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Risk Evaluation inRoutine Pharmacovigilance Activities inSKIMS: Analysis of3 Years Data

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Abstract

Introduction: The study was undertaken for risk evaluation of ADR's from the wide spectra of drugs that are used in a tertiary care hospital.
Methods: Data from 1225 ADR's reported spontaneously to the center during the three year study period from 1-1-2012 to 31-12 2014 was used.
Results: The overall incidence of ADR's among inpatients that occurred during their stay in the hospital was 0.79%. The M: F ratio was 0.98 and maximum numbers of cases were seen in the 41-60 year age group. Majority of the ADR's (240, 20%) were assessed as probable on the W.H.O causality assessment scale and most of the reactions were classified as Type H (782; 64%). Severity assessment showed that majority of ADRs (832; 68%) were classified as mild. Eighteen fatal ADR's were reported, fourteen of which were attributed to pentavalent vaccine and one each to Ciprofloxacin, Levofloxacin, Cefixime and iodinated contrast. The commonest implicated drug class was antibiotics (632; 51.5%) followed by anticancer drugs (193; 15.8%), anticonvulsants (102; 8.3%). Medicine department reported the maximum number of ADRs (397; 32.5%). Rash and itching were the commonest reported ADR's and Vancomycin, levofloxacin and Ceftriaxone were the most commonly implicated drugs.
Conclusion: Drug safety signals will continue to come mainly from the reporting of alert health care professionals and every effort should be made to enhance and to ease this process. Continuous sensitization, training and feedback are needed for ensuring safe and effective use of drugs.
Keywords: Adverse Drug reactions (ADR's), Adversedrug reaction Monitoring Center (AMC), Individual case safety reports (ICSR's), Pharmacovigilance Programme of India (PvPI).

1. Introduction

Adverse drug reactions (ADRs) are iatrogenic diseases which may persist even after the offending drug has been withdrawn and largely eliminated and may vary in severity from mild to fatal. The aims of pharmacovigilance are to enhance patient care and safety in relation to use of medicines and to support public health programmes by providing balanced information for effective assessment of risk benefit profiles of medicines.[1] A Meta-analysis estimates the incidence of serious and fatal ADRs in hospital patients at 6.7% and 0.32%. This makes ADRs between 4th and 6th leading cause of death in USA.[2] In India a study carried in Mumbai in 2007 showed that 6.7% of hospital admissions were due to ADRs; 60% of which were avoidable. The median duration of hospitalization was 5 days and the average hospitalization cost incurred per patient was INR 6197/- (USD 150).[3] Adverse Drug Reaction problem is the outcome of a variety of factors e.g., availability of a large number of drugs to the doctors, the inability of any physician to be expertly informed on all aspects of new drugs, and the pressure by sales promoters to create a demand for the drug, canvassing by detail men and even colleagues, and the persuasion of patients themselves to use the new drugs on them promptly before much becomes known about the human toxicity of the drug.[4]ADRs are seen frequently in hospitals due to a combination of factors such as, complexity of diseases, drug interactions, poly-pharmacy and possible negligence.

WHO established its Programme for International Drug Monitoring in response to the thalidomide disaster in year 1961.[1] Together with the WHO Collaborating Centre for International Drug Monitoring, Uppsala, WHO promotes Pharmacovigilance at country level.As of December 2014, 120 countries have joined the WHO Programme for International Drug Monitoring, and in addition 28 'associate members' are awaiting full membership while compatibility

between the national and international reporting formats is being established.[5]

The Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the aegis of Ministry of Health & Family Welfare, Government of India in collaboration with the Indian Pharmacopeia Commission, has initiated a nationwide programme; Pharmacovigilance Programme of India (PvPI) in 2010. PvPI was started with enrolment of 22 ADR Monitoring Centres in 2010,at present ninety ADR Monitoring Centres are fully functionaland sixty new are under proposal, throughout the length and breadth of the country, in various MCI approved medical colleges and hospitals, autonomous institutes, public and corporate hospitals, Pharm D, pharmacy, dental and paramedical colleges.Target is to cover all medical colleges of country to recognise them as AMCs.21,000 plus reports were entered into Vigiflow through PvPI in the first year.

PvPI is to boost the spontaneous reporting of ADRs which is the most sensitive, powerful, cost effective way of identifying unknown drug related risks. The purpose of PvPI is to collect, collate and analyze data to arrive at an inference to recommend regulatory interventions, besides communicating risks to healthcare professionals and public.

In the Kashmir Division of J&K state ADR Monitoring Centre was established in the Department of Clinical Pharmacology SKIMS Srinagar under the PvPI in Jan. 2012. The functions of ADR monitoring centre are: - 1.Collection of ADR reports. 2. Perform follow up of the report to check completeness as per SOPs 3. Data entry into Vigiflow. 4. Reporting to National Coordination Centre through Vigiflow with the source data (original) attached with each individual case safety report (ICSR). 5. Training/ sensitization / feedback to physicians.

2. Material and Methods

Spontaneous ADR reports collected prospectively in the adverse drug reaction monitoring centre (AMC) SKIMS for 3 consecutive years from 1st Jan 2012 to 31st Dec. 2014 from inpatient departments were included. They were followed up to check completeness as per SOPs. The ADRs had already been uploaded on Vigiflow for communication to the National Coordinating Centre and thence to UMCSweden. Causalitywas assessed by the WHO scale.[6] The ADRs were classified according to Wills and Brown.[7] Severity of recorded ADR's was determined according to Hartwig *et al*.[8]No re-challenge was done in any case except when the drug was prescribed by the physician inadvertently without patient's history having elicited such a possibility of drug reaction.

2.1 Statistical Methods

Data is presented as numbers and percentage.

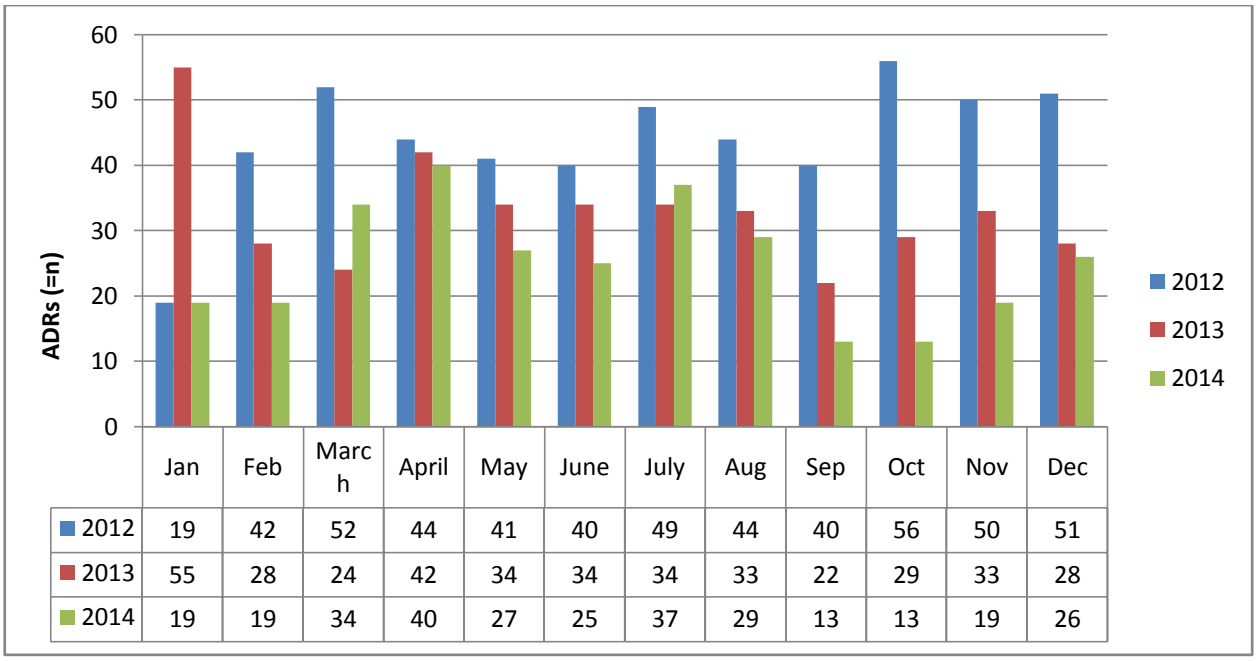
3. Results

During the study period 1225 ADRs were reported to the AMC SKIMS (Figure I). The total number of in-patient admissions during the same period was 1, 54,686 giving an incidence of 0.79% (Table I). Table 2 shows that females experienced a slightly higher incidence (618; 50.5 %) than males (607, 49.5 %). The frequency of ADR's increased with increase in age in an ascending order as depicted by age related analysis of frequency distribution except (147; 12%) were above 60 years as shown in Table II. Majority of the ADRS (887; 72.4%) were assessed as probable, (240, 20%) were assessed as possible and (86, 7%) ADRs were assessed as Unlikely/Unassessable/Unclassified. Only (12, 1%) ADRs were assessed as certain. (Table III)

Classification of the ADRs showed that (416; 34%) of the recorded ADRs were classified as Type A reactions, (782; 64%) were Type H, (14; 1.1%) ADRs were classified as Type U and (13; 1%) ADRs were classified as type C (Table IV). Severity assessment showed that majority of ADRs (832; 68%) were classified as mild; (368; 30%) were classified as moderate and (25, 2%) ADRs were classified as severe (Table V). Eighteendeaths were reported due to ADRs 14 of which were attributed to pentavalent vaccine and one each to ciprofloxacin, levofloxacin, cefixime and iodinated contrast. The cause of death was neurotoxicity and anaphylaxis. Most common class of drugs showing ADRs were antibiotics responsible for maximum number of cases(632; 51.5%) followed by anticancer drugs (193; 15.8%). anticonvulsants (102; 8.3%) antimanics (37; 3%), anti-tubercular drugs (30; 2.5%),blood and blood products (25, 2%),vitamins and supplements (22; 1.8%), steroids (21; 1.7%); NSAIDs (20; 1.6%) anticoagulants; (16, 1.3%). Other drugs collectively contributed to (127; 10%) of ADR reports (Table VI). There is no separate haemovigilance programme running at the Institute. Skin and mucosa was involved in (685; 56%) cases, followed by GIT (118; 9.6%), CNS (153; 12.5%); blood (98; 8%); kidney (92; 7.5%) endocrine/metabolic (30; 2.5%); CVS (24;2%); respiratory (18; 1.5%); ophthalmic (7; 0.6%) as shown in Table VII. Medicine department reported the maximum number of ADRs (397; 32.5%) followed by Medical Oncology (124; 10%); Clinical Pharmacology (123; 10%); Clinical Haematology (91; 7.5%), Paediatrics (67; 5.5%),Neurology (63; 5%),Plastic surgery (61; 5%), Cardiology(44; 3.6%), Nephrology (43; 3.5%), Surgery (42; 3.4%) and others (154, 12%).Sixteen cases (1.3%) were reported from outside SKIMS which were all related to pentavalent vaccine (Table VIII). Rash and itching

were the commonest ADR's reported and Vancomycin, levofloxacin and ceftriaxone were the commonest drugs implicated (Table IX).

Figure I: No. of ADR's Reported monthly from 1st Jan 2012 to 31st Dec. 2014



	Jan	Feb	March	April	May	June	July	Aug	Sep	Oct	Nov	Dec
2012	19	42	52	44	41	40	49	44	40	56	50	51
2013	55	28	24	42	34	34	34	33	22	29	33	28
2014	19	19	34	40	27	25	37	29	13	13	19	26

Table I: Incidence of Reported ADR's

Year	ADR's reported	Admissions(n)	(%)
2012	528	50312	1.05
2013	396	50332	0.78
2014	301	54042	0.55
Total	1225	154686	0.79

Table II: Demographic Distribution

Gender	(n)	(%)
Male	607	49.5
Female	618	50.4
Age		
<20	269	21.9
20-40	392	32.0
41-60	417	34.0
>60	147	12.0
Total	1225	

Table III: WHO Causality Assessment [6].

Causality	(n)	(%)
Certain	12	1.0
Probable	887	72.4
Possible	240	19.6
Unlikely	86	7.0

Table IV: Classification Based on type of Reaction (Wills & Brown scale [7])

Type	(n)	(%)
Type A	416	33.9
Type C	13	1.0
Type H	782	63.8
Type U	14	1.1

Table V: Severity of reported ADR's(Based on Hartwig Scale [8])

Severity	**(n)**	**(%)**
Mild	832	67.9
Moderate	368	30.0
Severe	25	2.0
Total	1225	
Deaths due to ADRs		
Drug	**(n)**	
Pentavalent	14	
Ciprofloxacin	1	
Levofloxacin	1	
Cefixime	1	
Iodinated Contrast	1	
Total	18	

Table VI: Class of drugs responsible for ADR's.

Drug class	**(n)**	**(%)**
Antibiotics	632	51.5
Anticancer	193	15.7
Anticonvulsants	102	8.3
ATT	30	2.4
Supplements	22	1.8
Antimaniacs	37	3.0
Steroids	21	1.7
Anticoagulants	16	1.3
NSAIDS	20	1.6
Blood & Blood Products	25	2.0
Others	127	10.3

Table VII: Organ system affected by reported ADR's

System	**(n)**	**(%)**
Skin & Mucosa	685	55.9
GIT	118	9.6
CNS	153	12.4
Blood	98	8.0
Kidney	92	7.5
CVS	24	1.9
Endocrine/Metabolic	30	2.4
Respiratory	18	1.5
Eye	7	0.5

Table VIII: Department wise No. of reported ADR's.

Department	**(n)**	**(%)**
Medicine	397	32.4
Medical Oncology	124	10.1
Cl. Haematology	91	7.4
Cl. Pharmacology	123	10.0
Nephrology	43	3.5
Paediatrics	67	5.5
Plastic Surgery	61	5.0
Surgery	42	3.4
Cardiology	44	3.6
Neurology	63	5.1
Others	154	12.6
Outside SKIMS	16	1.3

Table IX: - Commonly Reported ADR's and causative Drugs.

Rash	98	87	87	20	30	14	1	1	19	2	2	-	-	-	42	13	4	-	1	-
Itching	79	56	53	26	6	17	-	-	-	3	4	-	-	-	27	3	3	-	-	-
Sweating	9	3	7	4	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-
Fever	7	2	4		-	-	-	1	1	-	1	1	-	2	-	3	-	-	1	-
Chills	5	4	2	9	3	-	-	-	-	-		-	-	-	-	6	-	-	-	-
Breathlessness	2	2	2	3	-	-	-	-	-	-	1	-	-	-	-	4	-	-	-	-
Palpitation	4	4	-	2	-	-	-	-	-	1	-	-	-	-	1	-	-	-	-	-
Anaphylaxis	11	4	4	-	-	3	1	1	-	-	4	1	-	-	-	1	-	-	-	-
Marrow Depression	2	1	-	1	-	-	-	20	10	21	3	14	9	11	-	-	-	-	-	-
Thrombocytopenia	1	1	1	2	-	-	-	1	1		-	1	-	-	-	-	2	-	-	-
Mucositis	1	3	-	0	-	1	-	13		4	-	3	5	1	-	-	-	-	-	-
Vomiting	4	1	2	3	-	-	-	9	7	3	1	2	1	1	8	1	6	-	-	-
Diarrhoea	2	-	-	2	-	-	-	5	8	-	-	-	-	-	1	-	-	-	-	-
Hepatitis	-	-	-	-	2	-	-	-	-	-	-	-	-	-	-	-	14	-	-	-
Neurotoxicity	-	-	-	-	-	-	-	-	-	-	9	-	1	-	25	-	2	7	-	-
Nephrotoxicity	1	-	-	1	-	-	-	1	-	-	-	-	1	1	-	-	-	-	-	-
Pain at Inj. Site	1	3	-	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	-	-
SJS/ TEN	-	-	-	-	-	1	-	-	-	-	-	-	-	-	2	-	-	-	-	-
Redman syndrome	22	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Polyuria	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	15	-	-
Polydipsia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4	-	-
Gum Hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	18	-	-	-	-	-
Death	-	1	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	14	1
Total	249	172	162	73	41	37	3	52	46	34	25	23	17	17	124	32	31	26	16	1
	Vancomycin	**Levofloxacin**	**Ceftriaxone**	**Piperacillin/Tazobactam**	**Amoxicillin / Clavulanate**	**ciprofloxacin**	**Cefixime**	**Cisplatin**	**5 Flurouracil**	**Cyclophosphamide**	**L Asparaginase**	**Methotrexate**	**Vincristine**	**Daunorubicin**	**Phenytoin**	**Blood & blood products**	**Anti Tubercular**	**Lithium**	**Pentavalent vaccine**	**Iodinated contrast**

4. Discussion

Drug safety signals will continue to come mainly from the reporting of alert health care professionals and every effort should be made to enhance and to ease this process.[9] Spontaneous ADR reporting forms the backbone of Pharmacovigilance and is the most sensitive, powerful and cost effective way of identifying unknown drug related risks. Spontaneous reports are almost always submitted voluntarily. One of this system's major weaknesses is under-reporting[10] which may be as high as 98% for several clinical events believed to be associated with drug treatment,[11] though the figures vary greatly between countries and in relation to minor and serious ADRs. It has been a general observation worldwide that physicians do not routinely report ADRs and USFDA Med watch programme has attributed following reasons to under-reporting of ADRs by the Physicians:-[12]

1. Not part of regular routine - 20 %
2. Lack of time to complete ADR forms - 15 %
3. Inability to determine causality - 13 %
4. Most reactions are already reported and not unique -10%
5. Reporting to govt. agencies is too much work - 9 %
6. Responsibility rests with the attending physician -7%

1225 ADRs were reported to the AMC SKIMS for the stipulated period under assessment. The total number of in-patient admissions during the same period was 1,54,686 giving an incidence of 0.79%.A previous study shows that the median overall incidence of all in-patient adverse events was 9.2%, majority of these events were associated with surgical care provider, and more than half of events were operation or drug related.[13] The low incidence in our study could be because the system is largely spontaneous and no biochemical investigations and diagnostic tools were used to aid detection of ADRs.[14] The incidence estimated by a previous study at the same Institute in 2011 was only 0.2%.[15] The total number of ADR's reported annually is showing a downward trend probably because of the reasons as put forth by

W.H.O as limitations of spontaneous reporting. Although all the ADR reports received at the AMC are meant to be spontaneous and voluntary, the ICSR generation and its voluntary reporting by the health care providers was persistently encouraged and driven by the motivational efforts of the resident staff of Clinical Pharmacology department in general and the technical associates in particular who take daily round of all inpatient areas and interact with various cadres of health care providers and prescribers regarding ADR's and facilitate reporting as far as possible. Almost similar frequency of ADRs was seen in both the sexes. This finding is in contradiction with other studies where the incidence of ADRs has been showed to be higher in females,[16,17] though there are some studies[18] which show that sex has no influence on incidence rate of ADRs. Majority of ADRs reported (417; 34%) were seen in the age group of 41-60 (392; 32%). Although previous studies show large percentage of ADRs reported in geriatric and paediatric population,[19,20] the results are in agreement with some recent studies[15,16] and the reason could be that such age groups are more vulnerable to diseases like hypertension and diabetes and frequently visit physicians and take medicines. Patients above 60 years showed only (147; 12%) ADR's in the study probably due to either the number of reports was less or due to they being a special physiological group.

Majority of ADRs were classified as Type H (782; 63.8%) followed by Type A (416; 34%).Similar results have been shown by some other studies[17,22] although some studies report Type A reaction to be more common.[2] Fourteen ADRs were unclassifiable because the mechanism underlying them was not understood at present. Most of the reactions were classified as mild, (832; 68%) followed by moderate (368; 30%) and only (25; 2%) were severe. Similar results have been seen in the past.[15,21]Eighteendeaths were reported due to ADR's. The commonest offending drug class was antibiotics (632; 51.5%) followed by anticancer drugs (193; 15.8%), anticonvulsants (102; 8.3%) of reports. Similar pattern has emerged from some earlier studies from south India.[22] Skin, GIT and CNS were the most common organ systems affected by the ADRs as reported by Arulmani *et al*.[17]Medicine department reported maximum no of ADRs (397, 32.5%) similar to other studies.[21] Department of medicine has the highest number of admissions, use a wide variety of medicines or are better sensitized to the Pharmacovigilance programme.

4.1 Limitations ofthe Study

This study suffers the main drawback of spontaneous reporting system i.e. underreporting. Preventibility of the reported ADR's was not assessed and no biochemical investigation or diagnostic tool was used to aid detection of ADR's as data was collected using spontaneous reporting system as proposed by PvPI.

5. Conclusion

ADR monitoring is yet to be fully developed and implemented in India. There are two ADR monitoring centres functional in our state, one at SKIMS Srinagar and one at GMC Jammu. Two new centres are coming up; one at GMC Srinagar and other at Acharya Shri Chander College of Medical Sciences & Hospital. In the first three years 1225 ADR reports were entered into Vigiflow by AMC SKIMS mainly ADRs occurring among hospitalized patients. Twelve deaths suspected to be due to pentavalent vaccine were reported from children's hospital and peripheral health care of Kashmir division. India stands at 7th position among top ten countries contributing to global ICSR's safety database for the year 2013. Despite the limitations and variations in the study, data obtained from this research will be an invaluable feedback for health care professionals for their careful selection and therapeutic decision making including limiting use of antimicrobial agents. It may a beginning of more serious efforts on part of physicians to report each and every ADR they come across while administering the drugs in a tertiary care hospital where patients are exposed to large spectra of drugs. The pattern of ADRs reported in our hospital is comparable with the results of studies conducted in hospital set up elsewhere. AMC SKIMS will continue to sensitize/train and provide valuable feedback to physicians for ensuring safe and effective use of drugs.

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References

[1] Varghese S.S. Pharmacovigilance. *Hygeia. J. D. Med.* 2014; 6 (2):1-2.

[2] Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA.* 1998 Apr 15; 279(15):1200-5.

[3] KJ Patel, MS Kedia, D Bajpai, *et al.* Evaluation of the prevalence and economic burden of adverse drug reactions presenting to the medical emergency department of a tertiary referral centre: a prospective study.*BMC Clin Pharmacol.* 2007 Jul 28; 7:8.
[4] Bhargava KP. Mechanisms of ADRs. *Ind. J. Pharmacol*. 1972; 4(2): 35-50.
[5] Who-umc.org [homepage on the Internet].Pharmacovigilance: The WHO Programme, introduction to the WHO Programme for International Drug Monitoring [December 2014]. Available from: http://www.who-umc.org
[6] Edwards IR, Aronson JK. Adverse drug reactions: Definitions, diagnosis and management. *Lancet.*2000; 356:1255-9.
[7] Wills S, Brown DA. A proposed new means of classifying adverse drug reactions to medicines. *PharmJ* 1999; 262:163-5.
[8] Hartwig SC, Siegel J, Schneier PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm.* 1992; 49:2229-32.
[9] Edwards IR. Spontaneous ADR reporting and drug safety signal induction in perspective. *Pharmacol Toxicol*. 2000; 86Suppl 1:16-9.
[10] Hazell L, Shakir SA. Underreporting of adverse drug reactions: a systemic review. *Drug Saf.* 2006;29:385–96.
[11] Fletcher A. Spontaneous adverse drug reaction reporting vs event monitoring: a comparison. *J R Soc Med* 1991; 84:341-4.
[12] Chyka PA and McCommon SW. Reporting of adverse drug reactions by poison control centres in the US. *Drug Safety*. July 2000; 23 (1): 87-93.
[13] De Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: A systematic review. *Qual Saf Health Care.* 2008;17:216–23.
[14] Tandon VR, Khajuria V, Raina K *et al.* First Indian Study Evaluating Role of Biochemical Investigations and Diagnostic Tools in Detection of Adverse Drug Reactions. *J. Clin Diagn Res*. 2014 Sep; 8(9): HC23–HC26.
[15] Singh Surjeet, Wafai ZA. Adverse drug reaction monitoring in a tertiary care hospital SKIMS Srinagar. JK-Practitioner 2012; 17(1-3): 58-63.
[16] H Singh, N Dulhani, BN Kumar, P Singh, P Tewari, and K Nayak. A Pharmacovigilance Study in Medicine Department of Tertiary Care Hospital in Chhattisgarh (Jagdalpur), India. *J Young Pharm*. 2010 Jan-Mar; 2(1): 95–100.
[17] Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. *Br J Clin Pharmacol*. 2008 Feb; 65(2):210-6.
[18] Gor AP, Desai SV. Adverse Drug Reactions (ADR) in the in Patients of Medicine Department of a Rural Tertiary Care Teaching Hospital and Influence of Pharmacovigilance in Reporting ADR. *Indian J Pharma* 2008; 40; 37-40.
[19] Gonzalez-Martin G, Caroca CM, Paris E. Adverse drug reactions (ADR's) in hospitalized pediatric patients. A prospective study. *Int J Clin Pharmacol Ther* 1998 Oct; 36(10):530-3.
[20] Somers A, Petrovic M, Robays H, Bogaert M. Reporting adverse drug reactions on a geriatric ward: a pilot project. *Eur J Clin Phramacol* 2003 Feb; 58(10):707-14.
[21] Shrivastava M, Uchit G, Chakravarti A, Joshi G, Mahatme M, Chaudhari H. Adverse drug reactions reported in Indira Gandhi Government Medical College and Hospital, Nagpur. *J Assoc Physicians India*. 2011 May; 59:296-9.
[22] Padmaja U, Adhikari P, Pereira P. A Prospective Analysis of Adverse Drug Reactions in a South Indian Hospital *Online J Health Allied Scs*. 2009; 8(3):12.