Original Research Article

ADVERSE DRUG REACTIONS (ADRs) ASSOCIATED WITH HOSPITAL ADMISSIONS – MALE PATIENTS ARE AT HIGHEST RISK

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Abstract

Adverse Drug Reaction (ADR) may occur following a single dose or prolonged administration of a drug or may result from the combination of two or more drugs. The meaning of this term differs from the term "side effect" because side effects can be beneficial as well as detrimental. The study of ADRs is also known as pharmacovigilance. During this study ADRs assessed according to World Health Organization (WHO)–Uppsala Monitoring Centre (UMC) causality assessment criteria, Naranjo scale, Karch and lasagna scale, the result indicate symptoms of ADRs in male patient of adults and geriatrics common and it may be due to combination drug therapy. When ADRs assessed by using WHO Possible scale & Naranjo's probability scale it was found that only 05.13% have certain ADRs which required treatment while possible ADRs are between 39.84 to 55.68% also required strict monitoring. The main aim of this study was to find out the cause of ADRs and their assessment during hospital stay and developing a monitoring system and actively electronic submission of identified ADRs as per WHO ADRs monitoring system to prevent risk of ADRs.

Keywords : ADR, WHO-UMC, Preventability, Prevalence.

Introduction

ADRs represent a significant problem in drug utilization. The prevalence of admissions caused by ADRs varies depending on the observational site, studied population, data collection method and the used definitions. An adverse drug reaction (ADR) is a harmful, unintended result caused by taking medication[1,2]. Adverse Drug Reaction (ADR)may occur following a single dose or prolonged administration of a drug or may result from the combination of two or more drugs. The meaning of this term differs from the term "side effect" because side effects can be beneficial as well as detrimental[3,4]. The study of ADRs is the concern of the field known as pharmacovigilance[5]. An adverse event (AE) refers to any unexpected and inappropriate occurrence at the time a drug is used, whether or not the event is associated with the administration of the drug[6,7]. Adverse Event (AE)an ADR is a special type of AE in which a causative relationship can be shown[2,8,9]. ADRs are only one type of medication-related harm. Another type of medication-related harm type includes not taking prescribed medications, which is also known as non-adherence. Non-adherence to medications can lead to death and other negative outcomes. Adverse drug reactions require the use of a medication[10,11,12].

Causality assessment is used to determine the likelihood that a drug caused a suspected ADR[13,14]. There are a number of different methods used to judge causation, including the Naranjo algorithm, the Venulet algorithm and the WHO causality term assessment criteria. Each have pros and cons associated with their use and most require some level of expert judgement to apply[15].

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An ADR should not be labeled as 'certain' unless the ADR abates with a challenge-dechallenge-rechallenge protocol (stopping and starting the agent in question)[16]. The chronology of the onset of the suspected ADR is important, as another substance or factor may be implicated as a cause; co-prescribed medications and underlying psychiatric conditions may be factors in the ADR[17].

MATERIAL METHODS

World Health Organization (WHO)–Uppsala Monitoring Centre (UMC) causality assessment criteria WHO causality assessment scale is majorly used scale for the assessment of the causal relationship of case reports and has been developed during the International Drug Monitoring Programme in discussion with national centers. This scale has been categorized into 6 groups considering the basic criteria of 4 requirements in each category. These 4 criteria include a) temporal relationship b) plausibility and absence of other factors c) laboratory findings and d) de-challenge and re-challenge. Unclassified is applicable when additional information is necessary to evaluate the relationship[16,17].

Naranjo scale

Naranjo scale assesses the causality using the traditional categories of definite, probable, possible and doubtful. A ten elemental questionnaire with yes, no and unknown replies are developed. Based on the replies, the score has been determined into categories. Limitation: The Naranjo Scale does not address the points needed in the assessment of the causality of possible drug interactions[18,19].

Karch and lasagna scale

Karch and lasagna scale have been made known in the early 1970s and have a correlation to that of the WHO causality scale. Causality has been classified as definitive, probable, possible, conditional or unlikely. It has not been featured as there are no distinct advantages compared to other scales. Some of the studies had been conducted and the results of the studies found attributed to karch and lasagna scale over the WHO-UMC scale. Limitation: Duplicability and validity of results are not well established which will influence the quality of reports for further validation[20,21,22].

Results and Discussion

ADRs Observed During the Hospital Stay

Among the 328 cases, 540 adverse drug reactions were identified, which shows the probability of multiple adverse drug reactions in a single patient.

In the following table, 328 patients were distributed according to the age considering 10 as class interval.

Table 1: Age wise distribution

Sr. No.	Age -	No. of patients	Percentage (%)
1	1-10	12	03.66
2	11-20	21	06.40
3	21-30	29	08.84
4	31-40	22	06.71
5	41-50	53	16.16
6	51-60	75	22.87
7	61-70	54	16.46
8	71-80	41	12.50
9	81-90	21	06.40
Total		328	100

Among 328 patients the higher prevalence of adverse drug reactions was observed in patients of age 51-60yrs (22.87%) followed by 61-70yrs (16.46%), 41-50yrs (16.16%), 71-80yrs (12.50%), 21-30yrs (08.84%) while 81-90yrs (06.40%) and 11-20yrs(06.52%), and same in 31-40yrs (05.74%) and minimum in age group 1-10yrs (03.66%).

In the following table 328 patients were distributed according to their class of age group and sex.

Table 2: Distribution according to Age Group and sex

Sr. No.	Age group	Frequency N (%)	Gender		Ratio
			Female	Male	
1.	Children	39 (11.89 %)	20 (51.28%)	19 (48.72%)	1:1
2.	Adults	179 (54.57%)	61 (34.08.14%)	118 (65.92%)	1:05
3.	Geriatric	110 (33.54%)	49 (44.55%)	54 (55.45%)	1:0.9

Among age groups adults 179 (54.57%) were predominant over geriatric 110 (33.54%) and children 39 (11.89%) in terms of prevalence, while males have higher risk to develop adverse drug reactions among adults and geriatrics, and in Children both the genders have high risk in developing adverse drug reactions.

In the following table 383 patients were distributed according to their sex.

Table 3: Sex wise distribution

Sr. No.	Sex	No. of patients	Percentage (%)	Ratio
1	Male	218	66.46	
2	Female	110	33.54	
Total		328	100	1.98 :1

Among the 328 cases documented 218 (66.46%) were male and 110 (33.54%) werefemale, showing 1.98 times higher risk for males to develop adverse drug reactions.

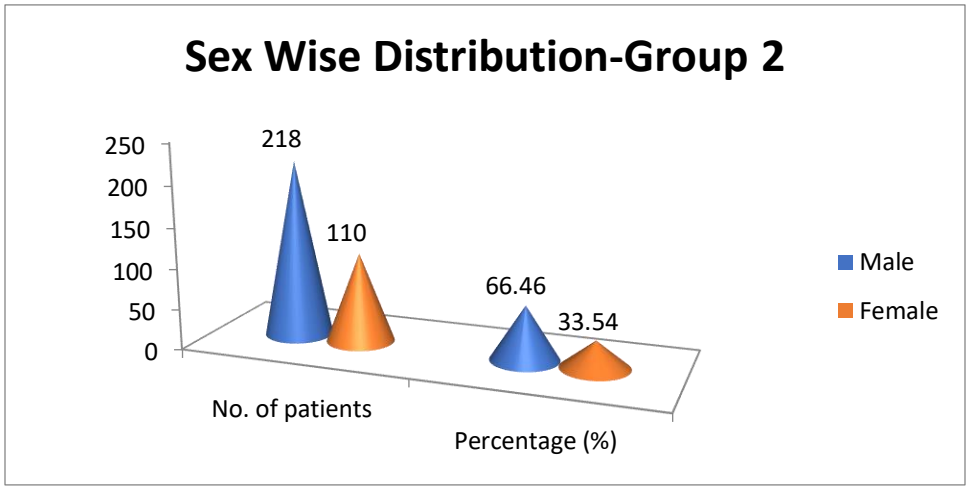

Fig. 1: Sex wise distribution

In the following table 328 cases were distributed according to the patient area of residence.

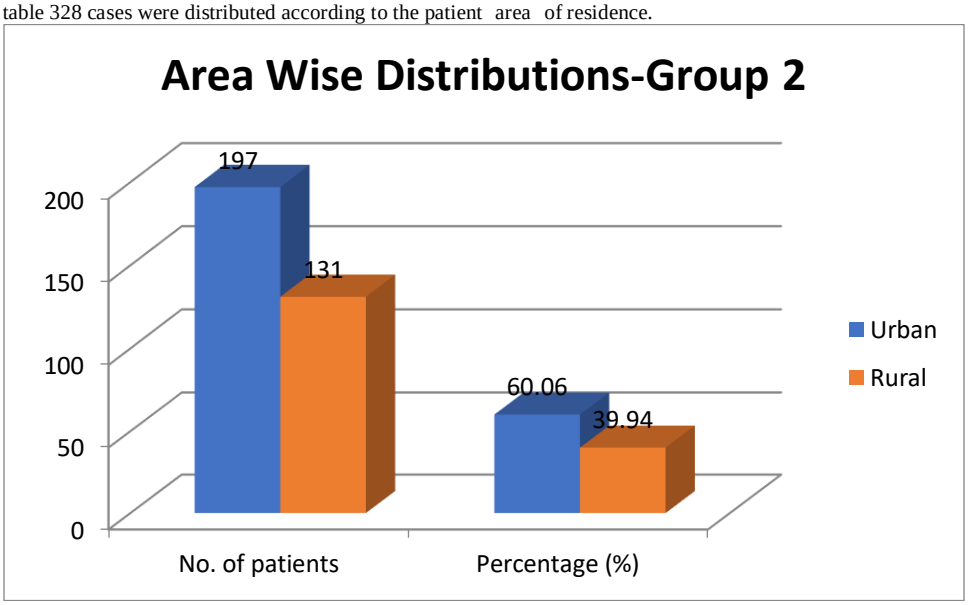

Fig. 2: Area wise Distribution

Graf show among the 328 cases documented predominance of adverse drug reactions was observed in patients belonging to urban area 197 (60.06%), showing 1.5 times higher risk for adverse drug reactions in individuals of urban area compared to rural area.

Table 4: Sex and Area wise distribution

Sr. No.	Gender	Area		Ratio
		Rural	Urban	
1.	Female	43 (41.54)	68 (58.45)	1:1.58
2.	Male	121 (56.19)	96(43.08)	1.23:1

Among all the individuals regardless of sex the distribution of adverse drug reactions issignificant over rural areas.

Distribution of the 328 cases documented according to the past medical history isdepicted in the following table.

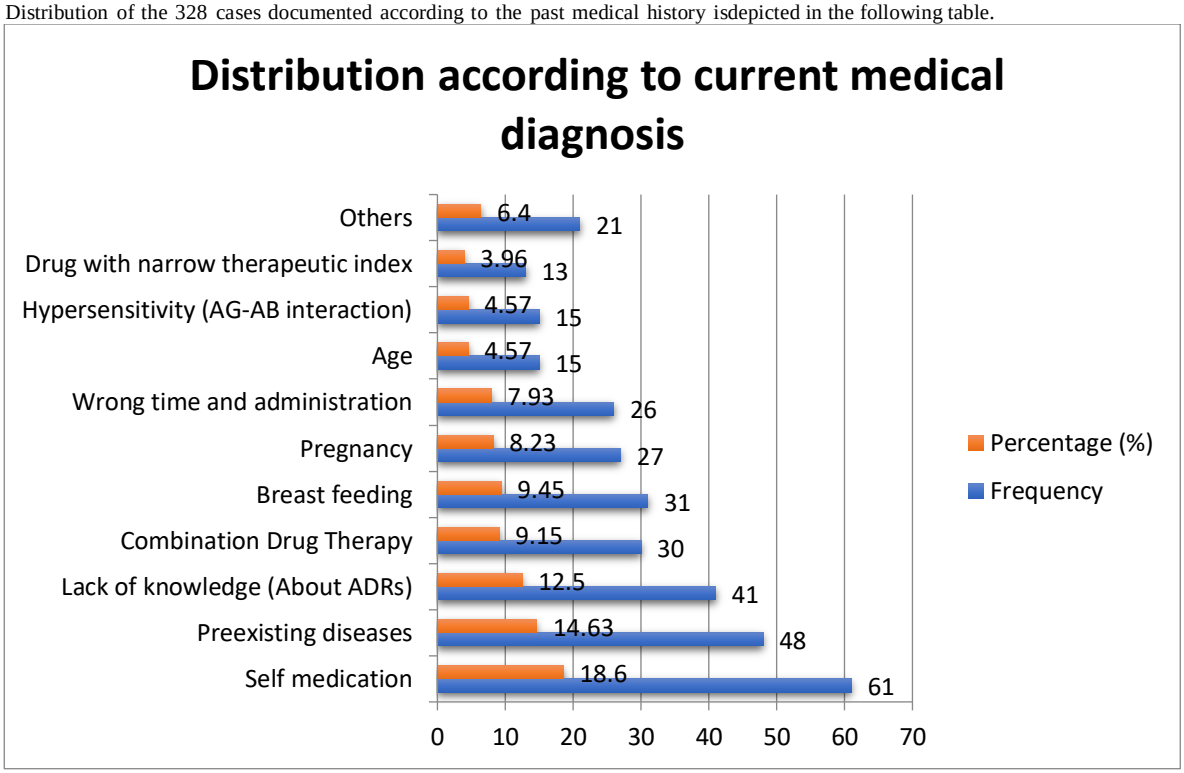

Fig. 3: Distribution according to current medical diagnosis

Among 328 cases the higher prevalence of current medical diagnosis was observed in patients having habit of self medication 61 (18.6%), followed by preexisting disease 48 (14.63%), lack of knowledge of ADRs 41 (12.5%) combination drug therapy 30 (09.15%), breast feeding

women 31 (09.45%), pregnancy 27 (08.23%), wrong time medication and administration of drug 26 (07.93%), age of patient and hypersensitivity 15 (04.57%), drug with narrow Therepeutic Index 13 (03.96) and others 21 (06.40%).
In the following table 487 ADRs identified and assessed in 328 documented cases were represented according to the type.
The 487 ADRs were distributed according to the WHO ART system codes in table 28.

Table 5: ADRs were distributed according to the WHO ART system codes

Sr. No	System	ART Codes	No. of ADRs	Percentage
1	Dermatology	(100)	127	26.08
2	Muscular skeletal	(200)	11	02.26
3	Central nervous	(410)	31	06.37
4	Ophthalmic	(420)	13	02.67
5	Otic system	(431)	12	02.46
6	Gastrointestinal	(600)	88	18.07
7	Hepatic system	(700)	51	10.47
8	Endocrine	(900)	44	09.03
9	Cardiovascular	(1000)	23	04.72
10	Heamatology	(1200)	67	13.76
11	Renal system	(1300)	20	04.11
	Total		487	100

The above table show that most of ADRs were experienced by Dermatology department 127 (26.08%) followed by gastrointestinal department 88 (18.07%) then hematology 67 (13.76%), while the list are found in otic 12 (02.46%) and ophthalmic 13 (02.67%).

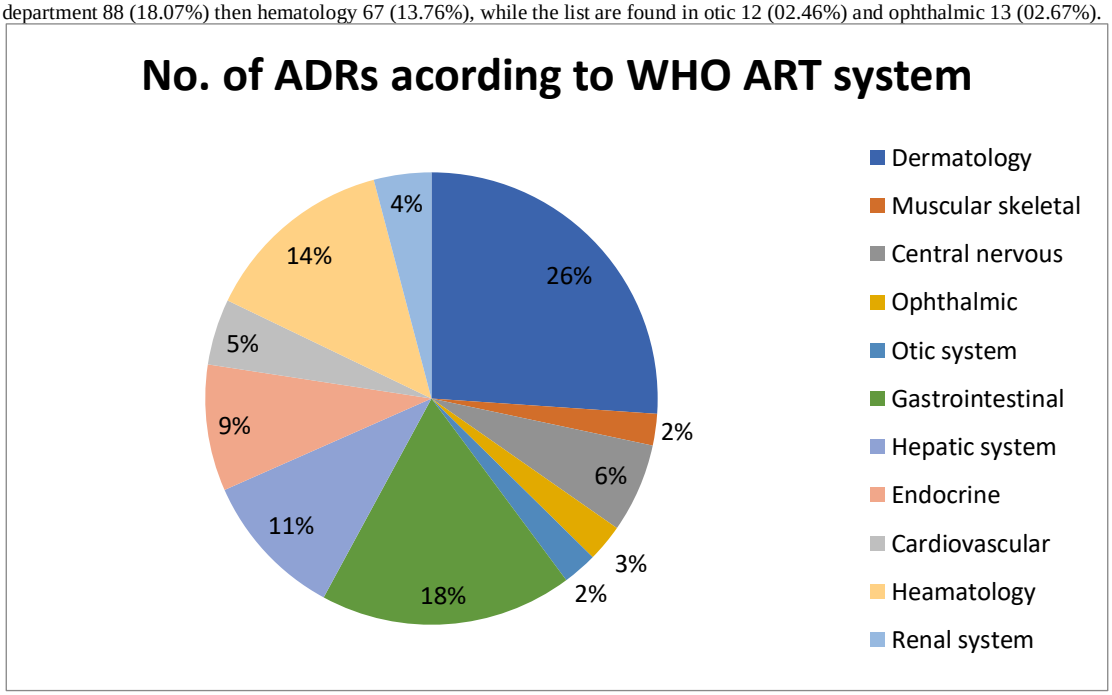

Fig. 4: ADRs were distributed according to the WHO ART system codes

Risk factors which are responsible for 487 adverse drug reactions as assessed are represented in the following table.

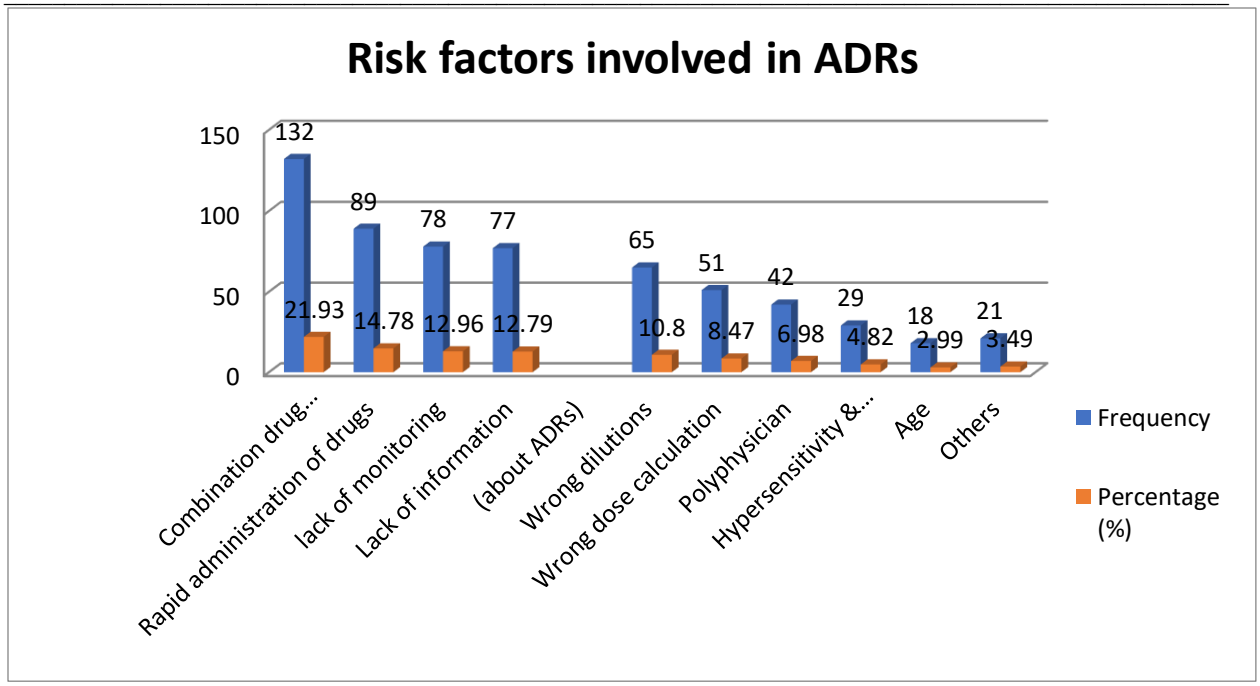

Fig. 5: Risk factors involved in ADRs

The risk factors which are highly involved among 487 adverse drug reactions are combination drug administration without indication 132 (21.93%) followed by Rapid administration of drugs 89 (14.78%), lack of monitoring 78 (12.96%), Lack of information (about ADRs) 77 (12.79%), Wrong dilutions 65 (10.80%), wrong dose calculation 51 (08.47%), Polyphysician 4 2 (06.98%), Hypersensitivity & Pharmacology of drugs 29 (04.82%) and Age of the patient 18 (02.99%) while others are 21 (03.49).

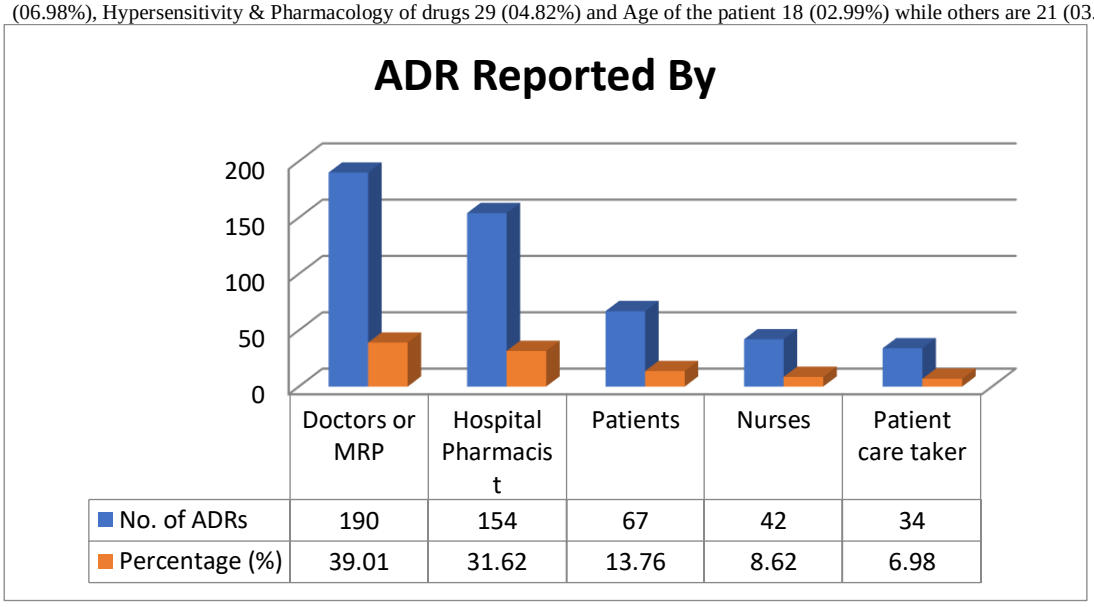

Fig. 6: ADR's reported by

Most of ADRs were identified by Doctors or Prescribers 190 (39.01%) followed by Hospital Pharmacist1 154 (31.62%), Patient 67 (13.76%), nurses 42 (08.62%) and patient care taker are reported 34 (06.98%).

In the following table 4 8 7 adverse drug reactions were distributed according to the agegroup of 328 patients considered for the project.

Management of the Adverse Drug Reaction

Causality assessment of adverse drug reactions

592 adverse drug reactions were causality assessed by using WHO Probability scales

Table 6: Causality assessment of ADRs according WHO probabilityscale

Sr. No	WHO probability scale	No. of ADRs	Percentage (%)
1	Certain	25	05.13
2	Possible	194	39.84
3	Potential	147	30.18
4	Unclassifiable	85	17.45
5	Dubious	35	07.19
	Total	487	99.79

Among 487 patients, causality assessment of ADRs according to WHO probability scale was as follows, possible reactions in 194 (39.84%) patients followed by potential reactions in 147 (30.18%) patient, unclassified in 85 (17.45%) patients, while dubious 35 (07.19) patient reactions.

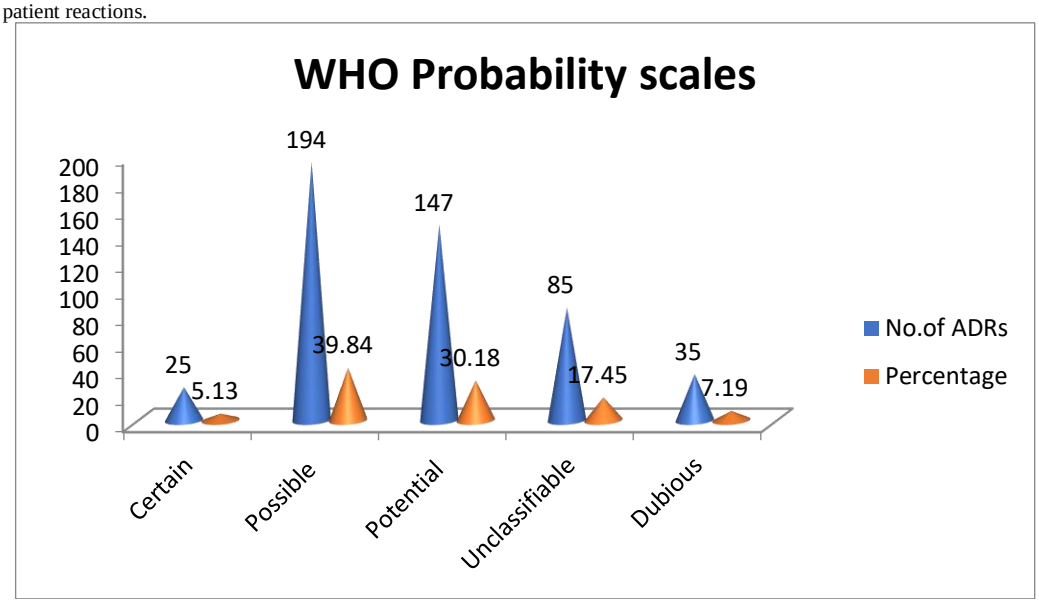

Fig. 7: Causality assessment of ADRs according WHO probability scale

487 adverse drug reactions were assessed by using Naraonjo's scale

Table 7: Causality assessment of ADRs according Naronjo's scale

Sr. No	Naronjo's scale	No. of ADRs	Percentage (%)
1	Definite	24	04.93
2	Probable	271	55.65
3	Possible	157	32.24
4	Unlikely	35	07.18
	Total	487	100.00

Among 487 patients causality assessment of ADRs according to Naronj's scale was as follows, probable reactions in 271 (55.65%) patients followed by possible in 1 5 7 (32.24%) patients, unlikely in 35 (07.18%) while definite ADRs are only in 24 (04.93%) patients.

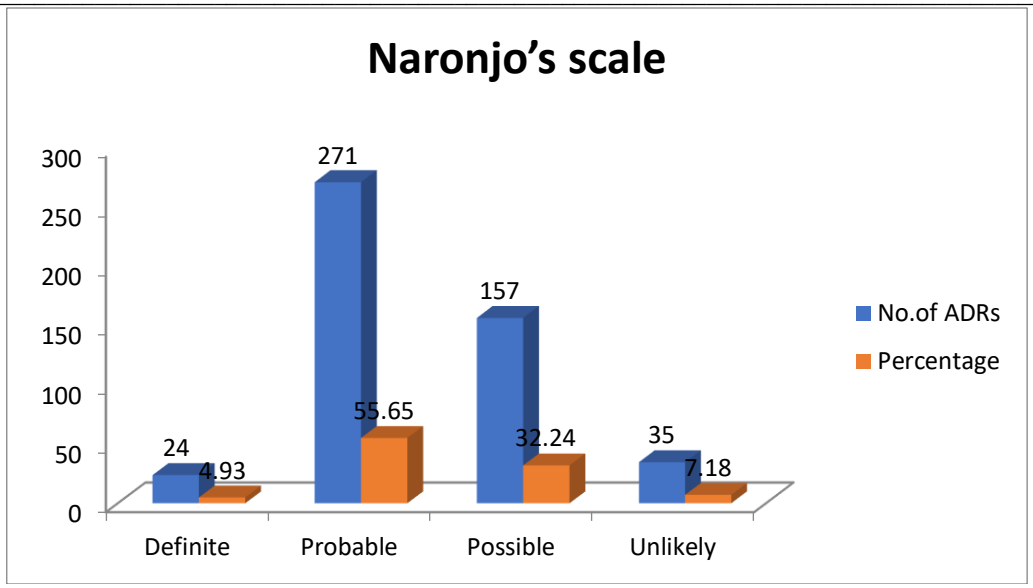

Fig. 8: Causality assessment adverse drug reactions according Naronjo's scale

487 adverse drug reactions were assessed by using Karch & Lasagna's Scale

Table 8: Causality assessment adverse drug reactions according Karch &Lasagna's Scale

Sr. No	Karch & Lasagna's Scale	No. of ADRs	Percentage
1	Definite	24	04.93
2	Probable	271	55.65
3	Possible	157	32.24
4	Unlikely	35	07.18
	Total	487	100.00

Among 487 patients causality assessment of ADRs according to Karch & Lasagna's scale was as follows, probable reactions in 271 (55.65%) patients followed by possible in 1 5 7 (32.24%) patients, unlikely in 35 (07.18%) while definite ADRs are only in 24 (04.93%) patients.

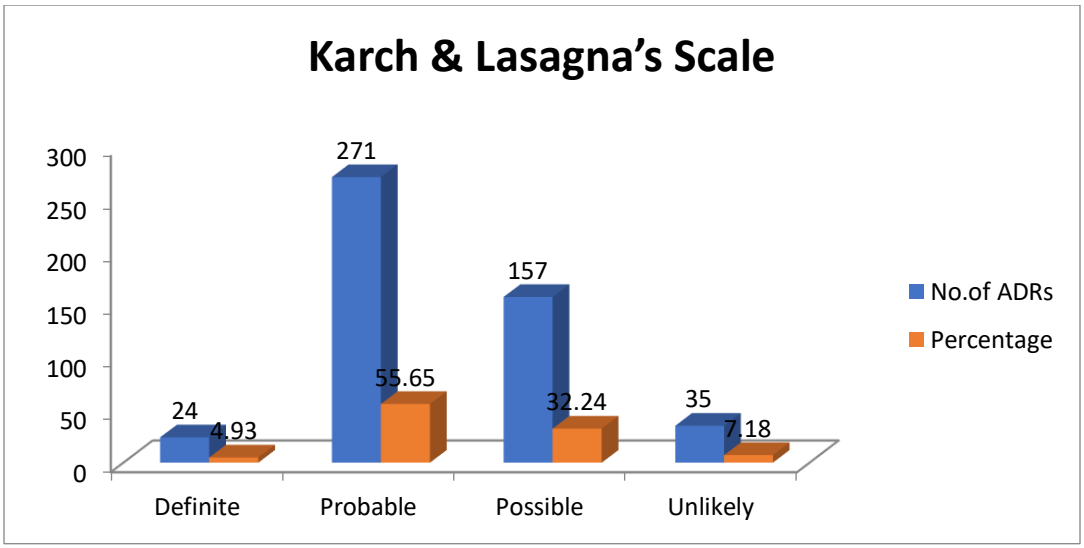

Fig. 9: Causality assessment adverse drug reactions according Karch& Lasagna's Scale

487 adverse drug reactions severity were assessed by using Modified Hartwig and Siegel scales.

Table 9: Assessment of severity of ADRs according ModifiedHartwig and Siegel scales

Sl. No.	Age group	Adverse Drug Reactions	Frequency	Percentage (%)
1.	**Mild**	Level 1	125	25.67
		Level 2	109	22.38
		Level 3	134	27.52
		Level 4	75	15.4

2.	**Moderate**			
3	Severe	Level 5	38	07.80
		Level 6	05	1.03
		Level 7	01	0.21
	Total		487	100.00

The 487 ADRs severity was assessed, most of the patients are at level – 3, 134 (27.52%) followed by lavel-1, 125 (25.67%), at level-2, 109 (22.38%) of patients, 7 5 (15.4%) patients at level-4, 38 (07.80) patients severe at level -5, while 05(01.03%) and 1 (00.16%) patients are at level-5, level-6 and level-7 respectively. 487 adverse drug reactions Preventability were assessed details were given in table 9

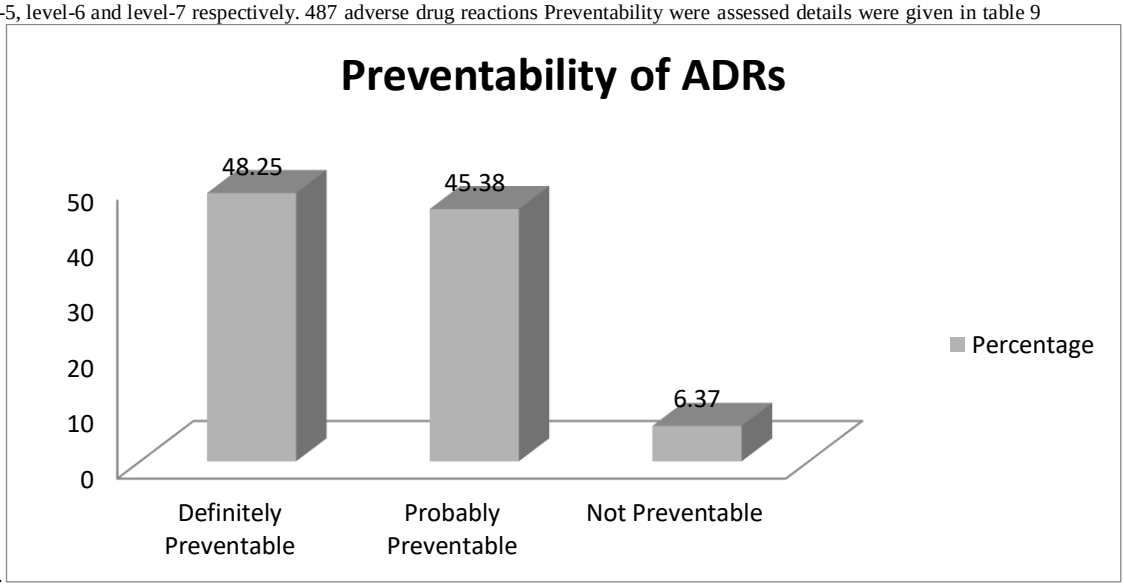

Fig. 10: Assessment adverse drug reactions Preventability

In 487 ADRs Definitely Preventable adverse drug reaction are 235 (48.25%) followed by probably preventable adverse drug reaction are 221 (45.38%) and not preventable are 31 (06.37%)

Conclusion

In this study total 6930 patient was involved out of which 540 (07.79%) experienced ADRs. Among 540 patient only 328 patient experienced ADRs during hospital stay in which 540 ADRs was identified. Out of these 328 the male patient are 218 (66.46%) which indicate the male patient are more sensitive. The study also indicates adults and geriatrics age group male show higher rate of ADRs. During the study it was also found that prevalence of ADRs in urban area i.e. 60.06% is higher compare to rural which is 39.94%.This study indicates the main cause of ADRs during hospital stay is combination drug therapy followed by rapid administration of drug.

When ADRs assessed by using WHO Possible scale & Naranjo's probability scale it was found that only 05.13% have certain ADRs which required treatment while possible ADRs are between 39.84 to 55.68% also required strict monitoring.

The main aim of this study was to find out the cause of ADRs and their assessment during hospital stay and developing a monitoring system and actively electronic submission of identified ADRs as per WHO ADRs monitoring system to prevent risk.

References

1. Guideline For Good Clinical Practice. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. 10 June 1996. Retrieved 16 April 2022.
2. Nebeker JR, Barach P, Samore MH. "Clarifying adverse drug events: a clinician's guide to terminology, documentation, and reporting". Annals of Internal Medicine. 140 (10): 795–801
3. Why You Need to Take Your Medications as Prescribed or Instructed". *U.S.* Food & Drug Administration. 16 February 2016. Retrieved 17 April 2023.
4. Aronson JK, Ferner RE "Joining the DotS: new approach to classifying adverse drug reactions". *BMJ. 327 (7425): 1222–1225.* PMID 14630763.
5. Davies EC, Rowe PH, James S, Nickless G, Ganguli A, Danjuma M, et al. "An Investigation of Disagreement in Causality Assessment of Adverse Drug Reactions". Pharm Med. 25 (1): 17–24.
6. Holvey C, Connolly A, Taylor D (August 2010). "Psychiatric side effects of non-psychiatric drugs". British Journal of Hospital Medicine. 71 (8): 432–6.
7. Shehab N, Lovegrove MC, Geller AI, Rose KO, Weidle NJ, Budnitz DS "US Emergency Department Visits for Outpatient Adverse Drug Events, 2013-2014". JAMA. 316 (20): 2115–2125.
8. Otero López MJ, Alonso Hernández P, Maderuelo Fernández JA, Ceruelo Bermejo J, DomínguezGil Hurlé A, Sánchez Rodríguez A. Prevalence and factors associated with preventable adverse drug events leading to hospital admission. Farm Hosp. 2006; 30: 161-170.
9. Leendertse AJ, Egberts ACG, Stoker LJ, van den Bemt PMLA; HARM Study Group. Frequency of and risk factors for preventable medicationrelated hospital admissions in the Netherlands. Arch Intern Med. 2008; 168: 1890-1896
10. Howard RL, Avery AJ, Howard PD, Partridge M. Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study. Qual Saf Health Care. 2003; 12: 280-285.
11. Winterstein AG, Sauer BC, Hepler CD, Poole C. Preventable drug-related hospital admissions. Ann Pharmacother. 2002; 36: 1238-1248.
12. Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. Ann Pharmacother. 2008; 42: 1017-1025.
13. C. Hofer-Dueckelmann, E. Prinz, W. Beindl, J. Szymanski, G. Fellhofer, M. Pichler and J. Schuler Adverse drug

reactions (ADRs) associated with hospital admissions – elderly female patients are at highest risk international Journal of Clinical Pharmacology and Therapeutics, Vol. 49 – No. 10/2011 (577-586)

14. Karel Allegaert, Johannes N. van den Anker "Adverse drug reactions in neonates and infants: a population-tailored approach is needed" British Journal of Clinical Pharmacology, 2023, 788-795.
15. Jamie J Coleman A and Sarah K Pontefract B, "Adverse drug reactions" Clinical Medicine 2016 Vol 16, No 5: 481–5
16. World Health Organization (WHO), Uppsala Monitoring Centre. The use of the WHO-UMC system for standardized case causality assessment. WHO [Internet]. Available from: http://www.who-umc.org/graphics/4409.pdf. [Last accessed on 10 Jan 2020].
17. Macedo AF, Marques FB, Ribeiro CF, Texeira F. Causality assessment of adverse drug reactions: comparison of the results obtained from published decisional algorithms and from the evaluations of an expert panel. Pharmacoepidemiol Drug Saf 2005;14:885-90.
18. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clinical Pharmacology Thereputics 1981; 30:239-45.
19. Naranjo CA, Lanctot KL. A consultant ″s view on the role of Bayesian differential diagnosis in the safety assessment of pharmaceuticals. Drug Information Journal 1992; 26:593-601.
20. Kyonen M, Folatre I, Lagos X, Vargas S. Comparison of two methods to assess causality of adverse drug reactions. Rev Med Chile 2015; 143:880-6.
21. Benahmed S, Picot MC, Dumas F, Demoly P. Accuracy of a pharmacovigilance algorithm in diagnosing drug hypersensitivity reactions. Arch Intern Med 2005; 165:1500-5.
22. Smyth RL, Peak M, Turner MA, Nunn AJ, Williamson PR, Young B, et al. Development of the liverpool adverse drug reaction avoidability tool. In ADRIC: Adverse drug reactions in children– a programme of research using mixed methods. NIHR Journals Library; 2014.

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