Original Article

Defaulter rate of follow-up of patients with gonorrhoea at the Genitourinary Medicine Clinic

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Abstract

Background. Gonorrhoea is the third most common sexually transmitted infection (STI) in the Genitourinary Medicine Clinic. Despite high cure rates achieved with the use of intramuscular ceftriaxone, all patients with gonorrhoea are followed up with one test of cure (gonococcal culture) after treatment. This is essential to ensure success of cure hence preventing complications, to screen for and treat concomitant STIs, and to reduce the possibility of re-infection through repeated patient education. A defaulter is defined as a patient who fails to attend follow-up and undergo test of cure within a period of 2 weeks after completion of treatment. Previous studies showed high defaulter rates of 41.1% and 43.8% in 1996 and 1997 respectively. This study aims to determine the defaulter rate of follow-up of patients with gonorrhoea, and to formulate remedial measures to reduce defaulter rate and thereby improve the management of gonorrhoea specifically and all sexually transmitted infections in general.

Materials and Methods. An audit of defaulter rate of patients diagnosed as gonorrhoea was performed from January 1998 to December 2005 in the Genitourinary Medicine Clinic, Department of Dermatology, Kuala Lumpur Hospital. All patients who failed to attend follow-up visit within 2 weeks after treatment were recorded as defaulters. An analysis was performed on all defaulters from January to December 2005.

Results. Defaulter rates for patients with gonorrhoea were generally high throughout the years studied, ranging from 35.0% to 48.2%, the highest being in year 2001. Despite continuous and relentless efforts in patient education and counseling, there has been no decreasing trend. In the year 2005, all defaulters were males. Majority (72.1%) of the defaulters were young adults aged between 21 and 40 years. 67.4% of the defaulters were Malay, followed by Indian 14.0%, Chinese 7.0% and other ethnic groups 11.6%. Among the defaulters, 30.2% had repeated gonococcal infection and 38.5% had comitant STIs.

Conclusions. More effort is necessary in educating patients to attend follow-up visit after treatment of gonorrhoea. Emphasis has to be made on the importance of confirming cure and thereby preventing complications and transmission to sexual partners. Counseling should also be given to all patients regarding practice of safe sex to prevent gonococcal re-infection and other STIs.

Keywords. gonorrhoea, defaulter, defaulter rate

Introduction. Gonorrhoea is the third most common sexually transmitted infection (STI), after syphilis and non-gonococcal urethritis, in the Genitourinary Medicine (GUM) Clinic, Hospital Kuala Lumpur. In our clinic, high cure rates (100%) have been achieved with the use of directed observed therapy using single dose of intramuscular ceftriaxone. Despite this, all patients are followed up after treatment. A test of cure i.e. gonococcal culture from urethral swab is performed after 72 hours post-treatment in all patients (Figure 1). Follow up is essential to ensure success of cure, thereby preventing complications. It also provides us with an opportunity to screen for and treat concomitant STIs, detect development of resistant gonococcal strains, evaluate risk of re-infection, pursue partner screening and treatment, as well as reinforce patient education and counseling.

In view of the importance of follow-up in the management of gonorrhoea, rate of defaulting follow up visits has thus been used as a negative marker of success in the management. This has been one of the quality indicators monitored annually in the Continuous Quality Improvement activities of the Department of Dermatology, Hospital Kuala Lumpur, since 1998. It is hoped that efforts taken to reduce defaulter rates may improve the overall management of gonorrhoea as well as other STIs.

The aims of the study was to improve the management of all sexually transmitted infections, using gonorrhoea as the main proxy indicator. It aims to determine the defaulter rate of follow up of patients with gonorrhoea, to formulate remedial measures to reduce defaulter rate and to ensure continuous improvement by re-evaluating the defaulter rate annually.
Materials and Methods
Annual audit of defaulter rates of all patients diagnosed as gonorrhoea was performed throughout an 8-year period from January 1998 to December 2005 in the GUM Clinic, Department of Dermatology, Hospital Kuala Lumpur. All patients who did not attend pre-scheduled follow-up visits within one week post-treatment were identified. Attempts were made to contact them via telephone and urge them to attend the clinic at an earliest possible date. Patients who failed to attend follow-up visit and undergo one test of cure within 2 weeks post-treatment were recorded as defaulters. A defaulter rate of less than 20% was adopted as an arbitrary standard of good care.

A retrospective review of all gonorrhoea defaulters from January to December 2005 was performed. The study focused on their demographic pattern, reasons of default, whether it was the first or repeated gonococcal infection, and concomitant STIs, if any, detected by screening at the first visit.

Results
The number of new cases of gonorrhoea seen in the GUM Clinic ranged from 83 to 123 per year (median 92.5) during the study period. This had markedly reduced from more than 400 new cases per year in the early 1990’s (Figure 2).
Defaulter rates remained high throughout the years studied, ranging from 35.0% to 48.2%. Overall mean defaulter rate was 41.3%, much higher than the arbitrary standard of < 20%. Defaulter rates for the later period from 2001 to 2005 were higher than that of the earlier years from 1998 to 2000 (mean 44.6% vs 35.7%) (Figure 3).

From January to December 2005, all defaulters were males. All female gonorrhoea patients, who constituted only 6% of all gonorrhoea cases, attended follow-up within two weeks post-treatment. Majority (72.1%) of the defaulters were young adults aged between 21 and 40. Patients aged between 31 to 40 had the highest defaulter rate of 73.3% (Figure 4).

The ethnic distribution of the defaulters was similar to that of all gonorrhoea cases. 67.4% of the defaulters were Malay, followed by Indian 14.0%, Chinese 7.0% and other ethnic groups 11.6%. Although about half of all patients who attended the GUM clinic were Malays, more than two-thirds of gonorrhoea cases were Malay patients (Figure 5).
Common reasons for defaulting given by the gonorrhoea defaulters included feeling cured after treatment, unable to spare time to come for follow up, and refusal of a repeat test (Table 1).

<table>
<thead>
<tr>
<th>Reasons for defaulting follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Felt cured after treatment</td>
</tr>
<tr>
<td>Unable to get time off work</td>
</tr>
<tr>
<td>Too busy</td>
</tr>
<tr>
<td>Clinic too far to come for follow up</td>
</tr>
<tr>
<td>Was out-station</td>
</tr>
<tr>
<td>Do not want repeat test</td>
</tr>
</tbody>
</table>

Among the defaulters, 30.2% had repeated gonococcal infection. From the screening of STIs during the first visit, 38.5% of the defaulters had concomitant STIs detected. These included chlamydial urethritis (23.1%), syphilis (5.1%), HIV (2.6%), hepatitis B (2.6%), hepatitis C (2.6%), and a combination of HIV, hepatitis B and hepatitis C (2.6%) (Figure 6).

All patients were educated and counseled during their first visit, particularly emphasizing the importance of confirming cure during follow-up visits. Practice of safe sex was actively promoted in preventing spread and re-infection. Education pamphlets printed in different languages were distributed to all patients during their first visit.

Follow-up appointments were made to patients’ convenience. Moreover, unscheduled walk-in follow-up visits, though not encouraged, were all attended and seen at the same clinic session. Patients who did not attend follow-up one week after treatment were reminded by phone calls from the clinic staff. Time-off slips or medical certificates were given for follow-up visits to all working patients.

Clinic environment was improved, with spacious patient waiting area and tinted window glasses. Patients’ privacy has always been maintained, with spouses or partners interviewed, managed and counseled individually. Clinic waiting time was shortened by streamlining the process of registration, consultation, laboratory tests, treatment and counseling to minimise patient waiting time for each section. Clinic parking spaces were increased. Friendly and non-judgmental approach to patients has been a policy and practised by all doctors and clinic staff.

**Discussion**

Although antibiotic treatment is usually simple and straightforward, the widespread occurrence of gonococcal strains resistant to commonly used antibiotics in recent years demands vigilance in ensuring treatment success. Absence or resolution of symptoms following treatment may not indicate cure of infection. Almost half of treatment failures in gonococcal urethritis are asymptomatic. Treatment inadequacy may lead to complications such as epididymitis and prostatitis in males, and pelvic inflammatory disease, ectopic pregnancy and infertility in females. It also perpetuates the silent spread of gonorrhoea to sexual partners and enhances the transmission of human immunodeficiency virus (HIV) and other STIs.

According to current international guidelines, routine follow up of gonorrhoea cases after treatment is recommended. Test of cure may not be routinely necessary if treated with recommended antibiotic and sensitivity of organism to the antibiotic is confirmed. However, test of cure is routinely performed in our centre due to its value in ensuring eradication of infection thus preventing complications, prevention of spread to community, and detection of emerging resistant strains. Gonococcal culture from direct plating of the urethral swab in males and endocervical swab in females is used as a test of cure in our clinic. Alternative tests which have been used in other

*Figure 5. Concomitant STI in gonorrhoea defaulters in 2005*
centres include nucleic acid amplification tests (NAATs) which may be more sensitive (>90%) for genital as well as extragenital sites, and results are less affected by the adequacy of specimens. However, specificity of NAATs is not 100%, and hence confirmation of positive results by culture is recommended\(^4\).

A previous study in the same centre showed defaulter rates of 41.1% and 43.8% in 1996 and 1997 respectively\(^1\). Several centres in UK reported defaulter rates ranging from 24% to 53%\(^5\)\(^6\)\(^7\). Defaulter rates of 35.0% to 48.2% in our centre are high, and should be a cause for alarm. Majority of the defaulters are young men. Almost one-third of them had repeated gonococcal infection and hence had been given counseling repeatedly. The lack of awareness and lackadaisical attitude of this group is worrying. More than a third of the defaulters carry concomitant STIs, for which potential opportunity of treatment may be missed. The efforts put into partner tracing and screening are often hindered.

To reduce the alarmingly high defaulter rates in our GUM Clinic, additional remedial measures should be implemented. Patient education and counseling should be further consolidated with additional training given to professional counselors, and emphasis put on creating awareness at the importance of follow-up. Clinic environment will be further improved by a proposed plan of moving to a new building with more consultation rooms, and a more comfortable fully air-conditioned patient waiting area with television. With consent given at the first visit, patients can be reminded of their follow-up appointments via mobile phone short-message services (SMS) delivered through an automated system. Use of non-invasive and more sensitive tests such as NAATs for test of cure should be considered. These tests enable the use of first-pass urine sample, obviating the need for uncomfortable urethral swab and exposure of genitals. Only positive test results require confirmation and sensitivity testing by culture methods.

**Conclusion**

Much more effort is needed in improving the rate of follow up of gonorrhoea patients after treatment. Emphasis has to be made on the importance of confirming cure thereby preventing complications and transmission to sexual partners, as well as the detection and treatment of concomitant STIs. Counseling should also be given to all patients regarding practice of safe sex to prevent gonococcal re-infection and other STIs.

**References**

Original Article

HIV infection among patients attending the Genitourinary Medicine Clinic, Hospital Kuala Lumpur (2000-2005)

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Abstract

Background According to the Department of Public Health Malaysia, the total number of HIV patients up to December 2006 was 76,389. More than 90% were males with Malays being the majority. IVDU was the main mode of transmission followed by heterosexual contact.

Objectives To determine the sociodemography, associated risk factors and clinical presentation of patients with HIV attending the Genitourinary Medicine (GUM) clinic.

Method A retrospective study analyzing the data using a standard questionnaire. All HIV patients seen in the GUM clinic between 1/1/2000-31/12/2005 were recruited

Results A total of 191 patients with HIV were seen, with 84% being males and 16% females. This constituted 4.2% of the total number of patients seen in the clinic. 64% were Chinese, 18% Malays, 15% Indians and 2% other races. 90% were between 21-50 years of age. The major risk factors for males were sexual promiscuity (61%) and IVDU (14%). 41% frequented commercial sex workers. 74% were heterosexuals, 18% homosexuals and 8% bisexuals.

The major risk factors for females were being sexual partners of HIV infected males (48%), IVDU (16%) and sex workers (6%). Majority reported no usage of condom.

The main diagnoses at presentation were herpes genitalis (24%), genital warts (22%), gonorrhoea (10%) and syphilis (10%). Non venereal disease accounted for 23%.

Conclusions The major risk factor for HIV transmission in patients attending the GUM clinic was exposure to sex workers, and the predominant race was Chinese. According to the national figure the main mode of HIV transmission was IVDU with Malays being the majority. The main diagnoses at presentation were herpes genitalis, genital warts, gonorrhoea and syphilis.

Keywords HIV, Sexually Transmitted Infection, risk factors

Background According to the Department of Public Health Malaysia, the total number of HIV patients up to December 2006 was 76,389. More than 90% were males with Malays being the majority. IVDU was the main mode of transmission followed by heterosexual contact. The proportion of reported HIV infections transmitted through heterosexual and homosexual/bisexual contacts has increased from 7.4% in 1995 to 17.4% in 2002.

The presence of sexually transmitted infection (STI) particularly genital ulcer disease and also genital discharge can enhance both acquisition and transmission of HIV. The increased susceptibility to HIV is related to the STI causing damaged mucosa or skin and the increased presence of HIV susceptible macrophages. The increased transmission of HIV is related to increased shedding of the virus when STI is present

Objectives The main objective of this study is to determine the sociodemography, associated risk factors and diagnoses at presentation of patients with HIV attending the Genitourinary Medicine Clinic, Department of Dermatology, Hospital Kuala Lumpur.

Method This is a retrospective study analyzing the patients’ data obtained using a standard questionnaire. The questionnaire contains the patients’ basic demographic information, risk factors for HIV, presenting complaint and diagnosis. The questionnaire was filled in by the attending doctor on the
patients' first visit to the GUM clinic. All HIV patients seen in the GUM clinic, Department of Dermatology, HKL between 1/1/2000 and 31/12/2005 were recruited in the study. The National Statistics figures were obtained from the Department of Public Health, Malaysia.

**Results**

A total of 191 patients with HIV were seen in the GUM clinic during the study period of six years. This constituted 4.2% of the total number of 4521 patients seen in the clinic. Out of these 191 patients, 65% were Chinese, 18% were Malays, 15% were Indians and the remaining 2% were of other races (Figure 1). There were more males (84%) than females (16%) infected with HIV in the GUM clinic (Figure 2).

Ninety percent of HIV patients were between 21-50 years of age (Figure 3). The major risk factors for males were sexual promiscuity (56%), combination of IVDU and promiscuity (12%) and IVDU (2.5%). Out of these male patients 74% were heterosexuals, 18% homosexuals and 8% bisexuals. Forty six percent of males frequented sex workers. Information regarding precaution during sexual intercourse in the questionnaire did not specify the use of condoms. However from the data available it appears that the usage of condom is low.

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**Figure 1.** Racial distribution of patients with HIV (n=191)

**Figure 2.** Gender distribution of patients with HIV (n=191)

**Figure 3.** Distribution of patients with HIV by age and sex (n=191)
The major risk factors for females were being sexual partners of HIV infected males (48%), IVDU (16%) and being sex workers (6%). The main diagnoses at presentation were herpes genitalis, genital warts, gonorrhoea and syphilis (Table 1).

### Table 1. Diagnosis of HIV patients at presentation

<table>
<thead>
<tr>
<th>Diagnosis at presentation</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes genitalis</td>
<td>24</td>
</tr>
<tr>
<td>Genital wart</td>
<td>22</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>10</td>
</tr>
<tr>
<td>Syphilis</td>
<td>10</td>
</tr>
<tr>
<td>Non venereal disease</td>
<td>23</td>
</tr>
</tbody>
</table>

### Discussion

The racial distribution of patients with HIV in GUM clinic differs from the National Statistics. Chinese made up the majority of patients with HIV in GUM clinic (64%) as opposed to the national figures which showed Malays (72.6%) as the majority with HIV in the country.

Most of the male patients with HIV attending the GUM clinic acquired the infection through heterosexual contacts and 46% had exposure to sex workers. Most of the HIV infected females in the clinic had sexual partners who were HIV positive and only a smaller number were sex workers. IVDUs form a much smaller group for both sexes. These findings differ from the National Statistics where the main mode of HIV transmission in the country was IVDU (76.2%) followed by heterosexual contact (17.5%). This is because HIV patients attending the GUM clinic represents a biased group where sexual exposure is a high risk behaviour with predisposition to HIV infection.

Recent studies have shown that heterosexual transmission is becoming more important in the country, with rates increasing from 20% to 38.9%. The percentage of females infected with HIV in the country has risen from 1.4% in 1990 to 7% in 2003. This is because HIV patients attending the GUM clinic represent a biased group where sexual exposure is a high risk behaviour with predisposition to HIV infection.

Most patients presented in the GUM clinic with ulcerative STIs which have been shown to increase susceptibility to HIV infection. In fact both ulcerative STIs such as genital ulcer disease and syphilis, as well as non-ulcerative STIs such as gonorrhoea, chlamydia and non-gonococcal urethritis may be associated with increased risk of HIV transmission. HIV patients with STI are more likely to transmit HIV through sexual contact than those without STI. Thus early STI treatment should be part of the HIV prevention strategy. Patients should also be advised to use condoms and practice safe sex as most of the GUM clinic attendees do not use condoms.

There are several limitations in this study. As it is a retrospective study, the accuracy of the data depends on good case documentation. The number of patients with HIV infection may not be representative of the actual figure as the HIV test is voluntary, thus some patients may refuse to be tested.

### Conclusions

The sociodemography and risk factors of patients with HIV attending the GUM clinic are different from those of the country. This could be explained by the fact that HIV patients attending the GUM clinic belong to a high risk group where sexual exposure is a potential risk of HIV transmission. Thus they should be educated, counseled, screened and treated for STIs to reduce the risk of HIV transmission.

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7. Section of AIDS/STD, Division of Disease Control, Dept of Public Health, Malaysia
Original Article

Cutaneous Adverse Drug Reactions in a General Hospital in Singapore: A One-Year Retrospective Analysis

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Abstract

Background Rashes are the most common adverse reaction to drugs. Our aim is to describe (i) the prevalence of cutaneous adverse drug reactions in hospitalised patients over a 1-year period in our hospital; (ii) the variety of cutaneous drug reactions; (iii) the characteristics of patients with cutaneous drug reactions and (iv) the drugs implicated.

Methods A retrospective analysis of all adverse drug reactions from the pharmacists’ database from January to December 2003 was conducted. Patients’ records were reviewed to extract demographic data, drug implicated, route of administration, drug allergy history, type of cutaneous reaction, severity and presence of underlying chronic disease.

Results Sixty-five patients met our inclusion criteria, giving an estimated prevalence of 1.8/1000 among hospitalised patients. The cases were mostly from the general medicine department (64.6%), with a slight male predominance (males, 53.8%; females 46.2%). Cutaneous adverse drug reactions were more common in the Malay population (32.3%). The mean age was 41.6 years (range, 13 to 85 years). The main drugs implicated were antibiotics (49.2%), mainly penicillins and cephalosporins, and non-steroidal anti-inflammatory agents (16.9%). Urticarial (46.1%) and generalised maculopapular eruptions (40.0%) were the most common patterns encountered. Others included Stevens-Johnson syndrome/toxic epidermal necrolysis (7.7%), drug reaction with eosinophilia and systemic symptoms (1.5%) and erythroderma (1.5%). 29.2% of cases were considered to be severe. There were no deaths. 44.6% had an associated chronic disease and 24.6% had a previous documented drug allergy.

Conclusion Antibiotics and NSAIDs were the major drugs involved. The commonest cutaneous manifestations were urticarial and maculopapular eruptions. A high proportion of reactions were considered severe and almost one-quarter had a previous drug allergy.

Keywords exanthema, hypersensitivity, skin

Introduction

Cutaneous adverse drug reactions (ADRs) are a common occurrence in hospitalised patients, causing significant morbidity and mortality. However, there is a lack of local data on this subject. We therefore conducted a retrospective descriptive study over a 12-month period in a local general hospital with the aims of (i) describing the prevalence of cutaneous ADRs in this population, (ii) the types of drugs implicated, (iii) the clinical spectrum of cutaneous ADRs seen and (iv) the characteristics of patients with cutaneous ADRs. This information will help to update the spectrum of cutaneous drug reactions seen locally.

Materials and Methods

This was a retrospective hospital-based descriptive study carried out in Changi General Hospital, Singapore. All ADRs from the pharmacists’ database were reviewed over a 12-month period from January to December 2003. Information from the database had been mainly gathered through healthcare staff, including doctors and nurses, who had reported these adverse events to the central database.

Inclusion criteria included all inpatients with a reported ADR with a cutaneous component. Outpatients and patients whose adverse reactions were non-cutaneous were excluded from the study. Patients’ records were reviewed for demographic data, including age, gender, race and admitting department. In addition, we determined the drug implicated and route of administration.

The patterns of cutaneous reaction were classified into the following groups: (i) maculopapular, (ii) urticaria/angioedema, (iii) Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN), (iv) drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, (v) erythroderma (vi) fixed drug eruption, (vii) acute generalised exanthematous pustulosis (AGEP) and (viii) vasculitis.
The ADR was considered severe if it was the reason for hospitalisation or prolonged the stay; if it caused hypotension, fever or blisters; if it was life-threatening or caused death; or if there were systemic abnormalities such as liver or renal dysfunction.

The patients’ medical histories were reviewed to determine if they had a documented previous drug allergy and any associated chronic diseases. These included cancer, chronic renal failure, asthma and other respiratory diseases, connective tissue disease, chronic liver disease, diabetes mellitus, hypertension, ischaemic heart disease and human immunodeficiency virus infection.

Data were tabulated on Microsoft Excel spreadsheets and prevalence rates were calculated based on data collected by the operations department of our hospital. Data were analysed using goodness of fit test.

**Results**

A total of 65 patients met our inclusion criteria. A prevalence of 1.8/1000 among hospitalised patients was estimated. The mean age was 41.6 years (range, 13 to 85 years). There was a male predominance (males 53.8%, females 46.2%). The ethnic distribution is shown in Table 1. Compared to the ethnic distribution of hospitalised patients in 2003, cutaneous ADRs were more common in the Malay population (P = 0.007). There was no specific drug that was implicated more commonly in the Malay population, with the antibiotics (penicillins, cephalosporins and quinolones) and NSAIDs accounting for the majority (57.1%) of reactions. The majority of patients who experienced cutaneous ADRs were from the general medicine department (64.6%). The rest were from the departments of general surgery (13.8%), orthopaedics (12.3%), and cardiology (4.6%), and equal numbers (1.5%) were from the departments of psychiatry, ophthalmology and geriatric medicine.

Five patterns of cutaneous drug reactions were seen in our population. In order of decreasing incidence, these were urticaria/angioedema, maculopapular, SJS/TEN, DRESS, and erythroderma (Table 2). Fixed drug eruption, acute generalised exanthematous pustulosis, and vasculitis were not observed. In 2 patients, the cutaneous reaction was not specified.

Nineteen patients (29.2%) had severe reactions, but there were no reported deaths. Of these 19 patients, hypotension or anaphylaxis occurred in 10.5% and biological abnormalities such as renal or liver dysfunction were observed in 15.8%. The ADR was responsible for hospitalisation or prolonged stay in 73.7%.

The list of causative drugs and their frequency are shown in Table 3. Antibiotics, particularly penicillins and cephalosporins, and non-steroidal anti-inflammatory agents (NSAIDs) accounted for the majority (66.1%) of cases. Together with anti-convulsants, they were also responsible for the more serious reaction patterns of erythroderma, TEN or SJS. Of these drugs, 55.4% were administered via the intravenous route, 43.1% orally and 1.5% by intramuscular injection.

There were 44.6% of patients that had at least 1 concurrent chronic disease. These include hypertension (44.8%), ischaemic heart disease (27.6%), diabetes mellitus (24.1%), asthma (17.2%), chronic liver disease (17.2%), other respiratory diseases (10.3%), cancer (6.9%), chronic renal failure (6.9%), connective tissue disease (3.4%) or human immunodeficiency virus (HIV) infection (3.4%).

**Discussion**

Cutaneous drug eruptions are the most common drug-induced adverse reaction, and have been reported in 2% of hospitalised patients. The estimated prevalence rate of 1.8/1000 hospitalised patients in our study is lower than that of most reports, and this may be due to an underreporting of ADRs to the database on the part of healthcare workers. Our study showed that the commonest drugs causing cutaneous ADRs were antibiotics. When compared to previous local studies, a higher number of

<table>
<thead>
<tr>
<th>Ethnic group</th>
<th>Number of hospital admissions in 2003 (%)</th>
<th>Number of patients who reported cutaneous ADR (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>22,795 (62.2)</td>
<td>38 (58.5)</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>6548 (17.8)</td>
<td>21 (32.3)</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>3469 (9.5)</td>
<td>4 (6.2)</td>
<td>0.007</td>
</tr>
<tr>
<td>Others</td>
<td>3851 (10.5)</td>
<td>2 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>36,663 (100.0)</td>
<td>65 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

ADR: adverse drug reaction
cutaneous ADRs were found to be due to newer drugs like cephalosporins and quinolones. This is probably due to an increased usage of such drugs in the hospital setting today.

From previous studies, the incidence of ADR varied greatly amongst departments\(^2\). We found this to be true in our study, with the largest proportion of patients coming from the general medicine department. There was also a slight male predominance in our study, which is consistent with previous data\(^2,5\).

Maculopapular exanthems and urticaria/angioedema were the most common manifestations of cutaneous ADRs whatever the suspected drug, accounting for 86.1% of the cutaneous reactions seen. This is consistent with previous retrospective studies\(^3,5,6\), but our study demonstrated an unusually higher proportion of urticarial eruptions. More severe reactions like SJS/TEN, DRESS and erythroderma

### Table 2. Patterns of Cutaneous Adverse Drug Reactions and Its Occurrence in a Hospital Setting

<table>
<thead>
<tr>
<th>Reaction pattern</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urticaria/angioedema</td>
<td>30 (46.2)</td>
</tr>
<tr>
<td>Maculopapular</td>
<td>26 (40.0)</td>
</tr>
<tr>
<td>SJS/TEN</td>
<td>5 (7.7)</td>
</tr>
<tr>
<td>DRESS</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Erythroderma</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Not specified</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>Total</td>
<td>65 (100.0)</td>
</tr>
</tbody>
</table>

SJS/TEN: Stevens-Johnson Syndrome/toxic epidermal necrolysis
DRESS: Drug reaction with eosinophilia and systemic symptoms

### Table 3. Drugs Implicated in Adverse Cutaneous Reactions in a Hospital Setting

<table>
<thead>
<tr>
<th></th>
<th>URT/AE</th>
<th>MP</th>
<th>SJS/TEN</th>
<th>DRESS</th>
<th>ERY</th>
<th>Not specified</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporin</td>
<td>9</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13</td>
</tr>
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were associated mainly with anti-microbials, NSAIDs and anticonvulsants. The single patient who developed DRESS had, in addition to the usual features of fever, malaise, dermatitis and lymphadenopathy, rare manifestations of reversible hypersensitivity myocarditis and thyrotoxicosis. The culprit drug was maloprim (comprising dapsone 100 mg and pyrimethamine 12.5 mg), which was administered for anti-malarial prophylaxis. Our study also emphasises the high proportion of severe cutaneous ADRs (29.2%).

In addition, a large proportion of the patients (44.6%) had an associated chronic disease. The commonest associated diseases were hypertension, ischaemic heart disease and diabetes mellitus. This may be an additional risk factor for the development of cutaneous ADR due to the increased use of medication, polypharmacy, and drug interactions, leading to decreased clearance of drug metabolites. Almost one-quarter of the patients had a documented previous cutaneous ADR. Although the exact mechanism is not known, some authors have suggested that a genetic susceptibility to drug-induced cutaneous ADR may play a role. For example, N-acetyltransferase activity may vary between individuals due to genetic polymorphism.

Underreporting of cutaneous ADRs by ward doctors is likely to be a limitation in our study. In addition, we took the reported data at face value, and did not attempt to take into account the causal association of the drug implicated. However, we feel that this study provides insight into local data on this topic and helps to update the spectrum of cutaneous ADRs seen in hospital practice. This is important as new drugs are constantly being introduced into the market.

Our study highlights several important findings: antibiotics and NSAIDs were the major drugs involved, a high proportion of patients had severe reactions, the proportion of patients with urticaria/angioedema was higher than in most previous studies, and the Malay population may be at a higher risk for cutaneous ADRs. We recommend a prospective investigation of ADRs in the hospital setting in Singapore.

Acknowledgements
The authors thank Ms Liew Siew Huey for her help in generating the patient database and the NUH-NUS Medical Publications Support Unit, Singapore, for its assistance in the preparation of this manuscript.

References
Original Article

Cutaneous Adverse Drug Reactions observed in a Dermatology Clinic, Penang General Hospital

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Abstract

Background Cutaneous Adverse Drug Reaction (CADR) is commonly encountered in our daily clinical practice. Knowledge of the various patterns of CADR and the common offending agents will certainly help the physician in assessing the likelihood of the drug induced eruption as opposed to another dermatological diagnosis.

Objectives
To improve the understanding of CADRs in Penang General Hospital, To evaluate the incidence of CADR in Dermatology clinic Penang General Hospital, to identify the common offending drugs and to describe the characteristics of CADR and to identify the associated risk factors of developing CADR.

Materials and Methods
This prospective study covers a 12-month period from April 2005 to March 2006. Demographic characteristics, causative drugs, management and treatment outcome were analysed.

Results
A total of 174 cases were referred to the Dermatology Clinic over 1-year period (Incidence of 4.9% of Dermatology Clinic new case attendees). Chinese comprises of 51.4%, followed by Malay 32.4%, Indian 10.8% and others 5.4%. Male to female ratio was 1.2:1. 74.1% of CADR occurred between 13 - 59 year age group. The offending drugs included antimicrobials 28.6%, antituberculous 19.7%, analgesics 17.7%, allopurinol 8.4%, anticonvulsants 5.4%, HAART 1.0%, traditional medicines 2.0% and others 17.2%. High proportion of erythema multiforme syndrome cases was observed (23.5%). Toxic epidermal necrolysis has a high mortality rate. It was caused by amoxicillin, sulphonamide and phenytoin. 80.5% of CADR occurred within 2 weeks of drug introduction. Overall mortality rate secondary to CADR was 2.3%. Risk factors identified included poly-pharmacy (37.9%), renal insufficiency (31.0%), personal history of previous drug allergy (19.0%), liver disorder (18.4%), tuberculosis (16.7%), HIV infection (10.3%), autoimmune disorders (6.3%) and hematological malignancy (4.0%).

Conclusions
Diagnosis of CADR requires a high index of suspicion especially in those having symmetrical eruption within 2 months in relation to initial dose of medication, particularly the high risk groups.

Keywords
Cutaneous adverse drug reaction, toxic epidermal necrolysis, drug rash

Introduction
Cutaneous Adverse Drug Reactions (CADR) is commonly encountered in our daily clinical practice. Cutaneous adverse drug reactions to drugs are common, affecting 2 to 3 percents of hospitalized patients. Knowledge of the various patterns of cutaneous adverse drug reactions and the common offending agents will certainly help the physician in assessing the likelihood of the drug induced eruption as opposed to another dermatological diagnosis. The true incidence and prevalence in any community is probably difficult to determine as it depends on the prescribing pattern, availability of medication and surveillance system of the specific medical community.

The aim of this study is to improve the understanding of CADRs in Penang General Hospital, to evaluate the incidence of CADR in Dermatology clinic Penang General Hospital, to identify the common offending drugs and to describe the characteristics of CADR, including the type and severity and to identify the associated risk factors of developing Cutaneous ADR.

Materials and Methods
The Penang General Hospital is a tertiary centre and teaching hospital in the state of Penang, Malaysia. It is a 1090 bedded hospital that serves a population of 1.4 million (47% Chinese, 40% Malay, 10% Indian and others).

This prospective study covered a 12-month period from April 2005 to March 2006. Reporting forms were filled up by the doctor in-charge. Demographic characteristics, causative drug, management and treatment outcomes were noted and analysed.
All patients including inpatient and outpatient in the Department of Dermatology Penang General Hospital, with diagnosis of CADR seen within the study period were included. Diagnosis of CADR was based on clinical impression and relevant investigations including a skin biopsy.

The drug responsible for the condition was determined from the history based on the timing of the drug reaction and the attending dermatologist's impression with the best available information.

- **Inclusion criteria:**
  - Clear history of drug induced reaction.
  - De-challenge improved the skin condition.

- **Exclusion criteria:**
  - Absence of a causative drug according to our definition
  - Lack of recorded date when the causative drug was started / stopped or disease evolution.
  - Allergic contact dermatitis
  - Skin disorder attributable to infection

- **Data analysis:**
  All analyses were performed using SPSS 13.0 version.

**Results**
A total of 174 cases were referred to the Dermatology Clinic from April 2005 to March 2006, over a 1 year period. This represents 4.9% of Dermatology Clinic new case attendees (Total of 3539 new cases during the study period). This was a conservative figure and only reflected perhaps the cases which needed referral for diagnosis or management.

There were 82 Chinese (51.4%); 73 Malay (32.4%); 12 Indian (10.8%); 7 others (5.4%). Male to female ratio was 1.2:1. 74.1 % of CADR occurred in 13 - 59 year age group (ranged from day 7 of life to 83 years).

The offending drugs included antimicrobials 28.6%, antituberculous 19.7%, analgesics 17.7%, allopurinol 8.4%, anticonvulsants 5.4%, Highly Active Antiretroviral Therapy (HAART) 1.0%, traditional medicines 2.0% and others 17.2% (**Figure 1 & 2**).

Among the antimicrobials, the penicillin group was the commonest offending agent (31.0%), followed by sulphur based drugs (27.6%), cephalosporin (20.0%), tetracycline (8.6%), and quinolones (5.2%).

For antituberculous drugs, pyrazinamide and rifampicin each contributed to 27.5% of reactions, ethambutol (20.0%) and isoniazid (20.0%). Among the analgesics, the NSAIDS group was the commonest identified agents 88.9%.

In the anticonvulsants, phenytoin was the commonest culprit, causing 54.5% of reactions, carbamazpine 36.4% and sodium valproate 9.1%. Interestingly to note that, all the CADR cases in patients taking HAART were due to NNRTI.

Allopurinol caused significant numbers of CADR (8.4%). The frequency of the various morphological types seen were morbiliform 23.6%, SJS 23.6%, erythroderma 17.6%, photodermatitis 17.6% and EM minor 17.6%.

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**Figure 1.** Offending agents that identified among CADR patients in dermatology Clinic Penang Hospital
The commonest drug implicated for morbilliform rashes was NSAIDS and antituberculous drugs (25.0%), allopurinol for SJS (28.6%), NSAIDS for EM (38.5%), NSAIDS for FDE (38.5%) and NSAIDS for urticaria (28.6%).

Various types of CADR were observed in our series (Figure 3). A high proportion was due to erythema multiforme syndrome 23.5% (the second commonest type of CADR observed). Toxic epidermal necrolysis was the most serious CADR among all with a high mortality rate. It was mainly caused by amoxycillin, sulphonamide, phenytoin, carbamazepine and cephalosporin.

As for the onset of CADR in relation to the initial dose of medication taken, 80.5% of CADR occurred within the first 2 weeks and none was observed after 2 months (Figure 4).

Among the patients with CADR, 53.4% were managed as out-patient, 43.7% required hospitalization and 2.9% needed ICU admission. Intravenous Immunoglobulin (IV IG) was given to 11 patients (10 TEN; 1 SJS). In our series, mortality rate of TEN was 15.4% and SJS was 0.0%. Overall mortality rate of CADR was 2.3%. 10.3% of patients recovered but with sequelae including pigmentary problems.

In our study population, risk factors for CADR identified included poly-pharmacy (37.9%), renal insufficiency (31.0%), personal history of previous drug allergy (19.0%), liver disorder (18.4%), TB (16.7%), HIV infection (10.3%), autoimmune disorders (6.3%) and hematological malignancy (4.0%) (Figure 5).
**Discussion**

The increasing use of new drugs especially growth factors, hormones and chemotherapeutic agents have resulted in increasing number of cutaneous adverse drug reactions (CADR). Besides western medicine, traditional and alternative medications can also cause CADR².

CADR is defined as unwanted skin reaction in response to a systemic administration (oral / subcutaneous / intramuscular / intravenous / inhalation) drug, which is noxious and unintended, which occurs at doses used in human for prophylaxis, diagnosis or therapy. CADR can mimic all the morphologic expressions in dermatology³.

The types of CADR observed in our series were similar to those reported worldwide. But we observed a high proportion of erythema multiforme syndrome cases 23.5% (the second commonest type of CADR observed). This may be due to the fact that Penang Hospital is a tertiary referral centre. Common CADR like morbilliform and urticaria usually do not get referred.
CADR should be considered as one of the differential diagnoses of a suddenly appearing symmetrical skin eruption. The diagnosis of cutaneous ADR is heavily dependent on history & physical examination. Previous drug allergy history, morphology & distribution of rashes and chronology of drug intake are the key factors in diagnosis. CADR usually occurs within 2 months of initiation of drug therapy\(^3\). This was also observed in our series.

It is important to be familiar with the various morphology of cutaneous eruption to drugs. Recognizing them will help to pinpoint the most likely offending agent especially in the case of poly-pharmacy.

It is equally important to recognize those at high risk of developing a CADR. The at risk groups include those with underlying multi organ failure\(^1\), elderly\(^3\), poly-pharmacy\(^3\),\(^6\),\(^7\), malignancy especially hematological\(^3\),\(^5\), underlying infection like HIV / Epstein-Barr Virus (EBV) / tuberculosis\(^2\),\(^3\),\(^4\), certain autoimmune diseases (Rheumatoid arthritis, Sjogren’s disease or Systemic Lupus Erythematosus)\(^3\),\(^5\) and genetic susceptibility\(^10\),\(^11\). Similar picture also observed in our series. Interestingly it was observed that, 19.0% of CADR (33 cases) were preventable. These involved patients with a personal history of previous drug allergy who have been given same group of medication.

Management of CADR involves a multi-disciplinary approach\(^12\). Early diagnosis and prompt withdrawal of the most likely offending medication is crucial\(^13\). The patient should be informed and given in writing, the name of the offending medication and the type of reaction seen in allergy notification card. Medic alert bracelet is encouraged in those with severe CADR.

All cases should be notified\(^14\),\(^15\) to the Malaysian Adverse Drug Reaction Advisory Committee (MADRAC). This helps to create awareness by sharing information and developing a database, in the hope of reducing the incidence of CADR.

**Conclusion**

The diagnosis of CADR requires a high index of suspicion especially in those with symmetrical cutaneous eruption within 2 months after a new medication, particularly the high risk groups.

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**Acknowledgements**

We are most grateful to all the staff of Department of Dermatology, Penang General Hospital for their help in collecting and compounding data.

**References**

Hansen’s Disease in Penang: A 10-year Retrospective Analysis

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Abstract

Background Leprosy is a chronic granulomatous infection caused by Mycobacterium leprae. The principal manifestations are skin lesions and peripheral neuropathy. The aims of the study is to improve the understanding of leprosy cases managed in Penang General Hospital and to analyse the demographics, clinical patterns, treatment regimen and outcome of leprosy in Penang Hospital.

Materials and Methods This retrospective study covered a 10-year period from 1997 to 2006. Demographic characteristics, clinical patterns, treatment regimen of leprosy and outcome were analysed.

Results A total of 95 patients were diagnosed to have leprosy (prevalence rate of 0.68 per 100,000). The mean age at presentation was 40.4 years ± 17.9 (range from 3 to 91 years old). There were 35 Malays (36.8%), 34 Chinese (35.8%), 5 Indians (5.2%) and 21 others. Patients experienced symptoms for a mean of 21.4 months before being referred to our clinic. Only 29 patients (30.5%) had a family history of leprosy. 34 patients (35.8%) presented with lepromatous leprosy. 95 patients (100%) presented with skin lesions, 61 patients (61.2%) with nerve lesions, 17 patients (17.9%) with deformities and 12 (12.6%) with reactions. The skin lesions occurred predominantly over the lower limbs, face and trunk. 95.8% of skin lesions were hypo/anaesthetic. Common thickened nerves observed were ulnar nerve (40.0%), great auricular nerve (38.9%) and posterior tibialis nerve (25.3%). The lepra reaction rate was 51.6%. Type 1 reaction commonly involved those with borderline spectrum but type 2 reaction commonly involved those with lepromatous spectrum. Common side effects observed with MDT were dapsone induced hemolytic anaemia (10.5%), cutaneous adverse drug reaction (8.4%) and drug induced hepatitis (2.1%). None of them experienced severe drug toxicity. In terms of treatment for leprosy, 71.6% of patients had completed their treatment and 18.9% were still on treatment. 24.1% of patients had their regimen changed because of side effects and drug resistance. 6 patients died (due to unrelated cause) and another 3 patients defaulted treatment.

Conclusions Our study showed similar epidemiological findings as other studies except for a higher reaction rate. There was a significant delay in diagnosis in our cohort. Identification of the reasons of delay in diagnosis, and the risk factors of lepra reaction are important in the management of leprosy. Anti-leprotic treatment is relatively safe and effective in treating leprosy.

Keywords Epidemiology, leprosy, lepra reactions

Introduction

Leprosy is a chronic granulomatous infection caused by Mycobacterium leprae. The principal manifestations are skin lesions and peripheral neuropathy. Complications are caused by nerve damage, immunological reactions and bacillary infiltration. Drug treatment is effective in killing the bacilli, but does not prevent nerve damage and reaction. The aim of the study was to improve the understanding of leprosy cases managed in Penang General Hospital and to analyse the demographics, clinical patterns, treatment regimen and outcome of leprosy in Penang Hospital.

Materials and Methods

The Penang General Hospital is a tertiary centre and teaching hospital in the state of Penang, Malaysia. It is a 1090 bedded hospital that serves a 1.4 million population (Chinese 47%, Malay 40%, Indian 10% and others 3%).

This retrospective study covered a 10-year period from 1997 to 2006. Reporting forms were filled up by the doctor in-charge. Demographic characteristics, clinical patterns, treatment regimen of leprosy and outcomes were noted and analysed.

All patients (inpatient and outpatient) in the Department of Dermatology Penang General Hospital, with a diagnosis of leprosy within this period were included.

Due to paucity of cases and difficulty in doing a skin biopsy in young children, some cases were diagnosed clinically without a biopsy. Slit skin smears were taken from the site of the lesion and stained with Ziehl-Neelsen’s staining method. Skin biopsy was done after obtaining an informed consent.
The tissue specimens were processed for routine histopathological examination (i.e. staining with Hematoxylin-Eosin and Fite-Faraco stains). A definite histological diagnosis of leprosy requires: a) presence of infiltration within dermal nerves and b) the presence of Acid Fast Bacilli (AFB).

The diagnosis of leprosy is primarily clinical. Anaesthetic or hypoesthetic skin lesions with or without thickened peripheral nerves are virtually pathognomonic of leprosy. A full thickness skin biopsy from an anesthetic lesion showing granuloma and lymphocytic infiltration of nerves essentially confirms the diagnosis.

Leprosy is categorized as TT (Tuberculoid Leprosy), BT (Borderline Tuberculoid), BB (Borderline Borderline), BL (Borderline Lepromatous) and LL (Lepromatous Leprosy) types according to the Ridley Jopling classification.

"Lepra reaction" is the term given to a violent but often ineffective tissue response presenting as an acute deterioration in the clinical lesions of the patient undergoing treatment for leprosy.

Inclusion Criteria:
• Patients with Leprosy
  (With one or more of the following symptoms)
  1. Hypopigmented or erythematous skin lesion(s) with definite loss of sensation.
  2. Damage to the peripheral nerves as demonstrated by palpable thickening with or without impairment of sensation and/or weakness of the muscles of hands, feet or face
  3. Presence of acid-fast bacilli in slit skin smears
  4. Histological changes diagnostic of leprosy in skin biopsy
• Receiving standard MDT treatment for leprosy or completed treatment for leprosy

Exclusion Criteria:
• Presence of other skin or neurological disorders that may be confused with the clinical picture of leprosy.
• On oral corticosteroid or other immunosuppressive treatment for other disorder, not for the purpose of the treatment of lepra reaction.
• Concurrent participation in another clinical trial.

All analyses were performed using SPSS 13.0 version.

**Results**
A total of 95 patients were diagnosed to have leprosy during this period in the Dermatology Clinic, Penang Hospital. The mean age at presentation was 40.4 ± 17.9 years (ranged from 3 to 91 years old). The patients were predominantly male (70.5%). There were 35 Malays (36.8%), 34 Chinese (35.8%), and 5 Indians (5.2%) (Refer figure 1). The rest of the 21 patients (22.2%) were immigrants from neighbouring countries like Indonesia, Nepal, Bangladesh and Philippines.

Patients experienced symptoms for a mean of 21.4 months before being referred to our clinic. At presentation, patients had a mean Bacteriological Index (BI) of 1.38 and mean Morphological Index (MI) of 1.00. 66 patients (69.5%) had no family history of leprosy.

![Figure 1. Characteristic features of patients with leprosy seen at dermatology clinic, Penang General Hospital (1997 to 2006)](image)
34 (35.8%) of the patients presented as LL, 13 (13.7%) as BL, 13 as BB (13.7%), 18 (18.9%) as BT, and 17 (17.9%) as TT (Refer figure 2).

95 patients (100%) presented with skin lesions, 61 patients (61.2%) with nerve lesions, 17 patients (17.9%) with deformities and 12 (12.6%) with reactions. 2.1% of patients were detected to have leprosy during the contact tracing (Figure 3).

Majority of patients (55.8%) presented with > 5 skin lesions at presentation. The skin lesions occurred predominantly over the lower limbs, face, trunk, upper limbs, back and genital region. 95.8% of skin lesions were hypo/anaesthetic (Figure 4).

As for nerve dysfunction, 56 patients (58.9%) were noted to have thickened nerves, 32 patients (33.7%) had sensory loss and 11 patients (11.6%) had motor dysfunction. Common thickened nerves observed were ulnar nerve (40.0%), great auricular nerve (38.9%), posterior tibialis nerve (25.3%), peroneal nerve (9.5%) and radial nerve (2.1%).

In our series, the lepra reaction rate was 51.6%. Type 1 reaction commonly involved those with borderline spectrum but type 2 reaction commonly involved those with lepromatous spectrum. Lepra reaction can occur before, during or after completing treatment. At presentation, 12 patients (12.6%) had ongoing lepra reaction and majority of them had type 2 reaction. During treatment, 35 patients experienced a reaction, and following cessation of treatment an additional 2 patients experienced a reaction. Lepra reactions seen during treatment were mainly type 1 reaction. The majority of the reactions occurred within 6 months on MDT. They were rarely seen among those already on MDT for more than 12 months (Figure 5).
Common side effects observed with MDT were dapsone induced hemolytic anaemia (10.5%), cutaneous adverse drug reaction (8.4%) and drug induced hepatitis (2.1%). None of them experienced severe drug toxicity.

In terms of treatment for leprosy, 71.6% of patients had completed treatment and 18.9% were still on treatment. 24.1% of patients had their regimen changed because of side effects and drug resistance. 6 patients died (due to unrelated cause) and another 3 patients (foreigner) defaulted treatment (Figure 6).

**Discussion**

WHO introduced Multiple Drug Therapy (MDT) in 1982. The prevalence of leprosy has declined steadily. MDT was started in Malaysia since 1985. Malaysia achieved elimination with a prevalence < 1 per 10,000 & incidence rate of < 1 per 100,000 population in 1994. Malaysia achieved WHO’s target for control earlier than expected1. But leprosy is still considered a public health problem in Malaysia. Leprosy is regarded as a public health problem because of its capacity to cause permanent disabilities and their social consequences of discrimination and stigma.

The incidence of leprosy in Penang Hospital for the year 2006 was 15 patients. The incidence rate of Penang in 2006 was 0.11 per 10,000 and prevalence rate of 0.68 per 100,000.

Leprosy is a chronic granulomatous infection caused by *Mycobacterium leprae*, a non-cultivable, extremely slow-growing, acid-fast bacillus. *M. leprae* grows best in humans
at temperatures below 37°C. It therefore grows well in cooler areas of the body and is viable in the armadillo and rodents. The long incubation period of *M. leprae* is unique among bacterial diseases. The minimum and average incubation times are 2-3 and 5-7 years and can be as long as 40 or more years.

Leprosy demonstrates a wide spectrum of immunological, microbiological, histological and clinical sequelae as classified by Ridley and Jopling in 1962. Clinical manifestations are largely confined to the skin, upper respiratory system, eyes, testes and peripheral nerves, with subsequent physical deformities and nerve damage. At one polar is tuberculoid leprosy, which is characterized by a strong cell-mediated immunity towards *M. leprae*, giving rise to localized disease. This is clinically manifested by up to three small elevated erythematous cutaneous plaques with a well-defined border. The plaque has a healing center with anaesthesia with or without the presence of an enlarged peripheral nerve and associated sensory or motor dysfunction. It also contains an undemonstrable number of bacilli.

At the other end of the spectrum is lepromatous leprosy, which is characterized by numerous disseminated macules / nodules / papules having ill defined borders and no healing center. There is sensory nerve damage with significant presence of the bacilli in Schwann cells. Deformities of the hands and feet are common. If untreated, lepromatous leprosy progresses slowly with continuous bacteremia and subsequent death from renal failure or acute infections.

Leprosy is also classified according to the degree of skin-smear positivity based on the Ridley-Jopling classification system. This classification served as a basis for chemotherapy. Multicellular leprosy consists of the polar to borderline lepromatous leprosy, while paucibacillary leprosy consists of tuberculoid and borderline tuberculoid leprosy. Most leprosy cases fall between the two polar forms under borderline categories and can transform along this spectrum. They are stable at the two polar extremes and most labile at the mid-point of the spectrum. The polar forms of leprosy vary widely in different populations. In India and Africa, 90% of patients are tuberculoid, while in Mexico 90% are lepromatous. In our cohort, about 50% of leprosy patients are in lepromatous spectrum.

*Mycobacterium leprae* has the affinity for peripheral nerves and neuropathy is a cardinal manifestation of the disease. The nerve damage affects sensory, motor and autonomic fibers resulting in physical impairment and limitation of physical activities and social participation.

Type 1 lepra reaction is the most common type of reaction. It is mediated by delayed-type hypersensitivity (Type 4) directed against *M. leprae* antigens which usually localized to the skin and nerve and result in mycobacterial elimination. These reactions typically occur in immunologically unstable BT, BB and BL leprosy patients. A similar pattern was observed in our cohort (76.9% of type 1 reaction occurred among these groups). They manifest clinically as acutely inflamed skin lesions and acute neuritis. Type 1 reactions may not be associated with systemic symptoms such as fever or arthralgias. Systemic corticosteroid remains the treatment of choice for type 1 reaction.

Type 2 (erythema nodosum leprosum, ENL) reactions occur as a result of immune-complex deposition in the vascular endothelium and tissues and mediated by type 3 immune reactions (immune-complex mediated). ENL is an episodic reaction which occurs in about half of borderline lepromatous and lepromatous leprosy patients and mostly develops within the first 1 years of drug treatment. 90.9% of type 2 reaction cases in our cohort belonged to BL and LL leprosy. Precipitating factors include pyrogenic infection, pregnancy and parturition. ENL is usually a systemic disorder associated with fever, malaise, anorexia, leukocytosis and anemia. Classic clinical manifestations include crops of erythematous painful nodules in the skin and subcutaneous tissue anywhere in the body but mainly in the face, forearms, torso and medial thighs. There may be accompanying nerve, ocular, hepatic, splenic, joint, musculoskeletal, reticuloendothelial, testicular (in males), cardiac and renal involvement.

Most of the ENL reactions are mild in nature and do not require any specific treatment except with some analgesics or antipyretics. In those suffering ENL-associated neuritis, the drug of choice is prednisolone. For chronic recurrent reactions the drug of choice is clofazimine (Pannikar 2003).

Lucio phenomenon is a rare occurrence reported mainly in Latin Americans, especially Mexicans. Patients have a form of lepromatous leprosy described as diffuse lepromatosis, resulting in necrotic lesions that ulcerate, especially below the knees. Lesions are the result of dermal ischemic infarction resulting in turn from endothelial proliferation and/or thrombosis in small vessels. Bacilli are often present along with endothelial cells. Unlike ENL, Lucio is present at the time of initial diagnosis. The only case of Lucio’s phenomenon in our series was a previously undiagnosed lepromatous leprosy patient and Lucio’s phenomenon was his initial presentation.

The lepra bacillus has not been successfully cultured in artificial media. But genetically susceptible armadillos, mouse foot pad and thymectomized irradiated rats can be used to grow bacilli. Diagnosis of leprosy is essentially clinical but there are several laboratory and clinical tests that provide bacteriologic, histopathologic, and immunologic evidence to support the clinical diagnosis.
The World Health Organization (WHO) recommends multiple-drug therapy (MDT) to prevent drug resistance. Three main drugs are used: dapsone, rifampin and clofazimine. Standard MDT for multibacillary leprosy consists of 600 mg rifampin once a month, 100 mg dapsone daily and 300 mg clofazimine once a month and 50 mg daily for 12 months. Paucibacillary leprosy is treated with 600 mg rifampin once a month and 100 mg dapsone daily for 6 months. Ofloxacin and minocycline have also been used in patients who developed side-effects. In contrast, the MDT regimen used in Malaysia is based on the Sungai Buloh Augmented Regimen. Sungai Buloh Augmented Regimen is an intensified regimen. Treatment duration for paucibacillary leprosy is 1 year. For multibacillary leprosy, the maintenance treatment duration is 3 years and intensive phase of daily Rifampicin, Clofazimine and Dapsone is for at least 3 weeks or until MI = 0. In our cohort study, 100% of leprosy patients received MDT as scheduled.

Multi-drug therapy (MDT) is well established. It is safe, effective and widely available. Those who presented late have an increased risk of nerve impairment or disability. Leprosy is a curable disease and treatment provided in the early stages will prevent the disability.

Conclusions

Our study showed similar epidemiological findings as other studies except for a higher reaction rate observed. There was a significant delay in diagnosis observed in our cohort. Identification of the reasons of delay in diagnosis, and the risk factors of lepra reaction are important in the management of leprosy. Anti-leprotic treatment is relatively safe and effective in treating leprosy.

References

Management of leprosy in the Department of Dermatology, Hospital Sultanah Aminah, Johor Bahru

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Abstract

Background Malaysia has achieved control of leprosy with an incidence rate of 1.1 case per 100,000 population, and a prevalence rate of 0.5 per 10,000 population since 1994. However, recently the incidence has increased with the influx of foreign workers, especially from Indonesia, Nepal and Bangladesh. In order to eliminate leprosy, certain issues of need to be addressed namely, imported cases, default from treatment and drug-resistant cases.

Objectives
1. To determine the demography of leprosy patients who attended the Skin Department at Hospital Sultanah Aminah Johor Bahru (HSAJB) for treatment.
2. To determine the clinical subtypes of Hansen's Disease, the incidence of erythema nodosum leprosum (ENL) and reversal reactions.
3. To review the management, side effects of treatment, and disease surveillance

Materials and Methods A 15-year retrospective study of all new cases of Hansen's disease attending the Skin Clinic from 1992 to 2006 was undertaken.

Results
A total of 166 patients were treated in the study period, of whom 74.4% were male. The median age at presentation was 37 years (range 4 to 85 years). 33% of the patients were immigrants, 34% local Malays, 27% local Chinese and 6% local Indians. Of the 166 patients, 59% had lepromatous leprosy (LL), 22% tuberculoid leprosy (TT), 9% borderline tuberculoid leprosy (BT), 8% borderline lepromatous leprosy (BL), 1% indeterminate leprosy and 1% neural leprosy.

The mean bacteriological index (BI) was 1.63 ± 1.63 std deviations, and the mean morphological index (MI) was 0.77 ± 1.24 std deviations at the time of diagnosis.

All patients achieved an MI of zero after three weeks of intensive therapy. 84.6% of the patients received multiple drug therapy (MBCOMBI) in the blister pack distributed by WHO. The remainder was put on modified regimens, because of side effects or drug resistance. 43% of patients developed reactions. Of these, 21.1% had type I reaction and 22.9% had erythematous nodosum leprosum (ENL). 2 patients developed Lucio's phenomenon at initial presentation. 53% of these developed reaction at presentation while 47% had reaction after a few months' treatment. 9.6% of the patients developed side effects secondary to multidrug therapy which necessitated withdrawal of the drugs. The defaulter rate was 15%.

Limitations Retrospective analysis with inadequate documentation is a limitation of this study. In addition, the population studied was limited to referrals being made to the Skin Clinic, which is a tertiary referral center.

Conclusions Control and elimination of leprosy still posed a problem as the majority of the foreign patients had lepromatous leprosy, and a high defaulter rate. Although leprosy in Malaysia has reached the elimination target set by the WHO, new cases will continue to be observed in small numbers due to the long incubation period of this disease.

Background
In 1991, the World Health Organization formed a campaign to eliminate leprosy as a public health problem by the year 2000. Elimination was defined as a prevalence rate of less than 1 per 10,000 population. Although this goal was achieved at the global level by the end of the year 2000, extra effort is still needed to achieve such rates at the national level in some countries.

Malaysia has achieved control of leprosy with an incidence rate of 1.1 case per 100,000 population and a prevalence rate of 0.5 case per 10,000 population since 1994. With the influx of foreign workers, especially from Indonesia, Nepal and Bangladesh, the incidence of leprosy is again increasing.

In order to eliminate leprosy, issues like imported cases, default from treatment and drug-resistant cases have to be addressed.
The objectives of the study are:
1. To determine the demography of leprosy patients who attended the Skin Department HSAJB for treatment
2. To determine the clinical subtypes of Hansen’s Disease, the incidence of erythema nodosum leprosum (ENL) and reversal reactions
3. To review the management, side effects of treatment and surveillance

Materials and Methods
This is a cross-sectional retrospective study of all the registered patients with leprosy referred to the Skin Clinic over the past 15 years (January 1992 - December 2006). This study is based on patient records of the Dermatology Clinic, Hospital Sultanah Aminah, Johor Bahru. A database of the main parameters was created from information extracted from the case records. Statistical analysis was done using Microsoft Excel.

We used the following terminology and definitions in our study.
1. Multiple Drug Therapy (MDT) consists of a combination of Rifampicin, Dapsone and Clofazimine which is given for 3 years in patients with multibacillary leprosy and 1 year for patients with paucibacillary leprosy.
2. Monotherapy refers to single-drug treatment with Dapsone.
3. For monotherapy, a defaulter is one who has absconded from treatment for 2 years or more. For MDT, a defaulter is one who has not presented for treatment for at least 3 consecutive months.
4. MDT Relapse refers to patients who have completed an adequate course of MDT, but who subsequently develop new signs and symptoms of the disease either during the surveillance period or thereafter.
5. Monotherapy Relapse refers to patients who have completed an adequate course of monotherapy (Dapsone) and who subsequently develop new signs and symptoms of the disease after the surveillance period (Release from Control (RFC)
6. Reactivation refers to patients who have completed an adequate course of monotherapy but who subsequently develop new signs and symptoms of the disease during the surveillance period.

Results

Demographic data
The number of new cases from 1992 till 2006 is depicted in (Figure 1). A total of 166 cases were included in the study of which 74.4% were male. (Figure 2)

The median age at presentation was 37 years (range 4 to 85 years old). 33% of the patients were immigrants; 34% local Malays, 27% local Chinese and 6% local Indians (Figure 3)

Clinical subtypes of Hansen’s disease
Out of the 166 patients, 59% had lepromatous leprosy (LL), 22% tuberculoid leprosy (TT), 9% borderline tuberculoid (BT), 8% borderline lepromatous (BL), 1% indeterminate leprosy and 1% neural leprosy. (Figure 4)
According to the WHO classification, 111 patients (67%) were classified as having multibacillary leprosy (MB) and 55 patients (33%) paucibacillary leprosy (PB). Of the 111 MB cases, 99 patients (89%) were found to be skin smear positive, and 12 patients (11%) were skin smear negative. All patients had a skin biopsy consistent with Hansen's disease. As for the remaining 17 patients currently under treatment, 10 had MB leprosy while 7 PB leprosy.

**Reactional states and treatment of reactions**
A total of 72 patients (43%) developed reactions. 34 patients (21.1%) had type I reaction while 38 patients (22.9%) had erythematous nodosum leprosum (ENL). 2 patients developed Lucio’s phenomenon at initial presentation. 53% of the patients developed reaction at time of presentation while 47% had a reaction after a few months of treatment. Drugs that were used to treat reactions are depicted in the pie chart below (Figure 5).

**Figure 4.** Clinical subtypes of leprosy

**Figure 4.** Drugs used to treat reversal reaction

**Table 1.** Types of MDT Treatment Regimes

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>FREQUENCY</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MB COMBI</td>
<td>138</td>
<td>84.60%</td>
</tr>
<tr>
<td>ROM</td>
<td>6</td>
<td>3.61%</td>
</tr>
<tr>
<td>ROD</td>
<td>3</td>
<td>1.80%</td>
</tr>
<tr>
<td>ROC, RCM</td>
<td>3</td>
<td>1.80%</td>
</tr>
<tr>
<td>MB COMBI RCM</td>
<td>2</td>
<td>1.20%</td>
</tr>
<tr>
<td>ROC</td>
<td>2</td>
<td>1.20%</td>
</tr>
<tr>
<td>MB COMBI ROD</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>MB COMBI ROM</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>RMD</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>RC</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>MC</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>RC ETHIONAMIDE</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>RD ETHIONAMIDE</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>RCD</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>CMD</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>RD</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>ROD ROM</td>
<td>1</td>
<td>0.60%</td>
</tr>
<tr>
<td>MB COMBI RC</td>
<td>1</td>
<td>0.60%</td>
</tr>
</tbody>
</table>

MB COMBI - Blister pack distributed by WHO
ROM - Rifampicin, ofloxacin, minocycline
ROD - Rifampicin, ofloxacin, dapsone
ROC, RCM - Rifampicin, ofloxacin, dapsone, clofazimine, minocycline
MB COMBI RCM - MB COMBI follows by Rifampicin, clofazimine, minocycline
ROC - Rifampicin, ofloxacin, clofazimine
MB COMBI ROD - MB COMBI follows by Rifampicin, ofloxacin, dapsone
MB COMBI ROM - MB COMBI follows by Rifampicin, ofloxacin, minocycline
RMD - Rifampicin, minocycline, dapsone
RC - Rifampicin, clofazimine
MC - Minocycline, clofazimine
RC Ethionamide - Rifampicin, clofazimine, Ethionamide
RD Ethionamide - Rifampicin, dapsone, Ethionamide
RCD - Rifampicin, clofazimine, dapsone
CMD - Clarithromycin, minocycline, dapsone
RD - Rifampicin, dapsone
RD ROM - Rifampicin, ofloxacin, dapsone, by Rifampicin, ofloxacin, minocycline
MB COMBI RC - MB COMBI follow by Rifampicin, clofazimine
Treatment, side effects of treatment and surveillance

A total of 138 patients (84.6%) received multiple drug therapy (MBCOMBI) in a blister pack provided by WHO. The remainder were put on modified regimens because of side effects of drugs or drug resistance. (Table 1) As for the 17 patients still under treatment, 10 patients had MB leprosy while 7 patients had PB leprosy. 9.6% of the patients developed side effects secondary to multidrug therapy which necessitated withdrawal of the drugs.

Five patients developed a greyish pigmentation due to minocycline, 3 had hepatitis from rifampicin, and 5 had hemolytic anaemia with dapsone. A single patient had toxic epidermal necrolysis due to ofloxacin. One patient had urticaria due to ofloxacin, while another developed severe neutropenia following azathioprine.

Four patients had concurrent pulmonary tuberculosis (PTB) and were referred to the chest physician for treatment. 2 patients had preexisting renal failure prior to diagnosis of leprosy. For all patients with a positive skin smear, a skin biopsy was taken and sent to Sungai Buloh Leprosy Centre for mouse foot pad inoculation, and MDT sensitivity testing. Ten of our patients proved resistant to dapsone, and 1 patient had partial resistance to clofazimine. (Table 2) The treatment regimes were modified accordingly.

Twelve patients relapsed after completing treatment. 7 out of these had been treated with monotherapy with dapsone in 1948-1979. Twenty two patients (13.3 %) developed deformities. Table 3 showed the breakdown of the deformities seen among the cases over the past 15 years. A total of 25 patients defaulted follow-up. The defaulter rate was 15 % despite rigorous surveillance.

Discussion

Malaysia has achieved control of leprosy with an incidence rate of 1.1 cases per 100,000 population and a prevalence rate of 0.5 case per 10,000 population since 1994. With the influx of foreign workers, especially from Indonesia, Nepal and Bangladesh, the incidence is again increasing. Over the past 15 years, a total of 166 new cases were seen in our skin clinic. The majority of these cases were referred to our clinic either by the district hospitals, out-patient departments or private clinics. The number of new cases has declined significantly from 1992 (21 cases) till 2003 (5 cases), with a small increase between 2004 and 2006. One third of the patients were foreign nationals from Indonesia, Myanmar, Nepal and India.

Leprosy affects all age groups, ranging from early infancy to the very old. Prevalence rates usually peak between the age of 30 and 50 years. The youngest patient reported in the medical literature is a 3 week old child in Martinique by Montestruc and Berdonneau in 1954.

In our case series, the peak incidence occurred between the ages of 30 to 40 years. Our youngest patient was 4 years old and oldest 85 years old at presentation. In our series, leprosy affected the most productive age group and this poses an economic loss to the family and country. A delay in treatment may result in complications and the necessary rehabilitation would be even costlier.

In most parts of the world, males are affected more frequently than female in the ratio of 2 to 1. In our study, 74.4% of cases were males while 23.6 % were females. However, the male preponderance in leprosy is not universal. In Africa, leprosy affects both sexes equally. A higher prevalence of leprosy among females is observed in Uganda, Nigeria, Malawi, Gambia, Burkina Faso, Zambia, Thailand & Japan.

The epidemiology of the disease itself is still a problem because there is still no effective way to measure the level of infection and the incidence of the disease in the community. This is complicated by very long incubation period of the disease and the process of self-healing of many single lesions. There is also a tendency for patients to conceal their disease because of social stigma.

Table 2. Drug resistance

<table>
<thead>
<tr>
<th>DRUG TYPE</th>
<th>FREQUENCY</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLOFAZIMINE</td>
<td>1</td>
<td>0.61%</td>
</tr>
<tr>
<td>DAPSONE</td>
<td>10</td>
<td>6.10%</td>
</tr>
</tbody>
</table>

Table 3. Deformities

<table>
<thead>
<tr>
<th>Deformities</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leonine</td>
<td>4</td>
</tr>
<tr>
<td>Collapse of Nose + Exposure keratitis</td>
<td>1</td>
</tr>
<tr>
<td>Ulnar Claw Hand</td>
<td>3</td>
</tr>
<tr>
<td>Foot Drop</td>
<td>2</td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>7</td>
</tr>
<tr>
<td>Partial Absorption of Hands &amp; Feet</td>
<td>2</td>
</tr>
</tbody>
</table>
Thirty three percent of the patients were foreigners. More new cases were detected among immigrants since 2000. As majority of the immigrants do not come forward for treatment and do not possess a fixed abode, contact tracing, follow-up and surveillance is difficult. High defaulter rates were seen among this group of patients. This may well serve as a source of infection to the local population.

In 1960, Ridley and Jopling classified leprosy into 5 groups based on immunological and histological evidence namely tuberculoid leprosy (TT), borderline tuberculoid (BT) borderline borderline (BB), borderline lepromatous (BL) and lepromatous leprosy (LL). Out of the 166 patients, 59% had lepromatous leprosy (LL), 22% tuberculoid leprosy (TT), and 9% borderline tuberculoid (BT), 8% borderline lepromatous (BL), 1% indeterminate leprosy and 1% neural leprosy.

According to the WHO classification, 111 patients (67%) were classified as multibacillary leprosy (MB) while 55 patients (33%) were classified as paucibacillary (PB) cases. Of the 111 MB cases, 99 patients (89%) were found to be skin smear positive, 12 patients (11%) were skin smear negative. All diagnoses were confirmed by skin biopsy. As for the 17 patients currently under treatment, 10 patients had MB leprosy while 7 patients had PB leprosy. Comparing both classifications, most of the patients were diagnosed late.

Dapsone was first used to treat leprosy in 1943. Clofazimine was introduced in 1963 and Rifampicin in 1966. Monotherapy with Dapsone had resulted in resistant strains of Mycobacterium leprae. In 1981, the World Health Organisation (WHO) introduced Multiple Drug Therapy (MDT) comprising of Rifampicin, Clofazimine and Dapsone. MDT was introduced in Malaysia in 1985, and by 1994, almost all cases nationwide were on MDT. The program was reviewed in 1995 and integrated into the public health service. The WHO MDT regime is summarised in Table 4.

Out of the 166 patients, 59% had lepromatous leprosy (LL), 22% tuberculoid leprosy (TT), and 9% borderline tuberculoid (BT), 8% borderline lepromatous (BL), 1% indeterminate leprosy and 1% neural leprosy.

In our clinic, we have adopted the Sungai Buloh Augmented Regime as showed in (Table 5) where PB cases were treated for a year and, MB leprosy patients were treated for 3 years.

<table>
<thead>
<tr>
<th>Paucibacillary (PB)</th>
<th>Multibacillary (MB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months of:</td>
<td>Intensive Therapy</td>
</tr>
<tr>
<td>Rifampicin 600mg monthly</td>
<td>Rifampicin 600mg monthly</td>
</tr>
<tr>
<td>Clofazimine 300mg monthly</td>
<td>Clofazimine 300mg monthly</td>
</tr>
<tr>
<td>Clofazimine 100mg daily</td>
<td>Clofazimine 100mg daily</td>
</tr>
<tr>
<td>Dapsone 100mg daily</td>
<td>Dapsone 100mg daily</td>
</tr>
</tbody>
</table>

43% of the patients developed reactions, 21.1% type I reaction and 22.9% erythematous nodosum lepromus (ENL), 2 patients developed Lucio’s phenomenon at initial presentation and were successfully treated with prednisolone and MDT. 53% of the patients developed reaction at time of presentation while 47% had reaction a few months’ after initiation of therapy. Single-agent prednisolone is the drug of choice for treatment of reactions (66%), follow by combinations of prednisolone and aspirin (23%), prednisolone and azathioprine (9%), and aspirin alone (2%)

A total of 138 patients (84.6%) o received multiple drug therapy (MBCOMBI ) in the blister pack distributed by WHO. The blister pack is easy to understand and administer by most patients, regardless of their education level. The patients were requested to return the empty pack each month during follow-up. This allows a check on the compliance to treatment. The remainder were put on modified regimens because of side effects of drugs and drug resistance. As for the 17 patients currently under treatment, 10 patients had MB leprosy while 7 patients had PB leprosy. Nine point six percent of the patients had side effects secondary to multidrug therapy which necessitated withdrawal of the drugs.

The National Leprosy Elimination programme was launched in Malaysia in July 1992. The aim is to increase early detection of cases and early treatment with adequate follow-up to prevent transmission, as well as to reduce deformity rate. The national target for deformities was set below 10%. In our study, 22 patients (13.3 %) developed deformities which is higher than the national target. This problem should be addressed seriously. Health education to familiarize the public with the early signs and symptoms of leprosy should be carried out, as well as campaigns.
encouraging the public to seek treatment early. Training of healthcare professionals to have a high index of suspicion and recognize leprosy at an early stage is equally important.

For all patients with positive skin smears, skin biopsies were sent to Sungai Buluh Leprosy Centre for mouse foot pad inoculation and MDT sensitivity testing. Ten of our patients were resistant to dapsone, and 1 patient had partial resistance to clofazimine. The treatment regimes were modified accordingly.

Dapsone was used to treat leprosy since 1943, and was used as monotherapy for over 30 years. Emergence of drug resistant strains of Mycobacterium leprae was reported soon after the introduction of dapsone. Dapsone resistance was first reported in 1964. By 1982, secondary dapsone resistance was reported in more than 25 countries according to a report by WHO.

Clofazimine was found to be effective in the treatment of leprosy since 1962. The first case of clofazimine resistance was reported in 1982 by Warndoff and Van die pen.

Rifampicin was used as anti-leprosy drug since 1966. Secondary rifampicin resistance was first reported in 1976.

In 1989, 22 more strains of M. leprae resistant to rifampicin was detected in 39 multibacillary patients who relapsed. All cases reported were due to rifampicin monotherapy.

The first report of secondary resistance to rifampicin following 26 doses of MDT (Rifampicin 600mg and Clofazimine 600mg for 2 days, Inj Acedapsone 225mg IM every 8 weeks and dapsone 100mg daily) was reported in 2003 from India. Rifampicin resistant cases following MDT may have gone undetected. It is necessary to monitor and gather the information on it's magnitude. In order to prevent multiple drug resistant strains of M. leprae from developing, current leprosy control strategies are based on early detection of cases and treatment with multidrug therapy (MDT) as recommended by the WHO.

Twelve patients relapsed after completion of therapy. Seven out of them had been treated with monotherapy with dapsone from 1948-1979. Education on compliance to medication is important to prevent relapse and emergence of resistance strains. Early detection of drug-resistant bacilli among patients not improving clinically will need treatment with combinations of effective drugs to prevent resistance to current and new drugs for leprosy. Twenty-five patients defaulted follow-up and the patient default rate was 15% despite rigorous surveillance. High default rates were seen among foreign nationals, who pose a great challenge to our leprosy elimination programme.

Conclusions

Leprosy affects predominantly males (74.4%). Majority of the patients were in the economically active age group. One third of the patients were immigrants, and this serves as a source of infection to the local population. Sixty seven percent of study cohort had MB leprosy at initial presentation. The majority of the multibacillary Hansen's patients were immigrants. Despite a rigorous surveillance policy, the defaulter rate was 15%.

Control and elimination of leprosy still poses a problem in view of the fact that the majority of immigrants had MB leprosy and a high default rate. Although leprosy in Malaysia has reached the elimination target set by the WHO, new cases will continue to be seen in small numbers due to the long incubation period of this disease.

Early diagnosis and prompt referral for treatment is crucial to prevent deformities and permanent disability. Public health education is important to increase public knowledge, dispel false beliefs and reduce stigma of this dreaded disease.

Acknowledgement

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