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A study on assessment of knowledge about adverse drug reactions

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ABSTRACT

Adverse drug reaction (ADR) monitoring activity is in infancy in India. This study was conducted to determine the level of awareness of Health Care Professionals (HCP) about ADR reporting and extent of their involvement in pharmacovigilance activities. A questionnaire containing 19 questions was distributed to the teaching faculties, physicians, nurses and students of the study setting. The response rate of faculties, physicians, nurses and students for the questionnaire in phase-I were found to be 66.67, 40, 66.67 and 73.33 percent respectively. But the response rates were remarkably increased in the phase-II when compared with phase-I study viz 100 percent from faculties and students, 93.33 percent from physicians and 86.67 from nurses. Almost all the participants said that ADR monitoring was done in their institution. Majority of the participants said that ADR should be reported if it causes both inconvenience and death to the patients. In our study, Physician (93%) know the objectives of ADRs monitoring very well in phase-II, when compared with phase –I study (75%) which is followed by faculties (83), nurses (77%) and students (73%). Spontaneous reporting of ADRs denoted by all faculties, 93 percent physician, 80 percent students and 77 percent nurses in phase II study. All participants in the phase-II survey know any one method to monitor ADRs but in phase-I, 10 percent nurses and 9 percent students do not know about any one method of monitoring ADRs. Lack of knowledge about ADR reporting center is the mainstay in under-reporting or non-reporting of observed ADRs noted by only 6.67 percent of faculties, 19.23 percent nurses and 10 percent students. The reasons for underreporting was very much reduced in phase-II than in phase-I.

Keywords: Adverse drug reactions, knowledge, health care professionals, underreporting, barriers

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INTRODUCTION

India became a collaborating member of the WHO-ADR monitoring programme 30 years after its establishment. The pattern of drug use and ADRs in India is quite different due to the socio-economic, ethnic, nutritional and other factors. The Controller General of India (DCGI) and Indian Council of Medical Research (ICMR) have established ADR monitoring centers in many hospitals in major cities of India. Despite these efforts and the presence of a large number of tertiary care facilities, pharmacovigilance is still in its infancy. Gross Under reporting of ADRs is a cause of concern, the reasons for which may be due to lack of trained staff and lack of awareness regarding detection, communication and spontaneous monitoring of ADRs. As many physicians are not aware of importance of monitoring and reporting of ADRs, they may be under reported [1].

Spontaneous reporting of ADRs would enhance monitoring and evaluation activities related to drug safety. To improve the pharmacovigilance activities in India, the Ministry of Health and Family Welfare had initiated the National Pharmacovigilance Programe (NPP) on 1 January 2005 which was further reviewed in July 2010. This program is overseen by Central Drugs Control Organization (CDSCO), New Delhi. ADR reports will be collected at

the Monitoring centers which will then be dispatched to the coordinating center as per the standard operating procedures. The coordinating center will conduct causality assessment and upload the reports into the pharmacovigilance software. Lastly, the integrated ADR data will be transmitted through vigiflow software interface into the Uppsala Monitoring Center's ADR database where signal processing can be carried out [2].Recently, the Medical Council of India has recommended teaching of ADR monitoring to the undergraduate (UG) students [1]. We therefore studied the knowledge, attitude and practices (KAP) of Final year UG students and Health Care Professionals (HCP) (Physicians, nurses, pharmacist, faculty) towards the recording and reporting of ADRs. The primary objectives of this study were to assess the knowledge, attitude and skills of HCP regarding Pharmacivigilance and spontaneous reporting of ADR, to identify the reason for under-reporting and to suggest methods for improvement in the current spontaneous ADR reporting system.

Objectives of the current prospective observational spontaneous reporting study were to study the pattern and extent of occurrence of ADRs in the hospital, to analyze the ADRs reporting behaviors in health care professionals, to analyze the knowledge about ADRs in health care professionals, to analyze and compare the ADRs reported by health care professionals and to analyze the barriers involved in non-reporting of suspected ADRs.

MATERIALS AND METHODS

Study Site: The study was carried out at 800 bed private corporate multi-specialty tertiary care hospital, which has all facilities under one roof. All department of the hospital were included in this study, which has the potential of adverse drug reactions.

Study Design: Prospective, observational, spontaneous reporting study with both active and passive methods: a) Active method: Pharmacist actively looking for suspected ADRs, b) Passive method: Stimulating prescriber to report suspected ADRs

Study period: The study was carried for a period of one year between July 2011 and June 2012. Ethical committee clearance was obtained from the KMCH Ethics Committee to carry out the study in the hospital patients (Ref. No: EC/AP/103/09-2009).

Inclusion / Exclusion Criteria: Prescribers, nurses, pharmacist, patients and their volunteers of the hospital were included in the study. ADRs report of patients who develop an ADR due to accidental or intentional poisoning, ADR due to fresh blood or blood products, ADR due to over dose, patients with drugs abuse and intoxication are excluded from the study.

ADRs Notification and documentation form: Separate ADRs notification and documentation form was designed which consists of all relevant data including patient's demographic details, all drugs the patients received prior to onset of reaction, their route of administration, respective dosage, frequency, date of onset of reaction and the patient's allergy status to drugs and foods, ADRs management, details of reporter, etc. This form was made available in all nursing stations of the hospital and the out-patient areas for easy access to all healthcare professionals. It has two fold advantages; primarily to serve as an official medium of reporting back to the healthcare professional with necessary information pertaining to the suspected ADRs reported. Secondly, it as a method is to encourage their continuous reporting of suspected ADRs.

Assessment of Causality:
The extent of relationship between suspected ADR and the drug therapy was assessed using the WHO Probability assessment scale [3]. It was further classified into Certain, Probable/likely, Possible, Unlikely, Conditional/unclassified and Un-assessable/unclassifiable. The causality relationship between a drug and suspected reaction was established by using the Naranjo's causality assessment scale [4], further the causal relation were classified into Definite, probable, possible, and unlikely. It consists of 10 questions, Yes, No and Not known are the three options, based on this Definite > or equal to 9, Probable 5-8, Possible 1-4 and Unlikely < or equal to 0 were determined.

Assessment of Severity and Preventability:
Severity of the reaction was assessed by using the Modified Hartwig and Siegel Severity assessment scale [5] and the severity is broadly categorized in to "mild", "moderate" and "severe" for each ADR. All the reported ADRs

were assessed for their preventability using the modified criteria of Schumock and Thornton's by Lau et al. [6] and were categorized into "Definitely preventable", 'probably preventable" and "not preventable"

Preparation, implementation of questionnaire and assessment of knowledge about ADRs and Reason(s) for not reporting by HCP

A questionnaire was prepared and developed which contains 19 different questions; the first 8 questions were focused to assess the knowledge about ADRs among Health Care Professionals (HCP) [7], and the rest of 11 questions were focused to assess the reason for not reporting ADRs. The prepared and developed questionnaire was distributed to the prescribers of the study hospital, teaching faculty of the institution and final year undergraduate students of the study settings. The questionnaire was distributed twice, that is before implementing the study in the hospital and after implementing the study with an interval of one year duration. In the mean time, ADRs notification form, ADRs alert card, were prepared and implemented. Respondents were requested to fill the answer for the simple questions in front of the clinical pharmacist. Sufficient time was given to complete the questionnaire. Finally the filled questionnaire was collected for analyzing knowledge about ADRs and the reason for not reporting suspected ADRs.

Data analysis, interpretation and statistical analysis:

The collected data were analyzed for its appropriateness and suitability. The interpretation was made for the collected data. Finally statistical analysis was performed with SPSS software, version17.0. P-values <0.05 were considered to be statistically significant. From the data analysis, results were obtained and conclusion was drawn.

RESULTS

In the current study, the severity of suspected ADRs were assessed by using the modified Hartwig and Siegel Severity assessment scale, it revealed that majority of the suspected ADRs were found to be moderate (n=583; 61.37%). Mild ADRs were found to be 308 (32.42%), which is followed by severe ADRs. 4 (0.42%) lethal effects were observed in the study patients. Causality assessment was used to describe the causal relationship between offending drugs and the reaction and it was done by using the Naranjo's causality assessment scale and shown that 20 (2.11%) ADRs were definitely related to drugs, 759 (79.89%) ADRs were probably related to drugs, 165 (17.37%) ADRs were possibility related to drugs and 6 (0.63%) ADRs were unlikely related to drugs.

Probability of the suspected ADRs were assessed by using the WHO probability assessment scale and revealed that 22 ADRs were certain, 758 ADRs were probable or likely, 160 ADRs were possible, 5 ADRs were unlikely, 5 ADRs were un-assessable or unclassifiable and none of the ADRs was conditional or unclassified. Preventability of the suspected ADRs were assessed by using the Schmock and Thornton criterion modified by Lau, et al. and showed that 384 (40.42%) ADRs were definitely preventable. Probably preventable ADRs were 294 (30.95%) and 272 (28.63) ADRs were identified as not-preventable. Management of ADRs in the study population shown that in 89.89 (n=854) percent of patients, the offending drug was withdrawn, dose was altered in 10.11 (n=96) percent of the patients.

In this prospective observational spontaneous reporting study, pharmacist played a major role in reporting the suspected ADRs. Pharmacist reported the most number of ADRs in this study it was around 40.18 (n=493) percent of ADRs, next to pharmacist the nurses reported good percent of ADRs (n=310; 25.26) that is one fourth of the ADRs were reported by nurses and prescriber reported 13.04 (n=160) percent of ADRs. Patients reported 7.82 (n=96) percent of ADRs but more than this their volunteers reported 11.65 (n=143) percent of ADRs. Other peoples reported only 2.04 (n=25) percent of ADRs in this study.

Regarding the mode of reporting of suspected ADRs (n=1227), 1131 ADRs were reported through ADRs notification or reporting form, 46 ADRs were reported through referral mode and 20 ADRs were reported through telephone. 30 ADRs were reported through direct contact with the pharmacist. A total of 1227 ADRs were reported, from this 950 ADRs were accepted and the rest of reports were not accepted due of lack of information or the reactions were not coming under the category of ADRs. In this accepted ADRs (n=950), 887 ADRs were reported through ADRs notification or reporting form, 22 from referral mode and 12 ADRs reported through telephone. From the 30 ADRs reported by direct contact, 29 ADRs were accepted.

A questionnaire was developed to assess the knowledge about ADRs among the Health Care Professionals (HCPs), teaching faculties, nurses and students of the study settings. The developed questionnaire was distributed by direct approach with the HCPs, teaching faculties, nurses and students, they were requested to fill and return the questionnaire. Enough time was given to fill the answer in the questionnaire and finally the filled or completed questionnaire were collected. The questionnaire was distributed two times, one at the time of beginning of Phase-I study and the second at the end of Phase-II study. The response rate was found out by dividing the number approached by number responded with filled questionnaire.

In the phase-I, 30 faculties of the pharmacy college was approached and 20 were responded well with the filled questionnaire, 20 physicians were approached and 8 responded well. Thirty nurses and 30 students were approached to fill the questionnaire, 20 nurses and 22 students were responded with the filled questionnaire. The response rate of faculties, physicians, nurses and students were found to be 66.67, 40, 66.67 and 73.33 percent respectively. In the phase-II, 30 faculties of the pharmacy college were approached and all are responded well with the filled questionnaire, 30 physicians were approached and 28 were responded well. Equal number (n=30) of nurses and students were approached to fill the questionnaire in the phase-II, 26 nurses and 30 students were responded and returned the filled questionnaire with the response rate of 86.67 and 100 percent respectively. The response rates were remarkably increased in the phase-II when compared with phase-I study.

The demographic study of respondents revealed that in the Phase-I study, 33 were male and 37 were female; 5 respondents were Undergraduate (UG) teachers and 15 were Postgraduate (PG) teachers; 22 respondents were UG students and PG students were not included in this study. 42 respondents were found to have undergraduate qualifications and 28 were Postgraduates.

A good response was observed in the Phase-II study, in which 72 respondents were male and 42 were female; only 4 were UG teacher and 26 were PG teachers. Undergraduate students were found to be 30 and PG students were not included. Respondents with educational qualification revealed that, 55 were undergraduates and 59 were postgraduates. A questionnaire was prepared to assess the knowledge about ADRs among Health Care Professionals (HCP), which contains 19 different questions; the first 8 questions were focused to assess the knowledge about ADRs and the rest of 11 questions were focused to assess the reason for not reporting ADRs.

In the phase-I study, 8 (40%) faculties, 3 (37.5%) physicians, 1 (5%) nurse and 6 (27.27%) students wrote correct definition for ADRs. 6 (30%) faculties, 1 (12.5%) physician and 9 (40.90%) students classified the ADRs and none of the nurses classified correctly. Regarding the objectives of ADRs monitoring, 12 (60%) faculties, 6 (75%) physicians, 16 (80%) nurses and 12 (54.5%) students noted that ADRs were monitored to identify quickly important or serious ones and give early warning to concerned authorities; 5 (25%) faculties, 2 (25%) physicians, 1 (5%) nurse and 5 (22.72%) students reported that ADRs monitoring for attempt to establish a cause–effect relationship between drug and reaction; 3 (15%) faculties and 3 (13.63%) students reported that ADRs monitoring were done to find out the incidence of particular reaction. Three (15%) nurses and 2 (9.09%) students replied that they do not know about the objectives of ADRs monitoring.

Regarding the monitoring methods of ADRs, 14 (70%) faculties, 7 (87.5%) physicians, 11 (55%) nurses and 7 (31.81%) students noted the spontaneous reporting system is used for ADRs monitoring; 4 (20%) faculties, 6 (30%) nurses and 11 (50%) students mentioned that intensive monitoring for a particular drug; 1 (5%) faculty and 2 (9.09%) students mentioned cohort or case control study; Randomized trials was reported by 1 (5%) faculty, 1 (12.5%) physicians and 1 (5%) nurse. 2 (10%) nurses and 2 (9.09%) students do not know about the ADRs monitoring methods. Twenty (100%) faculties, 8 (100%) physicians, 15 (75%) nurses and 22 (100%) students know the present status of ADR monitoring in the hospital. Only 5 (25%) nurses don't know about the present status of ADR monitoring in the hospital. Twenty (100%) faculties, 8 (100%) physicians, 15 (75%) nurses and 21 (95.45%) students answered 'Yes' for the question ADR monitoring should be done routinely for better patient care. 5 (25%) nurses and 1 (4.55%) answered 'No' for the same question.

One (5%) faculty, 1 (12.5%) physician, 1 (5%) nurse and 2 (9.09%) students answered ADR should be reported if it causes inconvenience to the patient; 3 (15%) nurses replied it should be reported when it cause death of the patient; 19 (95%) faculties, 7 (87.5%) physicians, 16 (80%) nurses and 20 (90.90%) students replied ADRs should be reported if it causes both inconvenience and death of the patient. Three (15%) faculties, 3 (37.5%) physicians, 9 (45%) nurses and 4 (18.18%) students mentioned ADR should be reported to head of the unit or department,

whereas 10 (50%) faculties, 3 (37.5%) physicians, 5 (25%) nurses and 6 (27.27%) students mentioned it should be reported to department of pharmacy practice of pharmacology. National ADR monitoring center was reported by 3 (15%) faculties, 2 (10%) nurses and 4 (18.18%) students but not even a single physician mentioned these centers. Four (20%) faculties, 2 (25%) physicians, 2 (10%) nurses and 7 (31.81%) students mentioned WHO ADR monitoring cell (regional office) to report an ADR but 2 (10%) nurses and 1 (4.55%) student replied they don't know where to report an ADR.

In the reason for not reporting of suspected or observed ADRs, Five (25%) faculties, 2 (25%) physician, 15 (75%) nurses and 2 (9.09%) students told not aware of pharmacovigilance programme. 15 (75%) faculties, 6 (75%) physicians, 5 (25%) nurses and 20 (90.90%) students were aware about the pharmacovigilance programme. Nine (45%) faculties, 6 (75%) physicians, 11 (55%) nurses and 14 (63.63%) students replied they will report the observed ADR. 11 (55%) faculties, 2 (25%) physician, 9 (45%) nurses and 8 (36.36%) students do not report the observed ADRs. Twelve (60%) faculties, 3 (37.5%) physician, 17 (85%) nurses and 12 (54.54%) students don't know the National Monitoring Center (NMC) or Regional Monitoring Center (RMC) to report ADRs. Eight (40%) faculties, 5 (63.5%) physicians, 3 (15%) nurses and 10 (45.45%) students have knowledge about the National or Regional Monitoring Center as reporting centers. Eight (40%) faculties, 5 (63.5%) physicians, 2 (10%) nurses and 14 (63.63%) students were aware of ADR reporting center in Coimbatore and the rest of participants were not aware about the reporting center.

Six (30%) faculties, 2 (25%) physicians, 2 (10%) nurses and 6 (27.27%) students told we have phone number and address of National Pharmacovigilance Programme (NPP) reporting in their organization. Fourteen (70%) faculties, 2 (25%) physicians, 11 (55%) nurses and 17 (77.27%) students mentioned we have set procedure of ADR reporting in their organization. Each of 6 faculties and physician, 9 nurses and 16 students mentioned do not have set procedure of ADR reporting. Twelve (60%) faculties, 6 (75%) physicians, 18 (90%) nurses and 16 (72.72%) students were not reporting the suspected ADR due to lack of knowledge about center. Seventeen (85%) faculties, 4 (50%) physicians, 16 (80%) nurses and 17 (77.27%) students were uncertain about the drug causing ADR. Two (10%) faculties, 1 (5%) nurse and 4 (18.18%) students' feel all ADRs are well known to them. Six (30%) faculties, 4 (50%) physicians, 7 (35%) nurses and 7 (31.812%) students replied they have ADR reporting form. (Table: 1).

We had a tremendous response from the participants for the questionnaire in the Phase-II. In this phase-II, 27 (90%) faculties, 21 (75%) physicians, 14 (53.85%) nurse and 25 (83.33%) students wrote correct definition for ADRs. 22 (73.33%) faculties, 24 (85.71%) physicians, 15 (57.69%) nurses and 21 (70%) students wrote the exact classification of ADRs. Regarding the objectives of ADRs monitoring, 25 (83.33%) faculties, 26 (92.86%) physicians, 20 (76.92%) nurses and 22 (73.33%) students were reported that ADRs were monitored to identify quickly important or serious ones and give early warning to concerned authorities; 3 (10%) faculties, 2 (7.14%) physicians, 5 (19.23%) nurses and 4 (13.33%) students reported that ADRs monitoring for attempt to establish a cause–effect relationship between drug and reaction; 2 (6.67%) faculties, 1 (3.85%) nurse and 2 (6.67%) students reported that ADRs monitoring were done to find out the incidence of particular reaction. 1 (3.33%) faculty and 2 (6.67%) students replied that they do not know about the objectives of ADRs monitoring.

Regarding the monitoring methods of ADRs, all 30 (100%) faculties, 26 (92.86%) physicians, 20 (76.92%) nurses and 24 (80%) students noted the spontaneous reporting system is used for ADRs monitoring; 2 (7.14%) physician, 4 (15.38%) nurses and 4 (13.33%) students mentioned that intensive monitoring for a particular drug; 1 (3.85%) nurse and 1 (3.33%) student mentioned cohort or case control study; Randomized trials was reported by 1 (3.85%) nurse and 1 (3.33%) student. No one made comment on the do not know about the ADRs monitoring methods. All thirty (100%) faculties, 28 (100%) physicians, 22 (84.62%) nurses and 25 (83.33%) students know the present status of ADR monitoring in the hospital. Only 4 (15.38%) nurses and 5 (16.67%) students don't know about the present status of ADR monitoring in the hospital.

All Thirty (100%) faculties, 28 (100%) physicians, 26 (100%) nurses and 30 (100%) students answered 'Yes' for the question ADR monitoring should be done routinely for better patient care. Two (6.67%) faculties, 2 (7.69%) nurses and 3 (10%) students answered ADR should be reported if it causes inconvenience to the patient; 2 (6.67%) faculties, 4 (15.38%) nurses and 2 (6.67%) students noted it should be reported when it cause death of the patient; 26 (86.67%) faculties, 28 (100%) physicians, 20 (76.92%) nurses and 25 (83.33%) students answered ADRs should be reported if it causes both inconvenience and death of the patient. Ten (33.33%) faculties, 2 (7.15%) physicians, 5 (19.23%) nurses and 10 (33.33%) students answered ADR should be reported to head of the unit or department,

whereas 20 (66.67%) faculties, 10 (35.71%) physicians, 10 (38.46%) nurses and 30 (100%) students replied it should be reported to department of pharmacy practice of pharmacology. National ADR monitoring center was reported by 25 (83.33%) faculties, 25 (89.29%) physicians, 15 (57.69%) nurses and 25 (83.33%) students. All thirty (100%) faculties, 28 (100%) physicians, 15 (57.69%) nurses and 28 (93.33%) students mentioned WHO ADR monitoring cell (regional office) to report an ADR but 2 (6.67%) students replied they don't know where to report an ADR.

In the reason for not reporting of suspected or observed ADRs in Phase-II study, only 2 (7.69%) nurses and 3 (10%) students do not have awareness of pharmacovigilance programme. But all thirty (100%) faculties, 28 (100%) physicians, 24 (92.31%) nurses and 27 (90%) students were aware about the pharmacovigilance programme. All our respondents agreed they will report the observed ADR. Thirty (100%) faculties, 28 (100%) physicians, 22 (84.62%) nurses and 25 (83.33%) students have knowledge about the National Monitoring Center (NMC) or Regional Monitoring Center (RMC) as reporting centers but 4 (15.38%) nurses and 5 (16.67%) students mentioned they don't know about reporting centers.

Thirty (100%) faculties, 28 (100%) physicians, 23 (88.46%) nurses and 28 (93.33%) students were aware of ADR reporting center in Coimbatore but 3 (11.548%) nurses and 2 (6.67%) students were not aware of ADR reporting center in Coimbatore to report the observed ADRs. Ten (33.33%) faculties, 5 (17.86%) physicians, 6 (23.08%) nurses and 8 (26.67%) students told they don't have phone number and address of National Pharmacovigilance Programme (NPP) reporting in their organization. Twenty (66.67%) faculties, 23 (82.14%) physicians, 20 (76.92%) nurses and 22 (73.33%) students told we have phone number and address of National Pharmacovigilance Programme (NPP) reporting in their organization.

Two (6.67%) faculties, 6 (21.43%) physicians, 3 (11.54%) nurses and 11 (36.67%) students mentioned we don't have set procedure of ADR reporting in their organization. Twenty eight (93.33%) faculties, 22 (78.57%) physicians, 23 (88.46%) nurses and 19 (63.33%) students mentioned we have set procedure of ADR reporting in their organization. Two (6.67%) faculties, 5 (19.23%) nurses and 3 (10%) students were not reporting the suspected ADR due to lack of knowledge about center. Twelve (40%) faculties, 15 (57.69%) nurses and 15 (50%) students were uncertain about the drug causing ADR. Eighteen (60%) faculties, 22 (78.57%) physicians, 14 (53.85%) nurses and 14 (46.67%) students' feel all ADRs are well known to them. All thirty (100%) faculties, 28 (100%) physicians, 26 (100%) nurses and 30 (100%) students replied they have ADR reporting form and none of the participants mentioned do not have ADR reporting form to report the suspected of observed ADRs (Table: 2).

DISCUSSION

In this study, the severity assessment of suspected ADRs by modified Hartwig and Siegel scale shown, majority of the suspected ADRs were moderate (n=583; 61.37%), followed by mild (n=308; 32.42%) and severe (n=55; 5.79%). These observations were consistent with other studies, the severity of ADRs was either moderate (urticaria, abnormal LFT) or severe (neutropenia) [8]. Most of the ADRs (96.5%) were moderately severe while 3 cases were severe in nature and were preventable. At least one in five patients was admitted to the hospital due to the severe ADRs and a small portion (0.07%) of patients died in Emergency department [9]. We observed some distinct findings from some other studies in that a higher percentage of patients with severe ADRs were male (44%) compared with patients with mild ADRs (38% male).[9] The degree of severity was minor in 72.9% of the reports, moderate in 22.4%, severe in 4.4%, and fatal in 0.3% (4 cases) [10].

In our study, 4 (0.42%) lethal effects were observed in the study patients, among this 3 (0.32%) from female and 1 (0.11%) from male patients, which is contrast to an study showed 28 (2.3%) patients died as a direct result of the index ADRs and gastrointestinal bleeding was responsible for 15 (54%) deaths, while aspirin in isolation or in combination with other drugs was implicated in 17 (61%) deaths [11].

Causality assessment was used to describe the causal relationship between offending drugs and the reaction and it was done by using the Naranjo's causality assessment scale and shown that 20 (2.11%) ADRs were definitely related to drugs, 759 (79.89%) ADRs were probably related to drugs, 165 (17.37%) ADRs were possibility related to drugs and 6 (0.63%) ADRs were unlikely related to drugs. Similar findings were noted from other studies also, most of the reported ADRs belonged to the category of probable (70%) followed by possible in 30% of the cases [12]. All ADRs were found to be probably related to the antibiotic administration [13]. Causality assessment

revealed that no reactions were certain or definite, 9 were probable and 52 were possible reactions [14]. Probability of the suspected ADRs were assessed by using the WHO probability assessment scale and revealed that 22 ADRs were certain, 758 ADRs were probable or likely, 160 ADRs were possible, 5 ADRs were unlikely, 5 ADRs were un-assessable or unclassifiable and none of the ADRs was conditional or unclassified. This is contrast to a study in that causality assessment showed 46% possible, 23% probable and 29% were un-assessable because the drug was unknown [15].

Preventability of the suspected ADRs were assessed by using the Schumock and Thornton criterion modified by Lau, et al. and showed that 384 (40.42%) ADRs were definitely preventable, among this 256 (26.95%) ADRs were present in female and 128 (13.47) in male patients; probably preventable ADRs were 294 (30.95%) in which 198 (20.84%) ADRs were identified in female and 96 (10.11%) ADRs in male patients; 272 (28.63) ADRs were identified as not-preventable and it was observed in 183 (19.26) female and 89 (9.37) male patients. These findings were similar to a study, of the 316 reported ADRs, majorities (56%) of the reaction were predictable and 33 % of the reactions were preventable [12]. The findings were different from other studies in that a majority of ADRs were not preventable (n=57; 79%) [15]. None of the ADRs were definitely probable, 84 ADRs were probable preventable and 12 ADRs were not preventable [16].

In our study, management of ADRs in the study population shown that in 89.89 (n=854) percent of patients the offending drug was and dose was altered in 10.11 (n=96) percent of the patients. In one study, the suspected drug was withdrawn in 90% of the cases, whilst no change was made with the suspected drug in 9% of the cases, and dose was altered in 1% of cases [12]. Fifty six percent of ADRs were managed by withdrawing the drug and altering of the dose, 43.75% of ADRs were treated with other drugs in another study [16].

In this prospective observational spontaneous reporting study, pharmacist played a major role in reporting the suspected ADRs. Pharmacist reported the most number of ADRs in this study it was around 40.18 (n=493) percent of ADRs, next to pharmacist the nurses reported good percent of ADRs (n=310; 25.26) that is one fourth of the ADRs were reported by nurses and prescriber reported 13.04 (n=160) percent of ADRs. Patients reported 7.82 (n=96) percent of ADRs but more than this their volunteers reported 11.65 (n=143) percent of ADRs. Other peoples reported only 2.04 (n=25) percent of ADRs in this study. Similar findings were observed in that clinical pharmacist reported 257 (45.6%) of the ADRs, nurses reported 204 (36.2%), and physicians reported 85 (15.1%) of the ADRs. The remaining 18 (3.2%) were reported by the patient or family members [17]. Out of 65 ADRs reported, 42 (64.6%) were identified and reported by physician and nurses, while the remaining 23 (35.4%) were identified and reported by clinical pharmacist [18].

Regarding the mode of reporting of suspected ADRs (n=1227), 1131 ADRs were reported through ADRs notification or reporting form, 46 ADRs were reported through referral mode and 20 ADRs were reported through telephone. 30 ADRs were reported through direct contact with the pharmacist. A total of 1227 ADRs were reported, from this 950 ADRs were accepted and the rest of reports were not accepted due to lack of information or the reactions were not coming under the category of ADRs. In this accepted ADRs (n=950), 887 ADRs were reported through ADRs notification or reporting form, 22 from referral mode and 12 ADRs reported through telephone. From the 30 ADRs reported by direct contact, 29 ADRs were accepted.

In the phase-I study of the questionnaire survey, 30 faculties of the pharmacy college were approached and 20 were responded well with the filled questionnaire, 20 physicians were approached and 8 responded well. Thirty nurses and 30 students were approached to fill the questionnaire, 20 nurses and 22 students were responded with the filled questionnaire. The response rate of faculties, physicians, nurses and students were found to be 66.67, 40, 66.67 and 73.33 percent respectively. In the phase-II, 30 faculties of the pharmacy college were approached and all are responded well with the filled questionnaire, 30 physicians were approached and 28 were responded well. Equal number (n=30) of nurses and students were approached to fill the questionnaire in the phase-II, 26 nurses and 30 students were responded and returned the filled questionnaire with the response rate of 86.67 and 100 percent respectively. The response rates were remarkably increased in the phase-II when compared with phase-I study.

We developed a questionnaire to assess the knowledge about ADRs among health care professionals and to identify the barrier in reporting of suspected ADR. We had a tremendous and very good response for the questionnaire survey in phase-II study when compared with phase-I study. In the phase-I study, 40 percent faculties wrote correct definition of ADRs but in phase-II the percentage was increased to 90, this shows the ability of teaching faculties

towards improving and updating their knowledge and the interest in patient care. Next to faculties students have much knowledge about ADR (83%) followed by physician (75%) and nurses (54%) in phase-II study. 85 percent physicians, 73 percent faculties able to classify the ADRs in phase-II, this percentage was increased from the 12.5 and 30 percent respectively in phase-I.

Similar findings were observed in a study, about 68% of the nurses did not even know the correct definition of the term "pharmacovigilance" and most of the nurses in the study (79.0%) were not aware of what kind of ADR should be reported [19]. In another study, the overall knowledge of ADRs and pharmacovigilance activity was found poor in undergraduate medical students [20].

In our study, Physician (93%) know the objectives of ADRs monitoring very well in phase-II, when compared with phase –I study (75%) which is followed by faculties (83), nurses (77%) and students (73%). Another study stated identifying previously unreported ADR was the most important goal for ADR reporting in before and after the interventions of the study [21]. Lacking suspicion of an ADR could be a problem. There are doctors who believe that it is necessary to confirm the ADRs and they do not report anything if they are not completely sure about the causality assessment of the ADR. A problem in reporting is to establish a causality relationship between several drugs taken by patients and suspicions of adverse reactions [22].

Spontaneous reporting of ADRs is very essential in the current scenario, which is denoted by all faculties, 93 percent physician, 80 percent students and 77 percent nurses in phase II study. All participants in the phase-II survey know any one method to monitor ADRs but in phase-I, 10 percent nurses and 9 percent students do not know about any one method of monitoring ADRs. Almost all faculties and physicians know the present status of ADR monitoring in the hospital in both the phases. Twenty five percent of the nurses in Phase-I; 15.38 percent of nurses and 16.67 percent of students in phase-II reported ADR monitoring was not done presently at the hospital, this is the fact due to newly appointed nurses and fresher's in the pharmacy course don't know much about the routine work in the hospital. All the faculties, physicians in phase-I and all respondents in phase-II mentioned ADR monitoring should be done routinely for better patient care and it is essential for improving the health outcome of the patient.

All of our physicians stated ADR should be reported if it causes both inconvenience and death of the patient, because they know well about the necessary of ADR reporting when compared to faculties, students and nurses. Almost all of our respondents know very well, where to report an ADR but only 7 percent of the students do not know the reporting center. Lack of reporting is the main underlying cause to have reduced quality of life of the patient after experiencing and seeing a mild or moderate form of ADRs. Under-reporting of ADR may be associated with poor knowledge, attitudes and practices to pharmacovigilance [23].

In the current study, awareness about pharmacovigilance was created through regular monitoring of patients and their profiles with other HCPs, providing pamphlets, hand outs and thank you note to the reporter. In phase-II study, most of our participants were aware of pharmacovigilance programme when compared to phase-I study. Only 2 (7.69%) nurses and 3 (10%) students do not aware of pharmacovigilance programme in phase-II study. Consistent with our study, most doctors know about the pharmacovigilance programme, there are some who still do not. Many doctors are not acquainted with the objectives and potential usefulness of the pharmacovigilance programme. Many doctors think that barriers to contact and access to people working in the hospital pharmacovigilance system are an important problem in spontaneous reporting. A lack of reporting cards or forms for reporting is another problem that doctors described [22].

All our participants in the phase-II were accepted and reported the observed ADRs to the reporting centers. Majority of the participants know the national monitoring center or regional monitoring centers to report the suspected or observed ADRs, but 4 (15.38%) nurses and 5 (16.67%) students do not know the national monitoring center or regional monitoring centers to report the suspected or observed ADRs. All our faculties and physicians were aware of reporting centers in Coimbatore to report the observed ADRs, only 11 percent nurses and 7 percent students do not know the correct reporting centers.

Table 1 Assessment of knowledge about adverse drug reactions among Health Care Professionals, Faculties and Students in Phase-I

Questions	Answers	Faculties n=20(%)	Physicians n=8(%)	Nurses n=20(%)	Students n=22(%)
Definition	Correct	8(40)	3(37.5)	1(5)	6(27.27)
	Incorrect	6(30)	1(12.5)	9(45)	13(59.09)
	Partially correct	6(30)	3(37.5)	3(15)	3(13.63)
	Not attempted	0(0)	1(12.5)	7(35)	0(0)
Classification of ADRs	Correct	6(30)	1(12.5)	0(0)	9(40.90)
	Incorrect	8(40)	3(37.5)	3(15)	3(13.63)
	Partially correct	4(20)	0(0)	2(10)	9(40.90)
	Not attempted	2(10)	4(50)	15(75)	1(4.54)
Objectives of ADR Monitoring	Identify quickly important or serious ones and give early warning to concerned authorities	12(60)	6(75)	16(80)	12(54.5)
	Attempt to establish a cause –effect relationship between drug and reaction	5(25)	2(25)	1(5)	5(22.72)
	Find out the incidence of particular reaction	3(15)	0(0)	0(0)	3(13.63)
	Do not know	0(0)	0(0)	3(15)	2(9.09)
Monitoring methods	Spontaneous reporting	14(70)	7(87.5)	11(55)	7(31.81)
	Intensive monitoring for a particular drug.	4(20)	0(0)	6(30)	11(50)
	Cohort or case control study	1(5)	0(0)	0(0)	2(9.09)
	Randomized trails	1(5)	1(12.5)	1(5)	0(0)
	Do not know	0(0)	0(0)	2(10)	2(9.09)
Present status of ADR monitoring in your hospital	Done	20(100)	8 (100)	15(75)	22(100)
	Not done	0(0)	0(0)	5(25)	0(0)
ADR monitoring should be done routinely for better patient care	Yes	20(100)	8(100)	15(75)	21(95.45)
	No	0(0)	0(0)	5(25)	1(4.55)
ADR should be report if it causes	Inconvenience to the patient	1(5)	1(12.5)	1(5)	2(9.09)
	Death of the patient	0(0)	0(0)	3(15)	0(0)
	Both of the above	19(95)	7(87.5)	16(80)	20(90.90)
ADR should be report to	Head of the unit/dept	3(15)	3(37.5)	9(45)	4(18.18)
	Department of Pharmacy Practice/ Pharmacology	10(50)	3(37.5)	5(25)	6(27.27)
	National ADR monitoring center	3(15)	0(0)	2(10)	4(18.18)
	WHO ADR monitoring cell (regional office)	4(20)	2(25)	2(10)	7(31.81)
	Do not know	0(0)	0(0)	2(10)	1(4.55)
	REASON FOR NOT REPORTING ADRS				
Aware of pharmaco-vigilance	Yes	15(75)	6(75)	5(25)	20(90.90)
	No	5(25)	2(25)	15(75)	2(9.09)
Report observed ADR	Yes	9(45)	6(75)	11(55)	14(63.63)
	No	11(55)	2(25)	9(45)	8(36.36)
Knew NMC/ RMC as reporting centers	Yes	8(40)	5(63.5)	3(15)	10(45.45)
	No	12(60)	3(37.5)	17(85)	12(54.54)
Aware of ADR reporting center in Coimbatore	Yes	8(40)	5(63.5)	2(10)	14(63.63)
	No	12(60)	3(37.5)	18(90)	8(36.36)
Have phone number and address of NPP reporting in their organization	Yes	6(30)	2(25)	2(10)	6(27.27)
	No	14(70)	6(75)	18(90)	16(72.72)
Have set procedure of ADR reporting in their organization	Yes	14(70)	2(25)	11(55)	17(77.27)
	No	6(30)	6(75)	9(45)	5(22.72)
Non reporting due to lack of knowledge about center	Yes	12(60)	6(75)	18(90)	16(72.72)
	No	8(40)	2(25)	2(10)	6(27.27)
Uncertain of drug causing ADR	Yes	17(85)	4(50)	16(80)	17(77.27)
	No	3(15)	4(50)	4(20)	5(22.72)
Feel all ADRs are well known	Yes	2(10)	0(0)	1(5)	4(18.18)
	No	18(90)	8(100)	19(95)	18(81.81)
Have ADR reporting form	Yes	6(30)	4(50)	7(35)	7(31.81)
	No	14(70)	4(50)	13(65)	15(68.18)

Table 2 Assessment of knowledge about adverse drug reactions among Health Care Professionals, Faculties and Students in Phase-II

Questions	Answers	Faculties n=30(%)	Physicians n=28(%)	Nurses n=26(%)	Students n=30(%)
Definition	Correct	27 (90)	21(75)	14(53.85)	25(83.33)*
	Incorrect	0(0)	0(0)	5(19.23)	2(6.67)
	Partially correct	3(10)	4(14.29)	7(26.92)	3(10)
	Not attempted	0(0)	3(10.71)	0(0)	0(0)
Classification of ADRs	Correct	22(73.33)	24(85.71)	15(57.69)	21(70)*
	Incorrect	2(6.67)	0(0)	4(15.38)	3(10)
	Partially correct	4(13.33)	3(10.71)	7(26.92)	6(20)
	Not attempted	2(6.67)	1(3.57)	0(0)	0(0)
Objectives of ADR Monitoring	Identify quickly important or serious ones and give early warning to concerned authorities	25(83.33)	26(92.86)	20(76.92)	22(73.33)*
	Attempt to establish a cause –effect relationship between drug and reaction	3(10)	2(7.14)	5(19.23)	4(13.33)
	Find out the incidence of particular reaction	2(6.67)	0(0)	1(3.85)	2(6.67)
	Do not know	1(3.33)	0(0)	0(0)	2(6.67)
Monitoring methods	Spontaneous reporting	30(100)	26(92.86)	20(76.92)	24(80)*
	Intensive monitoring for a particular drug.	0(0)	2(7.14)	4(15.38)	4(13.33)
	Cohort or case control study	0(0)	0(0)	1(3.85)	1(3.33)
	Randomized trails	0(0)	0(0)	1(3.85)	1(3.33)
	Do not know	0(0)	0(0)	0(0)	0(0)
Present status of ADR monitoring in your hospital	Done	30(100)	28(100)	22(84.62)	25(83.33)*
	Not done	0(0)	0(0)	4(15.38)	5(16.67)
ADR monitoring should be done routinely for better patient care	Yes	30(100)	28(100)	26(100)	30(100)*
	No	0(0)	0(0)	0(0)	0(0)
ADR should be report if it causes	Inconvenience to the patient	2(6.67)	0(0)	2(7.69)	3(10)
	Death of the patient	2(6.67)	0(0)	4(15.38)	2(6.67)
	Both of the above	26(86.67)	28(100)	20(76.92)	25(83.33)*
ADR should be report to	Head of the unit/dept	10(33.33)	2(7.14)	5(19.23)	10(33.33)
	Department of Pharmacy Practice/ Pharmacology	20(66.67)	10(35.71)	10(38.46)	30(100)*
	National ADR monitoring center	25(83.33)	25(89.29)	15(57.69)	25(83.33)
	WHO ADR monitoring cell (regional office)	30(100)	28(100)	15(57.69)	28(93.33)*
	Do not know	0(0)	0(0)	0(0)	2(6.67)
	REASON FOR NOT REPORTING OF ADRS				
Aware of pharmaco-vigilance	Yes	30(100)	28(100)	24(92.31)	27(90)*
	No	0(0)	0(0)	2(7.69)	3(10)
Report observed ADR	Yes	30(100)	28(100)	26(100)	30(100)*
	No	0(0)	0(0)	0(0)	0(0)
Knew NMC/ RMC as reporting centers	Yes	30(100)	28(100)	22(84.62)	25(83.33)*
	No	0(0)	0(0)	4(15.38)	5(16.67)
Aware of ADR reporting center in Coimbatore	Yes	30(100)	28(100)	23(88.46)	28(93.33)*
	No	0(0)	0(0)	3(11.54)	2(6.67)
Have phone number and address of NPP reporting in their organization	Yes	20(66.67)	23(82.14)	20(76.92)	22(73.33)*
	No	10(33.33)	5(17.86)	6(23.08)	8(26.67)
Have set procedure of ADR reporting in their organization	Yes	28(93.33)	22(78.57)	23(88.46)	19(63.33)*
	No	2(6.67)	6(21.43)	3(11.54)	11(36.67)
Non reporting due to lack of knowledge about center	Yes	2(6.67)	0(0)	5(19.23)	3(10)
	No	28(93.33)	28(100)	21(80.77)	27(90)*
Uncertain of drug causing ADR	Yes	12(40)	0(0)	15(57.69)	15(50)
	No	18(60)	28(100)	11(42.31)	15(50)
Feel all ADRs are well known	Yes	18(60)	22(78.57)	14(53.85)	14(46.67)
	No	12(40)	6(21.43)	12(46.15)	16(53.33)*
Have ADR reporting form	Yes	30(100)	28(100)	26(100)	30(100)*
	No	0(0)	0(0)	0(0)	0(0)

** indicates the p<0.001*

Only 19 (45.2%) of the clinicians were aware of the existence of a pharmacovigilance centre and only 6 of them had reported ADRs to the Pharmacovigilance Centre. Only 28 (66.7%) felt that ADR reporting was necessary [24]. This finding was similar to our study in phase-I, but the awareness of clinicians or physicians increased in phase-II. Similar finding was observed in another study, in that 89 percent of responders were aware of existence of ADR

reporting and monitoring system at their hospital [25]. Many of our study participants told the organization having phone number and address of the national pharmacovigilance programme, and having set procedure for reporting ADR in the organization; the percentage was considerably increased from phase-I to phase-II. But in one study, 43 (41.35%) nurses agreed that their organization does not have set procedure of reporting ADR [26].

Lack of knowledge about ADR reporting center is the mainstay in under-reporting or non-reporting of observed ADRs noted by only 6.67 percent of faculties, 19.23 percent nurses and 10 percent students. The reasons for under-reporting was very much reduced in phase-II; 40 percent faculties, 58 percent nurses and 50 percent students told not sure or uncertain about drug causing ADRs, this indicates in depth of knowledge of drugs and their reactions are needed in these groups. A consistent results were found in one study and stated that the reasons of not reporting ADRs given by nurses were uncertainty about causal drug (49.04%), ADR is well known (40.38%), unawareness of ADR reporting centers (83.65%).[26] The physicians and nurses in this private hospital have insufficient knowledge about pharmacovigilance and ADRs reporting [27]. Education interventions also should be targeted at student pharmacists, who have been found to have inadequate knowledge of ADR reporting [28].

A study showed that the most frequently mentioned barrier to reporting were the ADRs assumed to be already known or uncertainty about the causal relationship between the ADRs and a drug and the reporting procedure being too time consuming [29]. The major barrier to ADR reporting was a lack of knowledge about ADR reporting processes. To increase ADR reporting rates, some participants suggested that educational interventions are needed from organizations and academia [30].

The spontaneous reporting system of the pharmacovigilance programme has contributed significantly to improve the ADR reporting rates worldwide. Nurses' attitude towards ADRs report and their practice need major change. Education and training can have a strong influence on knowledge and attitude towards reporting [24]. Most of participants answered 'No' for the question, feel all ADRs are well known? at phase-I, but in Phase-II the percentage was reduced much and most of them told 'Yes'. Increase of knowledge about ADRs among the HCPs increased the percentage of answering as 'Yes'.

In phase-I, only little percentage of the study participants reported they have ADR reporting form to report the suspected or observed ADRs. But in phase-II, all of our study participants have ADRs reporting form and answered 'Yes' to reach us 100 percent. This highlights the need for the encouraging medical practitioners to report suspected ADRs and therefore there is a greater potential for the pharmacists to increase the reporting rate of ADRs through creating awareness and educating the medical practitioners about the importance of reporting of ADRs. Underreporting of ADRs is a problem that should be taken seriously and given higher priority with regard to increasing the amount of knowledge [31].

The pharmacist is a key member of the health care team and is often the patient's main point of contact for health information and guidance. Continuing education and knowledge exchange are important tools for the pharmacists and most respondents indicate that they keep abreast of ADR related information through various sources. Pharmacists are particularly well equipped to recognize and report on ADRs, the entire focus of pharmacy training is almost exclusively on drugs, while knowledge of drugs forms a relatively small proportion of clinicians and nurse training [32]. The deficiencies in knowledge regarding ADRs and Pharmacovigilance need the urgent attention on priority basis, not only for the success of the Pharmacovigilance program but for the better clinical management of the patients in general [20]**.** The pharmacovigilance programme should take strong steps to motivate physicians and other HCPs for ADR reporting in order to increase the numbers [33]. There is an urgent need to do more research to improve the understanding of the barriers to report ADRs and overcome.

CONCLUSION

Adverse drug reactions are a significant cause of morbidity and mortality and contribute to the incidence of adverse events, resulting in increased healthcare costs. It is important to motivate health care professionals to understand their role and responsibility in the detection, management, documentation and reporting of suspected ADRs and all essential activities for optimizing patient safety. Patients were also considered responsible for the development of avoidable ADRs. Reasons for the improper use of prescribed medication may include poor understanding of instructions given by physicians during the consultation, by pharmacist at the time of dispensing, or contained in product information leaflets. Improved patient education would help minimize these patient attributable adverse

drug reactions. Dose adjustment according to the needs of individual patients and therapeutic drug monitoring can help to minimize these ADRs, and pharmacogenetics has the potential to identify patients at an increased risk of such problems. A thorough knowledge of ADRs and a well established ADRs reporting system will help to reduce the occurrence and the costs of avoidable ADRs related admissions.

A limitation of the study was that the rate of ADR related hospitalization was probably an underestimate because of underreporting or misclassification, because all ADRs possibly were not identified. The actual number of ADRs in the study population might also have been higher than the number of ADRs detected and reported during hospitalization because of relatively short length of stay in our hospital.

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