Incidence and Severity of Adverse Drug Reactions and Spontaneous Adverse Drug Reporting in Hospital Settings of Lahore

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***Abstract*- Objective:** The aim of the study was to observe the incidence and severity of ADRs and spontaneous adverse drug reporting and role of pharmacist in ADR reporting in different hospital settings of Lahore.

Study Design: Descriptive / retrospective study.

Plan and duration of study: This study was conducted from the health care providers working in different hospital settings of Lahore from 10th July to 10th Sept, 2016.

Materials and methods: The data was collected through a preformed questionnaire about knowledge of incidence and severity of ADRs and second portion was about spontaneous adverse drug reporting. Data was entered, analyzed and presented in the form of graphs.

Results: 150 healthcare providers were included (50 clinicians, 50 pharmacists & 50 nurses), out of which 28% observed and reported the ADRs, 42% only observed but did not reported theADRs while 30% neither observed nor reported the ADRs. From the observed and reported ADRs, 54% were mild, 22% were moderate while 24% of ADRs were of severe nature. Most of the observed ADRs were due to the antibiotics (vancomycin 22%, amoxicillin+clavulanic acid 13%, ciprofloxacin 12%, clarithromycin 10%, penicillin 7%, metronidazole 3%, cephtriazone 3%). Other drugs include ibuprofen 8%, paracetamol 3%, heparin and aspirin 3%, dexamethasone 4% and sulphacetamide 2%. While 9% of the ADRs were due to unknown drugs. Gastrointestinal tract (GIT) and Skin were the most commonly involved systems in 26% of ADRs, followed by oral cavity (21%) and respiratory system (14%), in the heart and the CNS 3% ADRs were found while 7% ADRs were due to unknown symptoms.

Conclusion: Awareness about spontaneous ADR reporting is still poor amongst healthcare professionals in Lahore. The incidence and severity of ADRs are well documented. Antibiotics comprise the major drug family associated with ADRs so should be rationally prescribed. Geriatrics, pediatrics and females were most affected with ADRs.There is need for establishing ADR monitoring center at every multidisciplinary hospital.

***Index Terms*-** Adverse drug reactions, Spontaneous adverse drug reporting, pharmacotherapy

I. Introduction

Adverse Drug Reactions (ADRs) are inevitable consequences of pharmacotherapy. It is well known that all drugs carry the potential to produce both desirable and undesirable effects. No drug is absolutely safe under all circumstances of use or in all patients and ADRs may occur even if a drug is correctly selected and dosed. The World Health Organization defines an adverse drug reaction (ADR) as “a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis,diagnosis, or therapy of disease, or for the modification of physiological function”. **[1-2**]

Several classification methods have been proposed to describe ADRs such as by their severity (mild, moderate or severe), by reaction time (acute or latent) and whether the reaction is localized or systemic. However, the pharmacological classification which classifies ADRs into types A-F is the most commonly used.Type A (Augmented), Type B (Bizarre), Type C (Chronic), Type D (Delayed), Type E (End of use) and Type F (Failure of therapy).Many adverse drug reactions represent an exaggeration of the drug's therapeutic effects (called type 1 or overdose reactions). These reactions are usually not serious but are relatively common. Some adverse drug reactions result from mechanisms that are not currently understood (called type 2 or idiosyncratic reactions). This type of adverse drug reaction is largely unpredictable. [3-4]

ADR in hospital patients are divided into two categories: those that cause admission to to hospital and those that occur in hospital inpatients after admission. Hospital based ADR monitoring can provide valueable information on drug usage. ADR add an unnecessary cost to an to an already burdened health care system and are usually preventable.[5]

An ADR may result from both drug related and non-drug related factors. [6]The risk of ADRs is necessarily an inherent risk of all drug therapy and is modulated by several factors, including dose and frequency of administration, genotype and pharmacokinetic characteristics of special populations, such as pediatric and geriatric patients and those with hepatic or renal impairment. ADRs arising from inappropriate drug use can be due to inappropriate dosage or duration of treatment, drug interactions, off-label use or use in contraindicated circumstances all of which can occur in the general population or in a hospital setting. [7-9] Due to the high frequency and potentially serious consequences, ADRs may have a dramatic impact in clinical practice both from a clinical and economic perspective. ADRs may increase costs due to increased hospitalization, prolongation of hospital stay and additional clinical investigations in more serious cases. [10-13]

Adverse drug reactions (ADRs) are considered as one of the leading causes of death among hospitalized patients. Thus reporting of adverse drug reactions become an important

phenomenon. Reporting of ADR is done by various methods but the most commonly used method is spontaneous adverse drug reporting. It is the most likely method of detecting new, rare ADRs and frequently generates safety signals which need to be examined further. Spontaneous adverse drug reaction reporting form is an essential component and a major tool of the pharmacovigilance system of any country. This form is a tool to collect information of ADRs which helps in establishing the causal relationship between the suspected drug and the reaction. Every country has developed its own spontaneous ADR reporting form for data collection which is used by them to capture information about an adverse event. The guidelines have been developed to assist health care professionals on understanding the importance of ADRs monitoring, procedures of reporting an ADR and the four essential components of an ADRs case report to improve drug safety. The essential components include information about the patient, description of the adverse drug reactions, the suspected drug(s) and the reporter.[5,1415,16.17]
Spontaneous reports are a crucial element in the worldwide enterprise of pharmacovigilance and form the core of the WHO database.[9]. Pharmacists have been encouraged to participate and contribute the ADR and monitoring program this has considerably improve the rate of reporting.[18.19]

II. MATERIALS AND METHODS

This retrospective study was conducted for the period of two months from july10th to sep10th, 2016, to analyses the incidence and severity of ADRs and spontaneous ADR reporting. The data was collected from the health care providers of different hospital settings on a data collection form having the basic information about patient, adverse drug reaction and ADR reporting system. Patients of both sex and of any age who developed an ADR before or after hospitalization are included in this study while patients with intentional or accidental poisoning, patients who developed an ADR during transfusion of blood or blood products and vaccines, patients with drug abuse were excluded from the study. WHO definition of ADR was adopted. The data was collected from the 150 health care providers, out of which 50 were clinicians, 50 were pharmacists and 50 were nurses. Some of the health care providers observed and reported the ADRs while some only observed but not reported the ADRs while some neither observed nor reported the ADRs. For the reporting of ADRs they used either yellow card or the hospital's own ADR reporting form. The information about awareness of ADRs and ADR reporting system and demographic details of the patient were collected along with the ADR and its management details in a systematically designed data collection form. All relevant including the drugs patient received prior to the onset of reaction, respective dose and route of administration with frequency and the patient's allergic status were noted. Any drug treatment or supportive therapy given for management of the reactions was also noted.

The causality relationship between the ADR and the suspected drug therapy was assessed. The ADRs were classified. The severity of the ADRs were determined and classified as mild, moderate and severe. Mild reactions were defined as self-limiting and able to resolve over time without treatment and did not contribute to prolongation of length of stay. Moderate ADRs were defined as those that required therapeutic intervention and hospitalization prolonged by one day but resolved in less than 24 hours or change in drug therapy or specific treatment to prevent a further outcome. Severe ADRs were those that were life threating, producing disability and those that prolonged hospital stay or led to hospitalization, required intensive medical care or led to the death of the patient.

The most common class of drugs causing ADRs were identified and documented. Patients outcome were reported as recovering, recovered and death.

III. RESULTS

The data was collected from the 150 health care providers (50 clinicians, 50 pharmacists and 50 nurses) out of which 42 observed and reported the ADRs, 62 only observed but not reported the ADRs while remaining 46 neither observed nor reported the ADRs. (Fig 1).

100% of the clinicians and pharmacists and 92% nurses were aware of ADRs while 8% of the nurses had little knowledge about ADRs. (Fig 2).

A total of 104 suspected adverse drug reactions were recorded out of which 40% were reported and 60% were not. Majority of the health care providers 76% used hospital's own ADR reporting form while 24% used yellow card for reporting of ADRs which were then submitted to the ADR focal person in the hospital pharmacy. Out of 104 patients, 63% were female and 37% were male. Maximum patients (30%) belonged to the age group 41-60 years, followed by (25%) 21-40 years, (21%) 1day-1year, (14%) 41-60 year and (10%) belonged to >60 years.(Table 1).

Vancomycin caused highest 22% of the ADRs, Augmentin caused 13%, ciprofloxacin 12%, clarithromycin 10%, ibuprofen 8%, penicillin 7%, dexamethasone 4%, paracetamol, metronidazole, cephtriazone and heparin+aspirin caused 3%, sulphacetamide 2%, meronam+lenzolid 1% while 9% of the ADRs were due to the unknown drugs. (Table 2).

Gastrointestinal tract (GIT) and Skin were the most commonly involved systems in 26% of ADRs, followed by oral cavity (21%) and the heart and the CNS (8%) and in respiratory system 6% ADRs were found while the ADRs due to unknown causes involved5%. (Fig 3).

Out of 104 ADRs, 71% were of type B while 29% were type A. (Table 3).

54% of the ADRs were mild, 22% were moderate and 24% were severe. (Fig 4).

The 63% patients were fully recovered, 31% of the cases were recovering while 6% were died before coming to hospital or during hospital stay.(Fig:5)

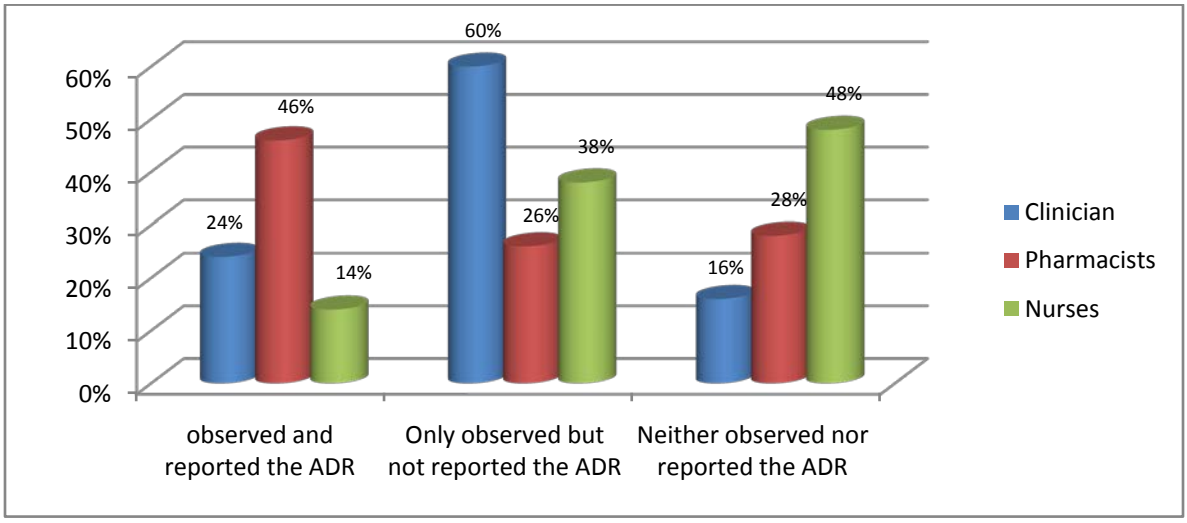

Figure 1: Spontaneous reporting of ADRs

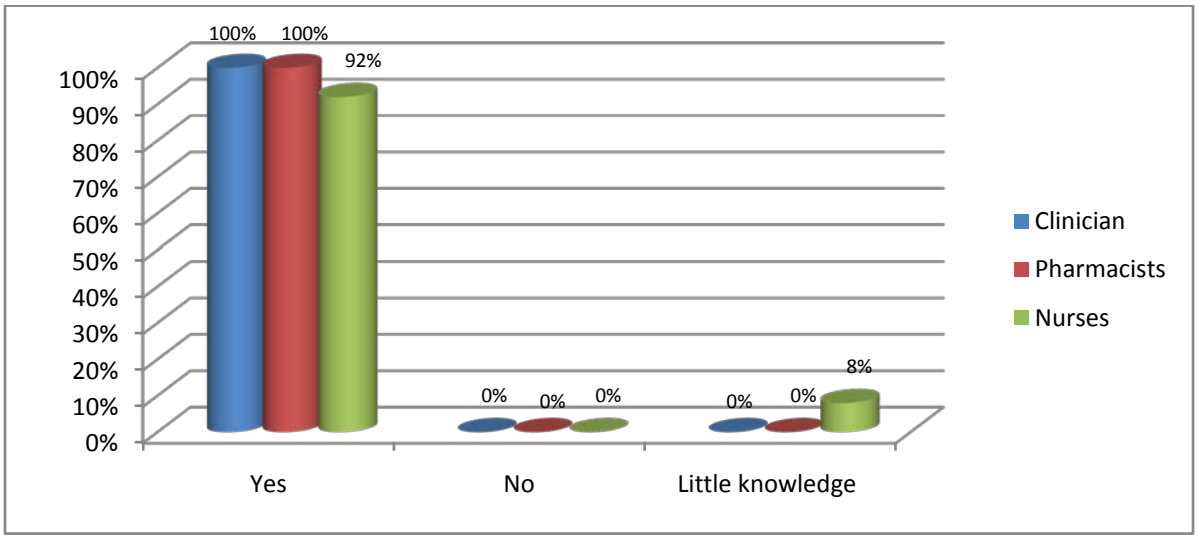

Figure 2: Awareness about ADRs

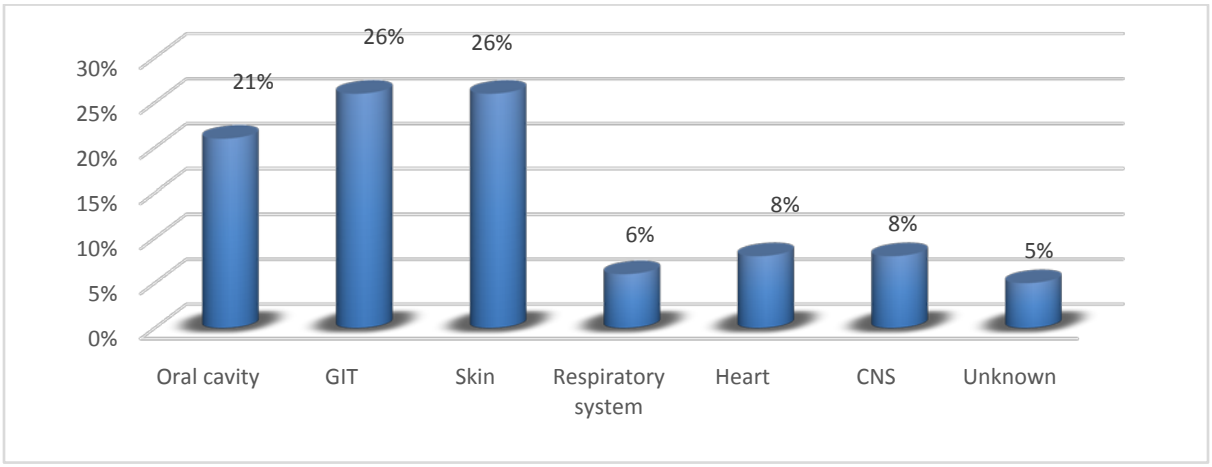

Figure 3: Systems affected due to ADRs

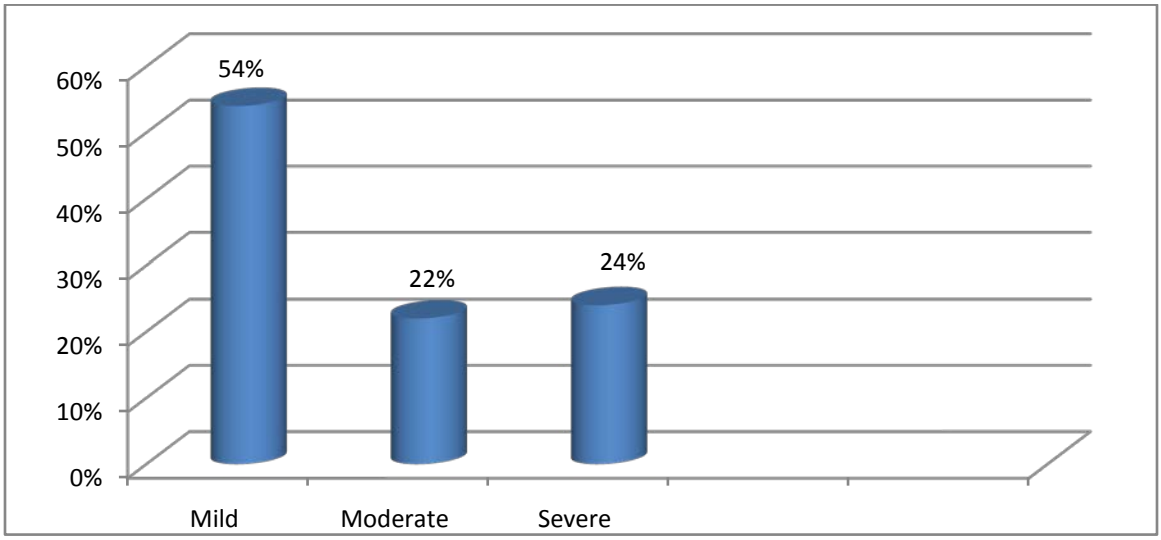

Figure 4: Level of Severity

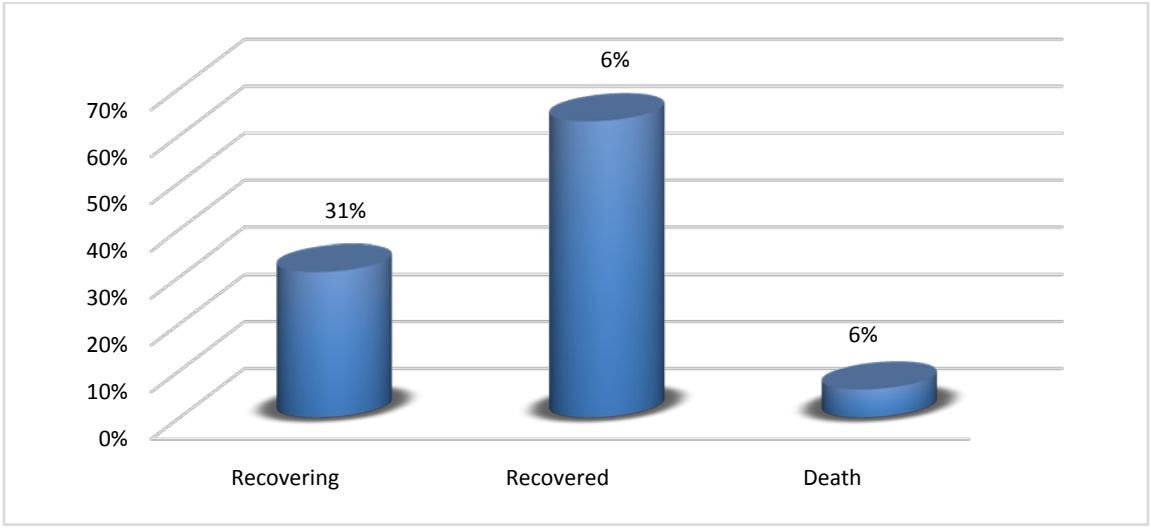

Figure 5: Outcome

Age	Male	Female	Total number of ADRs	Percentage (%)
1day-1year	11	11	22	21%
2-20 years	4	10	14	13%
21-40 years	6	20	26	25%
41-60 years	11	21	32	31%
>60 years	6	4	10	10%
Total	**38**	**66**	**104**	**100%**

Table 1: Sex and age wise distribution of ADRs

Name of Drug	Dosage form	No of ADRs
Vancomycin	Injection	23
Augmentin	Tablet/Injection	13
Ciprofloxacin	Injection	12
Clarithromycin	Syrup	12
Ibuprofen	Tablet/suspension	8
Penicillin	Injection	7
Dexamethasone	Injection	4
Cephtriaxone	Injection	3
Metronidazole	Tablet/injection	3
Paracetamol	Tablet	2
Sulphacetamide	Ointment	2
Heparin+Aspirin	Injection+tablet	2
Augmentin and ceftozidine	Tablet	1
Heparin	Injection	1
Paracetamol+Hydroxizine	Tablet	1
Meropenam+Lenzolid	Tablet/injection	1
Unknown drug	-	9

Table 2: Drugs causing ADRs

Category	No. of ADRs	Percentage
Type A	30	29%
Type B	74	71%
Total	**104**	**100%**

Table 3: Type of Reaction

IV. DISCUSSION

With the addition of a multitude of drugs to the physician's armamentarium, the treatment of many hitherto uncontrollable diseases has become possible. However, every progress has a price to pay, so is the case with the new drugs which have led to the iatrogenic diseases. Although most patients derive far more benefit than harm, a proportion of them experience adverse drug reactions (ADRs) from the use of the medicines at recommended doses and frequencies. [20,21]

This study was mainly conducted in general medical, surgical and derma units of the 5 government and 1 private hospital of Lahore. The data was collected from 150 health care providers (50 clinicians, 50 pharmacists and 50 nurses). Out of these 28% health care providers observed and reported the ADRs, 42% were only observed but not reported while 30% were those who neither observed nor reported the ADRs. In comparison with other studies for search of ADRs this can be considered as underreporting. It is a universal problem and many reasons were identified such as busy schedule of clinicians, lack of knowledge about the exact authority to report ADRs to, unavailability of ADR reporting forms, lack of incentives, reporting process being tedious and inadequate expertise. Our verbal discussion with health care providers revealed similar reasons for underreporting in many institutions.

The details of our study showed female gender predominance over males. This might be due to higher emotion quotient in females, which makes them more sensitive to the pharmacological actions of medicines. Rational dose titration may lead to minimization of ADRs in females. The larger percentage of ADRs was reported from geriatric and pediatric populations. In our study pediatric (21%) and geriatric patients (35%) experienced a higher percentage of ADRs than the adult population. Incidence of ADRs was found to be higher in older patients and pediatric patients due decreased basal metabolic rate, hypersensitivity, allergies, genetic causes, concomitant disease conditions and multiple drug regimens.

The antibiotics were the class of drugs which caused most of the adverse drug reactions. Out of these antibiotics vancomycin caused highest of the ADRs. These adverse drug reactions mainly affecting the GIT and skin. Thus implementation of antibiotic guidelines for the hospital scenario and strict adherence should be ensured to promote the rational use. Analysis of the type of reported ADRs revealed Type B predominance. Type B reactions comprise approximately 71% of all ADRs and include hypersensitivity drug reactions. Even though, most of them were mild reactions, they resulted in an increased health care cost due to an increased length of stay and need of some medical interventions as a result of incidence of Adverse Drug Reactions.

Treatment of ADR was provided to 94% of the patients. Mostly ADRs were allergic/hypersensitivity reactions. However, some reactions involved additional, poorly understood mechanisms that are not easily classified. Identifiable risk factors for drug hypersensitivity reactions include age, female gender, concurrent illness and previous hypersensitivity to related drugs. Treatment was largely supportive and includes discontinuation of the offending medication, symptomatic treatment and patient education. Patients with penicillin allergy should avoid carbapenams and caution should be used in prescribing cephalosporins in these patients. In case of vancomycinsensititvity, amikacin was used instead of vancomycin or reaction may be treated by slow administration of vancomycin. Usually for the allergic symptoms like fever, itiching and skin rash anti allergic medicines i.e. Avil injection (Pheniramine maleate) and SoluCortef (Hydrocortisone Sodium Succinate) and dexamethasone were used. Other includes prednisone, diphenhydramine and either ephedrine or a histamine H2- receptor antagonist. Different medicines were also used according to the symptoms of the ADR e.g. for skin reactions derma drugs were used.

Most of the adverse drug reactions are preventable. This calls for the urgent need to reinforce the monitoring of adverse reactions to drugs, public education against self-medication, inclusion of reaction monitoring, and an introduction to drug-safety in the curriculum of medical undergraduates, as well as systemic and periodic medical education of health professionals. This multi-pronged strategy could lead to a reduction in the incidence and severity of adverse drug reactions to be assessed in Pakistan. [22-24]

V. CONCLUSION

Awareness about ADR reporting is still poor ,amongst healthcare professionals in Lahore. The incidence and severity of ADRs are well documented. The incidence is more in hospitalized patients compared to ADR induced hospital admission. Antibiotics comprise the major drug family associated with ADRs so should be rationally prescribed. Geriatrics, pediatrics and females were most affected with ADRs. Improved communication between the physicians, pharmacists and nurses with the pharmacovigilance center in the hospital can reduce incidence of ADRs and improve patient quality of life. There is need for establishing ADR monitoring center at every multidisciplinary hospital. Also, more original studies need to be conducted in Pakistani population to know the exact prevalence of ADRs in Pakistani hospitals.

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