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Research Article

An Epidemiological Study on Adverse Drug Reactions in Indian Population: Meta-Analysis

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ABSTRACT

Adverse drug reaction (ADR) has been implicated as a leading cause of considerable morbidity and mortality. The raise of adverse drug reactions (ADRs) in present day setting in India is high due to many reasons like polypharmacy, medication errors, medication adherence, lacking in reporting. The aim of this study is to determine the prevalence and different parameters regarding ADRs in Indian population. We performed a review study of all epidemiological studies quantifying ADRs in Indian setting that were published between 2003 and 2017. Included studies also assessed the number of patients who were hospitalized due to an ADR, studies that assessed the number of patients who developed an ADR during hospitalization. In total, 25 Indian articles were studied and the parameters analysed were prevalence of ADR, causality, severity, age, gender, class of drugs mostly effected. The percentages of ADRs in total were found to be major age groups involved. According to Naranjo's causality assessment scale 44.93% of patients were found to have possible relation with drug. As per WHO scale the results obtained indicate probable (44.57%) as highest. As per Hartwig and Siegel severity assessment scale most of the reactions were mild (48.85%). According to Schumock and Thornton preventability scale the reactions are not preventable (41.77%). The major class of drugs leading to ADRs were reported as Antibiotics (35.33%).

Keywords: Adverse drug reaction, Pharmacovigilance, Naranjo's causality scale, WHO scale, Hartwig and Siegel severity assessment scale, Schumock and Thornton preventability scale.

INTRODUCTION

According to world health organisation (WHO), an ADR can be defined as any response of a drug which is noxious and unintended, that occurs at doses used in humans for the prophylaxis, diagnosis or therapy of disease; or for the modification of physiologic function purposely excludes therapeutic failures, overdose, drug abuse, non compliance, and medication error[2]. Pharmacovigilance is developed much only from a decade but there were many disasters happened in previous years. Some of the examples like thalidomide disaster in 1960s made the health care professional and pharmaceutical companies alert. Although many regulatory authorities like CDSCO (central drugs standard for control of organisation), DCGI (drug controller general of India), WHO-UMC (world health organisation-Uppsala monitoring centre) are concentrating on drug interactions and ADRs there is an increase in number of ADRs reporting every year. In USA, more than 90 per cent of adults aged 65 yr and older use one medication per week and 10-25 percent experience an adverse drug reaction. These ADRs are responsible for 3.4 to 7.0 percent of hospital admissions[4]. It is estimated that only 6-10% of all ADRs are reported to the regulatory authorities. India is lacking in reporting ADRs and conducting studies on ADRs.

ADR scales were assessed initially. Different scales included were, Naranjo's causality scale, WHO scale, Hartwig and Siegel severity assessment scale, Schumock and Thornton preventability scale to assess different parameters like causality, severity and preventability. Then by assessing scales the major risk of patient groups are categorised and reported in our study. We performed meta-analysis study by considering only Indian population to check the prevalence of ADRs in this population.

Methodology

A systematic review of 25 articles considering only Indian population was done in this study. Out of 25 articles studied 21680 patients and ruled out 4875 patients with ADRs. Different articles reported ADRs in different departments by conducting a prospective study in different hospitals in India.

Inclusion criteria

Studies conducted in Indian population
Epidemiological and Pharmacovigilance studies on ADRs
All age groups and clinical settings (outpatient and/or inpatient)
Studies that were published between 2003 and 2017

Exclusion criteria

Case reports
Meta analysis studies on ADRs
Studies conducted other than Indian population
No or insufficient information about causality analysis
Doubtful, unlikely, and/or unclassifiable type of reactions

Study design

Meta-analysis/Systematic review performed in India and which are published from 2003-17. Eligible study designs

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Table 1: A Summary of ADR studies on Indian population with sample size and ADR occurrence rate (incidence).

Author	year	Study design	Study period	Study setting	Sample size	ADR occurrence rate (%)
Dimple Gohel et al	2014	Prospective, observational	6months	dermatology	51	3.78
Akanksha Suman et al	2017	Prospective, observational	6months	pediatric	142	68
Prakash H. Bhabhor et al	2014	cohort study	2years	complete hospital	97	10.25
Gaur S et al	2016	retrospective	1 year	complete hospital	251	25
Asawari Raut et al	2011	Prospective	6months	complete hospital	58	4.75
Padmaja Uday Kumar et al	2009	Prospective	1 year	medical ward	1250	20
Kranthi Koushik Nalluri et al	2016	Prospective	6months	complete hospital	400	34.5
Farhan Ahmad Khan et al	2003	Prospective	5months	complete hospital	1200	
Rohan Hire et al	2014	Prospective, observational	9months	T.B patients	110	48.2
Jahirul Islam Laskar et al	2017	Prospective, observational	1 year	complete hospital	1000	0.41%
Ramesh M et al	2003	Prospective	7months	complete hospital	164	1.68
Davies EC et al	2006	Prospective	2week	complete hospital	3000	19.2
J. Kurian et al	2016	Prospective, observational		paediatric	1082	4.99
Kumarjit Sinha et al	2013	Prospective	17months	T.B patients	102	69.01
Jayanthi C. R et al	2013	Prospective, observational	1year	psychiatry	329	20.36
G Parthasarathi et al		Prospective	3years	medical ward	4815	
Abhishank Singh et al	2017	prospective observational study	1 year	complete hospital	220	11.8
V. K. Saini et al	2015	Prospective Observational	2 months	Oncology	174	87.36
Shanmugam Sriram et al	2011	prospective-observational	1 year	General Medicine	3117	1.8
Abhijeet Singh et al	2015	prospective cross sectional spontaneous		complete hospital		
D.Yadav et al	2015	reporting	6 months	Surgery	3565	1.26
Sivasankari Venkatachalam et al	2012	Prospective Observational	6 months	orthopaedic	200	5.50
S Kaur et al	2009	Prospective Observational	1 year	cardiology	188	19.50

Table 2: Gender wise distribution.

S.NO	Average
MALE	51.61%
FEMALE	48.39%

Table 3: Naranjo's causality scale.

S.No	Naranjo's scale score	prevalence %
1	Probable	44.93%
2	Possible	40.18%
3	Definite	14.89%

Table 4: WHO Causality assessment scale.

S.No	WHO scale score	prevalence %
1	Certain	3.18%
2	Possible	44.57%
3	Probable	51.28%
4	Unlikely	0.58%
5	Unclassified	0.36%
6	Unassessable	0.021%

were both prospective and retrospective observational studies which measured the ADR occurrence rate[1].
An electronic search of PubMed/MEDLINE was performed using the following search string: (adverse drug reaction OR adverse drug reactions OR drug induced OR drug related problems OR toxic effects of drug OR adverse effect OR adverse effects OR adverse event OR adverse outcome OR adverse outcomes AND (prevalence OR occurrence) AND (hospitalisation* OR admission* OR

Table 5: Hartwig Severity Assessment Scale.

S.no	Hartwig severity	prevalence%
1	Mild	48.85%
2	Moderate	36.9%
3	Severe	14.25%

Table 6: Schumock and Thornton preventability scale

S.no	Preventability scale	prevalence %
1	Definitely preventable	34.35%
2	Probably preventable	23.88%
3	Not preventable	41.77%

Table 7: Prevalence of drug classes causing risk of ADRs.

S.No	Drug classes	Prevalence%
1	Antibiotics	35.33%
2	Antiepileptics	5.63 %
3	NSAID'S	5.32%
4	Autocoids	3.21%
5	Antivirals	1.58%
6	Anti-tubercular drugs	1.37%
7	Antipsychotics	12.51%
8	Antidepressants	0.025%
9	DMARD'S	0.0015%
10	Cardiovascular agents	8.59%
11	Anti-diabetics	0.37%
12	Steroids	11.64%
13	Others	14.43%

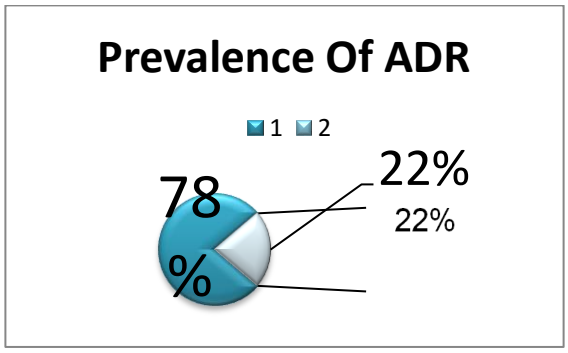

Figure 1: Prevalence of ADR occurrence in total population.

admitted OR visit) AND (observational OR retrospective OR prospective) NOT (clinical trial). All search terms were limited to the title and/or abstract, and only papers published in English were included[4].

The meta-analysis is performed by concentrating on ADR scales and to categorise the causality, severity, and preventability of ADR reaction. The below table summarised regarding the articles referred, their type of study, year of study, study setting either a particular department or patients hospitalized in particular period of time and ADR occurrence rate reported in those study. The main objective of the study is to find out the prevalence of ADRs in Indian population.

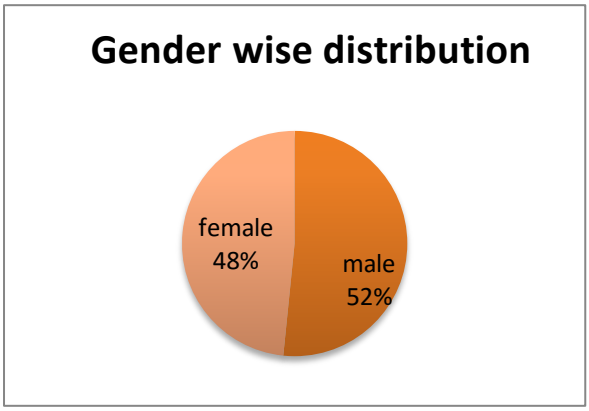

Figure 2: Gender wise distribution of ADRs.

By analysing all the studies, the prevalence of occurrence of ADR is found(Table 1). The population recruited in all the studies has no bias relating to sex. By the results obtained, there is no much significant distribution of ADRs in both the sexes.

Few articles only concentrated on only particular age group i.e., either paediatrics or adults or geriatrics. Akanksha Suman et al conducted a prospective observational study on Adverse Drug Effects of Antiepileptic Drugs used in Paediatric Patients in a Tertiary care rural Hospital. The prevalence of ADRs was found to be higher in adults followed by paediatrics and geriatrics[13]. Rohan hire et al performed a prospective observational study for 9 months on tuberculosis (T.B) patients and observed 64 ADRs in 55 patients out of total 110 patients recruited and assessed frequency and severity of ADRs[19].

The causality scales (Naranjo's and WHO) are assessed and the causal relationship is ruled out as probable, possible and definite. Severity assessment scales (Hartwig) were also performed and the level of severity is assessed as mild(level 1,2), moderate(level 3, 4), severe(level 5,6,7). and Preventable scales were also analysed to know the percentage of avoidable drug reactions. The percentages are mentioned in the tables 3,4,5,6. Dimple gohel et al performed a prospective observational study in dermatology in 2014 and discussed regarding incidence of causality, probability and class of drugs which are at risk of causing ADR[12]. A total of 15 studies have been conducted regarding drug classes which are at risk of causing ADR[12,13,15,16,17,21].

RESULTS AND DISCUSSION

In a total of 25 articles on ADRs, total numbers of patients recruited in the study are 21680. The average incidence rate of ADR occurrence in the patients was found to be 0.218% (in 21 studies). Among them the ADRs which leads to hospital admission were 0.046% (in 6 studies) and ADRs occurred during hospitalization were 0.212% (in 6 studies).

To assess the causality of ADR there were 2 scales considered i.e., Naranjo scale and WHO scale. Causality analysis according to Naranjo showed 12.4% were probable, 25.9% possible, 13.8% were definite in a total of

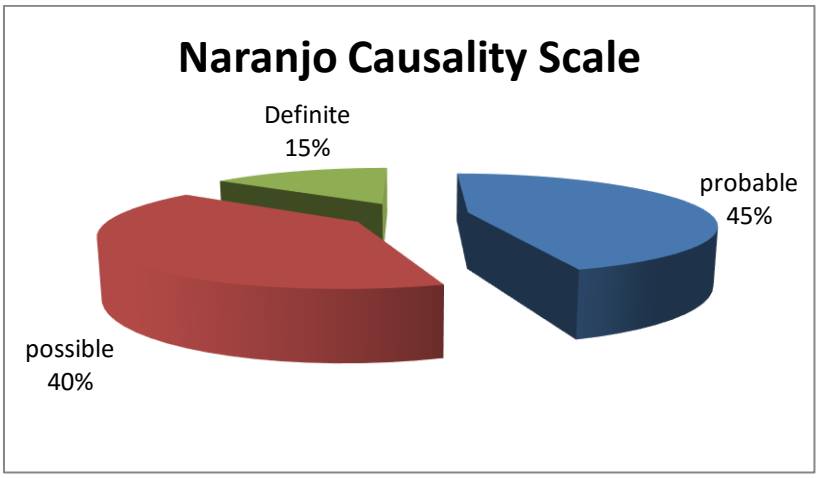

Figure 3: Causality scale of ADRs.

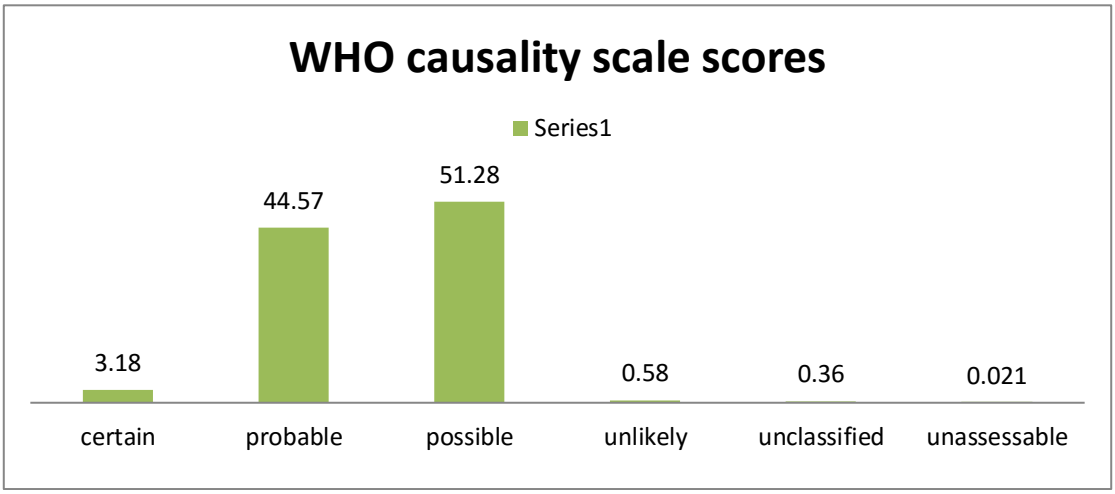

Figure 4: WHO causality scale scores.

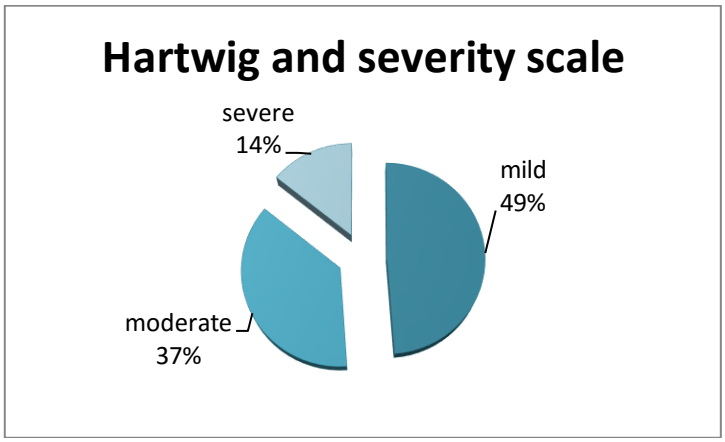

Figure 5: Severity of ADRs.

14 studies. Causality analysis by WHO scale showed 0% certain, 5.33% possible, 10.23% probable, 0.03% unlikely, 0.021% unclassified, 0.021% unassessable by considering a total of 8 studies.

By considering Hartwig severity assessment scale the Prevalence was found as 14% for mild, 37% for moderate and 49% for severe according to 16 studies. On an average the preventability score for 5 studies was found to be, 3.27% for definitely preventable, 16.114% for probably preventable and 20.828% for not preventable.

Drug classes which are more prone to ADRs risk were found to be Antibiotics (35.33%) by considering 12 studies, other drug classes average prevalence was found to be as Antiepileptics (5.63%), NSAIDS (5.32%), Autocoids (3.21%), Antivirals (1.58%), Anti-tubercular drugs (1.37%), Antipsychotics (12.51%), Antidepressants

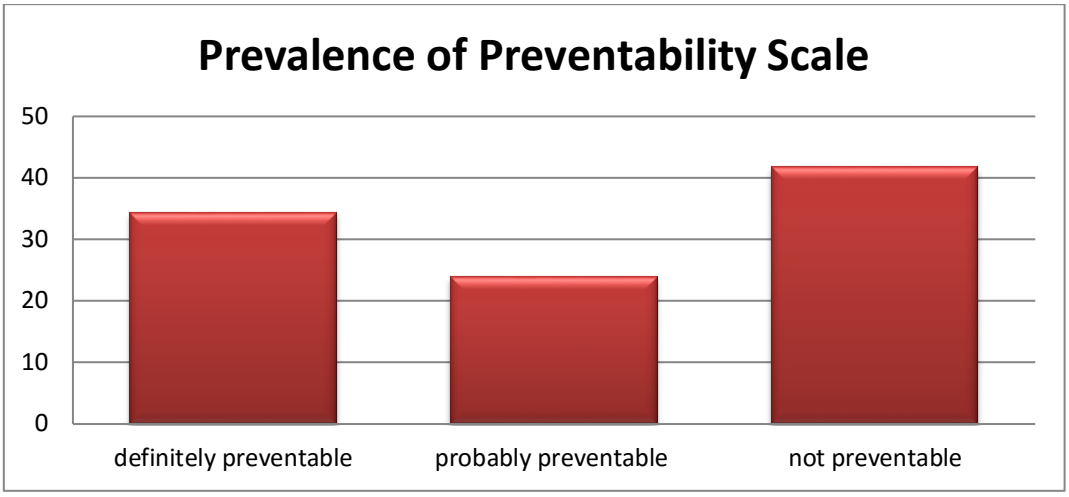

Figure 6: Preventability scale of ADRs.

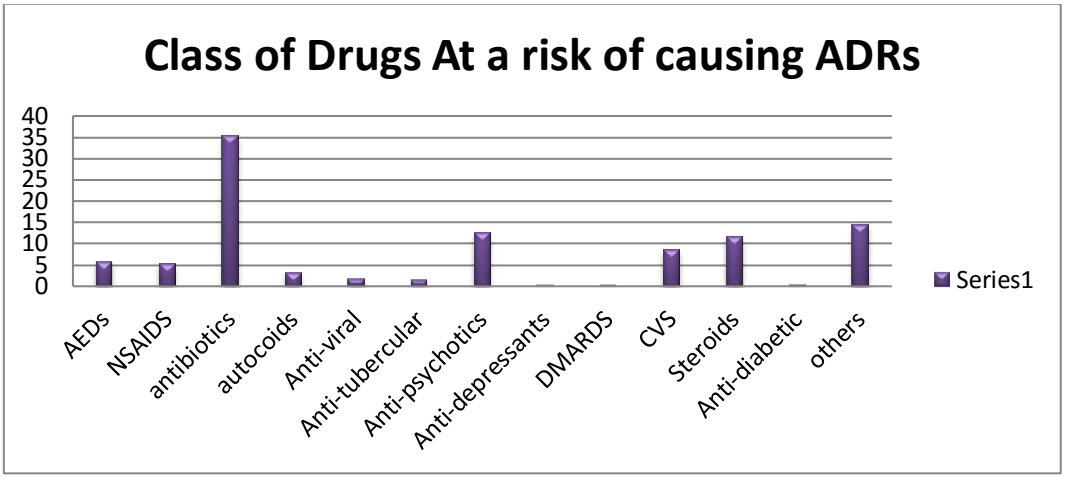

Figure 7: Class of Drugs At a risk of causing ADRs.

(0.025%), DMARD'S (0.0015%), Cardiovascular agents (8.59%), Anti-diabetics (0.37%), others (14.43%).

CONCLUSION

These results indicate the prevalence of ADRs in Indian population. There were very limited studies performed in India regarding identifying, reporting, detection and management of ADRs to the Pharmacovigilance. Our study revealed about the importance of Pharmacovigilance has to be provided among the health care professionals by different ways such as ADR bulletins, seminars and workshops. There is a need of conducting mores studies in Indian population to know the exact ADR occurrence rate and prevalence of ADRs in Indian hospitals.

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