DISCUSSIONS
A number of reports have shown that abuse of alcohol and other substances such as opiates, sedatives has reached alarming proportions in north eastern states of India including Sikkim.\cite{59,65} There are reports to evident analgesic abuse among youths of Sikkim\cite{56,59}, but to my knowledge, this is the first broad structured study to understand the epidemiology of prescription opioid abuse in Sikkim.

This study is an attempt to reveal the socioeconomic, demographic profile, pattern of substance use, employment status, high risk behaviour profile and quality of life of prescription opioid abusers in Sikkim and also to study their pain status, comorbid medical and psychiatric conditions etc. The current study brought out several trends & patterns of prescription opioid abuse which are of appreciable concern.

Study found that prescription opioid users of this study belonged to 17–51 years age group and mean age of first use of prescription opioid started around the age of 20 years, ranged between 11-46 years, when 43.3% (n=97) of the subjects had onset of prescription opioid use in the 15-20 years age range. This finding correlates with the 2006 NSDUH report\cite{66} –which confirms initiation of prescription opioid use non medically at adolescent age ( 12 years and older) and also correlates with Basu D et al\cite{67} study which documents lower age of subjects reporting for substance abuse treatment. Adolescent is a period in human growth and development that occurs after childhood and before adulthood from ages 10 to 19. Adolescence is also a period during which they have every possibility to put them in high risk behaviour either intentionally or unintentionally. Adolescents are different from young children and adults. Researchers from the University of Pittsburgh recorded neuron activity in the brains of adolescent rats while they
performed a reward-driven task, and found that adolescents’ brains react to rewards with much
greater excitement than adults’ brains. The researchers found that the stimulation in adolescent
brains varied throughout the study and with a greater degree of disorganization, whereas the
adult brains processed their rewards with a more consistent balance of stimulation and inhibition.
This could help explain why adolescents are more vulnerable to drug addiction, rash decisions,
and mental health problems. [Source: Science Daily, Teen Brains Over-Process Rewards,
Suggesting Root of Risky Behaviour, Mental Ills, January 26, 2011]. A behavioural-
temperamental trait (often termed disinhibition), characterized by difficulty of inhibiting
behavioural impulses, resulting in aggressive or otherwise problematic behaviour has been
widely recognized as an important risk factor for alcohol and other substance use disorders.
Childhood aggression predicts substance use problems in adulthood. While on the other hand,
affective traits such as anxiousness may increase the risk for problematic substance use.
Adolescents’ substance abuse problem is important to address because it causes several harmful
consequences such as physical deterioration, psychiatric problems, intellectual impairment,
personality deterioration, increased risks of accidents, legal risks and higher susceptibility to high
risk behaviour in the form of unprotected sex or use of unsterile needles.
The present study also found that adults 25 years of age and older are more likely than young
adults 15–24 years old to report co-occurrence of alcohol use and prescription opioid use non
medically. This finding does not counterparts with SE McCabe et al [68] study which compared
past-year drinking behaviours and nonmedical use of prescription drugs (NMUPD) in a
nationally representative samples of United States.
Number of female respondents in this study (0.04%) is too small to draw any meaningful conclusion on them. No significant gender differences in the use of prescription opioids were revealed. Finding indicates that there is limited turnover of women abusers at de-addiction centre for seeking treatment. Low turnover of female respondents to the treatment centre for treatment of any substance abuse is observed in several studies. \[^{69}\] This low prevalence of women abusers reported at de-addiction centre is supported by the finding of Drug Abuse Monitoring Survey (DAMS) with percentage of treatment seeking female substance abusers at 2.8%. Our finding indicates that women of Sikkim are less likely than men to have prescription opioid problems. This low turnover can be explained by the fact that drug abusing women receive little support from their relatives, husbands and other family members. Fear that people will identify them as addict, fear of withdrawal and concerns about social acceptability of their children as well as fear of losing custody of their children are also the other reasons for which drug abusing women did not sought treatment from drug de-addiction centres. Several studies have identified these possible reasons as barriers to treatment, leading to low turnover of women substance users at treatment centre in countries like Australia, India, Canada and six European countries. \[^{70-72}\] Lack of awareness, lack of resources and negative attitudes are therefore responsible for inadequate availability of gender related epidemiological data on prescription opioid abuse in Sikkim. This is of great concern because there are studies to indicate that women who inject opioids seem to be at higher risk of HIV infection \[^{73,74}\] and women who use heroin and other opioids during pregnancy has risk of miscarriage, preterm delivery \[^{75}\] and women drug abusers are more likely than men to report psychiatric problems \[^{33,76}\].
This study found higher rates of prescription opioid abuse and abuse related problems among Nepalese ethnic subjects and abuse observed almost equally by Hindu (42.9%) and Buddhist (43.3%) subjects. Only traditional inhabitants of Sikkim i.e. Lepcha’s contributed to only 6.3% to the total recruited subjects of this study. This can be explained by the fact that Nepalese [77] comprise major ethnic population (70%) in Sikkim and both ‘Hindu and Buddhist’ [78] are predominant religions in Sikkim. The findings are also in line with past researches that has shown high substance abuse rate by Nepalese in Sikkim. [56,79] This increased incidences of prescription opioid abuse by Nepalese Hindu and Buddhists are of particular concern because they are the dominant ethnic religion in the state who form society.

Study finds that over half of the prescription opioid abusers were unmarried. This was similar to a study from China [80, 81] with 54.7% unmarried opioid users seeking treatment for opioid dependence. Our finding is supported by findings of Amit Goel et al [79] study in 2009 on substance use in rural community in Sikkim representing 57.3% unmarried substance user. Only 20 of 224 (8.9%) prescription opioid abusers were either separated or divorced or widowed. This observation primarily indicates that the effect of divorce or separation was not the cause of subject’s prescription opioid abuse. Further studies are needed to establish it.

Subjects of our study had poor literacy rate, higher unemployment status. Majority of respondents either never attended school or dropped out of school even before completing eight standards. These finding were different from a similar kind of study from Amit Goel et al [79] as well as Nebhinani et al [82] study. It was also observed that mean age of first use of prescription opioid was lower among school dropouts than those who had any kind of formal education. Employment problems are found quite common among individuals receiving treatment for
prescription opioid abuse. It was observed that unemployed and student respondents had started first use of prescription opioid at much lower age than those who were involved in any kind of employment such as business and skilled work. A severe employment problem or difficulties such as inability to find work, problems with present job of over 20 days in current time and over half of the respondent’s dependency on family members for daily living were noticed in this study. Finding suggests that low rate of employment of prescription opioid abusers may be either due to lack of motivation to work and/or due to functional impairment directly related to prescription opioid abuse.

In our study prescription opioid abuse was found more among urban respondents. This is supported by the results of a meta-analysis by ‘Reddy & Chandrasekhar’ [83] indicating an overall substance use prevalence of 6.9/1000 for India with urban and rural rates of 5.8 and 7.3/1000 population. Our study also reported that there was no effect of migration on their pattern of prescription opioid abuse as most of them lived in and had started taking prescription opioid in the same place where they were born. Only 2.2% prescription opioid abusers had a history of migration.

Drinking of alcoholic beverages is very common and popular among Sikkim’s population. All the parents of the respondents reported to drink alcoholic beverages either occasionally or regularly. Regular use of substances such as opiates and others were not found more by them. Parents and siblings alcohol use was significantly higher than their prescription opioid use. On the other hand it was found that friends of the respondents were frequent user of both alcohol and prescription opioids. Therefore it can be said that ‘family history’ [84] and drug use by ‘friends’ [85] are two important risk factors for study respondents’ substance use. Study also revealed that
urban respondents have more friends with prescription opioid and alcohol use history. This is found statistically significant (Chi square = 13.38, df = 2, p = 0.0012).

In this study both prescription opioid and alcohol were reported as substance of major problem by more than half of the respondents, whereas prescription opioid alone was found to be the substance of major problem for over one fourth (30.8%) of respondents. Most commonly abused prescription opioids reported were dextropropoxyphene and codeine in both rural and urban Sikkim. Respondents did not report any shift or migration from their non-medical prescription opioid use to other illicit substance use. Rather reported concomitant alcohol and other substance use such as cannabis, heroin and nitrazepam. Prescription opioid abusers reported experiencing alcohol problems for nearly half a month (mean = 13 days) in past month. Alcohol problem or dependence was determined by using CAGE questionnaires. Study revealed that half of the subjects (53%) had alcohol problem (score ≥2). Although their biggest opiate problem at present recorded was prescription opioid only –i.e. opioids analgesics which are designed and used clinically for the treatment of severe / chronic pain. This is a clear indication of diversion from pharmaceutical shops. Although there are studies indicating shift from OxyContin (a prescription opioid) use to heroin use. Past month frequency of use of only prescription opioid was 79% in 20-30 days use group and majority reported to abuse prescription opioid for a period of 10 years or less in lifetimes. This shows that primary attention and concern about prescription opioid abuse and related harms has been in Sikkim-a north eastern state of India, where data from other parts of India also have documented increase in nonmedical use and abuse of prescription opioids in general populations. This correlates with findings of Basu D et al study indicating a decrease in use of natural opioids over three decades (1978-88, 1989-98, 1999-
(2008) while there is increase use of newer and prescription opioids such as buprenorphine, codeine and dextropropoxyphene in north India. In recent years, misuse and abuse of prescription opioids has been highlighted as a major and growing health problem globally.\textsuperscript{[90, 91]} Examination of various routes of administration revealed that all participants were taking prescription opioids orally in pill form and 23.2% were also taking by injection form. This is similar to the Sudie E et al\textsuperscript{[92]} study findings (orally, 100%) which collected information to help inform the design of a NIH-sponsored laboratory investigation to examine stress- and cue-induced craving among individuals with prescription opioid dependence. Proportion of IDUs of our study (23.2%, n=52), ranges between the findings of National Household Survey (0.1%) and that of Rapid Assessment survey of Drug Abuse (43%).\textsuperscript{[16]} Unmarried respondents reported higher rates of injecting prescription opioids (16.5% vs 4%) than the married respondents. But this difference did not reach statistical significance (Fisher’s exact test P value = 0.0712).

Injecting prescription opioid was observed less by the students in comparison to skilled workers. This was not found statistically significant (Fisher’s exact, p value = 1.00). The average monthly expenditure on prescription opioid (mean = 4896) was found almost half of the average past month income (mean = 9075) and was almost six times to the average monthly expenditure on alcohol (mean = 737). Past month expenses of Rs 5000 & above on prescription opioid was reported more by salaried and self-employed respondents in comparison to students and unemployed subjects (82.7% vs 17.2%). This was found statistically significant (Chi square = 31.27, df = 3, p =000). Average frequency of more than one substance use per day (including alcohol, excluding nicotine) in past month was 18 days. All the subjects endorsed either chewing or smoking nicotine products. Most of the prescription opioid abusers also endorsed using other illicit drugs (e.g. heroin, cannabis, benzodiazepines) in lifetimes, whereas only a limited (21%)
number of respondents had used any inhalants in lifetimes. Such types of patterns of poly substance use correlates with Sudie E et al [92] study.

Respondents identified initial and current reasons for their prescription opioid use. Half of the respondents mentioned that they had started using prescription opioids for the first time in order to experience ecstasy, but only few of the respondents said that they took prescription opioids for relief from depression, nervousness and anxiety. A significant number also reported to use it for the first time due to peer pressure. It was also found that none of the respondent had first received prescription opioids by physicians for the relief from chronic pain. Only 2.6% respondents among those who were interviewed reported to have pain for more than 2 years duration. Therefore it can be concluded that treatment need for the pain, coping with physical pain were not established in this study as important reasons or risk factors for subjects initiation of prescription opioid use. This research finding completely differ from Weiss RD et al [93] study where participants with chronic pain were more likely to report pain as their primary initial reason for use of prescription opioid. Our research noted that few subjects (16.5%) had used prescription opioids to get rid of pain which was not due to prescription opioid withdrawal symptoms in addition to other reasons. Many of them related that pain was not the reason why they were using prescription opioids. We found several reasons/motives such as anger, temptation to use, and craving, get rid of withdrawal symptoms and depressions etc. which were associated with subjects continued use of prescription opioids. Therefore, one of the major findings of this study is that this population often reports experiencing pain, although pain was not as an initial causal factor in why they sampled opioids and the fact that pain and
hypothesis can be manifestations of even mild opioid (or alcohol) withdrawal. Thereby, relationship of pain due to withdrawal symptoms can be established here.

In comparison to rural respondents, urban respondents were significantly more likely to report using prescription opioids in order to cope with depression and bad memories than anxiety and nervousness (Chi Square = 1.431, df = 2, p = 0.48). While grading the importance of motives of prescription opioid use by the subjects, we found that negative feelings such as feelings of pain, sadness, depression, and anger were not recognised as extremely important reasons rather their importance laid between moderate to very important reasons. On the other hand, only positive feelings of illicit substance use such as feelings of good mood, feelings of getting high either alone or along with peers were described as extremely importance reasons for continued use of prescription opioids either alone or along with other illicit substances like cannabis, benzodiazepines.

Respondents of the study reported that they first received their prescription opioids mostly from their substance using friends only at free of cost. It was reported that local drug peddlers were later introduced to the subjects by their friends who purchase prescription opioids regularly from them. Majority of the respondents had received prescription opioids most of the times from them. This establishes dealer’s role as major supplier or source of prescription opioids to both rural and urban Sikkim’s substance users in the next six months. It must be noted that dealer were not the first introducer. Simultaneously it was observed that friend’s initial free supply changed to paid supply in subsequent six months. At the same time more number of respondents reported to
purchase prescription opioids from medical shops without having legitimate prescription for such in the subsequent months than their initial period.

Pain status, health and psychiatric problems of prescription opioid abusers who reported for substance abuse treatment at various detoxification centres of Sikkim were studied and compared among various pain severity groups in our study. Subjects from all the pain severity group experienced pain at more than one joint than pain at any single site. It was also observed that moderate severity pain group had higher mean for both average as well as worst pain experienced in the past month category. Our study also evaluated pain qualities across pain severity groups and no significant differences were found. A higher percentage of subjects of all the three pain severity group (mild, moderate, severe) reported serious anxiety, tension both in past month and life time. Differences in current illicit substance use among the three pain severity groups were not found statistically significant. It was observed that all the prescription opioid abusers belonging to moderate pain group were using more than one illicit substance per day in the last month in comparison to mild and severe pain groups. Smoking was reported by all the subjects of all three pain severity groups for both past month and life time use history.

According to findings of this study, prescription opioid abuse can be linked with numerous morbidity indicator, e.g. health problems and consequences –both physical and mental health problems for which treatment demand generates. Chronic medical problems (12.5%), frequent hospitalisation (52%) and moderate to extreme intensity sufferings due to these problems were reported. Co-occurrence of mental health problems such as serious depression (lifetime, 68%), anxiety (lifetime, 96%) and thoughts of suicide both in lifetimes and past month, reported in this
study correlates with results of OPICAN [94] study (depression, 49.2%) which compared social, health and drug use characteristics of untreated non-medical prescription opioid using populations in five cities of Canada and Sproule B et al [95] study (depressive symptoms, 53%; anxiety, 25%) where a high mental health/psychiatric problem levels of Toronto’s non-medical prescription opioid users than the general population average was recorded. Reports of serious anxiety in lifetimes at Sproule B et al [95] study (25% vs 96%) was found far below than this study report. Male female ratio in this study is 223:1. All the prescription opioid abusing female had co morbid mental illness.

Our study also recorded several incidences of criminal charges due to either possession or dealing with prescription opioids and other illicit substance as well as numbers of incarcerations for the same. Incidences of major driving violations, disorderly conduct and public intoxications under the influence of alcohol and other illicit substances including prescription opioids were also reported. Therefore it can be concluded that ill effects of prescription opioid abuse –i.e. both physical & mental health problems as well as legitimate problems, were well observed in this study and correlates with several other studies as mentioned above. This increases concerns over illicit substance abuse related problems in Sikkim. This urges needs of education among general populations about deleterious effects of illicit substance use.

Entry into treatment were found to be influenced by a host of factors, including mandates from criminal justice proceedings (on parole, 4.9%) and perceptions of risk of continued illicit substance use (withdrawal symptoms and physical side effects) and the perceived benefits of treatment. Several subjects of this study availed inpatient and outpatient counselling, various
alcohol anonymous (AA) and narcotic anonymous (NA) programmes in addition to treatment at detoxification centre.

During the treatment course, majority reported to have somewhat to much better health condition in comparison to last year, which was confirmed by grading their ability to perform moderate to vigorous activities. Most of them reported to perform physical activities without much limitations.

IDU’s are subject to dual risk of unsafe injections and sexual practices with non-primary sex partners. Needle sharing was found common among IDU’s (8 of 13) in past month. First visit to CSW was reported at the age of 19.5 years. Lifetime history of precocious sexual activity (42%), MSP behaviour (47.3%), and unprotected sex (31.3%) were reported in this study. Majority reported to have sexual intercourse with 1-4 numbers of female partners in past month, whereas homosexuality (MSM) was reported only in 0.4% of prescription opioid abusers. This low reporting of MSM behaviour by respondents may be due to response bias. Past month safe intercourse practice rate with their female was found very low (8.5%). This indicates unprotected sex practices with partners other than spouse were quite common, which supports the similar findings of Rapid Assessment Survey of Drug Abuse (RAS) with percentages of 4-24%. Vaginal sex was reported mostly than oral sex by respondents during past month. Lifetime history of CSW behaviour (37.5%), MSP behaviour, unsafe sexual practices and needle sharing are recognised as important risk factors. This is life-threatening because injection-related problems may result in increased likelihood of Blood-spills and poor injection practices. These along with CSW behaviour and unprotected sex can aggravate transmission of blood borne...
Research has shown that IDU who share needles are significantly more likely to have unsafe sex than IDU with safe needle practices, contributing to the risk to needle sharing.

While comparing socio-demographic characteristics and type of drug use among prescription opioid abusers, we found some significant associations. Non-medical use of more than one substance was found prevalent among salaried respondents (p<0.005) and also among those who have business (p<0.05).

Our study has several strengths and limitations. Subjects that fulfill criteria according to my protocol were only accessible / available from de-addiction centers of Sikkim. As the study planned to enroll only clinically diagnosed PO abusers; therefore subjects selected from rehabilitation centers only can broadly represent the population of Sikkim. Secondly, all the subjects were interviewed by same interviewer, thus eliminates inter-rater error.

Several limitations of this study need to be acknowledged. We relied on subjects self-report for all the data including their health and mental status. However psychiatric status of the subject was not verified/confirmed by health care provider or by doing psychiatric clinical diagnosis. Detailed information was collected regarding subjects various characteristics of pain, however further studies needed to determine the exact cause of pain. Area that hurt most by pain was recorded by showing body map containing various sites. Therefore, chances of under reporting for above parameters and misclassification in body map by subjects may arise. A detailed note was also taken regarding substance use pattern and characteristics but data were not verified with urine toxicology testing. This study fails to capture the full extent of the opioid abuse problem in Sikkim because of the underrepresentation of women in the sample (and that fact that,
apparently, women too are abusing opioids and alcohol). While it is understandable why there was not a greater representation of women, this inherent bias is a limitation of this study. At the end the findings of our study may not be generalized to other parts of north eastern states of India even though there is geographical and socio cultural similarities exists among them. This is because substance use type and health care facilities widely varies among north eastern states. In our study alcohol problem was determined by analyzing CAGE questionnaire. We relied only on subjects self-report regarding data of alcohol intoxication and it was not assessed clinically.