DOI: 10.7860/JCDR/2014/8487.4907

Original Article

Pharmacology Section

Role of Biochemical Investigations and Diagnostic Tools in Detection of Adverse Drug Reactions

VISHAL R. TANDON[1], VIJAY KHAJURIA[2], KAPILA RAINA[3], VIVEK MAHAJAN[4], AMAN SHARMA[5] ZAHID GILLANI[6]

ABSTRACT

Aim of Study: To evaluate the role of biochemical investigations (BI) and diagnostic tools (DT) in ADR detection

Materials and Methods: An observational prospective cross-sectional study was done using suspected ADR data collection form.

Results: A total of 2381 ADR related events were recorded in two years. Total number/percentage of biochemical abnormalities (BA) related ADR detection rate was 14.57% and of DT was 1.091% in contrast to 84.33% recorded with clinical presentation. Maximum cases were inward patients (87.13%), 67.02% were recorded by active surveillance. ADR detection rate at one point & detection on follow up was 56.31% Vs 46.38%. ADR detection rate of ECG, endoscopy, X-ray were 0.57%, 0.22%, 0.22% and of CT scan, MRI, DEXA scan, USG and biopsy was 0.04% each. Maximum ADRs were severe/serious, latent and Type-A in nature. Anemia (4.6%), followed by liver dysfunction (2.8%), renal dysfunction, electrolyte imbalance, hyperglycemia (1.1% each), abnormal coagulation profile (1%), decrease platelet count (0.8%), hypoglycemia (0.7%) were the most common BAs. Anti retroviral drugs (ART), tirofiban and methotrexate accounted for anemia, ART and anti tubercular drugs for liver & renal dysfunction, insulin for hypoglycemia, tirofiban, paclitaxel, capecipabine and ifosfamide for thrombocytopenia, hematuria by enoxaparin & dyslipidemia with ART were common ADRs.

Conclusion: BI and DT can play very important role in ADR detection.

Keywords: Adverse drug reaction, Biochemical investigations, Diagnostic tools

INTRODUCTION

Adverse drug reactions (ADRs) account for considerable mortality, morbidity and in addition have immense economic impact on patients, health care providers and society at large [1]. Most of the ADRs are preventable [2]. Under reporting of ADRs is a big challenge in pharmacovigilance (PV) [3,4]. This is because primarily most of the countries follow spontaneous/voluntary system of ADR reporting including India.

There are patient and doctor related reasons for under-reporting. ADRs go unnoticed due to failure of medical teams to recognize ADR or correlate precisely with biochemical, pathological or radiological abnormalities [5].

However, intensive monitoring approach in PV amplifies the ADR detection [6]. Various approaches have been recommended to intensify the ADR reporting [7-13].

The role of biochemical investigation and various basic diagnostic tools like X-Ray, ECG, endoscopy, CT scan, MRI, DEXA, FNAC and ultra-sonography can be of immense value in picking up of various ADRs if active surveillance is carried out. However, their role in PV remains undermined. Moreover, there are various studies in the literature, where primarily clinical presentations have been used to describe trends of ADRs both from India [14-18] and Western world [19-22].

To best of our knowledge there exists no single study where the role of these valuable BI and DT in PV has been investigated. Hence, the first study of its kind was undertaken to underscore their role in ADR detection.

MATERIALS AND METHODS

An observational, cross-sectional prospective two year study was done in Adverse Drug Reaction Monitoring (ADRM) Centre, working under (PvPI) in a tertiary care teaching hospital from India w.e.f 1st November 2010 to 31st October 2012 using suspected ADR data collection form after IEC permission vide number Pharma/IEC/2014/3607/Research/6C/2012/2741.

The sample collection was based on both active surveillance and spontaneous ADR reporting.

Information about patient, suspected ADR, suspected medication and the reporter were recorded. Date of reaction, date of recovery and presentation of problem were also recorded. Suspected medication, name of drug, brand of manufacturer, generic name of manufacturer (if known), expiry date, dose used, route, frequency and therapy dates as well as reason for prescribing suspected drug were recorded. The information about de-challenge and re-challenge, concomitant medical treatment, the relevant laboratory biochemical investigation and various basic diagnostic tools like X-Ray, echocardiography (ECG), endoscopy, computed tomography (CT) Scan, magnetic resonance imaging (MRI), dual-energy X-ray absorptiometry (DEXA), and fine needle aspiration cytology (FNAC) were recorded separately. Other relevant history including pre-existing medical conditions like allergy, pregnancy, smoking and alcohol intake and any organ dysfunction was recorded. The seriousness of reaction, the outcome of reaction and onset time was recorded for every suspected ADR. The suspected ADRs were classified in term of causality using WHO-UMC scale as certain, probable, possible, unlikely, unclassified & unassessable and [23] using Naranjo scale as highly probable (score 9), probable (score 5-8), possible (score 1-4) and doubtful (score 0) [24].

Detailed subgroup analysis of ADRs detected by biochemical abnormality (BA) and diagnostic tools (DT) was carried.

STATISTICAL ANALYSIS

Analysis was carried out with the help of computer software SPSS Version 15 for windows.The data was expressed in number (n) and percentage (%). Chi-square test was applied for the parameters to prove their statistical significance. p-value < 0.05 was considered statistically significant.

Total Period of Study	2 years
Total number of ADR's reported	2242
Total number of ADR events	2381
Total number of Biochemical abnormality picked up as ADR	347
ADR Detection rate by biochemical investigations	14.57%
Total ADR picked up using Diagnostic Tools	26
ADR Detection rate by Diagnostic Tools	1.091%
Total Detection Rate	15.66%
Clinical Presentation(A) vs Biochemical Investigation(B) vs Diagnostic tools(C) detection rate A Vs B AVs C B Vs C	2008(84.33%) vs 347(14.57%)vs 26(1.09%) p<0.00001 ϖ^2 =2317.72, df-1 p<0.00001 ϖ^2 =3371.33, df-1 p<0.00001 ϖ^2 =299.73, df-1
Route of Drug Administration- Oral/I.V/ IM/SC	88.47%/2.6%/3.04%/5.89% p<0.00001 ϖ^2 =28680.72, df-3
Age wise classification-Adult, Geriatric & Pediatric	26.80% Vs 60.02% Vs 6.16% p<0.00000 ϖ^2 =6905.1, df-2
Sex Distribution- Male vs Female Ratio	1.69:1 p<0.000023 ϖ^2 =17.94, df-1
OPD VS Inward Patients	12.86% Vs 87.13% p<0.00000 ϖ^2 =11035.04, df-1
Urban vs Rural	67.02% Vs 32.97% p<0.00000 ϖ^2 =2317.44, df-1
One point detection Vs Detection on Follow up	53.61% Vs 46.38% p<0.00000 ϖ^2 =104.56, df-1
Specialty- Medicine/oncology/Chest Disease/ HIV Medicine/ Dermatology/ Rheumatology/others	53.61%/18.76%10.72%/8.04%/3.48%/ 2.68%/2.68% p<0.0000 ϖ^2 =12847.59, df-5
Severity of ADRS – Mild/ Moderate/ Severe/ Fatal	4.55%/ 18.49%/76.95%/0% p<0.00000 ϖ^2 =13209.74, df-2
Mode of onset – Sub acute/ Acute/ Latent	18.76%/4.55%/76.68% p<0.00000 ϖ^2 =13139.74, df-2
Nature of ADR- Serious vs Non serious	84.98% Vs 5.01% p<0.00001 ϖ^2 =14213.14, df-1
Type of reactions - A,B,C,D,E & Unclassified	92.49%/0%/7.50%/0%/0%/0% p<0.0000 ϖ^2 = 14448.05, df-5
Causality as per Naranjo's Scale - Definite/ Probable/Possible/Doubtful	0%/91.15%/8.84%/0% p<0.000000 ϖ^2 =13549.87, df-3
Causality as per WHO - UMC scale – Certain/Probable/Possible/Unlikely/ Unclassified/Un-assessable	0%/90.88%/9.11%/0%/0% p<0.00000 ϖ^2 =13372.67, df-5
Outcome of the ADRs - Recovered/ Recovering/Continuing	0%/80.42/19.57% p<0.0000 ϖ^2 =7405.45, df-2
Management of ADRs - Intervention required Vs No Intervention Required	100%Vs 0%
Picked and correlated by- Clinician/ Biochemist/Radiologist/Pharmacologist	69.70%/0%/0%/30.29% p<0.00000 ϖ^2 =3106.30, df-3

[Table/Fig-1]: Role of biochemical abnormalities and diagnostic tools in adr detection
Chi-Square test p<0.05 considered significant

RESULTS

A total 2242 ADR's and 2381 ADR related events were reported in a period of two year. Total percentage of BA related ADR detection rate was 14.57% and of DT was 1.091% in contrast to 84.33% recorded with clinical presentation. Clinical presentation significantly contributed more in comparison to biochemical investigations and various diagnostic tools with p<0.0001 in ADR detection. However, biochemical investigations contributed substantially and statistically more p<0.0001 in comparison to DT in ADR detection [Table/Fig-1].

ADR detection rate with ECG, endoscopy, X-ray, was 0.57%, 0.22%, 0.22%, while with CT scan, MRI, DEXA scan, USG and biopsy were the detection rate was 0.04% each [Table/Fig-2].

Diagnostic Tool	Findings	No
X-ray 0.22%	Deflazacort induced TB consolidation	2
	Prednisolone induced TB consolidation	1
	Hydroxychloroquine+methotrexate+sulfasalazine induced TB consolidation	1
	Methotrexate+sulfasalazine+leflunamide induced TB consolidation	1
CT 0.04%	Prednisolone induced osteoporosis	1
MRI 0.04%	Prednisolone induced osteoporosis	1
(DEXA) scan 0.04%	Methyl prednisolone induced osteoporosis	1
Endoscopy 0.22%	NSAID's induced upper GI bleed	5
ECG 0.57%	Digoxin induced bradycardia	1
	Acute Pancreatitis-ATT induced	1
	Carbamazepine induced hyponatremia and electrolyte imbalance leading to IHD Metoprolol induced Bradycardia Digoxin Induced Arrhythmia	1 7 1
Biopsy 0.04%	IgA nephropathy on tacrolimus and mycophenolate	1
USG 0.04%	Acute Pancreatitis-ATT induced	1
Total		**26**

[Table/Fig-2]: Profile of ADRs detected by various diagnostic tools

Oral (88.47%) administration of drugs followed by subcutaneous 5.89%, intramuscular (3.04%) and intravenous route contributed (2.6%) for the total ADRs detected by BI & DT. Age wise classification of total ADRs detected by BI & DT suggested geriatric population to be the largest contributor (60.02%) followed by adult (26.80%) & paediatric (6.16%) population. Male predominated in the study with male female ratio to be 1.68:1. Urban population was more in comparison to rural population 67.02% Vs 32.97% (p<0.00001). Maximum cases were picked up from inward patients (87.13%) in comparison to Out Patient Department (OPD) (12.86%) with p<0.00001. 67.02% and 32.97% with p<0.00001 of the total cases picked up by the BA and DT were by the medium of active surveillance in comparison to spontaneous reporting. ADR detection rates at one point was (56.31%) Vs detection on follow up (46.38%) however, varied significantly p<0.0000 among each other. Of the total ADR picked up by BA & DT 4.55, 18.49, 76.95, 0% was mild, moderate, severe and fatal in nature. 18.76%, 4.55% and 76.68% of the total ADRs picked up by BA&DT were sub acute, acute and latent as well as 84.98% and 5.01%. (p<0.00001) were serious and non serious in nature respectively. 92.49% and 7.50% were Type A and C reaction. Causality assessment of such reports both by Naranjo's (91.15%) and WHO UMC (90.88) scale showed maximum reactions to be probable. Type A & C 92.49% and 7.50% respectively. Till compilation of results 80.42 of the cases with ADR were recovering and 19.57% continuing at the time of collection of ADRs reports as well as 100% of ADRs required intervention.

Decreased hemoglobin (4.6%), followed by liver dysfunction (2.8%), renal dysfunction, electrolyte imbalance, hyperglycemia, 1.1% each were the most common BA in the current study [Table/Fig-3].

Anti retroviral drugs, tirofiban and methotrexate were the drugs maximally responsible for anemia. Anti-retroviral and anti-tubercular drugs were mainly responsible for liver dysfunction. Insulin was mainly responsible for hypoglycemia. Renal dysfunction was caused mainly by antitubercular drugs and injection ceftriaxone. Thrombocytopenia was mainly caused by anti cancer drugs like tirofiban, paclitaxel, capecipabine and ifosfamide. The detail of other drugs is shown in [Table/Fig-4].

ADR's With Altered Biochemistry	No. (Percentage) Out of Total ADR Events	No. (Percentage) Out of Total Picked by Biochemical Investigations
Decreased Hemoglobin	109(4.6)	109(31.41)
Liver Function Test (LFT) Dysfunction	66 (2.8)	66 (19.02)
Renal Function Test (RFT) Dysfunction	26 (1.1)	26 (7.49)
Electrolyte Imbalance	26 (1.1)	26 (7.49)
Increased Blood Sugar	25 (1.1)	25 (7.20)
Increased Prothrombin Time	24 (1.0)	24 (6.91)
Decreased Platelet Count	20 (0.8)	20 (5.76)
Decreased Blood Sugar	17 (0.7)	17 (4.89)
Increased Lipid	15 (0.6)	15 (4.32)
Increased Uric Acid	5 (0.2)	5 (1.44)
Decreased TLC Count	4 (0.17)	4 (1.15)
Raised ESR	3 (0.13)	3 (0.86)
Eosinophilia	2 (0.08)	2 (0.57)
Increased TSH	2 (0.08)	2 (0.57)
Decreased T3, T4	2 (0.08)	2 (0.57)
Increased CPK	1 (0.04)	1 (0.28)
Total	**34 7 (14.6)**	**347 (100)**

[Table/Fig-3]: Profile of ADR Detected by Abnormal Biochemical Investigations

DISCUSSION

Current PV programme worldwide is spontaneous/voluntary in nature. Thus, presently whatever literature exists regarding ADRs trends and pattern from India and western world primarily depend upon clinical manifestations [14-22]. However, the results of current study for the first time have indicated that BA & DT can contribute substantially in the ADR detection and thus contribute significantly in ADR detection. The study further endorses active surveillance approach and advocates the immense utility of biochemical tests and diagnostic investigations for intensified ADR detection.

Although, studies exist in the literature which recommends many strategies to intensify ADR detection like forming ADR reporting network within hospital [7] and patients directly reporting ADR [8,9]. Some have recommended compulsory ADR reporting by nurses [10]. Many research workers felt a need to improve knowledge and attitude for ADR reporting by healthcare professionals [11,12]. Even telephonic intervention help to intensify ADR reporting [13]. But to the best of our knowledge there exist no single study recommending close vigilance on BT and DT to help in intensifying the ADR detection. Intensive screening of the data and records of patient may help in overcoming biggest challenge of underreporting in current spontaneous/volunteer PV programme.

Maximum cases were picked up from inward patients in comparison to OPD patients indicating that inward patients if screened by the medium of active surveillance using biochemical investigations and diagnostic tools can prove to be a very important mode of ADR detection.

ADR detection at one point was more (56.31%) in comparison to detection on follow up (46.38%) indicating that follow up of the patient can further enhance ADR detection. As per specialty, ADR detection by BA & DT was maximally contributed by medicine department followed by oncology, chest disease, HIV medicine, dermatology, and rheumatology. The findings of current study endorse the finding

S.no	Biochemical abnormality	Most common suspected drugs (n=number of events)
1	Anemia	ART (29), Tirofiban (12), Methotrexate (11)
2	Jaundice	ATT (33), ART (5)
3	Hypoglycemia	Insulin (16)
4	Renal Dysfunction	ATT (12), Ceftriaxone (2)
5	Thrombocytopenia	Tirofiban (4), Paclitaxel (2),Capecitpabine (1),Ifosfamide(1)
6	Hematuria	Enoxaparin (13)
7	Dyslipidemia	ART (13)
9	Hyperglycemia	Deflazacort (3)
10	Hyperuricemia	Prednisolone (1), Torsemide(4), Pyrazinamide(4), Theophylline(1)
11	Hyperkalemia	Ramipril (3)
13	Hypokalemia	Insulin (3)
14	Hypothyroidism	Carbimazole (3)
15	Leucopenia	Anticancer Drugs (2)
16	Hyperthyroidism	Thyroxine (2)
17	Bone Marrow Suppression	Anticancer Drugs (2)
18	Oligozoospermia	Acyclovir (2)
19	Electrolyte Imbalance	Steroids (2)
20	Hypocalcemia	Phenobarbitone (1)
21	Hyponatremia	Furosemide(1)
22	Hypomagnesemia	Arsenic Trioxide(1)
26	Pancreatitis	ATT(1)
27	Haemolysis detected by abnormal coagulation profile	Acetaminophen (1)
28	Hypocalcemia	Phenobarbitone (1)
29	Arrhythmia	Digoxin (1)
30	Drug Reaction (or Rash) with Eosinophilia and Systemic Symptoms (DRESS)	Carbamazepine (1)

[Table/Fig-4]: Common Suspected Drugs Causing ADRs in the Form of Abnormal Biochemical

of the study carried by Goldstein LH et al., [7] suggesting a need to develop a network within hospitals to amplify the ADR detection. Collaboration with these specialties with department dealing with ADR reporting like Pharmacology can go a long way to amplify ADR detection.

Of the total ADR's picked up by BA & DT, maximum were severe and serious in nature requiring intervention and hospitalization indicating that ADRs picked up by the medium of BT and DT need to be promptly and comprehensively dealt in the interest of patient safety.

Maximum ADRs picked up by BA & DT were latent indicating great window of opportunity to pick them up and manage them as early as possible. Maximum of ADR detected by these tools were of type A and hence preventable. The study warrants a need to make a database of such drugs leading to preventable ADRs and update their prescribers about them, which shall help to improvise their clinical practice in favor of overall patient safety.

Causality assessment both by Naranjo's and WHO UMV scale showed maximum reactions to be probable indicating that evidence in the form of BA & DT add value to overall causality assessment.

Biochemist and radiologist failed to contribute any ADR by the medium of BA and DT. This probably is because of current hospital

management system in India, where biochemist and radiologist have least idea about the medication and disease history of the patient. Thus, current study stresses the need to have centralized sharing of patient's records including their medication record among all the concerned departments for early and effective detection of ADR.

Anemia, followed by liver dysfunction, renal dysfunction & electrolyte imbalance were the most common biochemical abnormalities in the current study. However, no similar study exist in the literature to make any comparisons regarding most common BA and most common drugs as most of the existing studies focuses on clinical presentations to describe trends and patterns of ADR presentation both from India [14-18] and Western world [19-22].

LIMITATIONS OF THE STUDY

There are some limitations in the current study that it may not represent the true ADR detection rates of BA and DT as data is largely generated by spontaneous reporting system as proposed by PvPI. Risk factor correlation was not studied. Thus, there may be many other confounding factors which could have affected the final outcome of the study which were beyond the scope of current cross-sectional study.

FUTURE SCOPE

The study stress upon the need of active surveillance to be adopted in current PV programme to increase the contributions of ADR detection by BA and DT.

CONCLUSION

Biochemical investigations and diagnostic tools can pick up substantial number of adverse drug reactions and can play very important role in ADR detection.

ACKNOWLEDGEMENT

The author acknowledge the Indian Pharmacopeia Commission, for all support provided under PvPI and WHO-For this important Initiative on Patient Safety.

REFERENCES

[1] Khan LM. Comparative epidemiology of hospital-acquired adverse drug reactions in adults and children and their impact on cost and hospital stay - a systematic review. *Eur J Clin Pharmacol*. 2013. [Epub ahead of print].
[2] Hakkarainen KM, Hedna K, Petzold M, Hägg S. Percentage of patients with preventable adverse drug reactions and preventability of adverse drug reactions--a meta-analysis. *PLoS One.* 2012;7(3):e33236.
[3] Irujo M, Beitia G, Bes-Rastrollo M, Figueiras A, Hernández-Díaz S, Lasheras B. Factors that influence under-reporting of suspected adverse drug reactions among community pharmacists in a Spanish region. *Drug Saf*. 2007;30(11):1073-82.
[4] Hazell L, Shakir SA. Under-reporting of adverse drug reactions: a systematic review. *Drug Saf.* 2006;29(5):385-96.
[5] Klopotowska JE, Wierenga PC, Smorenburg SM, Stuijt CC, Arisz L, Kuks PF, et al. Recognition of adverse drug events in older hospitalized medical patients. *Eur J Clin Pharmacol.* 2013;69(1):75-85.
[6] Khan LM, Al-Harthi SE, Saadah OI. Adverse drug reactions in hospitalized pediatric patients of Saudi Arabian University Hospital and impact of pharmacovigilance in reporting ADR. *Saudi Pharm J*. 2013 21(3):261-66.
[7] Goldstein LH, Berlin M, Saliba W, Elias M, Berkovitch M. Founding an adverse drug reaction (ADR) network: A method for improving doctors spontaneous ADR reporting in a general hospital. *J Clin Pharmacol.* 2013. doi: 10.1002/JCPH.149. [Epub ahead of print].
[8] Inch J, Watson MC, Anakwe-Umeh S. Patient versus healthcare professional spontaneous adverse drug reaction reporting: a systematic review. *Drug Saf.* 2012;35(10):807-18.
[9] Adams SA. Using patient-reported experiences for pharmacovigilance? *Stud Health Technol Inform.* 2013;194:63-68.
[10] Griffith R. Nurses must report adverse drug reactions. *Br J Nurs.* 2013;22(8):484-85.
[11] Santosh KC, Tragulpiankit P, Edwards IR, Gorsanan S. Knowledge about adverse drug reactions reporting among healthcare professionals in Nepal. *Int J Risk Saf Med.* 2013;25(1):1-16.
[12] Pérez García M, Figueras A. The lack of knowledge about the voluntary reporting system of adverse drug reactions as a major cause of underreporting: direct survey among health professionals. *Pharmacoepidemiol Drug Saf.* 2011;20(12):1295-302.
[13] Herdeiro MT, Ribeiro-Vaz I, Ferreira M, Polónia J, Falcão A, Figueiras A.Workshop- and telephone-based interventions to improve adverse drug reaction reporting: a cluster-randomized trial in Portugal. *Drug Saf.* 2012;35(8):655-65.
[14] Rehan HS, Chopra D, Sah RK, Mishra R. Adverse drug reactions: trends in a tertiary care hospital. *Curr Drug Saf.* 2012;7(5):384-88.
[15] Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacol Res.* 2006;54(3):226-33.
[16] Singh H, Dulhani N, Kumar B, Singh P, Tewari P, Nayak K. A pharmacovigilance study in medicine department of tertiary care hospital in chhattisgarh (jagdalpur), India. *J Young Pharm.* 2010;2(1):95-100.
[17] Dang A, Bhandare PN. The profile of voluntary reported adverse drug reactions at a tertiary care hospital: a fifteen month prospective study. *J Clin Diagn Res.* 2012 ;6(9):1504-09.
[18] Saha A, Das NK, Hazra A, Gharami RC, Chowdhury SN, Datta PK. Cutaneous adverse drug reaction profile in a tertiary care out patient setting in Eastern India. *Indian J Pharmacol.* 2012;44(6):792-97.
[19] Aagaard L, Strandell J, Melskens L, Petersen PS, Holme Hansen E. Global patterns of adverse drug reactions over a decade: analyses of spontaneous reports to VigiBase™. *Drug Saf*. 2012;35(12):1171-82.
[20] Aldea A, García Sánchez-Colomer M, Fernández Quintana E, García Sáiz M. Paediatric adverse drug reactions reported to the Spanish Pharmacovigilance System from 2004 to 2009. *Eur J Clin Pharmacol.* 2012;68(9):1329-38.
[21] Lobo MG, Pinheiro SM, Castro JG, Momenté VG, Pranchevicius MC. Adverse drug reaction monitoring: support for pharmacovigilance at a tertiary care hospital in Northern Brazil. *BMC Pharmacol Toxicol*. 2013; doi: 10.1186/2050-6511-14-15.
[22] Bárzaga Arencibia Z, López Leyva A, Mejías Peña Y, González Reyes AR, Fernández Manzano E, Choonara I. Pharmacovigilance in children in Camagüey Province, Cuba. *Eur J Clin Pharmacol.* 2012;68(7):1079-84.
[23] Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981;30:239-45.
[24] Edwards IR, Arsonson JK. Adverse drug reactions: Definitions, diagnosis and management. *Lancet*. 2000;356:1255-59.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate, Department of Pharmacology and Therapeutics Govt. Medical College Jammu- J&K, India.
2. Postgraduate, Department of Pharmacology and Therapeutics Govt. Medical College Jammu- J&K, India.
3. Postgraduate, Department of Biochemistry, Govt. Medical College Jammu- J&K, India.
4. Postgraduate, Department of Pharmacology and Therapeutics Govt. Medical College Jammu- J&K, India.
5. Postgraduate, Department of Pharmacology and Therapeutics, Govt. Medical College Jammu- J&K, India.
6. Postgraduate, Department of Pharmacology and Therapeutics Govt. Medical College Jammu- J&K, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Vishal R Tandon,
Assistant Professor, In-charge ADRM centre (Under PvPI)
Postgraduate, Department of Pharmacology and Therapeutics,
Govt. Medical College Jammu- J&K - 180001, India.
Phone : 09419195126, E-mail : dr_vishaltandon@yahoo.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jan 14, 2014**
Date of Peer Review: **Apr 22, 2014**
Date of Acceptance: **Jul 10, 2014**
Date of Publishing: **Sep 20, 2014**