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Editorial -----v

1. Knowledge, Attitude and Practices Concerning Sexually Transmitted Diseases/ Reproductive Tract Infection Among the Commercial Sex Workers, Dhaka City-----1
-Dr. Md. Rezaul Karim, Dr. Md. Mahmudul Haque
2. Prevalence of Pneumococcal Carriage in Children and Antimicrobial Susceptibility Pattern of Streptococcus Pneumoniae Isolates-----6
-Bijaya Malla, Jeevan Bahadur Sherchand, Rajendra Kumar B.C,
Prakash Ghimire , Basista P. Rijal
3. Acetylator status influences bioavailability of isoniazid in patients with advanced HIV disease---9
-Geetha Ramachandran, A.K.Hemanth Kumar, S.Rajasekaran, C.Padmapiyadarsini,
Soumya Swaminathan, P.Venkatesan, L.Sekar, Prema Gurumurthy, P.Paramesh
4. Burden of Tobacco Smoking in District Tharparkar, Sindh, Pakistan-----13
-Rano Mal Piryani, Nadeem Rizvi, Meva Ram
5. Delay in Detecting Tuberculosis Patients in Anuradhapura District of Sri Lanka-----16
-Deepthini RADKM Waidyaratne
6. First Panel Testing in SAARC Regional Networks of TB Reference Laboratories-----20
-B.P. Rijal, K.K. Jha, Rano Mal Piryani, M. Rahman, C.N. Paramasivan
7. Pharmacokinetics of isoniazid and rifampicin in patients with renal failure undergoing continuous ambulatory peritoneal dialysis (CAPD)-----23
-Geetha Ramachandran, Hemanth Kumar, A. K. Prema Gurumurthy, Prakash K.C., Venkatesan P., Bose S. C., Manjula Datta.
8. Status of AIDS Orphans In Chennai , South India-----28
-Meenalochani Dilip, Beena E Thomas, Fathima Rehman,
Vani Sundaram, Mohanarani Suhadev, Soumya Swaminathan

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It should state the purpose of the study and summarize the rationale for the study. It should have pertinent references but not extensive review of the subject.

Methods

Describe the criteria for selection of cases; identify the methods, apparatus (manufacturers name) and procedures in detail.

Results

Present the results in sequence in the text, tables and figures. Do not repeat all the data in the tables and/or figures in the text. Summarize the important points only. Mention the methods used for statistical analysis.

Discussion

Comment on the observations of the study and the conclusions derived from it. Do not repeat the data in detail already given in the results. Give implications of the findings, their limitations and observations to other relevant studies. Avoid unqualified statements and conclusions, which are not completely supported by the data. Avoid claiming priority. New hypothesis may be labeled as recommendations.

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Type, each table on a separate sheet, use double space. Give a brief title for each table. Cite each table in the text in consecutive order.

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Editorial

Around three billion people continue to depend upon solid fuel globally. Cooking with solid fuels results in high level of indoor pollution. Smoke in the home from cooking solid fuel, i.e., wood, cow-dung, crop waste and coal kills 1.6 million people every year. This means one life lost every 20 seconds. Smoke in the home is the fourth greatest risk factor to death and disease in the world's poorest countries. The incomplete combustion of the solid fuels from inefficient primitive type of earthen oven or Chulla is the main reason for producing smoke in the Kitchen. Women and children are predominantly the victims of smoke produced in Kitchen while cooking on solid fuels. Women spend three to seven hours a day near by the fire in villages. They are exposed to level of smoke more than 100 times above accepted safety levels. Children under five years of age spend most of the time with their mothers, so they are also exposed to smoke. Children are at greater risk of developing lower respiratory illnesses as their airways are small susceptible to inflammation, lungs are not fully developed and immune system is not well developed. Women have increased chance of developing chronic obstructive pulmonary disease (COPD), cancer of trachea, bronchi and lung parenchyma and lower respiratory infection. There is some evidence that smoke in the home contributes to low birth weight and infant mortality.

Earlier, the international community was slow to recognize this problem. Since last one decade this receives attention and the steps has been taken at international and regional level. Responds to global and regional initiatives such as MDGs (Goal 7: Ensure Environmental susceptibility) and SAARC Ministerial conferences/meeting on health and the environment, forming effective partnerships and alliances to respond to health, and environment with special emphasis on high-risk population groups such as children, women.

Health workers, NGO's workers and community based organizations need to aware the community about health hazards of indoor pollution and strengthen the international, regional and national efforts in resolving the problem.

Knowledge, Attitude and Practices Concerning Sexually Transmitted Diseases/ Reproductive Tract Infection Among the Commercial Sex Workers, Dhaka City

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Abstract

Objective: The study was conducted to assess the knowledge, attitude and practice regarding Sexually Transmitted Diseases (STDs) / Reproductive Tract Infection (RTI) among the Commercial Sex Workers (CSWS).

Methods: This cross sectional study was carried out among the Commercial Sex Workers (CSWS). Relevant information was collected through face-to-face interview. A pre-tested semi-structured questionnaire was used to collect the information.

Place and period of the study: The study was conducted in some different places of Dhaka city in Bangladesh from March 2000 to June 2000.

Results: Most of the respondents were below 25 years of age and out of total 102 respondents 63% came to this profession due to poverty. Students were the principal customers (62%). Of the respondents 93% knew about STDs/RTI. Among the respondents who know something about STDs/RTI a good number could say it's mode of transmission and some preventive measures. But 88.23% of the total did not use condom and it is mostly due to disliking by the customers.

Conclusion: It is widely accepted that commercial sex workers and their clients are major foci of risk in a number of areas, especially in their susceptibility to sexually transmitted infections. To prevent the spread of STDs/RTI proper health education regarding sign and symptoms of STDs/RTI, it's complications, mode of spread and preventive measures are to be enhanced among the Commercial Sex Workers (CSWS). This is also important in case of the other high-risk group of population.

Introduction

Bangladesh is a small country of 147,570 sq-km area and a land of disaster. She has to sustain the burden of a huge population boom (819 inhabitants/sq km).¹ Bangladesh has one of the lowest per capita income among the countries in the Asia Pacific region with a population of 122.8 million and per capita GNP of about

\$ 40. About 52% of the total population survives below the absolute poverty. At the same time, the urban population growth has been over 6% per annum during the last three decades compared with a national population growth rate of about 2%.² This high rate is due to the migration of rural people to the urban areas because of rural push and the urban pull.

In Bangladesh the situation of poverty is severe for women and children. The strains of deteriorating economic conditions couple with poverty have caused families to break up and the number of household headed by women has increased rapidly. Therefore a large number of women have been entering the labor. Due to lack of proper education and technical skill, a considerable number of girls are being brought to prostitution. It has been also reported that there are about 1000,000

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commercial sex workers (CSWs) in Bangladesh (VHSS, 1993).³ The floating sex workers are increasing in number and are more easily accessible to the young adults which cause an increasing trend in the prevalence of sexually transmitted diseases (STDs) and reproductive tract infections (RTIs) in Bangladesh.

Though the exact picture of STD problem in Bangladesh is not known due to lack of proper reporting system it seems to be quite high. Several reports showed that the STD/RTI/HIV and AIDS have been rampant in Bangladesh.⁴

The STDs are a major public health concern particularly since the early eighties after isolation of HIV, the agent of AIDS.⁵ For several decades STDs have ranked among the top five diseases for which adults in developing countries seek health care services.⁶

The presence of STD is a marker of high-risk behavior for HIV infection. STDs are biological co-factors of HIV transmission. The presence of a genital ulcer caused by chancroid or herpes increases ones risk of HIV infection 10-20 folds, and the risk increases 3-4 folds where gonorrhoea or clamydia is present.⁷ Social taboos, religion, stigmata and ambivalence in many countries make it extremely difficult to address the problem since in essence, it is not merely a health problem but a development problem of severe human and economic significance. Key issues related to STD management are prevention of new infection, treatment of individual with symptom of infection, notification and treatment of sexual partners and motivation towards health seeking behavior.⁸

The control of sexually transmitted diseases (STDs) is now recognized as a global priority (World Bank, 1993).⁵ HIV is clearly a major cause of premature death, and most cases are the result of sexual transmission. Other STDs cause considerable morbidity, particularly in relation to reproductive health of women, and are associated with increased transmission of HIV. A number of studies showed an exceptional increase of HIV infection among commercial sex workers in India and Thailand.⁹ About 44% of lower class prostitutes of Chiang Mai, Thailand and 35% prostitutes of Bombay, India are infected with HIV.¹⁰

The commercial sex workers are the specific high-risk group, almost all having STDs / RTI and they are transmitting the disease to the men who come to contact with them in silence. "With discovery of penicillin and its clinical application, since 1942, the incidence of STDs initially reduced. However in recent years, the world is again in grip of STDs and in fact venereal infections are at pandemic level around the globe".⁴

"In recent years, control of STDs has gained much more importance in the control of HIV / AIDS. This is because, evidence indicates that people with ulcerative STDs such as syphilis, chancroid and herpes are 100 times more prone to contact HIV infection during a single sex act without condom".⁴ WHO expert showed that the effective management of STDs in Mwanza, Tanzania has reduced HIV incidence by 42%. Similarly a 100% condom use drive in Pitsancoloke, Thailand has cut STDs among sex workers to virtually zero.¹⁰

This consideration has led to undertake this study to assess the knowledge of STDs and RTI and to determine the cause that promotes the transmission those among the commercial sex workers. Knowledge and information about these are useful developing appropriate strategy of prevention and intervention as well as creating advocacy role against this problem.

Materials and methods

This cross sectional study was carried out at different places of Dhaka city namely- Chandrima Uddyan, Kamlapur railway station, Court area of old Dhaka, around Moon cinema hall at old Dhaka and Drop in Center (DIC). Commercial sex workers residing in these places of Dhaka metropolitan city were the study population. Total 102 commercial sex workers were interviewed. Sample size was determined purposively. The study was conducted from March 2000 to June 2000. A semi-structured pre-tested questionnaire was used to collect the information.

Results

Majority of the respondents (47%) belonged to the age group 21-25 years. The mean age was 17.8 years and 26% of the respondents aged 15 years or below (Table-1).

Table-1 Distribution of respondents by age

Age group	Number	Percent
≤ 15 years	27	26
16 – 20 years	48	47
21 – 25 years	23	23
>25 years	4	4
Total	102	100

It was seen that majority of the respondents (63%) accepted the profession due to poverty, while 59% were seduced and 16% accepted the profession willingly (Table-2).

Table-2 Reasons for accepting the profession.

Reasons	Number*	Percent
Poverty	64	63
Seduced	60	59
Trafficking	4	4
Willingly	16	16

***Multiple responses**

Students were the major customer group (62%). Other customers were Businessmen 50%, Mastan (unemployed and terror) 42%, Driver 32% and Rickshaw puller 23% (Table-3).

Table-3 Distribution of the respondents according to their customer group

Customer group	Number*	Percent
Students	63	62
Businessmen	51	50
Mastan	42	41
Driver	33	32
Rickshaw puller	24	23
Police	13	13
Service holder	9	9
Shopkeeper	6	6

***Multiple responses**

There was wide variation in their income. Majority of the respondents had daily income of Taka 100-200. Only 8.82% had daily income more than 500 Taka (Table-4).

Table-4 Daily income of the respondents

Daily income (Taka)	Number	Percent
100-200	43	42.15
200-300	23	22.55
300-400	15	14.71
400-500	12	11.76
>500	9	8.82

On searching the knowledge of the respondents about STDs it was seen that out of total 102 respondents 95 (93%) heard about STDs and RTI. Among them 100% heard of AIDS, 75.79% and 64.21% of the respondents mentions syphilis and gonorrhoea as the names of STDs respectively (Table-5).

Table-5 Respondents by mentioning the names of STDs

n=95

Name	Number*	Percent
AIDS	95	100
Syphilis	72	75.79
Gonorrhoea	61	64.21

***Multiple responses**

About signs and symptoms of STDs 56.84% of respondents mentioned of vaginal discharge, 29.47% said Itching around vagina, 43.16% ulcer around vagina, 12.63% Burning micturition and 32.63% said lower abdominal pain (Table-6).

Table-6 Respondents according to the sign and symptoms of STDs / RTI

n=95

Sign and symptoms	Number*	Percent
Vaginal discharge	54	56.84
Itching around vagina	28	29.47
Ulcer around vagina	41	43.16
Burning micturition	12	12.63
Lower abdominal pain	31	32.63

***Multiple responses**

Of the 95 respondents who heard about STDs and RTI 100% mentioned that these are transmitted through sexual contact. Among them 34% said that sharing needles and 31% mentioned of blood transfusion as the cause of transmission (Table-7).

Table-7 Respondents' knowledge about prevention of STDs and RTI

n=95

Mode of transmission	Number*	Percent
Sexual contact	95	100
Sharing needle	32	33.68
Blood transfusion	29	30.53
Transplacental	5	5.26

***Multiple responses**

About the prevention of STDs and RTI 100% mentioned of condom use, 42.11% said of avoiding multiple sexes, 33.68% said of using disposable syringes and 30.53% mentioned of blood screening before transfusion (Table-8).

Table-8 Respondents' knowledge about prevention of STDs and RTI

n=95

Preventive measure	Number*	Percent
Condom use	95	100
Avoiding multiple sex	40	42.11
Using disposable syringes	32	33.68

***Multiple responses**

It was found that out of total 102 respondents 90(88.23%) did not use condom. Of them 3.33% did not use it because of self-disliking. On the other hand 84.44% said of disliking by the customers, 23.33% said that it is not always available and 4.44% said it to be costly (Table-9).

Table-9 Reasons for not using condoms

n=90

Reasons	Number*	Percent
Self disliking	3	3.33
Disliking by the customers	76	84.44
Not always available	21	23.33
Costly	4	4.44

*Multiple responses

Discussion

In this study it was seen that most of the commercial sex workers (CSW) were young in their late teen age. The mean age was 17.8 years. As the customers preferred and sought very young women, very few women were above 25 years of age (Table-1). In a similar study the mean age was found 22.2 years.³⁹ Majority of the respondents (63%) accepted this profession due to poverty and before coming to this profession most of them were in non-sex work. Study conducted by SHAKTI³⁹ also showed similar picture. People recognize STDs by symptoms. The symptoms of different STDs as perceived by the people were recorded. AIDS and its symptoms are not widely known. Some people termed AIDS as "English rog".⁵ In this study most of the respondents (93%) either knew or heard about STDs / RTI. They mentioned AIDS, syphilis and gonorrhoea (Table-5). Among the respondents who knew about STDs / RTI a good number could say something about the signs and symptoms of these diseases (Table-6). Of them 100% opined that these are transmitted through sexual contact and 100% said that use of condom can prevent the transmission of STDs/RTI (Table-7 & 8). But the most alarming picture is that they did not use condom and the principal cause behind it is 'disliking by the customers' (Table-9).

Conclusion

The magnitude of the problem of STDs/RTI is an increasing Public health concern in Bangladesh. STDs/RTI are widely spread in nature but are preventable and treatable diseases. It is widely accepted that commercial sex workers and their clients are major foci of risk in a number of areas, especially in their susceptibility to sexually transmitted infections. The analysis of the situation of CSWs of Dhaka metropolitan city, it is clear that the extent of the risk and the reason for the risk should be outlined. If preventive action is not taken immediately it may be difficult to control the spread of STDs among various population group as well as general population.

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Prevalence of Pneumococcal Carriage in Children and Antimicrobial Susceptibility Pattern of *Streptococcus Pneumoniae* Isolates

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Abstract

Introduction: *S.pneumoniae* is an important pathogen of childhood. Prevalence of resistant strains in nasopharynx can make the antibiotic treatment ineffective when becomes invasive.

Objectives: To find out the prevalence of *S. pneumoniae* carriage in nasopharynx and study the antimicrobial susceptibility patterns.

Methods: A total of 400 nasopharyngeal samples were collected from children during the period of Feb to Aug 2004. All the samples were processed at Research Laboratory, Tribhuvan University Teaching Hospital, Institute of Medicine. Bacterial identification and interpretation of antimicrobial susceptibility patterns was done by standard methodology.

Results: The study found that the Pneumococcal carriage in children was 83% (332/400). The organism showed lowest susceptibility to cotrimoxazole (6.62%). Among the 17 Oxacillin- resistant isolates, only two (11.76%) isolates demonstrated resistant to both Cotrimoxazole and Tetracycline.

Conclusion: The organism showed highest resistance to cotrimoxazole in comparison to others, which is commonly used drug against pneumonia. Crowding and lack of empirical use of antimicrobials is found responsible for high degree of prevalence of Cotrimoxazole resistance.

Keywords: Pneumococcal carriage, Oxacillin, Cotrimoxazole, drug resistance

Introduction

Streptococcus pneumoniae is a major cause of morbidity and mortality worldwide. It causes Acute Respiratory Infections (ARI) including bronchiolitis, otitis media, sinusitis, pneumonia, post measles-associated illness and severe infections such as meningitis and septicemia¹. In developing countries infants aged less than 3 months are also at risk, especially for Pneumococcal meningitis. However, based on available data, acute respiratory infections kill an estimated 1.9 million children aged 5 years and under annually. The Pneumococcus is estimated to cause over 1 million of these deaths, most of which occur in developing countries, where the pneumococcus is probably the most important pathogen of early infancy². In Nepal, it is common etiological agent

of pneumonia and meningitis with high mortality. Pneumococci are transient members of normal flora, colonizing the nasopharynx of 40% of healthy adults and children. Factors associated with Pneumococcal colonization are conditions of crowding, previous use of antibiotics, underlying medical conditions, human immunodeficiency virus infection, and hospitalization. In children with altered local defenses, malnutrition and viral factors, the aspiration of small amount of (upper) respiratory secretions could deliver enough inoculums to cause invasive infections into lungs. The nasopharynx is the usual source of pneumococci in clinical disease, and it is thought that resistance in carriage isolates is potentially predictive of the emergence of resistance in clinically significant isolates³. In developing countries because of higher probability of bacterial pneumonia, a stronger justification for empirical use of antimicrobials is needed. As nasopharyngeal *S. pneumoniae* may have a predictive potential for resistance in clinically significant isolates⁴. It has been suggested that pneumococci obtained from the nasopharynx of patients might be used

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as a surrogate for sensitivity testing as these are easier to isolate and can be obtained from a high proportion of patients. When this approach was followed in Pakistan⁴, concordance for capsular serotype between nasopharyngeal isolates and isolates from normally sterile sites was obtained in 99% of cases, suggesting that the same *Pneumococcus* was present at both sites.

The nasopharyngeal bacterial population is an important reservoir of infection, carriage and spread of pathogenic bacteria, including antibiotic-resistant clones. Antibiotic therapy should not only be active against both susceptible and resistant strains at concentrations achievable at the site of infection, but also reduce the prevalence of carriage to minimize the potential for the selection and spread of resistant strains.

The estimated worldwide prevalence of penicillin-resistant *Streptococcus pneumoniae* (PRSP) was 14.1% in 1997. Resistance to other agents, such as macrolide, chloramphenicol, co-trimoxazole and tetracycline, is also increasingly common. The estimated worldwide prevalence of macrolide-resistant *S. pneumoniae* was 22% in 1997 and was considerably higher in some areas, exceeding penicillin resistance in many countries⁵.

Material & Methods

Setting: The study was done in community children of Sarlahi aged below 5 years. Sarlahi is a rural, plain district in central terai of Nepal. About three quarters of population may be considered to live below the poverty line. The laboratory work was done in Institute Of Medicine, Tribhuvan University Teaching Hospital, Research Laboratory.

Isolation of strains: During the study period of Feb. to Aug. 2004, a total of 400 samples were collected from noninvasive infection site; nasopharynx of children using sterile calcium alginate tipped per nasal applicator (Hardwood Products Company LLC, MAINE, USA). The samples were stored in Skimmed milk Transport Glucose Glycerol (STGG) media at -70°C till further processing. The samples were plated on 5% sheep blood agar and incubated for 18 h at 37°C in 3-10% CO₂. Of these 400 subjects, 332 had cultures positive for *S. pneumoniae*. Bacterial identification was made on basis of Optochin (Ethylhydrocupriene Hydrochloride) test (inhibition zone >7mm), morphology of colony, bile solubility test, Gram stain.

Antimicrobial susceptibility testing

Susceptibility to antimicrobial agents was determined by the standard disk diffusion method on Mueller-Hinton agar plates containing 7% sheep blood and incubated at 37°C for 24 h in 3-10% CO₂. The antibiotic disks contained 1µg of Oxacillin, 15 µg of Erythromycin, 25 µg of Cotrimoxazole, 30 µg of Chloramphenicol, 30 µg of Tetracycline. Quality control testing was conducted with *S. pneumoniae* American Type Culture Collection (ATCC) 49619. The interpretation criteria of Inhibition zone of growth results was as directed by NCCLS standards.

Data analysis: The data was checked for accuracy and computerized using SPSS 10.5. Statistical tests including Chi-square test was carried out to test the differences in proportions of genders and association in carriage rates.

Results

Of the total samples, *Pneumococcus* could be isolated from 332 subjects. The percentage of *Pneumococcal* carrier cases between male and female was not significantly different ($p>0.05$) as presented in table 1.

Table 1 Sex-wise distribution of *Pneumococcal* carriage in children

Sex	No. of tested samples	No. of positive sample (%)
male	192	162 (84.37%)
female	208	170 (81.73%)
total	400	332

The in vitro activities of 5 selected antimicrobial agents tested against 332 isolates of *S. pneumoniae* are summarized in Table 2. Cotrimoxazole showed the lowest susceptibility rate (6.62%). All isolates showed susceptibility to Chloramphenicol (100%). Erythromycin demonstrated almost similar susceptibility (99.39%) except two that showed intermediate.

Only 17 isolates (5.12%) were resistant to Oxacillin (1µg). *Pneumococcus* can follow different pathways to acquire resistance to β -lactams, mostly by alterations in Penicillin Binding Proteins (PBP). Among the 17 Oxacillin-resistant isolates, only two (11.76%) demonstrated resistant to both Cotrimoxazole and Tetracycline and 8 isolates (47.05%) were Tetracycline -intermediate.

Table 2 Antimicrobial susceptibility patterns and no. of Pneumococcal isolates

No of isolates	Antibiotics				
	oxacillin	erythromycin	cotrimoxazole	chloramphenicol	tetracycline
2	O ^r	E ^l	Co ^r	Ch ^s	Tet ^r
6	O ^s	E ^s	Co ^s	Ch ^s	Tet ^s
7	O ^r	E ^s	Co ^r	Ch ^s	Tet ^s
8	O ^r	E ^s	Co ^r	Ch ^s	Tet ^l
10	O ^s	E ^s	Co ^l	Ch ^s	Tet ^r
10	O ^s	E ^s	Co ^r	Ch ^s	Tet ^r
16	O ^s	E ^s	Co ^s	Ch ^s	Tet ^s
273	O ^s	E ^s	Co ^r	Ch ^s	Tet ^s

^srepresents isolates susceptible, ^r represents isolates resistant to respective antibiotics and values underlined with ^l represents intermediate isolates.

Discussion and Conclusion

The present study showed a high prevalence of Pneumococcal carriage in child population. By contrast, in the Netherlands, the prevalence was found 37% in the not attend day-care centers (NDCC) children. Known risk factors for Pneumococcal carriage are young age, crowding, and antibiotic usage⁶. Since 11.76% of isolates showed resistance to Oxacillin, Cotrimoxazole and Tetracycline, crowding is presumed to be an important contributor to differences in those carriers.

Studies have revealed that previous use of antibiotics is a risk factor for infection with drug resistant pneumococci. Our study supports this conclusion. Sarlahi have both public and private medical coverage. In different parts of Nepal including Sarlahi antibiotics are available without prescription. Although this finding is not commonly observed in this study, various government data shows that antibiotic cotrimoxazole (cotrimoxazole pediatrics tablets) coverage is 35.20% in Sarlahi in accordance to the WHO recommendations of cotrimoxazole for home treatment of child pneumonia⁷. In this situation, the highest resistance (90.36%) to cotrimoxazole could have appeared due to frequent and misuse of it as a major drug.

This study suggests that the nasopharyngeal bacterial population is an important reservoir of infection and crowding as the factor responsible for spread of the organism. The prevalence of antimicrobial resistance in the key respiratory tract pathogens is high. In the case of *S. pneumoniae*, it is primarily due to the spread of drug-resistant strains. The patterns of resistance continue to change and antimicrobials that are effective today may become ineffective against resistant pathogens tomorrow. If the same cotrimoxazole resistant nasopharyngeal strain develops into invasive pneumonia,

antibiotics other than cotrimoxazole have to be used as the data shows high resistance (90.36%) to the antibiotic. A goal of antimicrobial therapy should be to cure the disease and to reduce the emergence and spread of resistant bacteria. Appropriate antibiotic therapy can decrease the nasopharyngeal carriage, carrying resistant pneumococci.

Acknowledgement

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Acetylator status influences bioavailability of isoniazid in patients with advanced HIV disease

Running Head: Bioavailability of isoniazid in HIV disease

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Abstract

Patients with advanced HIV disease may exhibit malabsorption of anti-tuberculosis (TB) drugs. We evaluated the effect of isoniazid (INH) acetylator status on the bioavailability of INH in HIV-infected patients with and without tuberculosis, based on urinary excretion of the drug. Estimation of INH in urine collected up to 8 hours after oral administration of 300 mg INH were undertaken in 23 TB, 40 HIV and 26 HIV-TB patients. Determination of acetylator status of all these patients was also carried by differential estimations of INH and acetyl INH in urine collected between 5 and 6 hours after oral administration of 300 mg INH.

Both slow and rapid acetylators in HIV and HIV-TB groups had significantly lower concentration of INH in urine compared to TB patients. The percent decrease in urinary excretion of INH was significantly higher in rapid than in slow acetylators, when compared to the corresponding TB patients. Acetylator status has an impact on the bioavailability of INH. Malabsorption in patients with advanced HIV disease may lead to decreased bioavailability of INH, particularly in rapid acetylators. Urinary estimation of INH provides reliable information on the bioavailability of the drug.

Key words: Acetylator status, Bioavailability, Isoniazid, HIV, Urine

Introduction

Isoniazid (INH) is an essential drug in the treatment of tuberculosis (TB). The primary step in its metabolism is acetylation to acetyl INH. The metabolising enzyme is a hepatic N-acetyl transferase, which displays genetic polymorphism. The rate of acetylation of INH is known to influence the response to treatment of TB patients with once-weekly regimens containing INH^{1,2} but it is of no prognostic significance when patients are treated with either daily, thrice-weekly or twice-weekly regimens containing the drug. It was observed that the failure of

once-weekly regimens was predominantly due to inadequate exposure (area under the time concentration curve) and coverage (hours for which a bacteriostatic concentration of INH 0.2 µg/ml are maintained)³. Weiner et al⁴ have reported that once-weekly INH / rifampentine therapy was less effective than twice-weekly INH / rifampicin in HIV sero negative TB patients. They observed an association between INH acetylator status and treatment outcome in these patients and further found that low INH concentrations in rapid acetylators was associated with failure/relapse. It is therefore essential that adequate INH concentrations are maintained in blood for good treatment outcome.

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In a recent pharmacokinetic study conducted in HIV-infected patients with advanced disease, we observed that peak concentration and exposure of INH were reduced in HIV-infected patients with and without TB compared to HIV seronegative pulmonary TB patients⁵. This study further showed that the differences in these pharmacokinetic variables were more pronounced in rapid acetylators than in slow acetylators of INH. However,

these differences (except for peak concentration in HIV-TB rapid group) failed to attain statistical significance. This could probably be due to the small number of patients in each sub-group (after classifying them based on their acetylator status). The study suggested that acetylator status could influence the bioavailability of INH in HIV-infected patients, and that rapid acetylators are likely to be affected more than slow acetylators, in the event of malabsorption.

Several reports suggest that malabsorption of antimycobacterial drugs occurs in selected HIV-infected patients, particularly those with advanced disease⁵⁻¹². This could lead to decreased blood levels of anti-TB drugs, thereby causing acquired drug resistance and treatment failure/relapse. The objective of the present study was to evaluate the effect of INH acetylator status on the bioavailability of INH in HIV-infected patients with and without TB, based on the urinary excretion of the drug. For this purpose, we carried out estimation of INH in urine and determination of INH acetylator status in urine samples collected from patients who participated in a previous study¹².

Methods

Participants

The study was conducted at the Government Hospital of Thoracic Medicine, Chennai, India. The study participants comprised of 23 HIV seronegative patients with pulmonary TB, 40 patients with advanced HIV disease and diarrhoea (history of recurrent episodes of watery stools, six to eight times a day for at least 10 consecutive days in a month at the start of study) and 26 patients with HIV infection and TB. The mean age and mean body weight of TB, HIV and HIV-TB patients were 41, 34 & 37 years and 40, 43 & 43 kg respectively. All the participants were males and were admitted to the hospital at least a day prior to the study. None of the patients was suffering from significant hepatic or renal dysfunction (liver transaminases, serum urea and creatinine were within normal limits). Diagnosis of pulmonary TB was based on bacteriological investigations (sputum smear and culture for mycobacteria), which were supported by clinical and radiological features. HIV infection was diagnosed on the basis of three positive results (two rapid tests and ELISA). All TB patients, with and without HIV infection were receiving standard anti-TB regimens. None of the HIV-infected patients were receiving antiretroviral treatment or any stool binders or other

medications known to interfere with the absorption of INH. The study was conducted after obtaining approval from the Institutional Ethics Committee and informed written consent was obtained from all the study participants.

Conduct of study

Isoniazid was withheld for a period of 72 hours before start of the study. All the patients were asked to empty their urinary bladder and this urine sample was discarded. They received INH (300mg) orally under supervision after an overnight fast. In addition to this, TB and HIV-TB received their other regular anti-TB medications. Uniform breakfast and lunch were provided to all the patients at 2 and 6 hours after drug administration. Urine excreted up to 8 hours was collected in a labeled container. The total volume of urine was measured, volume noted and aliquots were stored at -20°C until analysis. The concentration of INH in all the urine aliquots was estimated by a spectrophotometric method¹³. The percent dose of INH excreted in urine was calculated. All estimations were undertaken after coding the samples.

Determination of INH acetylator status

The INH acetylator status of all the patients was determined by differentially estimating the concentration of INH and its primary metabolite, acetyl INH in urine excreted between 5 and 6 hours after oral administration of 300 mg INH, and by calculating the molar ratio of acetyl INH to INH. A ratio of 2.0 or more denoted the acetylator status to be rapid¹⁴.

Statistical analysis

Analysis of data was performed using SPSS (version 10.5) package. The significance of differences in mean percent dose between two study groups was evaluated using unpaired t-test and between more than two groups using Bonferoni multiple comparison test (one-way Anova). The significance was taken at 5% level.

Results and Discussion

The number of slow and rapid acetylators of INH among TB, HIV and HIV-TB patients were 16 & 7, 22 & 18 and 11 & 15 respectively. The percent dose of INH excreted in urine up to 8 hours was compared between HIV (with and without TB) and TB patients among slow and rapid acetylators independently. Likewise, the percent

decrease in INH excretion in HIV and HIV-TB patients was calculated separately for slow and rapid acetylators against the corresponding TB patients in both these groups. There was a significant decrease in percent dose of INH excreted in urine in HIV and HIV-TB patients when compared to TB patients in both slow and rapid acetylators of INH ($p < 0.01$) (Table 1). While the percent decrease in urinary excretion of INH in slow acetylators in HIV and HIV-TB patients against TB patients was 28% and 27% respectively, the corresponding values among rapid acetylators was 47% and 55% respectively. The difference in urinary INH values between HIV and HIV-TB patients was not statistically significant.

The metabolizing enzyme of INH is a hepatic N-acetyl transferase, which displays genetic polymorphism. The difference in the two phenotypes of this enzyme, namely, slow and rapid acetylators of INH is due to difference in quantity rather than quality of the enzyme, the rapid acetylators having 4-5 times the quantity of the enzyme as the slow acetylators. It is therefore expected that rapid acetylators will have enhanced metabolism of INH than slow acetylators, and that blood levels and urinary excretion of INH will be lower in rapid than in slow acetylators. A significant effect of acetylator status on blood levels of INH has been reported^{4, 5, 11, 15}. This aspect was further confirmed in this study, where a significant decrease in urinary excretion of INH in rapid compared to slow acetylators in all three groups of patients was observed. This study further demonstrated that the percent decrease in INH excretion in HIV and HIV-TB patients was higher in rapid than in slow acetylators.

In the Revised National TB Control Programme, where INH is administered thrice-weekly, INH acetylator status may not play a role in treatment outcome as demonstrated in certain studies^{1, 2}. Despite a 50%

reduction in the percent dose of INH excreted in urine in rapid than in slow acetylators among TB patients, as seen in this study, the treatment outcome is expected to be similar irrespective of their INH acetylator status. However, the presence of malabsorption in rapid acetylators with advanced HIV disease (with and without TB) may lead to decreased bioavailability of INH. This could have implications for treatment of TB in a subset of HIV-infected patients who may require higher dose of INH or daily treatment. On the other hand slow acetylators are less likely to be affected, since their urinary INH levels were higher than TB patients who were rapid acetylators. This has been confirmed by our earlier study, where we observed differences in peak concentration and exposure between TB and HIV patients to be significant only among rapid acetylators of INH⁵.

To the best of our knowledge, there are no reports available on the effect of INH acetylator status on the bioavailability of INH in HIV-infected patients. Our findings suggest that patients with HIV, TB, diarrhoea who are rapid acetylators might have reduced bioavailability of INH. Urinary INH estimations offer a simple and reliable non invasive procedure to obtain information on the bioavailability of INH. A large prospective trial is required to correlate INH acetylator status with treatment outcome and emergence of mycobacterial drug resistance in patients with advanced HIV disease.

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Table 1 Urinary excretion of INH in the different study groups

INH acetylator status	Percent dose of INH (Mean \pm SD)		
	TB(S-16; R-7)	HIV(S-22; R-18)	HIV-TB(S-11; R-15)
Slow	31.71 \pm 7.98	22.80* \pm 7.19 (28%)	23.28* \pm 4.24 (27%)
Rapid	15.83 \pm 2.13	8.38* \pm 3.62 (47%)	7.12* \pm 3.02 (55%)

* $p < 0.01$ (vs TB patients)

Percent decrease vs TB patients are given in parentheses

S = Slow acetylator of INH, R = Rapid acetylator of INH

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Burden of Tobacco Smoking in District Tharparkar, Sindh, Pakistan

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Abstract

Background: Tobacco smoking is rising at an alarming rate in the developing countries. There is little information on money spent on it in poor countries. No such figures are available for Pakistan; but given the high prevalence of smoking there will certainly be a large figure. Tharparkar is one of the remote and most disadvantaged districts of Sindh Pakistan. Here most of the people live below poverty line. Nagarparkar is the remote village of the district situated near the Ran of Kutch. Tobacco smoking is common habit here.

Objectives

The objectives of the study were

- 1) to know the prevalence of Tobacco smoking in the village of Nagarparkar, Tharparkar
- 2) to assess the money spent on it and
- 3) to extrapolate the figures for the entire districts population.

Method

Community based random survey of the village Nagarparkar, District Tharparkar. Figures for the whole district were extrapolated from actual figures of the survey.

Results

Nearly 95% of the households had one or more smokers. Overall prevalence of smoking among surveyed population was 20% (all ages). Nearly half of them acquired this habit in their teens and were influenced by family members. Each smoker on an average was spending 4380.00 Pak Rupees per annum (1 US dollar was equivalent to around 55 Pak Rupees). Two hundred thousands people were estimated to be smokers in the entire district spending about 900 million Pak Rupees annually.

Conclusion

Despite of scarce means of communication and negligible propaganda run by transnational companies about their products in the district, a higher proportion of population is smoking Tobacco. These ever drought affected people are spending huge amount of money on "this silent killers habit", in fact they are consuming their flesh. It promotes the poverty one step more.

1. Introduction

Developing countries have been facing the burnt of the tobacco epidemic. The tobacco use is now more prevalent among the poor in developing countries.(1) The proportion of household expenditure used to purchase tobacco products in developing countries varies from 2.8% to 17%.(3) The amount spent on tobacco in poor countries exceeds that spent on health

care and education. It is fact that smoking exacerbates the poverty. The trends in expenditures on tobacco among poor in some developing countries are extremely worrying.(1,4,5) The money that poor households spend on tobacco products has very high opportunity costs, diverting scarce resources away from food and other basic needs.(6) Pakistan is a developing country with high prevalence of tobacco smoking and poverty; where studies on different aspect of tobacco smoking have been conducted including the prevalence of tobacco use in general population and specific groups but non on the tobacco expenditure.(7,8,9,10). This study was conducted in district Tharparkar, a very remote and underdeveloped district of province Sindh Pakistan with scarce means of transport and communication and very low per capita income, where drought use to visit regularly. (11) The objectives of the study were: to know

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the prevalence of tobacco smoking in village Nagarparkar district Tharparkar, to investigate the extent of tobacco expenditures by households of same population and to estimate the figures for entire district Tharparkar.

2. Methodology

This was a community-based survey of Households of all Mohallas of Village Nagarparkar, (Taluka Nagarparkar, District Tharparkar, Sindh, Pakistan) conducted in year 2001. Family members of households of all Mohallas of Village Nagarparkar were study population. There were around 280 households in village. Households were selected by systemic random sampling technique. Every fifth household were selected as 1,6,11, and so on. Pre-tested questionnaire was used for data collection. Principal investigator with the help of doctors and staff of Taluka Hospital Nagarparkar collected data by visiting households of all Mohallas of Village Nagarparkar as

per time convenient to community. Household heads were interviewed first for basic information and then rest of the family members. Data was entered into SPSS 11.0 version and analysed.

3. Results

I. Figures for Tobacco Smoking of Surveyed Population

Fifty-five households were surveyed and 454 persons were interviewed. Fifty-two households (94.5%) had one or more active smokers while three had none. The prevalence for all ages was 19.8% (90 persons) and for 18 years and above was 37%. Majority of the persons took up the habit of Tobacco smoking in their teens and twenties (Table I). Factors influencing to take up the habit of smoking and money spent to purchase tobacco by surveyed population are shown in Table 2 and Table 3 respectively.

Table 1 Age at which persons acquired habit of smoking

Age	Percent (No.)
Teens	46.7% (42)
Twenties	46.7% (42)
Thirties	4.4% (04)
Forties	2.2% (02)

Table 2 Influencing Factors for taking up habit of smoking

Factor/s	Percent (No.)
Friends	33.4% (30)
Family members	55.6% (50)
Both Friends and Family members	2.2% (02)
Personal ailment	5.5% (05)
Others	3.3% (03)

Table 3 Money Spent on Tobacco Smoking by Surveyed Population

	Daily	Monthly	Yearly
•Per smoker	Rs. 12.18	Rs. 365.00	Rs 4380.00
•Per Household	Rs. 20.00	Rs. 600.00	Rs. 7200.00
•Total	Rs. 1097.00	Rs. 32190.00	Rs.394920.00

II. Estimated Figures of Tobacco Smoking for District Tharparkar

The population of District Tharparkar was 914291 in 1998 as per census conducted in the same year. The estimated population for district Tharparkar in year 2001 was 992786 (nearly one million) calculated as per growth rate after census of 1998.(12) The figures for tobacco smoking for entire district were estimated on the basis of

actual figures of surveyed population. Nearly 200000 (0.2 Million) persons were estimated to smoke tobacco in year 2001 in entire district i.e. every fifth person as a whole and every third person of 18 years and above. Estimated figures for entire district on money spent to purchase tobacco are given in Table 4.

Table-4 Estimated Figures for Money Spent on Tobacco purchase in district Tharparkar

Daily	Rs. 2436000.00 (2.436 M)
Monthly	Rs. 73080000.00 (73.08 M)
Yearly	Rs. 876960000.00 (876.96 M)

Discussion and Conclusion

Prevalence of tobacco smoking in district Tharparkar in year 2001 was more or less similar to that in other districts of the country (8). These ever drought affected peoples have been living below poverty line (13) and spending huge amount of money on this "Silent Killer Habit", infact consuming their own flesh. The money diverted to purchase tobacco could undermine the schooling and food purchasing capacity of households in the area. This money could be saved and better utilized for nutrition, health and education of their children. It is evident from the study conducted in Bangladesh; accordingly average male cigarette smokers spend more than twice as much on the cigarettes as per capita expenditure on clothing, housing, health and education combined (6). Policy makers need to review the situation and develop comprehensive community based tobacco control programs, as anti smoking campaigns are the most cost-effective measures to improve health after childhood immunization (1, 14).

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Delay in Detecting Tuberculosis Patients in Anuradhapura District of Sri Lanka.

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Abstract

This prospective descriptive study was conducted at the Anuradhapura District Chest Clinic, Sri Lanka to ascertain whether there was any delay in detecting tuberculosis in patients, presented with common symptoms of TB, to identify the levels at which, the delays if any were occurring and to make suitable recommendations to overcome the problem.

All new tuberculosis patients diagnosed at Anuradhapura chest clinic from June 1 to September 30, 2003 were included into the study. A questioner was administered during the first interview.

Total number included was 85 patients whose ages were ranging from 7 months to 87 years, with a mean of 43.58 years. Majority were economically active. 59 (69%) were males. 53% had cough as first symptom, where as others had fever (18%), weakness (11%), chest pain (7%) and haemoptysis (6%). An average 133.8-day interval was noted between the onset of symptoms and commencement of ATT, though most of them had sought treatment by doctors, either of government or private sector, earlier.

A higher degree of professional sensitivity is required from the doctors to facilitate early detection of TB. As such there is a real need for continuing medical education of doctors in tuberculosis control activities.

Key words: Tuberculosis, delay in detecting, patient delay, continuing medical education

Introduction

Tuberculosis is a completely curable disease, if diagnosed in time and treated properly. Even though, a large number of people, through out the world, continue to become ill and die from tuberculosis². Many cases in Sri Lanka, as well as in other developing countries, remain undiagnosed due to lack of awareness on the part of the public (regarding the disease and the facilities available for diagnosis) and health staff (regarding diagnosis and treatment).

Un-treated pulmonary TB leads to serious complications and to death. One of the most important steps in preventing complications of TB and spread of the disease is "decreasing sources of infection through case-finding-

treatment"³. In 2002, 351 TB cases were diagnosed at the Chest Clinic, Anuradhapura. 149 were sputum direct-smear positive new cases out of which 15 (10.1%) patients died while on treatment, mainly during the initial intensive phase. This fact raised a suspicion of possible delay in detecting the patients⁴. In order to evaluate the situation a brief study was carried out in the Chest Clinic, Anuradhapura.

Objective of the study

1. To ascertain whether there was any delay in making the diagnosis of TB in patients presented with common symptoms suggestive of TB
2. To identify the levels at which, the delays were occurring and to make suitable recommendations to overcome the problem.

Method

All new TB patients seen at the Chest Clinic, Anuradhapura during the period of the study i.e. from June 1st 2003 to September 30th 2003 were included in the study. The doctor and nurse or PHI administered a

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questioner at the time of first interview and first registration in the TB register.

Results

During the period concerned, a total number of 85 patients were diagnosed to be suffering from tuberculosis. All of them were included into the study.

Profile of patients

- Gender and age distribution

The gender distribution of the patients in study was almost similar to that of the annual figures for the district. (Table 1)

There were patients from a wide range of ages, lowest being 7 months and the oldest, 87 years, with a mean age of 43.58 years. Majority of them were people of economically active age group. (Table 1)

- Economic background

The majority of the patients (41.2%) were farmers. (Table 2) Almost a half of them were earning less than 3000 rupees a month, placing them in the poorest category.

Clinical Presentation of Patients

- First Complaint

46 (53%) patients had cough as their first symptom, where as others had fever (18%), General weakness (11%), Chest pain (7%) and haemoptysis (6%). (Figure 1)

- The Delay in Detection

There was a significant time interval between the time of onset of first symptoms and the time that a patient finally arriving at the chest clinic. During this period, most of the patients had visited at least one doctor seeking treatment.

- Initial (Primary) delay in seeking treatment (patient delay)

There had been a delay in patient's attending to a medical institution or private doctor for the first time as well.

In average a patient had taken 59.6 days before seeing a doctor after onset of symptoms where as 22% of them had gone to the first doctor within 3 days. 54% had sought medical advice in first two weeks. (Table 3)

But 27% had delayed more than one month. A 5% had even remained at home without any treatment for more than 1 year.

- Delay in referrals of symptomatic patients to chest clinic by doctors.

Out of 85 patients, participants of the study, 78 (91.76%) had sought medical treatment from local doctors at some stage of their illness. Other 7 patients (8.24%) have directly come to the chest clinic although with a delay. One of them had been suffering from cough for 18 months, until family members advised to go to chest clinic. A field PHI had advised another patient, complaining of lethargy for 2 weeks to go to chest clinic. Others (5) who had cough, haemoptysis or chest pain more than one month had come to chest clinic on their own.

62 (79.5%) patients out of 78 who had gone to local doctors have been referred to chest clinic in variable time intervals ranging from a few days to one year from the date of first visit. Only 27 (34.7%) had been referred to chest clinic within the first month. (Table 4)

20.05% of patients, who had been treated for cough and other problems for more than one month (up to 2 years), had not been referred to a chest clinic by local doctors.

Patients were delayed at local doctors for an average of 65.7-days.

- Delay at the Chest Clinic

On 46% occasions, patients, who attended the Chest Clinic, were diagnosed, registered and anti TB treatment (ATT) was commenced within three days.

By the end of second week, 71% patients were on treatment. The mean delay at the chest clinic was 8.5 days. (Figure 2)

Summary

1. In our series, the most TB patients presented with Cough, Fever, Generalised Weakness, Chest Pain and Haemoptysis.
2. Middle-aged males are the main group to be affected.
3. An obvious delay was seen between the date of onset of first symptom and commencement of ATT.
4. Patients themselves, who had either neglected the early symptoms or had continued to attend the same doctor, even without any improvement, for long time, have significantly contributed to the delay in diagnosis and commencing treatment.
5. The contribution of doctors to the delay is considerable. (Figure 3)
6. Every fifth TB patient detected, had come to chest clinic on their own, after an average of almost 2 months treatment by local doctors for cough or other symptoms.

Table 1 Distribution of Patients by Gender and Age Groups

Age group	Female	Male	Total	
			No.	%
0-10 yrs	1	1	2	2.35
11-20 yrs	3	1	4	4.70
21-60 yrs	21	45	66	77.64
61 yrs>	1	12	13	15.31
Total	26 (31%)	59(69%)	85	100

Table 3 Distribution of patients by the time interval between onset of symptoms and seeking medical advice

Length of delay	N	%
Upto 3days	19	22
4d-1w	12	14
1w-2w	15	18
2w-1m	16	19
1m-3m	12	14
3m-12m	7	8
1 year>	4	5

Table 2 Distribution of Patients by Gender and Occupation

Occupation	F	M	Total	
			No.	%
Farmer	8	27	35	41.20
Unemployed.	14	6	20	23.50
Skilled	1	8	9	10.60
Unskilled	2	6	8	9.40
Business	0	6	6	7.05
Forces	0	4	4	4.70
Middle. Level	1	1	2	2.35
Pensioner	0	1	1	1.20
Total	26(31%)	59(69%)	85	100

Table 4 Distribution of patients by the time interval between first visit to a doctor and referral to chest clinic

Period of delay	N	%
Upto 3 days	5	6
4d-1w	4	5
1w-2w	6	7
2w-1m	12	14
1m-3m	21	25
3m-12m	13	15
1 y >	1	1
Not referred	16	19
Not gone to Dr.	7	8

Figure 1 Distribution of patients by first complaint

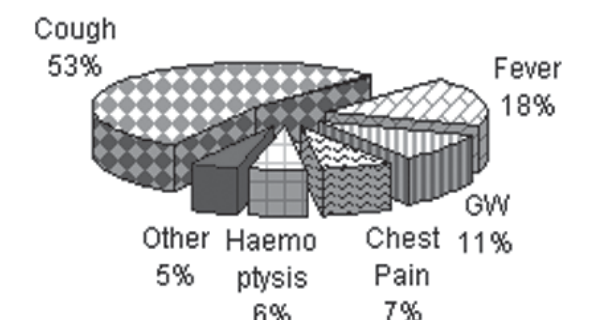


Figure 2 Time needed for diagnosis of TB at Chest Clinic

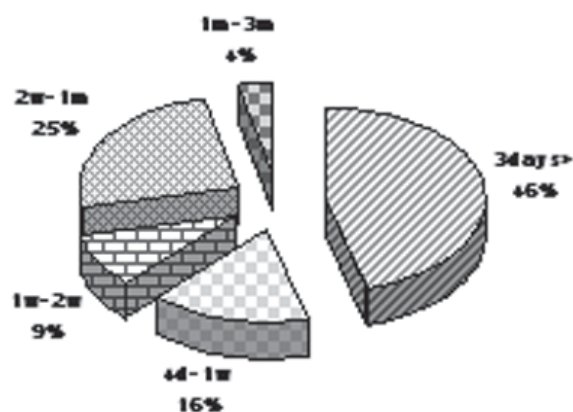
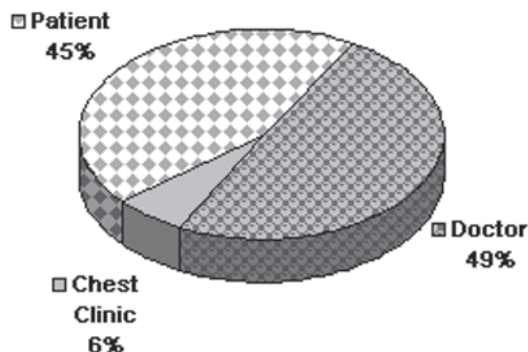


Figure 3 Delay in diagnosis of TB at different levels



Discussion and Conclusion

The presenting symptoms of TB in our series do not vary from well-known symptoms and signs of the disease⁵. But, some doctors have overlooked to suspect TB, as such, failed to refer them in time to chest clinic for investigation and management.

This brief study showed that, the average time gap between onsets of symptoms and commencement of ATT is 133.8 days.

In the context of tuberculosis being curable infectious disease⁶ up to date a higher degree of professional sensitivity is required from the doctors to facilitate early detection of TB by referral of patients with symptoms suggestive of the disease.

As such there is a real need for continuing medical education (in-service training) of doctors in tuberculosis control activities. It is note worthy that Rajeswary et. al. (2001) suggested that long total delay in the diagnosis of TB (in South India) could have been reduced by: 1) increasing public awareness about chest symptoms of TB and the availability and location of free diagnostic services. 2) educating government and private physicians about maintaining a high index of suspicion for TB while examining out –patients and 3) developing effective referral links for smear microscopy.⁷

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First Panel Testing In SAARC Regional Networks of TB Reference Laboratories

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Setting: South Asian Association for Regional Co-operation (SAARC) region with disproportionately high burden of TB in comparison of regional population.

Objective: To establish a quality assurance on sputum smear microscopy in SAARC regional network of TB reference laboratories.

Methods: Panel of slides were prepared and sent to national TB reference laboratories. The laboratory technician read the slides and sent report to SAARC TB center and report were analyzed.

Results: Seven laboratories had no error of any type and one laboratory got two minor types of errors.

Conclusion: Most of the laboratories had excellent performance in panel testing.

Key words: Panel testing, SAARC Region

Introduction

South Asian Association for Regional cooperation (SAARC) includes the seven countries- Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka. SAARC region has 22 percent of the global population and 29 percent of global burden of tuberculosis. 2.5 million new TB cases and 0.6 million TB deaths occur in SAARC region. Of the 22 high burden countries India, Pakistan and Bangladesh occupies first, 5th and 6th position among the high burden countries¹.

A network of nine National TB Reference Laboratories and SAARC TB laboratory has been established with the objective to share experience, capacity building, to harmonize the standard operating procedure of the TB laboratory and to establish a system of quality assurance within the network.

Panel testing is one of the activities conducted within the network. Panel testing refers to a system of retrospectively and objectively compared results from different laboratories by means of programme organized

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by external agency such as reference laboratory. The main objective of panel testing is to establish between laboratory comparability, in agreement with a reference standard².

The objective of the present study was to implement a panel testing for sputum microscopy within the Networks of SAARC Regional TB Reference Laboratories and SAARC TB Reference Laboratory in SAARC Region.

Materials and Methods

A panel of 25 slides consisting 7 negative slides, 7 with 1-9AFB/100 field, and 5, 3,3 slides with 1+ve, 2+ve and 3+ grading, respectively were prepared by Tuberculosis Research Institute (TRC) from the clinical samples. The slides were checked by three senior technicians and validated before including into the panels. Those slides were sent following to seven National TB Reference Laboratories in SAARC Region:

National TB Reference Laboratory (NTBR), Shyamoli, Dhaka; Public Health Laboratory (PHL), Bhutan; Public Health Lab (PHL) Maldives; Ojaha Institute of Chest Disease Laboratory(OICD) Laboratory, Karachi, National Reference Laboratory, NTP, Pakistan; National TB Reference Laboratory(NTBRL), Sri Lanka,; by courier service and SAARC Regional TB Reference Laboratory. Those slides were requested to examine by laboratory

Technician Laboratories and report according to WHO and IUATLD reporting criteria and send back report and slides. After receiving all the reports the reports were tabulated and analyzed.

Results

Hundred percent consistency was observed on reading negative and slides and the range was very high (50-100%), (Table I).

Analysis of the result

The result was interpreted on the basis WHO/IUATLD guidelines³. Of the eight laboratories participated, seven laboratories had no error of any type and only one laboratory had two minor errors (Table II).

Discussions

Panel testing is one of the three methods recommended for external quality assessment (EQA) in the recently released global consensus document. This method is considered to be less efficient than rechecking in higher level of the routine peripheral smears, as its result is not necessarily representative of routine performance⁴. This method has been selected in the initial phase of the TB reference laboratory activity and slides rechecking system should be adopted in future. Before this study none of the national TB reference laboratories were

tested by Supranational TB Reference laboratory in the SAARC region. National network of laboratory exists in different form in each country but the quality assurance on sputum microscopy seems far behind from the expected level. At the same time many countries in the region have not achieved the WHO target of 70% case detection. Study report revealed that the quality assurance services have been very heterogeneous in SAARC region^{5,6,7}. The first external proficiency panel testing was done when no national TB reference laboratory was being checked by any external agency. Of the eight laboratories participated in proficiency panel testing, seven laboratories had no error of any type and one laboratory had a low false negative (LFN) a quantitative error (QE). The study result demonstrated high level of performance in national TB reference laboratories.

Even though the performance of the national TB reference laboratories was very good, the consistency for reading 1-9AFB per 100 fields was only 61.8%, 72.5% to 1+slides, and 50% to 2+ slides but consistency to negative and 3+ was 100percent. The number of scanty positive identified at any level and confirmed during quality control itself already an indicator of the quality in that level⁸. Limited panel testing may be useful means to assess routine laboratory performance when no other method for quality assurance exists. Panel testing may also be useful in place where the intermediate laboratory structure necessary to support a re-checking program has not been established³.

Table I Proportion of consistency of slides reading by National TB Reference Laboratories

Grades of slide	Result of Ref Lab	Consistency of the participating National TB Reference Laboratories in reading different grade of slides										
		NTBRL Bangladesh	PHL Bhutan	PHL Maldives	NTC, Nepal	OICD, Pakistan	NTBRL, Rawalpindi Pakistan	NTBL Sri Lanka	SAARC TB Ref Lab	Total	%	
Neg.	7	7	7	7	7	7	7	7	7	7	56/56	100
0-9	7	6*	3	6	5	5	4	1	4	4	34/55	61.8
1+	5	5	2	4	3	4	5	3	3	3	29/40	72.5
2+	3	0*	2	1	3	3	0	1	3	3	13/23	50
3+	3	3	3	3	3	3	3	3	3	3	24/24	100
Total	25	21	17	21	21	22	19	15	20	20	156/198	78.8
%		71.9	68.0	84.0	84.0	88.0	66.9	60	80			

* One slide was broken on transport

Many problem of proficiency testing such as fading of the smear, contamination with saprophytic AFB, loss of AFB from heat fixed smear has been discussed previously⁹. There was not any kind of such problem observed in this study. Slide breaking during the transport of slide was one of the problems encountered in this study. In first proficiency panel testing two slides were broken in transport and slide was also broken in second proficiency testing (data not shown). The slide were broken, even though to prevent from breaking of slides in transport tissue paper was put as a cushion in between each slide and the slide box was sealed with thermo-cool cushion internally. After closing, the box was encircled with packing tape longitudinally and vertically. Another important factor for proficiency testing was slide transport cost. The panel of slides was sent by express delivery service to avoid in transport and prevent breaking. The average transport cost to deliver in the SAARC countries was \$50.(\$30-\$80). Therefore, the budgetary allocation should be made in time for panel testing.

Table II Analysis of the result

National TB Ref Lab	H F N	H F P	L F N	L F P	Q E	Total errors
National TB Reference Laboratory, Shyamoli, Dhaka	0	0	0	0	0	0
Public Health Laboratory , Bhutan	0	0	0	0	0	0
Public health Lab Maldives:	0	0	1	0	1	2
Ojaha Institute of Chest Disease, Karachi, Pakistan	0	0	0	0	0	0
Federal Government TB Ref Lab, Rawalpindi, Pakistan	0	0	0	0	0	0
National TB Ref Lab, Sri Lanka	0	0	0	0	0	0
National TB Ref Lab, Nepal	0	0	0	0	0	0
SAARC TB Ref Lab	0	0	0	0	0	0

Conclusions

The over all impact of the network was very good. The network has provided common forum for to share the experience, to learn for each other, to discuss problems and training opportunities. It was also felt that the proficiency panel testing has motivated national TB Reference laboratories for their quality assurance and to conduct quality assessment activities within the national network for TB laboratory.

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Pharmacokinetics of isoniazid and rifampicin in patients with renal failure undergoing continuous ambulatory peritoneal dialysis (CAPD)

Running Head : Pharmacokinetic of INH & RMP in renal failure (CAPD)

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Abstract

The pharmacokinetics of isoniazid (INH) and rifampicin (RMP) was determined in 22 renal failure patients, 11 each with low and high membrane permeabilities (LMP and HMP) undergoing Continuous Ambulatory Peritoneal Dialysis (CAPD). Blood samples were collected at different time points following oral administration of INH and RMP. Estimations of INH and RMP in blood were carried out by standard procedures and certain pharmacokinetic variables were calculated based on their concentrations in blood. The INH inactivation status was determined based on salivary levels of INH. The pharmacokinetic variables of INH and RMP did not differ significantly between LMP and HMP groups. The study results suggest that renal failure patients on CAPD may not require reduction in the dosage of RMP or INH in rapid acetylators. Slow acetylators might require dose reduction of INH. Determination of INH inactivation status is important when patients with renal failure and tuberculosis are treated with INH-containing regimens.

Key words: Rifampicin, Isoniazid, Pharmacokinetics, Renal Failure, CAPD

Introduction

Drugs are eliminated from the body by metabolism and excretion. The kidneys play a major role in the excretion of drugs and/or their metabolites. When they fail, such substances may accumulate and cause unwanted side effects. Therapeutic doses as administered to patients with normal renal function could lead to sustained high plasma levels in patients with renal failure and this could be toxic.

We have earlier demonstrated that in patients with chronic renal failure, the dosage of INH may be reduced in slow acetylators of the drug¹. However, the same may not be applicable to renal failure patients undergoing CAPD. Information on the pharmacokinetics of anti-tuberculosis (TB) drugs is therefore essential in renal failure patients undergoing CAPD, so that drug dosages

can be appropriately adjusted. No information is available to the best of our knowledge, on the pharmacokinetics of INH in such patients except for a study report on RMP carried out in two subjects². We, therefore, studied single dose pharmacokinetics of two first-line anti-TB drugs, namely, RMP and INH in patients with end stage renal failure on CAPD having different peritoneal permeability.

Methods

Subject: A total of 22 patients comprising of 13 males and 9 females who were undergoing treatment at the Nephrology Unit of Apollo Hospitals, Chennai were recruited to the study. All the study subjects were suffering from end stage renal failure and were undergoing CAPD. The patients were classified as having LMP or HMP based on peritoneal equilibration test. Those patients who had low or low average were classified as low peritoneal membrane permeability (LMP), and those with high or high average were classified as high membrane permeability (HMP). Patients in the LMP group received 3 exchanges of 2 litres, 8 hours dwell time; while patients in HMP group received 3 exchanges of 2 litres, 3-4 hours dwell time. The hepatic function, as assessed by liver function tests, was normal in all the patients. They were not suffering from any other ailment except renal failure at the time of study.

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The study was cleared by the Ethics Committees of the Tuberculosis Research Centre and Apollo Hospitals, Chennai. The nature of the study and possible side effects of the drugs were explained to the patients and informed written consent was obtained from them before they took part in the study.

Determination of acetylator phenotype

Prior to start of the study, the INH acetylator status was determined in all eligible patients according to the method of Kailasam *et al.*³. A uniform oral dose of INH (100mg) was administered and a sample of saliva was collected exactly at 5 hours after drug administration. The concentration of INH in saliva was determined according to the method of Gurumurthy *et al.*⁴. The criterion for a slow acetylator was taken as a concentration of INH $e^{-0.41}$ $\mu\text{g/ml}$.

Conduct of Study

On the day of the investigation, INH (7.5 mg/kg) and RMP (12 mg/kg) (according to the dosage schedule in Table 1) were administered on an empty stomach and blood samples were collected at 1,2,3,6, and 8 hours in heparinised containers. Plasma was separated from all the blood samples and stored at -20°C until drug estimations were carried out.

Plasma concentrations of INH were determined by the spectrofluorimetric method of Olson *et al.*⁵, and of RMP by the plate diffusion method of Dickinson *et al.*⁶. All the specimens were coded before drug estimations were undertaken.

Pharmacokinetic and Statistical Analysis: On each series of plasma INH and RMP concentrations, certain pharmacokinetic variables were calculated. Maximum concentrations (C_{max}) and the time to attain C_{max} (T_{max}) were determined by direct visual inspection of data. The linear trapezoidal rule was used to compute the exposure or area under the time concentration curve (AUC); the elimination rate constant (K_{el}) was calculated from the terminal log-linear decline of concentration; the terminal elimination half-life ($t_{1/2}$) was calculated as $0.693/K_{\text{el}}$; and $\text{AUC}_{0-\infty}$ was calculated by adding the sum of AUC

obtained from time zero until 8 hour concentration to the last quantifiable concentration (at 8 hours) divided by K_{el} . The plasma clearance (Cl) was calculated as $\text{dose}/\text{AUC}_{0-\infty}$.

The pharmacokinetic values were expressed as mean \pm standard deviation. Student's t-test (unpaired) was employed for testing the differences between the mean values of the LMP and HMP groups and the significance was taken at the 5% level.

Results

A total of 22 patients comprising of 13 males and 9 females were admitted to the study. Among them, 11 each belonged to the LMP and HMP groups. The mean age and body weight of the patients having LMP were 45.2 years (10-72 years) and 59.3 kg (24-90 kg) respectively. The corresponding values in patients having HMP were 49.8 years (16-67 years) and 58.1 kg (37-86 kg).

The mean dosages of INH administered to patients with LMP and HMP were 7.11 and 7.40 mg/kg bodyweight respectively, while the corresponding values for RMP were 10.69 and 11.20 mg/kg body weight. The numbers of slow and rapid acetylators of INH among patients with LMP were seven and four and with HMP were six and five respectively.

The distribution of patients having LMP and HMP according to the time at which the highest plasma concentrations of INH (amalgamating the findings in slow and rapid acetylators) and RMP were attained is presented in Table 2. The rate of gastro-intestinal absorption of INH appears to be similar in both the groups of patients as evident from the fact that in majority of the patients, peak concentrations were attained within one hour. However, in the case of RMP, there appeared to be a delay in the absorption in patients having HMP compared with that of LMP.

The mean serial plasma INH and RMP concentrations between LMP and HMP groups of patients did not show any statistical significance at all the time points tested. The pharmacokinetic variables calculated based on plasma concentrations of INH and RMP were not different between the LMP and HMP groups (Tables 3 and 4).

Table1 Dosage schedule:

Body-weight range (kg)	Isoniazid (mg)	Rifampicin (mg)
<30	200	300
30.0 – 44.9	300	450
45.0 – 59.9	400	600
≥ 60.00	500	750

Table 2 Distribution of patients based on peak concentrations of isoniazid and rifampicin

Group	Drug	No. of subjects with peak concentrations observed at				
		1 h	2 h	3 h	6 h	8 h
LMP	Isoniazid	6	1	4	-	-
n=11	Rifampicin	3	5	3	-	-
HMP	Isoniazid	6	5	-	-	-
n=11	Rifampicin	2	2	6	1	-

LMP – Low membrane permeability, HMP – High membrane permeability

Table 3 Pharmacokinetics of Isoniazid in patients with different membrane permeability:

Pharmacokinetic Variables	Mean ± SD			
	Slow		Rapid	
%	LMP(n=7)	HMP(n=6)	LMP(n=4)	HMP (n=5)
Peak Concentration (µg/ml)	11.73 ± 2.15	11.71±2.07	7.17±2.51	10.43±5.32
Exposure (0-8) (µg/ml.hours) (0-∞)	69.09±13.85	61.17±11.75	22.65±9.03	34.49±16.80
	213.47±55.89	139.39±28.00	25.78±11.64	38.83±19.84
Clearance (ml/min)	6.51±1.12	7.28±1.67	18.36±13.71	15.00±8.13
Half-life (hours)	8.16±1.23	6.15±1.04	2.42±0.75	2.46±0.12

LMP-Low membrane permeability, HMP – High membrane permeability

Table 4 Pharmacokinetics of rifampicin in patients with different membrane permeability:

Pharmacokinetic Variables	Mean ± SD	
	LMP (n=11)	HMP(n=11)
Peak Concentration (µg/ml)	10.37±4.21	10.44±4.00
Exposure (0-8) (µg/ml.hours) (0-∞)	56.49±24.73	50.90±20.37
	172.51±82.11	193.19±127.14
Clearance (ml/min)	12.35±4.67	15.61±12.99
Half-life (hours)	6.92±2.05	6.35±1.68

LMP-Low membrane permeability, HMP – High membrane permeability

Discussion

Isoniazid is eliminated from the system by acetylation as well as renal excretion. While elimination of the drug is predominantly through acetylation in rapid acetylators, approximately equal proportions are eliminated through acetylation and renal excretion in slow acetylators⁷. Therefore, exposure and elimination half-life are expected to be higher in slow acetylators. Several studies

conducted previously at our centre, both in healthy subject and in patients with pulmonary and extra pulmonary TB have reported half-lives ranging from 2.8 to 3.4 hours for slow and 1.2 to 1.9 hours for rapid acetylators of INH^{1, 4, 8-10}. The present study shows that, despite patients undergoing dialysis, plasma concentrations of INH in slow acetylators lead to higher half-life in LMP and HMP groups of patients. However, the mean C_{max} and AUC values in slow acetylators were

almost similar to our previous data^{1,4,8-10}. The elimination of INH in rapid acetylators did not seem to be affected. It may therefore be advisable to reduce the dosage of INH in slow acetylators with renal failure undergoing CAPD. However, with respect to rapid acetylators of INH, since the pharmacokinetic variables obtained in this study were almost similar to our previous study data, it may not be necessary to adjust drug dosages. This emphasizes the need to determine the INH acetylator status of patients suffering from renal failure and TB, and who require treatment with INH-containing regimens.

Methods to determine INH acetylator status in renal failure patients based on urinary excretion of acetyl INH and INH are obviously not suitable. On the other hand, estimating INH in saliva, collected at a particular time-point, as done in this study can be used to determine the acetylator phenotype in adults³ as well as in children¹¹.

Our recommendation with respect to the dosage of INH in patients with renal failure particularly with the slow acetylators is not in line with that of Reidenberg et. al.¹² who in their investigation of eight patients with renal failure did not find a need to reduce the dosage of this drug. A study conducted by Bowersox et. al.¹³ in 10 patients with chronic renal failure did not recommend reduction in the dose of INH (300mg) in rapid and slow acetylators with serum creatinine concentration less than 12 mg/dl. Neither of the investigators had classified patients as slow or rapid acetylators.

The elimination of RMP is mainly through hepato-biliary excretion¹⁴, with kidneys playing only a minor role. This is evident from this study data where we did not observe any difference in the pharmacokinetic variables between patients with renal failure undergoing CAPD and our previous study data^{1,4,8-10}. Also no differences were observed in patients having different membrane permeability. These findings suggest that there is no need to reduce the dosage of RMP in patients with renal failure undergoing CAPD. This is in agreement with that reported previously in patients with severe renal failure¹ and also by Woo et. al.² who observed that in patients with TB on maintenance dialysis, the dosage of RMP need not be reduced.

The risk of developing pulmonary and extra pulmonary TB is increased in patients undergoing peritoneal dialysis, especially in Asia^{7,15,16}. Since very scanty information is available on the pharmacokinetics of INH

and RMP in renal failure patients undergoing CAPD, we have attempted to obtain information on this aspect, and also compare the values between patients with different membrane permeability, namely, LMP and HMP. Although absence of a control group was a limitation of this study, the findings reported in this paper could be useful for the management of renal failure patients undergoing CAPD and suffering from TB, and requiring treatment with INH and RMP.

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Status of AIDS Orphans in Chennai, South India

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Short Summary

AIDS Orphans are children who have lost one or both parents to AIDS. In the Indian context, little is known about what happens to these children. This study was planned to assess the status of AIDS orphans. The sample was from a population of HIV-positive patients enrolled in clinical trials at the division of HIV/AIDS of the Tuberculosis Research Center, Chennai, India.

Some of the patients had succumbed to the illness and left behind children. Caregivers of these children were interviewed for the purpose of this study.

This paper discusses the status of 140 AIDS orphans belonging to 67 families who had lost one or both parents due to AIDS.

Abstract

As the AIDS epidemic progresses, there is a shift from focusing on the individual to the family. Often described as a family disease, the AIDS pandemic is leaving millions orphaned in its wake. AIDS Orphans are children who have lost one or both parents to AIDS. In the Indian context, little is known about what happens to these children. This study was planned to assess the status of AIDS orphans. The sample was from a population of HIV-positive patients enrolled in clinical trials at the division of HIV / AIDS of the Tuberculosis Research Center, Chennai, India. Some of the patients had succumbed to the illness and left behind children. Caregivers of these children were interviewed using a semi structured interview schedule. This paper discusses the status of 140 AIDS orphans belonging to 67 families who had lost one or both parent due to AIDS.

Twenty six percent had lost both parents and 50% of the surviving parents were sero positive. Ten percent of the children were sero positive while the sero status of 41% was not known. Their mothers cared more than half of the orphans for, while maternal relatives cared for 24%.

Key words: AIDS Orphans, Caregivers

Introduction

Defined as children suffering the death of one or both parents from the disease ¹ the number of AIDS orphans is rising. It is estimated that the total number of children (0-14 years of age) orphaned by AIDS and living at the end of 2003 was 2.1 million to 2.9 million ². The number of children in the developing world who have been

orphaned because of the AIDS related death of at least one parent will nearly double by 2010 from 13.4 million to 25.3 million according to a report released at 14th International AIDS conference in Barcelona ³.

Researchers noted that the number of children worldwide who are orphaned due to AIDS related causes could be even higher because the statistics did not account for India, which has the second largest number of people with HIV in the world ⁴.

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Since the beginning of the epidemic, well over 2 million HIV positive children under the age of 15 years have been born to HIV positive mothers, and thousands have acquired the infection from blood transfusion or through sex. Since the infected mothers are likely to die of AIDS within 5-10 years of giving birth, the uninfected infants will constitute a growing population of orphans ⁵.

The vulnerability of children orphaned by AIDS and that of their family starts well before the death of a parent. The emotional anguish of the children begins with their parent's distress and progressive illness. Eventually the children suffer the death of their parent(s) and the emotional trauma involved⁶. For orphans the stigma of having a parent die due to AIDS complication poses many obstacles. Besides the psychosocial trauma of having lost a parent, many children are unable to discuss their loss with others on account of AIDS being a highly stigmatized disease. This silence may lead to the child feeling isolated and depressed. In many communities, instead of receiving sympathy and care, these children are singled out and treated with suspicion. Many of them are denied access to public health facilities and education; those in foster homes are treated harshly and all too often, abused².

Obtaining data on the number of children orphaned by AIDS is difficult but it is believed that the proportion of children in India orphaned by AIDS is far lower than in sub Saharan Africa but because of India's huge population the actual number of children orphaned by AIDS is already high. In 2001 the number of orphaned children was estimated at 1.2 million⁷. The number of children in India orphaned by AIDS is approaching two million according to UN estimates⁸(UNICEF, 2004).

Although children are not being orphaned in a large scale in most cities studies have shown that the problem of orphans in some areas of India is already severe⁹. The number of children in India living with HIV currently is far greater than the number of children already orphaned. An increase in orphaning due to HIV/AIDS will not only raises the number of orphans but also will increase the difficulties in meeting the needs of these children. In India there is limited experience in terms of implementing care and support systems for orphans particularly children orphaned by AIDS¹⁰.

While AIDS has often been described as a family disease, there is a dearth of information available pertaining to orphans, from India. This study was undertaken to explore the status of children who had lost one or both parents to AIDS.

Aim: To assess the status of children orphaned by the death of one or both parents to AIDS.

Methods

This study is a descriptive study on the status of AIDS orphans. The study sample was from a population of HIV positive patients who were enrolled in clinical trials at the division of HIV/AIDS of the Tuberculosis Research

Centre, (Indian Council of Medical Research), Chennai, India between 2000 and 2003. For the purpose of the study 94 families who had lost a parent due to HIV complications, leaving behind children aged 0-15 years were contacted and caregivers were requested to attend for an interview with the Medical Social Worker. They were briefed on the need for the information, and the time that it would take for the interview.

Caregivers from 67 families responded, and interviews were conducted using a semi-structured interview schedule after obtaining informed consent. For those who were unable to attend in person, information was obtained through a mailed questionnaire in the local language.

Information gathered included socio demographic profile, family size, HIV status of the surviving parent, age, occupation, education of the child, if the child was institutionalized and current health status of the child. Details on who the caregivers were and if more than one caregiver cared for the child were also obtained.

HIV status of the child was obtained from hospital records, and unless it revealed by the surviving parent or the caregivers none of the respondents were directly questioned regarding child's sero status keeping in mind the best interest of the child.

Eligibility criteria

Children (0-15years) who had lost one or both parents to HIV/AIDS were eligible. Caregivers who were willing to spare their time and were willing to give the information required.

Results

Socio-demographic profile of AIDS orphans

One hundred and forty children belonging to 67 families were included in the study. Seventy-two children (51%) were male. Forty-three children (31%) were 1 –5 years of age while 59 (42%) were 6-10 years of age and the remaining 38 (27%) were more than eleven years. Sixty-two children (44%) were from urban areas and an equal number from suburbs, 16 children (11%) were from rural areas. Eighty children (57%) were attending school and had received some education. Only 2 children were employed and 5 had been institutionalized (Table 1).

Sero status of orphans

Fourteen of the children (10%) were known to be HIV positive and of these, 4 had died. Sixty-eight children

(49%) were HIV negative, however the sero status of 58 (41%) children was unknown (Table 2).

Sero status of parents

Thirty-six children (26%) had lost both parents. Fifty-two (37%) had one surviving parent who was already infected with HIV. The parents of 29 children (21%) were HIV negative while the sero status of the surviving parent was not known for 23 children (16 %). (Table 3).

Table 1 Demographic Profile

Sex	No	%
Male	72	51.4
Female	68	48.6
	140	100
Age group	No	%
1-5 years	43	30.6
6-10 years	59	42.2
11-15 years	38	27.2
	140	100
Area	No	%
Urban	62	44.3
Rural	16	11.4
Suburban	62	44.3
	140	100
Education/Occupation	No	%
Attending school	80	57.1
Not going to school	53	37.9
Institution	5	3.6
Employed	2	1.4
	140	100

Table 2 Sero status of Orphans

Sero status of orphans	No	%
Positive	10	7.1
Negative	68	48.6
Not known	58	41.4
Died	4	2.9
	140	100

Caregivers

Most of the children (56%) were cared for by their mothers, maternal grandparents or maternal relatives took care of nearly 24 % of the children while. While 15 % were cared for by paternal grandparents or paternal relatives (Table 4)

Ninety-one children (65%) received care from a single caregiver while 49 children (35%) had more than one caregiver. Caregivers of 50 children (36%) admitted that they had received small amounts of money given by relatives when they had come to visit but there was no consistent support or commitment. However caregivers of 90 children (64%) had to be taken care without any financial help from any other source. The caregivers had reported that 80 children (57%) were in good health, 43 (31%) in fairly good health and 17 children (12%) were falling ill often and their health status was causing concern for them.

Table 3 Sero status of Parents

Sero status of Parents	No	%
Positive	52	37
Positive/died	36	26
Negative	29	21
Not known	23	16
	140	100

Table 4 Caregivers

Caregivers	No	%
Mother	78	55.7
Maternal Grandparents	19	13.6
Maternal Relatives	14	10.0
Paternal Grandparents	10	7.1
Father	7	5.0
Paternal relatives	5	3.6
Institution	5	3.6
Employer	2	1.4
	140	100

Discussion

Socially the death of one or more parents is a devastating event in a child's life and it leaves the child in a pathetic situation and at an age when he or she is most vulnerable. ¹¹ "Care for orphans may be understood as a window to the situation of families and other social networks".

Studies in Rwanda have shown that the majority of new HIV infections are comprised of young people in the workforce ¹². This phenomenon of societies most productive age group falling ill and dying has drastic consequences both economically and socially.

The current study found that most of the deceased parents of the AIDS orphans belonged to the age group between 25 and 47 years, endorsing the widely held conclusion that HIV/AIDS affects the young economically productive age group, leaving behind young orphaned children. In this study, most of the children orphaned were less than 10 years of age.

In a similar study on AIDS orphans done at Namakkal in South India¹³ it was found that that about 45% of the children were above 10 years of age, 65% were attending primary school 16% were illiterates and 16% were drop outs.

Another finding that must be addressed is one of HIV testing in children. Caregivers who knew the sero-status of the children had revealed the same during the interviews. Being unaware of the HIV status could be a matter of concern as it influences the health seeking for the children by the caregiver and chances of child being denied proper health care exists.

Both caregivers and physicians must be made aware of the child's sero status in order to make informed decisions regarding the child's health. Children with compromised immune systems are especially susceptible to childhood infections and without proper health care and diet they could face desperate situations¹⁴. Caregivers who have knowledge and take adequate action could ensure a better quality of life for these children. It is strongly recommended that children with HIV positive parents get tested for HIV ¹⁴. In this study,

most children were reported to be in good health while about 12% were facing repeated sickness days.

In the high prevalence district of Kweneng, Botswana an orphan registration exercise conducted in mid 2000 found that only 22% of the people registered as care givers for orphans were employed. The others lacked productive employment, and fully 40% of them were grandparents or elderly relatives. In this study the major portion of the care giving was given by the mother who was the surviving parent.

The current study findings in regard to caregivers also has come out with the finding that caregivers are usually grandparents and maternal relatives. Among the 140 children, 111 were cared for by mothers or maternal relatives.

In a study done at Tanzania on AIDS orphans it was found that 70% of them had lost both parents to AIDS and care giving was mostly by the grandparents, and 60% of the children were in their care. Twenty percentage of the orphans lived with distant relatives and while the rest had no one to take care of them. Scholastic backwardness, lack of shelter, clothes, adequate food and sense of insecurity were some of the problems encountered¹⁵.

This shift of care to the grandparents has been called "skip generation parenting" ¹⁶. In Sub-Saharan Africa, HIV has been dubbed "the grandmothers disease" as the shift of care is increasingly towards this segment of the populace. Studies in Zimbabwe and Zambia found that over 45% of Zimbabwean caregivers and 57% of Zambian caregivers were grandparents ¹⁶. In these studies it was found that over one third of these caregivers were above 60 years of age.

Apart from the problems of taking care of the young at their advanced age, grandparents often face financial constraints as their capacity to earn is greatly diminished and they look for other sources of support. Some of them take care of their grandchildren by getting some form of support by means of shared care or through some amount of financial help from relatives.

A study done to assess the problems of family caregivers found that the primary cause of distress was inadequate

finance to house and care for the children. The government policy of providing higher financial assistance to unrelated caregivers was causing a lot of hardship to family caregivers¹⁷.

Other studies have established that the responsibility for HIV orphans often lay with relatively old and young generations of society^{11, 18-20}. In this study 49 children (35%) received shared care while 91(65%) were cared for by a single relative only.

Further caregivers of 50 children (35.7%) received small amounts of financial help from relatives, caregivers of 90 (64.3%) children however said that they did not get any help from other family members.

In our sample it was found that 80 (57.1%) were attending school and 53 children (37.9%) were not in school. This could be due to the fact that 43 children (30.6%) were below 5 years of age.

In Cambodia, a recent study by the Khmer HIV/AIDS NGO Alliance and Family Health International found that about one in five children in AIDS-affected families reported that they had to start working in the previous six months to support their family. One in three had to provide care and take on major household work. Many had to leave school, forego necessities such as food and clothes, or be sent away from their home. All of the children surveyed had been exposed to high levels of stigma and psychosocial stress, with girls more vulnerable than boys.

In the late 1990's a survey of 646 orphaned and 1239 non orphaned children in Kenya found that 52% of the children orphaned by AIDS were not in school compared to 2% of the non orphans. Among the orphaned 56% girls and 47% of boys had dropped out of school within 12 months of a parents death.

Three general observations about AIDS orphans provide a basis for analysis and planning²¹. First, most orphans are not infected with HIV. Second, the orphans create special stress on family and community resources, and third, they are highly vulnerable because families affected by HIV/AIDS usually have more than one ill or dying member.

While many families have absorbed orphaned children out of love, custom or moral obligation, they may not be able to do so indefinitely.

The issue of care is of vital importance in the allocation of funds for AIDS orphans. For the proper development of milestones and for them to be socially responsible adults, more studies are needed to assess orphan children with regard to their psychological upbringing, nutritional status, health status, and monitored so that they can grown up as socially responsible adults.

The well being of children orphaned by the HIV epidemic, like children in distress from other causes, is the test of our future commitment to social stability, economic development and human rights.

Policy makers and health providers must shift their attention to AIDS orphans who are growing in numbers. These orphans are equally entitled to quality care.

While it is fortunate that India can boast of an extended family and others are willing to share the responsibility of child care, it is important that this group of caregivers are also given assistance to help them shoulder the responsibility that is thrust on them. Often, financial constraints prevent these caregivers from giving orphans quality care. They must be made aware of the need to screen the children for HIV, and, if positive, to be attentive to the opportunistic infections that these children are prone to.

Conclusion

This is a preliminary study, which gives a brief profile of AIDS orphans. The study is limited to patients enrolled in clinical trials and therefore not representative of a larger community population. The information gathered was from the caregivers; hence an element of bias could be present. Though there were a number of AIDS orphans among this group only caregivers of 67 families were willing to be part of the study.

Future plans include detailed study and assessment of the children measuring milestones, nutritional status, psychosocial parameters, in order to provide some interventions, which would benefit the children. Caregivers need to be educated on the importance of HIV screening in view of the parents HIV status, and the importance of adequate health care for the children to improve the quality of life.

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