---|---|---|
| Patient's characteristics | | |
| Age (years) | 49.6 (17 - 74) | 65.2 (25 - 80) |
| Sex (M/F) | 6/10 | 4/7 |
| Race | | |
| Malay | 5 (31.3%) | 6 (54.5%) |
| Chinese | 8 (50%) | 4 (36.4%) |
| Indian | 2 (12.5%) | 1 (9.1%) |
| Indonesian | 1 (6.3%) | 0 |
| Duration of disease before diagnosis (months) | 7.1 (0.5 - 48) | 6.7 (0.3 - 36) |
| Treatment | | |
| Prednisolone alone | 4 (25%) | 2 (18.2%) |
| Prednisolone + 1 adjuvant | 6 (37.5%) | 5 (45.5) |
| Prednisolone + 2 adjuvants | 5 (31.3%) | 2 (18.2%) |
| No treatment* | 1 (6.3%) | 2 (18.2%) |
| Course of disease | | |
| Duration to disease control (months) | 12.4 | 11.2 |
| No. of patients with disease controlled | 5 | 1 |
| No. of patients in remission | 3 | 4 |
| No. of patients with active disease | 1 | 1 |
| No. of patients transferred to other centre | 1 | 0 |
| No. of patients who died of disease/sepsis | 0 | 1 |
| No. of patients who died of unrelated causes | 1 | 2 |
| No. of patients lost to follow-up | 5 | 2 |

** lost to follow-up before treatment was instituted*

**Table 3.** Therapy for bullous pemphigoid and pemphigus

| Combinations of Immunomodulators | BulIous pemphigoid | Pemphigus (PV + PF+ PVG) |
|---|---|---|
| Prednisolone alone | 23 | 23 |
| Prednisolone + Azathioprine | 9 | 9 |
| Prednisolone + Tetracycline | 2 | 2 |
| Prednisolone + Dapsone | 6 | 6 |
| Prednisolone + Cyclophosphamide | 2 | 2 |
| Prednisolone + Methotrexate | 0 | 0 |
| Prednisolone + Azathioprine + Dapsone | 3 | 3 |
| Prednisolone + Cyclophosphamide + Tetracycline | 0 | 0 |
| Prednisolone + Azathioprine + Tetracycline | 2 | 2 |
| Prednisolone + Mycophenolate +Tetracycline | 0 | 0 |

** 1 BP patient and 3 pemphigus patients defaulted follow-up before treatment was instituted.*

**Table 4.** Incidence of bullous pemphigoid and pemphigus in studies carried out in different regions of the world

| *Country and year of publication* | *Incidence (per 100,000 per year)* | |
|---|---|---|
| | BulIous pemphigoid | Pemphigus |
| Malaysia 1992[1] | 0.12 | 0.2 |
| France 1995[12] | 0.74 | |
| Germany 1995[13] | 0.662 | |
| Mali 1996[14] | | 0.29 |
| Bulgaria 2000[15] | | 0.47 |
| Southern Saudi Arabia 2001[16] | | 0.16 |
| Singapore 2002[5] | 0.76 | |
| Kuwait 2004[2] | 0.205 | 0.457 |
| Scotland 2005[9] | 1.4 | |
| Iran 2006[8] | | 0.67 |
| Greece 2007[6] | | 0.8 |
| Current study (Perak, Malaysia) | 0.47 | 0.28 |

distribution in pemphigus[4] but a striking female preponderance (M:F = 1:2) in their BP patients[5]. Similar female predominance was also observed in previous pemphigus studies from Greece[6] (M:F = 1:2.25 ), Turkey[7] (M:F = 1:1.41) and Iran[8] (M:F = 1:1.33). The factors responsible for this gender difference have yet to be elucidated.

While the Singapore study reported EBA to be their second commonest subepidermal immunobullous disorder[3], we had none during our study period. This could be explained by the fact that we did not have facilities for salt-split skin indirect immunofluorescence test at the time of the study period and therefore some of the cases may have been grouped together with BP since they share similar DIF findings. We also did not have any cases of BSLE despite SLE being a fairly common disease in this region. This could either be due to the incidence of BSLE being rare in this region or the cases were being treated by rheumatologists instead. We have had few cases of CP, PG and DH on our follow-up but no new cases during the 5 year study period. This finding is similar to the studies done in Singapore[5] and China[11] which reflects the rarity of these diseases in this region.

The first line of treatment for all cases of ABD was with oral prednisolone. Adjuvant therapy with various immunomodulators was added when prednisolone alone was not enough to achieve disease control. The choice for adjuvant therapy was azathioprine or dapsone as they are effective and relatively inexpensive. In the event of an adverse drug reaction or poor response to these 2 medications, other drugs like methotrexate, cyclophosphamide and mycophenolate mofetil were used instead. Tetracycline was usually added as a third agent when 2 drugs were not adequate to control the disease. We found mycophenolate mofetil to be an effective adjuvant therapeutic agent in 2 of our pemphigus patients who had failed to respond the other conventional agents. In addition to systemic therapy, most of our patients also received treatment with potent topical corticosteroids.

As expected, BP was easier to control compared to pemphigus. About half of the BP patients (47.9%) achieve disease control with prednisolone alone compared to only 25% of pemphigus patients. The duration to disease control was also shorter in BP compared to pemphigus, with a mean duration of 3.8 months and 13.6 months respectively **(Table 1)**. Although the number of deaths was higher in the BP group, all deaths were due to unrelated causes as most of the BP patients were older and had concomitant illnesses. It is noteworthy that none of them had active disease at the time of death. This result is in keeping with a previous study done in Scotland[9] which reported the first year mortality rate of 25%. Most deaths were related to old age and the general condition of the patient and rarely due to BP itself. Another study from Germany[10] demonstrated the first year mortality rate of 29% and they attributed low serum albumin, high dosage of corticosteroids and old age as risk factors for lethal outcome in BP.

Between PV and PF, PV appeared to be more difficult to control with about one third of them requiring 2 adjuvant agents to achieve disease control. The duration needed to achieve control was also longer. It is interesting to note that our PF patients present at an older age (mean 65.2 years) when compared to neighbouring Singapore[4] (57 years) and Turkey[7] (52 years). The reason for this is unclear but it could explain the higher mortality encountered in these patients.

## Conclusions

The results of our retrospective study demonstrate that BP is almost twice as common as pemphigus. This is comparable to reports from Singapore where they found BP to be three times more common than pemphigus[5]. The incidence rate is higher for both BP and pemphigus than previously thought. Chinese are more predisposed to ABD, especially BP and PV, while PF is more common in Malays. There is no evidence of a predilection for ethnic Indians as previously reported[1]. There is a female preponderance among BP and pemphigus patients and a low occurrence of other subepidermal blistering diseases like EBA, CP, DH, PG and BSLE in our patients. These results provide a basis on which future research activities in this region can be built.

## References


1. Adam BA. Bullous diseases in Malaysia: epidemiology and natural history. Int J Dermatol 1992; 31: 42-45.
2. Nanda A, Dvorak R, Al-Saeed K, Al-Sabah H, Alsaleh QA. Spectrum of autoimmune bullous diseases in Kuwait. Int J Dermatol 2004, 43: 876-881
3. Alsaleh QA, Nanda A, Al-Baghli NM, Dvorak R. Pemphigus in Kuwait. Int J Dermatol 1999; 38:351-356
4. Goon A, Tan SH. Comparative study of pemphigus vulgaris and pemphigus foliaceus in Singapore. Australasian J Dermatol 2001;42:172-5
5. Wong SN, Chua SH. Spectrum of subepidermal immunobullous disorders seen at the National Skin Centre Singapore: a 2-year review. Br J Dermatol 2002; 147: 476-480.
6. Michailidou EZ, Belazi MA, Markopoulous AK, et al. Epidemiologic survey of pemphigus vulgaris with oral manifestation in northern Greece: Retrospective study of 129 patients. Int J Dermatol 2007; 46: 356-361
7. Uzun S, Durdu M, et al. Pemphigus in the Mediterranean region of Turkey: A study of 148 cases. Int J Dermatol 2006, 45, 523-528
8. Salmanpour R, Shahkar H, Namazi MR, Rahman-Shenas MR. Epidemiology of pemphigus in South Western Iran: A 10-year retrospective study (1991-2000). Int J Dermatol 2006; 45,103-105.
9. Gudi VS, White MI, Cruickshank N, et al. Annual incidence and mortality of bullous pemphigoid in the Grampian Region of North-east Scotland. Br J Dermatol 2005; 153: 424-427.
10. Rzany B, Partscht K, Jung M et al. Risk factors for lethal outcome in patients with bullous pemphigoid: low serum albumin level, high dosage of glucocorticosteroids, and old age. Arch Dermatol 2002; 138: 903-8.
11. Jin P, Shao C, Ye G. Chronic bullous dermotoses in China. Int J Dermatol 1993; 32: 48-52
12. Bernard P, Vaillant L, Labeille B, et al. Incidence and distribution of subepidermal autoimmune bullous skin diseases in three French regions. Arch Dermatol 1995; 131: 48-52.
13. Zillikens D, Wever S, Roth A, et al. Incidence of autoimmune subepidermal blistering dermatoses in a region of central Germany. Arch Dermatol 1995; 131: 957-958.
14. Mahé A, Flageul B, Cissé I, et al. Pemphigus in Mali. A study of 30 cases. Br J Dermatol 1996; 134: 114-119.
15. Tsankov N, Vassileva S, Kamarashev J, et al. Epidemiology of pemphigus in Sofia, Bulgaria. A 16-year retrospective study (1980-1995). Int J Dermatol 2000; 39: 104–108.
16. Tallab T, Joharji H, Bahamdan K, et al. The incidence of pemphigus in Southern region of Saudi Arabia. Int J Dermatol 2001; 40: 570-572.

Original Article

# The effect of explanation and demonstration of topical therapy on the clinical response of atopic eczema

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**Abstract**

**Background** Atopic eczema is a common dermatological condition seen in our practice in which the mainstay of treatment is topical medications. One of the main reasons for poor clinical response to therapy in atopic eczema is the lack of understanding of topical preparation usage and thus poor adherence to treatment.

**Objectives** The aim of this study is to determine the effect of explanation and demonstration of topical medication on the clinical response of atopic eczema.

**Methodology** Twenty newly diagnosed patients with atopic eczema who fulfilled the study criteria were recruited and randomized consecutively into 2 groups - A & B. All patients were assessed on the severity of the eczema using the six area, six sign atopic dermatitis severity score (SASSAD) and patients' assessment of itch, sleep disturbance and irritability were recorded on 10-cm visual analogue scales. They were also assessed on their level of understanding on the proper usage of topical medications using a questionnaire. Group A then received explanation and demonstration on how to apply the topical medications while Group B was not educated on these. They were followed up 2 weeks after treatment and were re-evaluated on their understanding and the severity of their skin condition. This was followed by education by a dermatology nurse on the proper usage of topical medications for both groups. A third evaluation was done 2 weeks later.

**Results** At baseline, 70% of the patients did not understand the potency of topical corticosteroid and between 20-30% of them did not know the correct sites, frequency, time and duration of each topical application prescribed. About two thirds of the patients claimed that they did not receive any explanation or demonstration from either their doctors or the pharmacy dispensers. After education on the proper usage of topical medications, the level of understanding improved to 100% for group A at visit 2 and group B at visit 3. A clinical improvement as measured by SASSAD score reduction was seen in both groups. In group A, a significant SASSAD score reduction of 49.5% (P=0.003) was seen after 2 weeks and it was sustainable, as evidenced by a further reduction to 67% (p=0.001) by week 4. In group B, a significant SASSAD score reduction (64.8%; p=0.002) was seen only at week 4 after patient education and demonstration. The magnitude of improvement in patients' symptoms which included itch, sleep disturbance and irritability, measured by the patient using visual analog score, were only significant for group A after 4 weeks.

**Conclusions** This study reinforces the importance of explanation and demonstration on the proper usage of topical medications in achieving better clinical response. Failure to explain on the use of topical medications may lead to patient dissatisfaction, poor compliance and lack of treatment efficacy.

## Introduction

The cause of failure of response to therapy in many dermatological skin conditions including atopic eczema is poor adherence, rather than severity of disease. This can arise from a number of reasons, the most important of which is a lack of understanding of topical applications. Other reasons include failure to renew prescriptions, under-prescribing, lack of faith in the treatment, or insufficient time to apply the medication. About 80% of our patients are prescribed more than one topical medication at any one time. Confusion with treatment may arise when patients are not educated on the proper usage of the various topical medications. So far there is no published record of any studies carried out in Malaysia to support the fact that improving patients' knowledge of proper topical application by explanation and demonstration will improve the outcome of treatment. Atopic eczema is chosen for this study because it is one of the commonest conditions seen at our clinic; the modality of treatment is mainly by topical medications and the availability of a standard scoring system of severity of disease.

In this study, we aim to determine the effect of explanation and demonstration of topical medications by a trained dermatology nurse on the clinical response of atopic eczema.

## Materials and Methods

New patients who were diagnosed with moderate to severe atopic eczema using the Hanifin and Rajka Criteria[1] at the Dermatology Clinic Ipoh Hospital between February to August 2006 were recruited into the study. Patients who have had any previous consultations with a dermatologist or at any dermatology department were excluded. Those who have a skin disorder other than atopic eczema in the area to be treated were also excluded from this study.

Once the patients were enrolled, they were randomized consecutively into 2 groups, Group A and Group B. The severity of atopic eczema was determined by a global physician assessment using the Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score[2] **(Appendix 1)**. The patients' assessments of itch, sleep disturbances and irritability were recorded on 10-cm visual analogue scales.

After consultation, a prescription was given to the patients to collect their medications from the out-patient pharmacy. They were instructed to return to the clinic after collecting their medications to fill up a study questionnaire assessing their knowledge about the treatment given by their doctors. For patients below 17 years of age, their parents or guardians responded to the questionnaire. Patients who did not know how to read or write were interviewed by the study nurse. Following that, Group A received explanation regarding their disease followed by demonstration on how to apply the topical treatments by a trained nurse from the dermatology clinic. All their topical treatments were labeled with cartoon and multi-languages stickers. Patient information leaflets regarding the disease and the topical treatments which were available in 3 languages (English, Malay, and Mandarin), were handed out to the patients. Group B, on the other hand, did not receive additional explanation or demonstration from the nurse.

Both groups of patients were reviewed after 2 weeks (Visit 2). All patients were re-assessed on their knowledge of the correct usage of topical treatments. The disease severity was again assessed using SASSAD score and patients' assessments using visual analogue scale. They were given the same prescription as the first visit and were instructed to return to the clinic after collecting their medications from the pharmacy. This time, all patients from both Group A and Group B were educated on the methods of application of their medications. This was again reinforced using written instructions. Medications were labeled and information leaflets on the disease were also given.

Both groups were followed up 2 weeks later (Visit 3) and were re-assessed on their knowledge of the correct usage of topical treatments. The disease severity was assessed using SASSAD score and patients' assessments using visual analogue scale. All results were analyzed and interpreted using SPSS program version 10.0.

## Results

A total of 20 patients participated in the study. At baseline, 60% of the respondents recalled not receiving any demonstration from the doctors on how to apply the topical treatments and 55% claimed that the dispensers did not give any explanation to them. 70% of the respondents did not understand the potency of the topical corticosteroid prescribed and between 20-30% of them did not know the correct sites, frequency, time and duration of each topical application prescribed.

Only 14 patients were followed till the end of the study, 7 each for group A and B. The 6 patients who did not complete the study were excluded from further analysis. Out of the 6, 2 defaulted scheduled follow-up, 3 were not willing to spend additional time at the clinic for further assessment and explanation, and therefore left after collecting their medications from the pharmacy and 1 felt that the skin lesion had improved and did not want further consultation. After education on the proper usage of topical medications, the level of understanding had improved to 100% for group A at visit 2 and group B at visit 3.

Both groups showed a reduction in SASSAD score (clinical improvement) at Visit 2 and Visit 3 **(Figure 1)**. A significant reduction of 49.5% (p=0.003) in the severity of eczema was noted after 2 weeks (Visit 2) in Group A and a further reduction of 67% (p=0.001) was noted after 4 weeks (Visit 3). In Group B, a significant reduction of SASSAD score (64.8%; p=0.002) was only noted at week 4 **(Table 1)**.

For the improvement of symptoms based on visual analogue scores, there was a reduction of score at every visit for both groups **(Figure 2, 3, 4)**. At the end of the study, there was a significant improvement for itch, sleep disturbance and irritability for group A whereas in group B, only the score for sleep disturbance showed significant reduction at Visit 3 **(Table 2)**.

## Discussion

Due to the busy clinics and heavy workload, most doctors do not spend enough time explaining the nature of a disease and the proper use of medications prescribed to their patients. Moreover, doctors tend to depend very much on the pharmacists or dispensers to teach patients on the usage or administration of medications prescribed by them. In addition, patient educational materials are also insufficient for patients' reference after each consultation. Educating the patients or parents helps them to take charge of the management of their illness. One trial had demonstrated that education and demonstration of treatment for atopic eczema improved parents' knowledge and the outcome of their child's eczema[3]. Our current study is the first study done in Malaysia to support this finding.

From the literature review, only 5-20% of parents had received or recalled receiving any explanation of the causes of eczema or demonstration on how to apply topical treatments and the side effects of the topical corticosteroids[4, 5, 6]. Thirty to 60% of patients who were

**Table 1.** The Magnitude of SASSAD score reduction for Group A and B

| SASSAD score | Visit 1 (Baseline) | Visit 2 | % of reduction *(p value)* | Visit 3 | % of reduction at Visit 3 from Visit 2 *(p value)* | % of reduction at Visit 3 from baseline *(p value)* |
|---|---|---|---|---|---|---|
| Group A | 35.43 | 17.86 | 49.5* *(0.003)* | 11.57 | 35.2 *(0.054)* | 67.3* *(<0.001)* |
| Group B | 44.57 | 29.43 | 34 *(0.043)* | 15.71 | 46.6 *(0.03)* | 64.8* *(0.002)* |

**Table 2.** The Magnitude of Symptom Improvement using Visual Analog Score

| GROUP A | | | | | | |
|---|---|---|---|---|---|---|
| | Visit 1 | Visit 2 | % of change | Visit 3 | % of change at Visit 3 from Visit 2 | % of change at Visit 3 from baseline *(p value)* |
| Itch | 7.14 | 4.29 | 39.9 | 3.43 | 20.0 | 51.9* *(0.007)* |
| Sleep | 5.00 | 3.71 | 25.8 | 2.71 | 26.9 | 45.8* *(0.007)* |
| Irritability | 5.29 | 3.43 | 35.2 | 3.00 | 12.5 | 43.3* *(0.009)* |
| GROUP B | | | | | | |
| Itch | 8.00 | 6.29 | 21.4 | 4.57 | 25.9 | 42.8 |
| Sleep | 7.86 | 4.57 | 41.9 | 3.29 | 28.0 | 58.1* *(0.007)* |
| Irritability | 6.71 | 5.14 | 23.4 | 4.43 | 13.8 | 34.0 |

* Significant (p<0.01)

**Figure 1.** Global Physician Assessment on the severity of Atopic Eczema using Six Area, Six Sign Atopic Dermatitis severity Score (SASSAD)

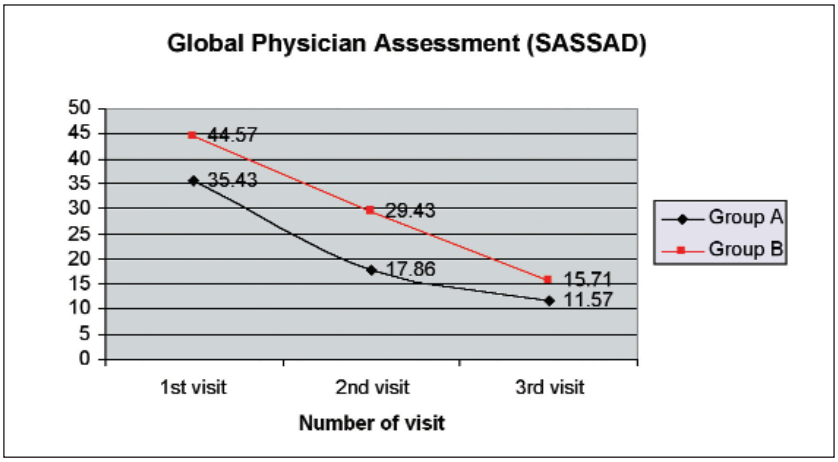


**Figure 2.** Comparison of Mean Reduction of Itch between Group A and B

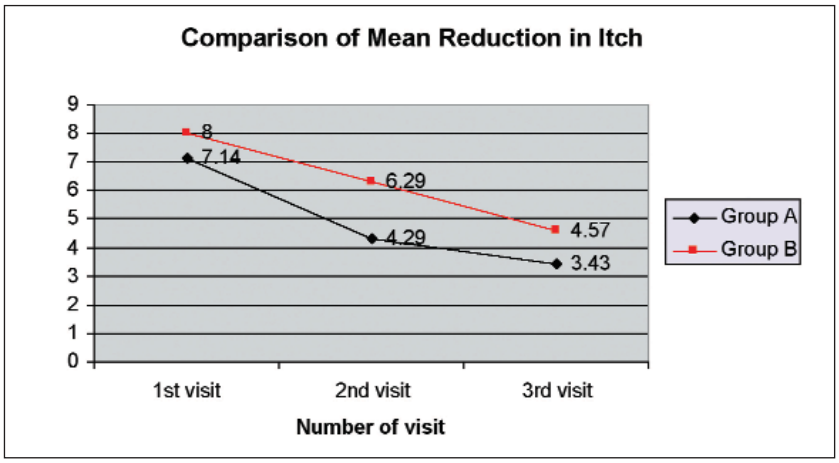



**Figure 3.** Comparison of Mean Reduction of Sleep Disturbances between Group A and B

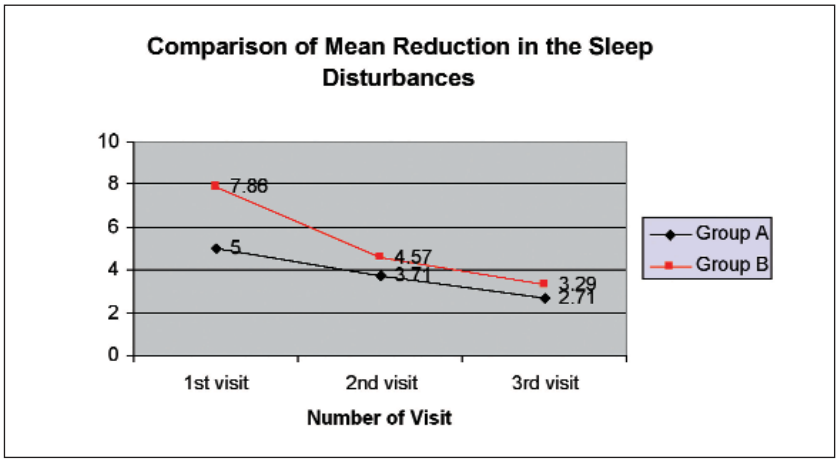
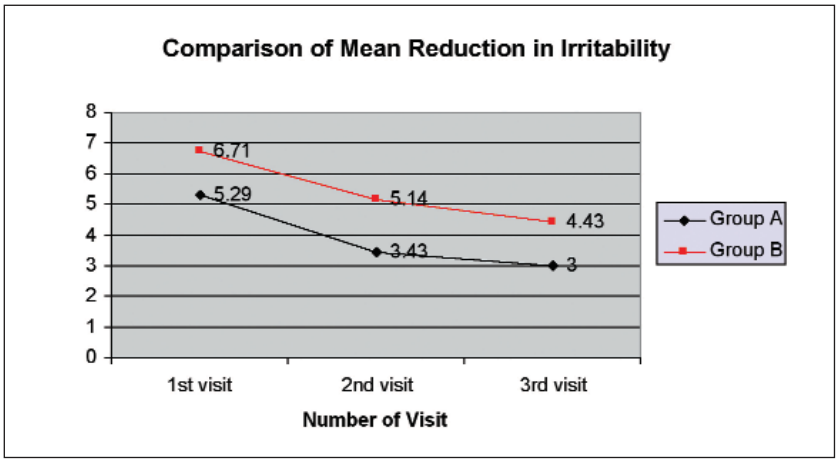



**Figure 4.** Comparison of Mean Reduction of Irritability between Group A and B



prescribed topical corticosteroid were not aware of the potency and resulted in either over or under usage of the topical application[5,7]. Following repeated education and demonstration of topical therapies by a specialist dermatology nurse, there was a 65% reduction in the severity of the eczema (SASSAD severity score) after 3 weeks[4].

We had excluded patients from entry into this study if they have had any previous consultation with any dermatology centre, in order to provide a population who had not been exposed to a dermatologist or specialist dermatology nurse in the past. At the first visit, which reflected the usual dermatology clinic consultation, majority of patients claimed they received neither explanation nor demonstration on how to apply topical medications from the doctors or dispensers at the pharmacy. After questioning, not all of them understood completely the correct use of topical medications. It is not possible to determine whether the lack of knowledge was due to failure of the healthcare providers in educating the patients/parents or because they had forgotten what they had been told. Either way, one can conclude that at the end of a consultation, appropriate medications were given to the patients but the information on the disease and proper usage of medications were not delivered to the patients.

Our intervention included recruitment of a trained dermatology nurse to explain regarding the disease and to demonstrate to the patients and/or parents on how to apply the topical medications. The patients were taught on the correct time, frequency, sites of applications, duration of use and the potency of the topical corticosteroid prescribed.

As reinforcement, all the topical medications were labeled with multi-languages cartoon labels and patient information leaflets on atopic eczema available in 3 languages were also given to the patients. We also spent some time answering to any queries from patients/parents.

There was an improvement in the disease severity in Group A as evidenced by a significant reduction of SASSAD score when proper education and demonstration on how to apply topical treatments were given during the first visit as compared to Group B, where the consultation was done in the usual manner but without further education or demonstration. This significant reduction was reproducible in Group B at the third visit when similar education and demonstration was given to them **(Table 1)**. Besides improvement in the disease severity, we also found that there was improvement in the patients' symptoms of itch, sleep disturbances and irritability.

The main limitation of this study is the small sample size. The disease severity of Group A appeared to be milder than Group B at baseline. We felt that this randomization bias was due to the small number of subjects in the study. In addition, the magnitude of symptom improvement of itch and irritability in Group B after education and demonstration were not statistically significant as compared to Group A **(Table 2)**. This, again, could be due to the small sample size.

At the end of the study, we noted that the key to the successful management of atopic eczema is to spend time to listen and to explain the nature of disease and how to use topical therapies and dressings. In addition to explanation, practical demonstrations on how to apply topical medications and dressings should be given to the patients or parents. Patients or parents should also be given written instructions and information to reinforce the therapies which have been explained and demonstrated. The quality of topical medications' labels could also be improved with the cooperation of the pharmacy department.

## Conclusion

We found a positive effect of explanation and demonstration of topical therapy on the clinical response of atopic eczema as evidenced by a significant reduction of disease severity score (SASSAD) as well as improvement in itch, sleep disturbances and irritability. This study reinforces the importance of having a trained dermatology nurse to explain and demonstrate on proper usage of topical applications in the management of atopic eczema. We suggest that all dermatology clinics utilize the services of these nurses especially in cases when the doctors themselves cannot afford to spend more time with the patients due to their busy schedule. Failure to explain on how to use topical applications may lead to patient dissatisfaction, poor compliance and lack of treatment efficacy.

## Acknowledgements

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**Appendix 1.** The Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score

- Six Signs: Erythema, Exudation, Excoriation, Dryness, Cracking, and Lichenification
- Six Sites: Arms; Hands; Legs; Feet; Head & neck; and trunk
- Grade of severity (Range of score: 0-108)

| | | |
|---|---|---|
| 0 | Absent | The sign cannot be detected with certainty even after careful inspection |
| 1 | Mild | The sign is certainly present but requires careful inspection to see it |
| 2 | Moderate | The sign is immediately apparent |
| 3 | Severe | The sign is very prominent |

## References


1. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockh) 1980; Suppl 92: 44-47.
2. Berth-Jones J. Six area, six sign atopic dermatitis (SASSAD) severity score: a simple system for monitoring disease activity in atopic dermatitis. Br J Dermatol 1996; 135: 25-30.
3. Broberg A, Kalimo K, Lindblad B et al. Parental education in the treatment of Childhood atopic eczema. Acta Derm Venereol (Stockh) 1990;70: 496-9.
4. Cork MJ, Britton J, Butler L et al. Comparison of parent knowledge, therapy utilization and severity of atopic eczema before and after explanation and demonstration of topical therapies by a specialist dermatology nurse. Br J Dermatol 2003;149: 582-589.
5. Basak PY, Ozturk M, Baysal V. Assessment of information and education about topical corticosteroids in dermatology outpatient departments: experience from Turkey. J Eur Acad Dermatol Venerol 2003;17: 652-658
6. Beattie PE, Lewis-Jones MS Parental knowledge of topical therapies in the treatment of childhood atopic dermatitis. Clin Exp Dermatol 2003; 28: 549-553.
7. Charman C.R., Morris A.D., Williams H.C. Topical corticosteroid phobia in patients with atopic eczema. Br J Dermatol 2000; 142: 931-936.