RATE OF ADHERENCE TO AND FACTORS ASSOCIATED WITH METHADONE MAINTENANCE TREATMENT PROGRAM (MMTP) COMPLIANCE AMONG INJECTING DRUG USE PATIENTS IN NEPAL

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Abstract. We conducted a survey to determine the rate of adherence to and factors associated with compliance with a methadone maintenance treatment program (MMTP) among injecting drug users in Nepal. We conducted face-to-face structured interviews with 165 methadone treatment patients aged 20-54 years during 5-20 April 2015. Data analysis included percentages, means, standard deviations, chi-square tests and multiple logistic regression analysis. Seventy-two point one percent of respondents had good adherence to a MMTP. Multiple logistic regression with 81.8% prediction showed respondents without a previous history of relapse were 2.7 times more likely to adhere to the MMTP than those with a history of relapse [Adjusted OR =2.772; 95% Confidence interval (CI): 1.163-6.605]. Respondents with a good knowledge of the MMTP 9.4 times more likely to be adherent to the MMTP than those with a poor to fair knowledge of the MMTP (Adjusted OR = 9.464; 95% CI: 3.873-23.126). The likelihood of MMTP adherence was 4.5 times more likely when methadone treatment services were available than those where the availability of methadone treatment services were low to moderate (Adjusted OR = 4.553; 95% CI: 1.883-11.008). Knowledge and availability of MMTP need to be improved in the study area in Nepal.

Keywords: methadone maintenance, adherence, injecting drug use, Nepal

INTRODUCTION

Injecting drug users are defined as those who abuse illicit drugs or prescription medications through infection (WHO, 1994). The types of drugs used for recreational purposes varies widely. The most commonly abused drugs are opiates, heroin, cocaine and methamphetamines (WHO/UNODC/UNAIDS, 2004). Individuals may start abusing drugs at a young age and soon become addicted (WHO/UNODC/UNAIDS, 2013). The drugs are injected via a syringe and needle intramuscularly, intradermally or intravenously. This behavior increases the risk contracting Human Immunodeficiency Virus (HIV), hepatitis B and C and other blood borne diseases (WHO/UNODC/UNAIDS, 2004). Other health

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problems occurring due to injecting drug use include arterial damage, cognitive damage, crime, financial problems and societal stigma (Raffa *et al*, 2007; Griffin and Khoshnood, 2010).

In 2013, the estimated number of people injecting drugs was about 11.2 to 22.0 million globally (WHO/UNODC/UNAIDS, 2013) with more than 10 million in developing countries like South Asia, Southeast Asia, Central Asia and the Pacific region (Aceijas *et al*, 2004). Eleven point five percent of those injecting drug users (1.6 million people) are people living with HIV (PLWH) (WHO/UNODC/UNAIDS, 2013). In 2008, it was estimated approximately 2-3% of people who inject drugs (PWIDs) die yearly from overdose, since they are unaware of the lethal dose of the drug they are abusing (WHO/UNODC/UNAIDS, 2004). The estimated number of PWIDs ranges from 434,000 to 726,000 in South-Asian countries including Nepal, of these 34,500 to 135,500 are PLWH (Rao *et al*, 2013). Most reside in Nepal, Bangladesh and the Maldives and are at risk for HIV infection due to injecting behavior (Rao *et al*, 2013). The estimated number of PWIDs was 16,100 to 28,000 in Nepal in 2013 (Rao *et al*, 2013). A national survey of drug users in Nepal during 2008 estimated 46,310 people abused drugs (WHO, 2010). However, this number could be higher since mixed drug use is common in Nepal. In Kathmandu and other urban areas of Nepal, there are more PWIDs. In Nepal, more than 5% of PWIDs have HIV, hepatitis B or hepatitis C infection (NCASC, 2012). Nepal is an epidemic area for HIV infection (NCASC, 2012). In 2012, 8.1% of PWIDs tested had HIV infection (NCASC, 2012). The sexually transmitted infections (STIs) were found to be 1.7% among people who inject drugs in eastern Terai highway districts of Nepal (NCASC, 2012). In 2008, the Kathmandu Valley had the largest number of drug users (*N*=17,458; 0.3% abused opiates) (WHO, 2010). In 2011, 6.3% of PWIDs in Kathmandu Valley tested had HIV infection (WHO SEARO, 2011).

Several approaches have been used to manage the drug abuse problem in Nepal. A common approach is abstinence along with detoxification such as rehabilitation homes, needle syringe exchange and oral substitution (WHO/UNODC/UNAIDS, 2004).

Methadone Maintenance Treatment Programs (MMTP) are a type of oral substitution therapy prescribed for injecting drug users (CDC, 2002). MMTP are a harm reduction strategy that can including counseling, case management, and medical and psychosocial support for clients with a history of injecting drugs (CDC, 2002; Kumar, 2012). Methadone maintenance is corrective, not curative for heroin addiction (CDC, 2002). These patients may remain in treatment for indefinite periods of time. Patients may work and live normal lives with their families during methadone maintenance therapy (Joseph *et al*, 2000). MMTP may reduce the risk of contracting HIV infection and participation in criminal activities. Harm reduction strategies, such as MMTP and abstinence are needed to achieve the target to reduce transmission of HIV by 50% among PWIDs in 2015 (WHO/UNODC/UNAIDS, 2013) set by United Nations General Assembly Special Session (UNGASS).

Medical adherence requires collaboration between patients and clinicians for planning and implementing the treatment regimen. Patients have a role in deciding to carry out the treatment and display self-regulatory activities (Midence and Myers, 1998). Adherence with the MMTP is important to reduce chance of contract-

ing HIV, and hepatitis B and C infections (CDC, 2002; Chang *et al,* 2015). In Kathmandu Valley, two sites provide MMTP: Tribhuwan University-Teaching Hospital, Kathmandu and Lalitpur Hospital, Lalitpur. At the Kathmandu site, 30% of clients are on maintenance methadone and in Lalitpur 53% were on maintence methadone in August 2014 (National Center for AIDS and STD Control, 2014). From this figure, the concern is raised why adherence is poor among PWIDs for this program. This is similar to all the sites of the country whether newly or old established sites.

Drug addiction is a social issue with multiple determinants and adherence is multidimensionally influenced. From previous findings several factors affect the adherence to treatment and are long term like methadone treatment including sociodemographic characteristics, knowledge and perceptions about treatment, accessibility to services, cost of treatment, social support, and government policies (Adorno *et al*, 2013; Go *et al*, 2013; Maehira *et al*, 2013).

This study aimed to assess factors related to adherence to methadone treatment based on the application of the PREECEDE-PROCEED model. The third phase of the model focuses on behavioral factors, including predisposing, reinforcing and enabling factors (Glanz *et al*, 2008). The predisposing factors included knowledge, attitudes and perceptions about methadone and injecting drug abuse problems (Adorno *et al,* 2013; Go *et al,* 2013). Reinforcing factors consist of social support. Enabling factors consist of accessibility and availability of methadone treatment services (Maehira *et al,* 2013; Adorno *et al,* 2013). This study provides baseline information for policy makers to effectively manage and plan MMTP programs to combat injecting drug abuse in Nepal.

MATERIALS AND METHODS

Study design

We conducted cross-sectional survey study among MMTP sites located in Kathmandu and Lalitpur Districts of Nepal. The clients were enrolled in two hospitals: Tribhuwan University-Teaching Hospital in Kathmandu, Maharajgunj and Patan Hospital in Lalitpur.

Sample size

The sample size calculation was based on Daniel (2009) using the prevalence of regular methadone users in Kathmandu Valley found in a previous study (Ambekar *et al*, 2013). That study found the adherence rate to methadone treatment was 37%. The total number of IDUs receiving methadone treatment in the two studied health facilities during the previous 3 months was presumed to be equal to 303 cases; using a 95% confidence level and a 5% absolute error for one sample test for proportion, the calculated sample size required for this study was 165 cases. With 15% added for incomplete answers and rounding up, the total sample collected was approximately 200 cases.

Inclusion and exclusion criteria

Inclusion criteria included clients with a history of injecting drugs before coming for treatment, >18 years, already completing at least one month of MMTP, willing to participate in the study and being willing and able to give informed consent. Exclusion criteria included patients with AIDS, tuberculosis or other opportunistic infections and those who did not complete the questionnaire.

Sampling method

A simple random sampling technique was used to select subjects from the study sites who met the inclusion criteria.

Data collection

We used a face to face interview questionnaire to collect data regarding subjects. This questionnaire was designed by the researchers based on a literature review. The interviews were conducted by the researchers and 2 trained research assistants between 5 April and 20 April, 2015. Each interview lasted 20-30 minutes. The questionnaire consisted of 6 parts. Part 1 covered sociodemographic factors comprised of age, sex, marital status, residence, religion, education, income, duration of IDU, types of IDU, and IDU status (relapse and disclosure). Part 2 consisted of predisposing factors comprised of 8 questions regarding knowledge about IDU and 10 questions about MMTP; this was constructed based on the Centers for Disease Control and Prevention tool kits (CDC, 2002) and a Family Health International booklet (FHI, 2011), and 11 questions about perceptions regarding methadone and methadone treatment. Part 3 evaluated enabling factors consisted of 6 questions about availability and 6 questions about accessibility to MMTP. Part 4 was comprised of 2 subsections about social support: 9 questions covered social support from family members and 9 questions covered support by health workers. Part 5 was a checklist recording adherence to the MMTP by evaluating the daily health service records.

The content validity of the questionnaire was determined by two doctors working in the MMTP and by two university lecturers in public health. The questionnaire was pretested for reliability among 30 study subjects from Podkhara District. The Kuder-Richardson-20 (KR-20) instrument was used to analyze knowledge about IDU and the MMTP and the Cronbach's alpha coefficient was used to analyze perception regarding the MMTP, availability and accessibility the MMTP and social support from family members and health workers. The KR-20 of knowledge on IDUs was 0.70; knowledge on MMTP was 0.726. The Cronbach's alpha coefficients were: perception about the MMPT = 0.670, availability of the MMTP = 0.760, accessibility of the MMTP = 0.804, social support from family members = 0.958 and social support from health workers = 0.897.

Using the Bloom BS classification (1971), the total scores for each part were classified into 3 groups: low (<60%), moderate (60-79%) and high (≥80%). For knowledge about IDU, the total scores were classified as low (<5); moderate (5-6), and high (>6). For knowledge about the MMTP the total scores were classified as: low (<6), moderate (6-7), and high (>7). For perception about the MMTP the total scores were classified as low (<20), moderate (20-25), and high (>25). Total scores for availability of the MMTP were classified as: low (<11), moderate (11-13), and high (>13). The total scores for accessibility of the MMTP were classified as: low (<11), moderate (11-13) and high (>13). The total scores for social support from family members and from health workers were also classified as: low (<16), moderate (16-21) and high (>21). MMTP adherence was classified as: good (completed 30 days of treatment in one month), fair (completed 27-29 days of treatment in one month) and poor (completed <27 days of treatment in one month).

Data analysis

Frequencies, percentages, means and standard deviations were used for descriptive statistics. The chi-square test was used to identify factors related to MMTP adherence. Predictive factors for

MMTP adherence were determined using forward multiple logistic regression analysis. Statistical significance was set at $p < 0.05$.

Ethical considerations

The study was approved by the Committee on Human Rights Related to Human Experimentation, Faculty of Public Health, Mahidol University (MU 2015-048).

RESULTS

Sociodemographic factors

A total of 165 subjects were included in the study. Forty-one point two percent of respondents were aged ≤30 years and 38.8% aged 30-40 years. The youngest respondent was aged 20 years, the oldest aged 54 years and the average age was 32.5 years (SD= 6.9 years). Ninety-six point four percent of respondents were male. Sixty-four point two percent were the Janajati ethnic group. Ninety-point nine percent of respondents came from Kathmandu Valley. Forty-one point eight percent of respondents had completed secondary school and 4.8% were illiterate. Fiffy-three point nine percent were married. Thirty-two point one percent of respondents were unemployed, 30% were employed in business, 14.5% in private jobs and 13.9% worked as craftspersons, singers or musicians. Forty-three percent had a sufficient family income. Forty-four point two percent of respondents used injecting drugs for <10 years; the minimum drug use was 1 year and the maximum was 33 years. The average duration of injecting drugs was 11.5 years (SD = 6.2 years). The most frequently abused substance was opium by 65.5% of respondents. Forty point six percent had a history of relapse into drug use within 3 months. Sixty-two point seven percent had a history of relapse at least once. Eighty-three point six percent had disclosed to their family they were IDUs. Seventeen percent also had hepatitis C and 4.8% had a combination of HIV, hepatitis B and hepatitis C (Table 1).

MMTP adherence

Seventy-two point one percent of respondents had good adherence to the MMTP and 18.8% had fair adherence (Table 2).

Factors associated with MMTP adherence by chi-square

Among sociodemographic factors, level of education, employment status, history of relapse, disclosure status and comorbidity were significantly associated with MMTP adherence. Among predisposing factors, level of knowledge about MMTP and perceptions about MMTP were significantly associated with MMTP adherence. Among enabling factors, only availability of MMTP was significantly associated with MMTP adherence. Among reinforcing factors, social support from family members and from health workers were significantly associated with MMTP adherence (Table 3).

Factors associated with MMTP adherence by multiple logistic regression analysis

Factors significantly associated with MMTP adherence using forward multiple logistic regression analysis were: history of relapse, knowledge about MMTP and availability of the MMTP. Respondents without a history of relapse during the previous 3 months were 2.7 times more likely to adhere to the MMTP (adjusted OR = 2.772; 95%CI: 1.163-6.605) those with a history of relapse. Respondents with a good knowledge level about the MMTP were 9.4 times more likely to adhere to the MMTP (adjusted OR = 9.464; 95%CI: 3.873-23.126) than those with fair to poor

Table 1
Socio-demographic characteristics of respondents (*N*=165).

Socio-demographic characteristics	Number (%)
Age (years)	
<30	68 (41.2)
30-40	64 (38.8)
>40	33 (20)
Mean ± SD=32.58±6.925, Min=20, Max=54	
Sex	
Male	159 (96.4)
Female	6 (3.6)
Ethnicity	
Brahmin/Chettri	58 (35.2)
Janajati	106 (64.2)
Madhesi	0 (0)
Dalits	1 (0.6)
Residence	
Kathmandu Valley	150 (90.9)
Outside Kathmandu Valley	15 (9.1)
Education	
Illiterate	8 (4.8)
Primary school	36 (21.8)
Secondary school	69 (41.8)
High school	36 (21.8)
College or university	16 (9.7)
Marital status	
Single	67 (40.6)
Married	89 (53.9)
Divorced/separated	9 (5.5)
Occupation	
Unemployed	53 (32.1)
Government officer	6 (3.6)
Business	51 (30.9)
Laborer	8 (4.8)
Private service/worker	47 (28.4)
Family income	
Insufficient	59 (35.8)
Sufficient	71 (43)
Sufficient with savings	35 (21.2)
Duration of intravenous drug use (years)	
<10	73 (44.2)
10-19	65 (39.4)
≥20	27 (16.4)
Mean ± SD=11.53±6.215, Min=1, Max=33	
Type of drugs most frequently abused	
Opium	108 (65.5)
Ecstasy	2 (1.2)
Heroin	36 (21.8)
Amphetamines	8 (4.8)
Barbiturates	11 (6.7)
History of relapse	
Yes	67 (40.6)
No	98 (59.4)
Number of relapses (times)	(*n*=67)
1-2	53 (79.1)
3-4	12 (17.9)
5	2 (3)
Mean +SD=1.67+ 1.067 Min=1 max=5	
Disclosure of history of intravenous drug use to family	
Yes	138 (83.6)
No	27 (16.4)
Presence of specified infections	
None	129 (78.2)
HIV, HBV and HCV	8 (4.8)
HCV only	28 (17)

HIV, human immune deficiency virus; HBV, hepatitis B virus infection; HCV, hepatitis C virus infection.

levels of knowledge. Those with a high level of MMTP availability were 4.5 times more likely to adhere to the MMTP (adjusted OR = 4.553; 95%CI: 1.883-10.596) than respondents with a moderate to low level of availability to the MMTP (Table 4).

DISCUSSION

MMTP adherence

Seventy-two point one percent of respondents in our study had good adherence to the MMTP. The World Health

Table 2
Level of adherence to the MMTP during the previous month (*N*=165).

MMTP adherence	Number (%)
Good (30 days)	119 (72.1)
Fair (27-29 days)	31 (18.8)
Poor (<27 days)	15 (9.1)

MMTP, methadone maintenance treatment program.

Organization (WHO), United Nations Office on Drugs and Crime (UNODC) and United Nations Office on AIDS (UNAIDS) in 2004 stated good adherence to the MMTP is necessary for success of the treatment (WHO/UNODC/UNAIDS, 2004). A large number of clients did not have good adherence in our study. In this study, a short term adherence within 30 days of one month and follow-up of the relapse rate within 3 months was used to identify the treatment adherence practices similar to the study done in San Francisco (Evans *et al*, 2009) in the young IDUs group reporting a 71.2% adherence rate. The adherence rate in our study was higher than the adherence rate two years after treatment in Malaysia (68.6%) (Musa *et al*, 2012), but lower than a study among clients in Vancouver (Li *et al*, 2013) with an adherence rate of 74.1% among aboriginals and 80% among non-aboriginals. The Nepal National Survey of methadone adherence in 2014 found the adherence rate in Kathmandu was 30% and in Latipur was 53% (National Center for AIDS and STDS Control, 2014), lower than our findings. Sanders *et al* (2013) suggested adherence to methadone treatment may vary based on both intrinsic and extrinsic factors. Intrinsic factors consisted of lack of control of treatment, concerns about methadone dependence, and desire to avoid adverse effects. Extrinsic factors consisted of shame and stigma surrounding the MMTP, pressures from family and peer relationships and medical conditions.

A history of relapse during the previous 3 months was negatively associated with adherence and a good knowledge level about the MMTP and high availability of the MMTP were positively associated with MMTP adherence. The factor with the most significant association with adherence to the MMTP was a good knowledge about the MMTP. This finding is similar to studies from Massachusetts (Adorno *et al*, 2013) and China (Zhou and Zhuang, 2014). Clients with a good knowledge about methadone maintenance therapy are more likely to be aware of the importance of the MMTP. Injecting drug abuse is more common among younger people (Ali and Howard, 2011; Li *et al*, 2013; Yang *et al*, 2013) perhaps because they are more curious about using it without having a knowledge about tis deleterious effects (Feng *et al*, 2012).

The second factor associated with MMTP adherence was the level of availability of the MMTP finding is similar to other studies (Maehira *et al*, 2013; Yang *et al*, 2013; Zhou and Zhuang, 2014). It can be assumed the availability of free methadone services and sufficient facilities would help make it easier for clients to maintain methadone treatment. Basically, if treatments were more easily available and accessable, clients would be more likely to use them (Glanz *et al*, 2008).

The other factor significantly negatively associated with adherence is a history of relapse during the previous 3 months. This finding was also reported by other studies (Regmi *et al*, 2004; Zhou and Zhuang, 2014). When the needs of a

Table 3
Factors related to MMTP adherence by chi-square test (N=165).

Factors	Methadone adherence		p-value
	Good n (%)	Fair to poor n (%)	
Age (years)			0.915
<30	50 (73.5)	18 (26.5)	
30-39	45 (70.3)	19 (29.70	
≥40	24 (72.7)	9 (27.3)	
Sex			1.000
Male	114 (71.7)	45 (28.3)	
Female	5 (83.3)	1 (16.7)	
Residence			0.763
Kathmandu	109 (72.7)	41 (27.3)	
Outside Kathmandu	10 (66.7)	5 (33.3)	
Ethnicity			0.585
Brahmin/Chettri	44 (75.9)	14 (24.1)	
Janajati	74 (69.8)	32 (30.2)	
Dalits	1 (100)	0 (0)	
Marital status			0.361
Single	50 (74.6)	17 (25.4)	
Married	61 (68.5)	28 (31.5)	
Divorced/separated	8 (88.9)	1 (11.1)	
Education			<0.001*
Primary school or lower	20 (45.5)	24 (54.5)	
Secondary school or above	99 (81.8)	22 (18.2)	
Occupation			0.032*
Employed	75 (67.0)	37 (33.0)	
Unemployed	44 (83.0)	9 (17.0)	
Income			0.375
Sufficient	45 (76.3)	14 (23.7)	
Insufficient	74 (69.8)	32 (30.2)	
History of relapse			<0.001*
No	83 (84.7)	15 (15.3)	
Yes	36 (53.7)	31 (46.3)	
Disclosure of IDU to family			0.010*
Yes	105 (76.1)	33 (23.9)	
No	14 (51.9)	13 (48.1)	
Presence of specified infections			<0.001*
No	102 (79.1)	27 (20.9)	
Yes	17 (47.2)	19 (52.8)	
Duration of drug use (years)			0.110
<10	55 (75.3)	18 (24.7)	
10-19	49 (75.4)	16 (24.6)	
>20	15 (55.6)	12 (44.4)	

Table 3 (Continued).

Factors	Methadone adherence		*p*-value
	Good n (%)	Fair to poor n (%)	
Types of drugs abused			0.155
Opioid	74 (68.5)	34 (31.5)	
Non-opioid	45 (78.9)	12 (21.1)	
Knowledge about IDU			0.859
Good	87 (72.5)	33 (27.5)	
Fair to poor	32 (71.1)	13 (28.9)	
Knowledge about MMTP			<0.001*
Good	105 (85.4)	18 (14.6)	
Fair to poor	14 (33.3)	28 (66.7)	
Perceptions about the MMTP			<0.001*
High	71 (84.5)	13 (15.5)	
Moderate to Low	48 (59.3)	33 (40.7)	
Social support from family members			0.006*
High	41 (87.2)	6 (12.8)	
Moderate to low	78 (66.1)	40 (33.9)	
Social support from health workers			0.001*
High	50 (87.7)	7 (12.3)	
Moderate to low	69 (63.9)	39 (36.1)	
Availability of the MMTP			<0.001*
High	97 (83.6)	19 (16.4)	
Moderate to low	22 (44.9)	27 (55.1)	
Accessibility to the MMTP			0.816
High	115 (72.8)	43 (27.2)	
Moderate to low	4 (47.1)	3 (42.9)	

MMTP, methadone maintenance treatment program.
IDUs, intravenous drug users; *Significant at $p < 0.05$.

Table 4
Factors significantly associated with MMTP adherence on multiple logistic regression analysis.

Factors	β	SE(β)	Exp(β)	95%CI	*p*-value
History of relapse[a]	1.020	0.443	2.772	1.163-6.605	0.021[d]
Knowledge about MMTP[b]	2.247	0.456	9.464	3.873-23.126	<0.001[d]
Availability of methadone treatment services[c]	1.516	0.450	4.553	1.883-10.596	0.001[d]
Constant	-2.024	0.490			

Reference group of comparison in parentheses: [a] = history of relapse; [b] = fair to poor level of knowledge about MMTP; [c] = Moderate to low level of availability of methadone treatment; [d] significant at $p<0.050$; MMTP, methadone maintenance treatment program.

client were managed properly (*eg*, craving drugs, dependence and withdrawal symptoms), the client is more likely to adhere to treatment (Amato *et al*, 2003). Clients with a history of mixed drug use, especially with opioids, and benzodiazepines and alcohol, their adherence to treatment is poorer (Evans *et al*, 2009; Ojha *et al*, 2014).

Our study had some limitations such as the sample selection, which was carried out in an institution-based setting rather than in a community-based setting. This limits the generalizability of the study results to other settings or treatment models. Our research focused only on the client's perspective not the provider's perspective, possibly excluding some factors responsible for MMTP adherence.

In conclusion, our findings are beneficial to healthcare providers in Nepal in setting up effective methadone maintenance services for injecting drug users, to improve better adherence. IDUs need to be better educated about MMTP to improve compliance with the program. MMTP should be more easily available to IDUs to improve better adherence. Follow-up and easier mechanisms for directly observe therapy, such as home visits, need to be improved to increase MMTP adherence and reduce relapses.

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Declaration of conflicts of interest

The authors declare they have no conflicts of interest.

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