CHAPTER: THREE

MATERIALS AND METHODS

3.1. THE STUDY
The present research was conducted in Imadol VDC of Lalitpur district. Lalitpur district is one of the three districts of the Kathmandu valley. The other two districts are Kathmandu and Bhaktapur. Kathmandu is the capital of Nepal. The 2011 population census, the population of the Kathmandu valley is 1081845, and that of Lalitpur city is 162991 and the total population of Lalitpur district is 466784 [43]. Population density (average number of population per square kilometer) is found to be highest in Kathmandu district (4,416 person per square km). Presence of many historic places and temples makes Lalitpur district as a famous place amongst foreign tourists in Nepal. The different group of people in this research were important stakeholders such as, healthcare professionals working in a hospital setup, pharmacists serving in the community and most importantly, the consumers who consume medicines.

3.2 STUDY POPULATION
Healthcare professionals working in KIST Medical College Teaching Hospital (KISTMCTH), including physicians, dental surgeons, nursing staffs, pharmacists, health assistants and other support staffs were considered as an important stakeholder in the pharmacovigilance systems. Community pharmacists, working in community settings were another important group of people selected to be interviewed and most importantly, consumers who were consuming the medicines were the third group of people included in the study. Besides, the director general from department of drug administration from the national drug regulatory authority were also interviewed. These people were interviewed because they are the people who make policies and are for monitoring and evaluating drug use inside the country. Drug regulatory authority can be taken as a key personnel for establishment and making guidelines for ADRs and pharmacovigilance process.

Initiating Consumers Pharmacovigilance in Lalitpur District
Patients from Lalitpur district, coming for health check-ups at KISTMCTH outpatient departments (OPD) were interviewed to identify areas where patients were lacking the information about ADRs and the ADR reporting processes and their willingness to report ADRs to KISTMCTH if a consumer pharmacovigilance centre was established in the institution. Community pharmacists registered in Department of Drug Administration (DDA) and running community pharmacies in Lalitpur district were considered as a population for interview for consumer pharmacovigilance. An interview was also conducted among fifty consumers who were from Imadol area for information required for designing an ADR reporting form for consumers.

3.3 STUDY DESIGN
Study design was descriptive and cross sectional for all the three groups. The design was one group pre-test, post-test (quasi experimental) for the healthcare professionals and one group pre-test, post-test and retention for the community pharmacist population. For consumers, baseline data about their KAP with regard to consumer pharmacovigilance was obtained.

3.4 SAMPLING METHOD
The sampling method used for the research work was a convenience sampling method for healthcare professionals and for the community pharmacists, a systematic sampling method with a sampling interval of three where the first pharmacy was selected randomly between one and three. The sampling interval was three as we were selecting 75 pharmacies from the total of 204 community pharmacies in the district. Similarly, for the consumers, the method used was systematic random sampling i.e. every fifth patient visiting the outpatient pharmacy. There were two pharmacy units existing at KISTMCTH. One is for the out patients and the other one is for admitted inpatients at KISTMCTH. These patients were interviewed using the questionnaire. The sampling method for consumers for obtaining their inputs
regarding designing an ADR reporting form for consumers was a convenience sampling method.

3.5 **SAMPLE SIZE CALCULATION**

Sample size calculation was done using the formula for sample size for a single proportion [78]. The knowledge was assumed to be 40% in all the three population. This was also obtained from the literature review. [79]

### 3.5.1 Sample size calculation for Health care professionals

Knowledge = 40%, \( P=0.4, Q=1-P=0.6 \)

\[
N = \frac{Z^2 \times P \times Q}{(M.E.)^2}
\]

Where \( Z = 1.96 \) from normal table, two tailed

\( P \) = Population proportion

\( M.E. \) = Margin of error = 10%

Now, \( n = (1.96)^2 \times (0.4) \times (0.6)/(0.1)^2 \)

\[= 92\]

Non-response correction = 10%

Total sample size needed with provision for drop outs from the study = 92 + 10% of 92 = 101

### 3.5.2 Sample size calculation for community pharmacists

Knowledge=40%, \( P=0.4, Q=1-P=0.6 \)

\[
N = \frac{Z^2 \times P \times Q}{(M.E.)^2}
\]

Where \( Z = 1.645 \) from normal table, two tailed
P = Population proportion
M.E = Margin of error

Now, $n = (1.645)^2 \times (0.4) \times (0.6)/(0.1)^2$

$= 65$

Non response correction = 10%

Total sample size needed with provision for drop outs from the study = 65 + 10% of 65 = 71

3.5.3 Sample size calculation for consumers

Knowledge=40%, $P=0.4$, $Q=1-P=0.6$

$N=Z^2 \times P \times Q/(M.E.)^2$

Where $Z_\alpha = 2.326$ from normal table, two tailed

$P= Population\ proportion$

$M.E = Margin\ of\ error$

Now, $n = (1.645)^2 \times (0.4) \times (0.2)/(0.1)^2$

$= 130$

Non response correction = 10%

Total sample size needed with provision for drop outs from the study = 130 + 10% of 130 = 143.

3.6 DEMOGRAPHICS

The demographics used in this research included variables like:
**Gender:** This parameter was noted for all the participants ranging from doctors, dentists, nurses, pharmacists, health assistants and consumers.

**Age:** Study participants were taken of any age excluding the children less than 14 years of age.

**Working experience:** The length of the working experience was noted for healthcare professionals and community pharmacists.

**Ethnic groups:** The caste/ethnic group of the study participants were noted. There are many ethnic groups in Nepal as per the report from CBS Nepal in 2012. According to it, Chetris are the largest ethnic group comprising of 16.6% of the total population followed by Brahmins (12.2%), and then by Janjati groups like Magars (7.1%), Tharu (6.6%), Tamangs (5.8%) and Newars (5%).

**Level of education:** Participants were categorized depending on their level of education as below class 10, Intermediate, bachelor, masters and PhD for consumers and healthcare professionals whereas for the community pharmacists, level of pharmacy education was noted. They were divided into three groups, diploma, bachelor and masters.

**Occupation:** the participant’s occupation was taken as the current job. The occupation was noted for the consumers surveyed.

### 3.7 STUDY METHOD

The data collection tools for evaluating the concept of pharmacovigilance and consumer pharmacovigilance were developed after consulting various studies and following inputs from the guide and co-guides. The questionnaire was developed for all three populations. Separate questionnaires were used for the three groups.
Initiating Consumers Pharmacovigilance in Lalitpur District

Questionnaires included a mix of statements and multiple choice questions. Respondents’ degree of agreement with each individual statement was studied using a Likert scale. As per the feedback from the experts, some statements were modified and others were reframed and restructured for better understanding. These questionnaires incorporated statements pertaining to knowledge, attitude and practice. Common topics included in all the three questionnaires were about pharmacovigilance, consumer pharmacovigilance, the existing system of pharmacovigilance and other important areas for pharmacovigilance, like information about the reporting process of the ADRs, location of the reporting centres and the reporting procedures.

3.7.1 STUDY DURATION
The pretesting of the questionnaire was done as a pilot study between March to June 2013 at Imadol, Lalitpur district. The study for the healthcare professionals was conducted from February 2013 to December 2013. Similarly, the Community pharmacists were studied from August 2013 to June 2014. Another group of population were studied from September 2013 to September 2014.

3.7.2 DATA COLLECTION
The questionnaire was administered to the healthcare professionals working at KIST Medical College. Similarly, the community pharmacists from Lalitpur district were chosen and the questionnaire was used for them to get the data. Consumers were the patients coming to the KIST Medical College’s outpatient department. They were administered the questionnaire framed for them. Interview was taken for them about the open ended and multiple choice questions.

3.7.3 TRANSLATION OF THE QUESTIONNAIRE
The structured questionnaires framed for the healthcare professionals, community pharmacists and the consumers were created by using first
language as English, and then was back translated into the local language Nepali and again back translated to English.

3.7.4 SCORING SYSTEM
The questionnaires consisted of various sets of statements for knowledge, attitude and practice. The system used for scoring of the statements were 5=strongly agree, 4=agree, 3=neutral, 2=disagree, and 1=strongly disagree. The questionnaire for healthcare professionals contained 20 statements as knowledge items to assess knowledge. The maximum possible score for knowledge was 100 and 19 statements were for assessing attitude with a maximum possible score of 95. The scores of knowledge and attitudes were obtained by adding the scores for knowledge and attitude scores for pre and post educational intervention group. The maximum total score was 195. The median scores and interquartile range were calculated for the knowledge, attitude and the total scores. The same system of scoring was used for community pharmacists also. There were twelve statements for assessing knowledge with a maximum possible score of 60 and nine statements for attitude with a maximum possible score of 45. Similarly, there were five statements for practice, with a maximum possible score of 25. The total score obtained by adding the knowledge, attitude and practice scores was 130. The median and interquartile range was calculated for total knowledge, attitude, practice and overall scores.

The scoring system was different for consumers and it was done as: The scores for knowledge items were given 1 for each possible option. Since the questions were with multi option answer, the score for each question depended on the number of options available. Similarly, the scores for attitude questions, positive attitude was given as 1 and the negative attitude as 0. Similarly, for practice, the score was calculated by giving 1 for each possible options from the multiple choice questions. This questionnaire for consumers was made in this manner for allowing the patients to answer in a multiple way. They could get the liberty to express their views about any particular statement for KAP.
3.7.5 PRETESTING OF THE QUESTIONNAIRE

The questionnaire developed was validated by using this data collection tool for 12 healthcare professionals and 10 community pharmacists.

The questionnaire was validated for face and content validation. Face validation was done by sharing the questionnaire with colleagues from the department where the candidate was working and the subject expert’s opinion was taken for the content validation. The data obtained during pretesting of the questionnaire was not used for further analysis. The Cronbach’s alpha value was used as a measure of the internal consistency of the questionnaire. The values were 0.78 for the questionnaire for healthcare professionals and 0.67 for community pharmacists. This value was 0.71 for consumers questionnaire indicating good reliability. The values above 0.62 were considered as good and reliable.

3.8 CONDUCT OF THE STUDY

The research for healthcare professionals was done in three phases. The first phase was the pilot test for both the groups. The second phase was the pre intervention phase, where the participants responded to the questionnaire with the existing levels of their knowledge to the issues related to pharmacovigilance and consumers pharmacovigilance. After getting the pre data of the respondents, an educational intervention was planned to make the deficiencies corrected and had an emphasis on the concepts of pharmacovigilance. The time interval between these two phases was two months. Similarly, for the community pharmacists, the study was also done in three phases as pre post and retention assessment phases. The time gap in between these three phases were 6 weeks each. The educational intervention included an informative presentation with issues related to medicines, their roles towards safety of medicines. The sessions also included the information about ADR reporting process, whom to report ADR and about the form to be used for ADR reporting. The areas for intervention were identified from the response made to the questionnaires by the respondents in the pre intervention phase. The intervention phase also had a poster session where the respondents

Initiating Consumers Pharmacovigilance in Lalitpur District
were further clarified about pharmacovigilance and consumers pharmacovigilance. The posters were obtained from the department of drug administration, DDA, Nepal. Besides these, there were discussions for all the queries made by the participants for the ADR reporting process and the common medicine use problems. The interactive sessions aimed to include the recognized the importance and epidemiology of ADR reporting and pharmacovigilance. This also aimed for the current status of ADR reporting process in Nepal. The intervention also highlighted the importance of community pharmacists in the system for ADR reporting. The third group of population was the group of consumers. The participants were chosen who came for their treatment in the study site for assessing the KAP for the ADRs and pharmacovigilance. Similarly, for the ADR report designing, people were asked from the Imadol area. Their opinion were taken for making an appropriate ADR form. The awareness about the subject matter was tried to spread by the help of publishing articles in the national English and Nepali newspapers.

3.9 STATISTICAL ANALYSIS

For the data with healthcare professionals, after the intervention, scores for knowledge and attitude were again measured using the same questionnaire. The collected data was analysed using SPSS version 19.0 for Windows. The knowledge, attitude, and total scores before and after the educational intervention were tested for normality of distribution using one sample Kolmogorov-Smirnov test. The samples did not follow a normal distribution and the median was calculated as a measure of central tendency, interquartile range as a measure of variance, and non-parametric tests were used for comparison between different subgroups of respondents pre-intervention. Scores before and after the intervention were compared using the Wilcoxon signed-rank test. Median knowledge, attitude, and total scores were also compared among different subgroups of respondents both before and after the intervention across categories. A \( p \) value less than 0.05 was taken as statistically significant.

Similarly for the community pharmacists, the samples were noted not to
follow a normal distribution and median was calculated as a measure of central tendency, interquartile range as a measure of variance and non-parametric tests were used for comparison between different subgroups of respondents. A cross tab evaluation of the variables like gender, age and education were done for various statements from the questionnaire. Comparisons were made by using Fisher’s Exact chi square test and Pearson’s chi square test. This analysis was performed for thirteen statements out of twenty six statements from the questionnaire to assess whether specific knowledge, attitude and practice variables are related to gender, age and level of education also. The Kruskal-Wallis test confirmed that at least one of the median knowledge, attitude and practice score pairs are different among the categories. A post-hoc test was done to find the pair/s that had statistically different median knowledge, attitude and practice scores. Data from consumers were also found not to follow a normal distribution and the median was calculated as a measure of central tendency, interquartile range as a measure of variance and non-parametric tests were used for comparison between different subgroups of consumers. A cross tab evaluation of the variables like gender, age and education were done for various statements from the questionnaire. Comparisons were made by using Fisher’s Exact chi square test and Pearson’s chi square test. This analysis was performed for six statements with their possible options out of twenty two statements from the questionnaire to assess whether specific knowledge, attitude and practice variables are related to gender, age and level of education also. The Kruskal-Wallis test confirmed that at least one of the median knowledge, attitude and practice score pairs are different among the categories. A post-hoc test was done to find the pair/s that had statistically different median knowledge, attitude and practice scores.

3.9.1 ETHICAL CONSIDERATIONS

This methodology was also presented before the Departmental Review Committee (DRC) of Suresh Gyan Vihar University (SGVU), Jaipur, India on 20th September 2012. The study protocol was been approved by the DRC committee. After this, the ethical approval was obtained from Institutional Research Committee of KIST Medical College for the ethical consideration for
all the tree study population. All healthcare professionals and community pharmacists were informed and explained about the aims and objectives of the study and invited to participate. Written informed consent was obtained from all participants. For the consumers, the verbal consent was taken for their participation in the research. The participants were explained about the research and they were given the liberty for not giving their consent if they are not willing to participate.

3.9.2 DATA COLLECTION TOOLS

The following questionnaires were used as study tools for conducting:
1. Questionnaire for healthcare professionals (annex-2).
2. Questionnaire for community pharmacists (annex-4).
3. Questionnaire for the consumers (annex-6 and 7). This questionnaire was back translated into Nepali language for better understand ability for the patients and consumers for data collection.
4. Questionnaire for interviewing stakeholders in Department of Drug Administration (DDA) (annex-8).