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Original article

Unveiling medication errors in liver transplant patients towards enhancing the imperative patient safety

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ABSTRACT

Background: Medication errors (MEs) are a significant healthcare problem that can harm patients and increase healthcare expenses. Being immunocompromised, liver-transplant patients are at high risk for complications if MEs inflict harmful or damaging effects. The present study reviewed and analyzed all MEs reported in Liver Transplant Patients.

Methods: All MEs in the Liver Transplant Patients admitted between January 2016 to August 2022 were retrieved through the computerized physician order entry system, which two expert pharmacists classified according to the type and severity risk index.

Results: A total of 314 records containing 407 MEs were committed by at least 71 physicians. Most of these errors involved drugs unrelated to managing liver-transplant-related issues. Antibiotic prescriptions had the highest mistake rate (17.0%), whereas immunosuppressants, routinely used in liver transplant patients, rank second with fewer than 14% of the identified MEs. The most often reported MEs (43.2%) are type-C errors, which, despite reaching patients, did not cause patient harm. Subgroup analysis revealed several factors associated with a statistically significant great incidence of MEs among physicians treating liver transplant patients.

Conclusion: Although a substantial number of MEs occurred with liver transplant patients, the majority are not related to liver-transplant medications, which mainly belonged to type-C errors. This could be attributed to polypharmacy of transplant patients or the heavy workload on health care practitioners. Improving patient safety requires adopting regulations and strategies to promptly identify MEs and address potential errors.

1. Introduction

Albert Einstein once said, "A person who never made a mistake never tried anything new." Medication errors (MEs) are a common and serious problem in healthcare, resulting in harm to patients and increased healthcare costs. According to the World Health Organization (WHO), the global yearly cost of medication errors exceeds $40 billion US dollars (WHO 2017). Healthcare professionals must accept responsibility and acknowledge their errors to move forward and learn to prevent repeating the same mistakes in the future. These errors may occur at any stage during the medication use process. Various MEs were realized, including prescribing, dispensing, administration, documentation errors, and inaccuracies while monitoring patient responses (Chen et al

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2019). A study investigated the medication related problems in liver transplantation patients. The majority were identified as unintentional nonadherence, drug use, or questions regarding drugs. The prevalence of identified medication related problems was reported as a percentage of a limited number of reported problems (n = 248) (Mulder et al 2022). Similar results including kidney transplant patients showed that documented significant or severe medication related problems occurred in 8% of 476 patients. The most common medication errors were patients taking the wrong dose of immunosuppressant, stopping some medications abruptly, or not starting some prescribed drugs. (Taber et al., 2012).

Healthcare professionals and researchers have identified several factors contributing to MEs, such as lack of communication, inadequate training, and system failures (Odukoya et al 2014, Ryan et al 2014). Healthcare organizations implemented several strategies to reduce the frequency of MEs, including employing the computerized physician order entry (CPOE) system and improving communication between healthcare providers and their patients (Colpaert et al 2006, Williams et al 2020). The pharmacist- driven intervention was shown to be crucially important and reduced medication list discrepancies significantly (from 95% to 28%) (Cohen et al 2020).

Hence, it is pivotal for all healthcare providers to be aware of these types of MEs to take the necessary precautions to prevent MEs from occurring or provide necessary treatment in cases of deleterious effects due to these mistakes. Therefore, systemic research is still warranted to recognize the most common MEs in any clinical healthcare setting, identify effective strategies for reducing these errors, and prioritize medication safety toward improving patient therapeutic outcomes. The present study aims to review and analyze the retrieved MEs detected in Liver Transplant Patients between January 2016 until August 2022.

2. Study design

This is a retrospective cross-sectional review study conducted at King Abdulaziz Medical City (KAMC), in Riyadh, the capital city of Saudi Arabia. KAMC is a tertiary-care hospital affiliated with the Ministry of National Guard Health Affairs (MNGHA) that provides various healthcare services to all kinds of patients and their families. All reported MEs with liver transplant patients from January 2016 to August 2022 were retrieved. Data were collected using a structured data collection format, which includes the age and gender of patients in addition to the prescription elements containing physician code, department, drug(s) details, and instructions of use. Random codes were assigned to the physicians involved in the MEs to maintain anonymity and avoid prejudice. Due to specified cohort and limited number of documented medication error reports, the sampling was inclusive to all reports which might be underpowered statistically.

Initially, the retrieved MEs were reviewed and classified by two expert pharmacists. Then, the potential hazardous outcomes of MEs were categorized according to the revised medication error index by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP 2022). This index considers all preventable events due to inappropriate medication use leading to MEs, whether the error reached the patient, and the extent of injury if the patient was harmed. No patients or physicians involved in the MEs were contacted. No names or other private information were collected.

3. Methods

Medication errors can be tracked and collected through different modalities one of these modalities is the voluntary reporting of events through a designated hospital reporting system. There is a hospital policy addressing the processes of reporting and managing these events. Following are some of the policy subjects but not limited to type of errors reported including mandate reporting any witnessed medication error within 24 h, classification of medication error based on a risk assessment tool, time frame to take action and close each event, and how to manage the event reported. The hospital classify medication errors either based on the process stage of medication use that adapted from ASHP such as planning, selection and procurement, storage, patient admission, Ordering, transcribing, reviewing, preparing, dispensing, administration, monitoring, patient discharge, evaluation.* Errors can also be classified based on the harm level formed by NCC MERP$ or classified by the class of medications e.g., chemotherapy, antithrombotic, anti-infective agent, etc.

Once the medication errors are submitted through the hospital reporting system the medication safety team will review the event and assign the proper classification to each incident. Some of these events required prompt analysis and investigation to take proper action to avoid reoccurrence of the error in the future however others were trended for further analysis to look for any common or special causes. Medication errors were reviewed in monthly basis as a task of Medication Use Process Error Subcommittee (MUPES) that consist of a different specialty member in the meeting such as a member from pharmacy, nursing, IT and medical to review, analyze, and identify the root cause of medication errors and make recommendations to prevent re-occurrence. Then a quarter of the reports of medication events reported to medication safety committee who reported to Quality and Patient Safety Department. The latest committee will further discuss the events and look for any area for improvement in a larger scope (Billstein-Leber et al 2018).

Results are summarized as mean ± standard deviation (SD) for continuous variables or as frequencies for categorical variables. Descriptive and statistical analyses were performed using GraphPad Prism Version 9.0 Software Package (San Diego, CA, USA). When appropriate, the unpaired *t*-test or Kruskal-Wallis one-way ANOVA test was used to estimate the significant difference between recognized variables and the various characteristics of the retrieved MEs. Statistical significance is considered at p-values less than 0.05.

4. Results

A total of 314 records containing 407 reported medication errors (MEs) were retrieved through the computerized physician order entry (CPOE) information system from KAMC, Riyadh, Saudi Arabia. The system recognized and documented these events from January 2016 to August 2022. The MEs involving male patients were slightly higher than their female counterparts (57.8% vs. 42.2%, respectively). Table 1 displays a summary of the general characteristics of patients and physicians who were involved in the recognized MEs. Of the 407 MEs, none were neonates or infants. Two-thirds (65.5%) of the patients involved in these MEs were adults over 46. On average, physicians were responsible for 5.7 ± 11.0 MEs. Almost half of the physicians (49.3%) had frequently committed MEs ranging from 2 to 67 times. Sixteen incidents of the identified MEs involved more than five flaws.

Table 2 shows the characteristics of the retrieved MEs. Peculiarly, the most encountered error was that medication was administered without an order (14.0%). For example, the charge nurse served an order for holding the morning dose of Tacrolimus under general instruction in the CPOE system. In another instance, Lasix (furosemide) was ordered to be administered once after a unit of packed red blood cells (pRBCs), unfortunately, given twice by a

Table 1
General characteristics of patients and physicians involved in the recognized Medication error.

	n (%)
Patient's gender (n = 255)	
Male	144 (57.8%)
Female	105 (42.2%)
Missing data n = 6 [¶]	
Patient's age (in years)	
Mean ± (SD)	54.2 (18.3)
Median (range)	58 (14 – 95)
Patient's age group (n = 255)	
Neonates and infants (birth to 1 year)	0 (0%)
Children and adolescents (1 to 17 years)	4 (1.6%)
Young adults (18 years to 30 years)	29 (11.9%)
Middle-aged adults (31 years to 45 years)	43 (17.7%)
Older adults (46 years to 65 years)	91 (37.7%)
Geriatric patients (above 65 years)	76 (31.3%)
Missing data n = 12 [¶]	
Frequency of errors per patient (n = 255)	
Once	184 (72.2%)
Twice	43 (16.9%)
Repeatedly (ranging from 3 up to 11 times)	28 (11.0%)
Prescription per medical department/unit n (%) [†]	
Internal Medicine	5 (1.6%)
Oncology Adult	14 (4.5%)
Transplant Unit	284 (90.4%)
Others	5 (1.6%)
Not identified	6 (1.9%)
Frequency of errors per prescriber n (%) [‡]	
Once	36 (50.7%)
Repeatedly (ranging from 2 up to 67 times)	35 (49.3%)

[¶] Not included in the descriptive analysis.
[†] Calculated out of n = 314 prescriptions.
[‡] Calculated out of n = 71 prescribers.

nurse at the ICU, even though no further pRBCs unit was administered. Missing drug dose(s) came in second (12.5%), followed by delayed drug administration and incorrect dosing (11.5% and 9.5%, respectively). In an inopportune case, an IV 1gm Ceftriaxone dose was missed at 0900hr by the day-shift nurse, and the patient went to the MRI department at 1000hr, then hemodialysis started at 1330hr and was completed at 1805 h. For other types of MEs, refer to Table 2. The most frequently committed MEs involved antimicrobial agents followed by immunosuppressants and analgesics (69 (17.0%), 54 (13.3%), and 51 (12.5%), respectively).

Remarkably, the most reported medication error-harm category was type-C errors (43.2%) (i.e., "errors occurred that reached the patient but did not cause patient harm"). Type-A errors (i.e., "events that have the potential to cause harm") came second, followed by type-B errors, where the "errors occurred, but the medication did not reach the patient" (i.e., "near-miss" type). Hardly in 26 (6.4%) cases, the "errors had reached the patient and required increased patient monitoring to confirm no harm/damage or intervention to preclude harm." Fig. 1 displays the distribution of MEs and the harm categories by the event year. Fortunately, most errors were minor to moderate, and no fatalities were recorded.

Table 3 shows analyses of factors associated with an increased risk of the recognized MEs among prescribers. Auspiciously, merely one-fifth of these events had included high-alert medications. Almost one-third of these cases involved prescribing and handling opioid analgesics (n = 27, 32.1%), followed by anticoagulant drugs, particularly warfarin and heparin (n = 25, 29.8%). However, among the other high-alert medications, various insulin products displayed the most remarkable statistically significant incidence rate of errors (p = 0.039). No statistically significant difference was found between the other drug groups (p = 0.6778).

Table 2
Characteristics of the recognized medication errors, n = 407.

	n (%)
Types of Errors	
Medication Given Without Order	57 (14.0%)
Dose Omitted	51 (12.5%)
Delay	47 (11.5%)
Incorrect Medication	37 (9.1%)
Incorrect Dose or Dosage Form	37 (9.1%)
Medication Duplicates or extra doses	25 (6.1%)
Medication Lost	24 (5.9%)
Wrong Patient	17 (4.2%)
Incorrect Route	16 (3.9%)
Incorrect Duration or Frequency	14 (3.4%)
Medication Discontinued	14 (3.4%)
Allergy	2 (0.5%)
Others [#]	66 (16.2%)
Medications Therapeutic Classifications	
Antimicrobial agents	69 (17.0%)
Immunosuppressants	54 (13.3%)
Analgesics	51 (12.5%)
Blood (i.e., Anticoagulants/Antiplatelets)	33 (8.1%)
Gastric acid-related disorders	27 (6.6%)
Electrolytes IV fluids	27 (6.6%)
Cardiovascular system drugs	26 (6.4%)
Nervous system drugs	17 (4.2%)
Antidiabetics and insulin analogs	16 (3.9%)
Diuretics (Furosemide)	15 (3.7%)
Total parenteral nutrition (TPN)	10 (2.5%)
Cholesterol-lowering drugs	6 (1.5%)
Respiratory system drugs	5 (1.2%)
Others	51 (12.5%)
Medication Error-Harm Category	
A-Potential to cause Harm/Damage	128 (31.4%)
B-Near-Miss, Error did not reach the individual	77 (18.9%)
C-Event reached individual, No Harm/Damage	176 (43.2%)
D-Required monitoring to confirm No Harm/Damage	26 (6.4%)
Date of the event n (%)	
Jan 2016–Dec. 2016	31 (7.6%)
Jan 2017–Dec. 2017	100 (24.6%)
Jan 2018–Dec. 2018	115 (28.3%)
Jan 2019–Dec. 2019	65 (16.0%)
Jan 2020–Dec. 2020	37 (9.1%)
Jan 2021–Dec. 2021	50 (12.3%)
Jan 2022–Aug. 2022	9 (2.2%)

[#] Others include dispensing expired medication, inappropriate storage, incomplete ordering, damaged medication packages, and lack of proper documentation.

A prominent statistically significant difference was realized among the four Medication Error-Harm Categories (p = 0.011). Type-C errors were statistically significantly higher than type-B and type-D errors, with p-values equal to 0.0036 and 0.0015, respectively. Remarkably, many (n = 34, 47.0%) participated in prescribing drugs belonging to different medication error-harm categories. Finally, despite reaching the patient, the substantially high incidence of type-C errors (n = 176, 43.2%) is not of great concern as they did not cause harm to patients.

5. Discussion

MEs are well-recognized issues leading to potential harm to patients and increased costs. Literature findings on MEs reveal they are ubiquitous in any healthcare setting. Being immunocompromised individuals, liver-transplant patients are at high risk for complications in the event of medication-related problems. MEs can inflict harmful or damaging effects on liver-transplant patients, including adverse drug reactions, delayed treatment, and increased healthcare costs (Kahriman and Öztürk, 2016, Ahsani-Estahbanati et al 2022).

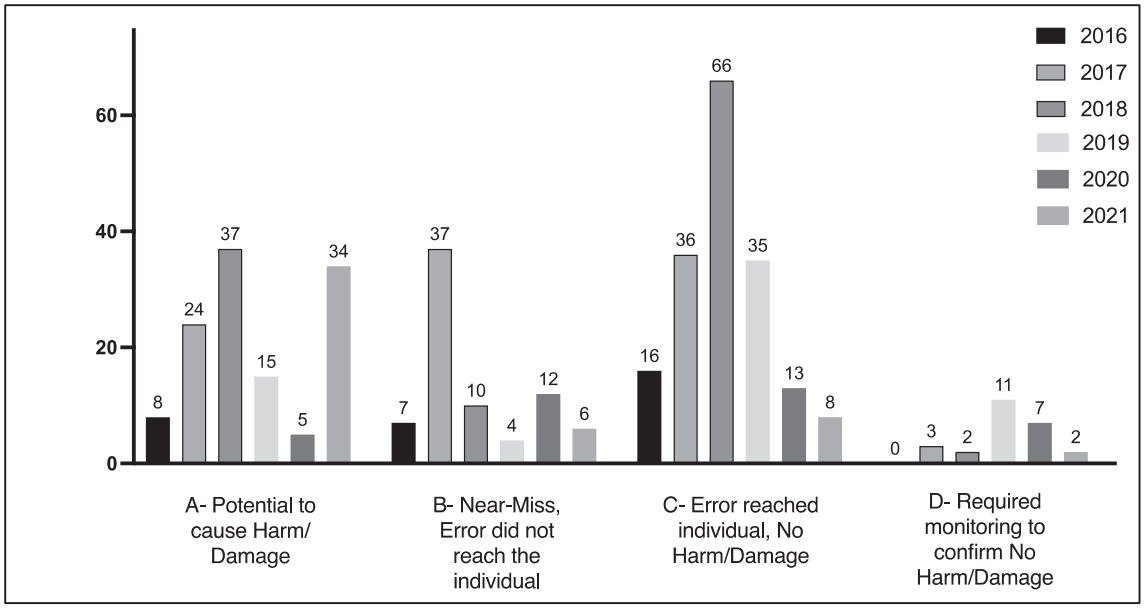

Fig. 1. Distribution of the Medication errors and harm category between January 2016 and December 2021. Total number = 398 (Data for the year 2022 are also not included because they are not representative of the entire year).

Table 3
Analysis of factors associated with the recognized medication errors (n = 407) among physicians, n = 71.

	Number of errors (%)	Mean ± SD	P-value
Physician Department		5.7 ± 11.0	
Internal Medicine (n = 5)	17 (4.2%)	3.4 ± 2.9	<0.0001
Oncology Adult (n = 7)	18 (4.4%)	2.6 ± 2.1	
Transplant Unit (n = 49)	356 (87.5%)	7.3 ± 12.9 *	
Others (n = 4) ¶	6 (1.5%)	1.5 ± 1.0	
Not identified (n = 6) ¶	10 (2.5%)	1.7 ± 1.2	
High-Alert Medication †			
No (n = 54)	323 (79.4%)	6.0 ± 10.7 *	0.003
Yes (n = 34)	84 (20.6%)	2.5 ± 2.4	
What type of High-Alert Medication? ‡	n = 84		
Opioids (n = 18)	27 (32.1%)	1.5 ± 0.6	0.039
Anticoagulants (n = 14)	25 (29.8%)	1.8 ± 1.3	
Insulin (n = 3)	11 (13.1%)	3.7 ± 4.6 *	
Electrolytes &TPN (n = 7)	12 (14.3%)	1.7 ± 1.1	
Immunosuppressants (n = 2)	4 (4.8%)	2.0 ± 1.4	
Others (n = 5) ¶	5 (6.0%)	1.0 ± 0	
Medication Error-Harm Category			
A-Potential to cause Harm or Damage (n = 34)	128 (31.4%)	3.8 ± 4.9	0.011
B-Near-Miss, Error did not reach the individual (n = 27)	77 (18.9%)	2.9 ± 2.9	
C-Event reached individual, No Harm/Damage (n = 34)	176 (43.2%)	5.2 ± 7.6*	
D-Required monitoring to confirm No Harm/Damage (n = 10)	26 (6.4%)	2.6 ± 2.0	

§Calculated for 105 physicians since 34 of them participated in prescribing drugs belonging to different medication error-harm categories.
¶ Not included in the statistical analysis.
† Calculated for 88 physicians since 17 participated in prescribing both high-alert and regular medications.
‡ Calculated for 34 physicians who participated in prescribing the 84 high-alert medications.

The present study reviewed and analyzed all MEs recognized by healthcare professionals, particularly pharmacists-in-charge, at the Liver Transplant Units. Pharmacists had done a great job of identifying and documenting these MEs in an inventory and monitoring system dedicated to medication errors. Due to the discretion and privacy of the identified data, access to this system is restricted to employees of the Quality & Patient Medication Safety Department. A substantial number of MEs have been found in prescribing medications to patients treated in the Transplant Units, with an average of 5.7 ± 11.0 MEs per physician, which far exceeds most MEs reported by other researchers in similar clinical settings (Mulder et al 2021). However, the retrieved MEs in the present study show a rather distinct distribution. Most of these errors do not relate to managing liver-transplant-related issues. For example, the most frequent MEs include antibiotic medications, whereas immunosuppressants, commonly used in liver-transplant patients, come in second with less than 14% of the identified MEs. However, the most often reported MEs belong to type-C errors, where, despite reaching patients, these errors did not cause patient harm. The subgroup analysis shows a statistically significantly more significant incidence of MEs among physicians treating liver transplant patients compared to physicians treating patients in other departments who also participated in treating patients in the transplant units. This could be attributed to the work-related stress because of the considerable burden that falls on treating physicians with liver transplant patients compared to other physicians who scarcely treat liver-transplant patients.

MEs were common, and their prevalence varies greatly depending on the concerned country and the healthcare setting. In a United States study that included 36 hospitals, the MEs occurred in 19.7% of hospitalized patients (Barker et al 2002). Another study in the United Kingdom found that MEs occurred in 8.9% of medication orders (Ashcroft et al 2015). Comparable ME rates were also found in Saudi Arabia (Ali et al 2017) and Canada (Wilmer et al 2010). However, MEs were remarkably lower in outpatient settings (Walsh et al 2009). Nonetheless, considerably greater incidences of MEs were also realized in Saudi Arabia (Alshammari et al 2022) and other Countries in the Middle East (Alsulami et al 2013) and Asia (Salmasi et al 2015). On the other hand, investigating MEs among patients in critical care settings such as intensive care (Shulman et al 2005), oncology (Abdel-Razaq et al 2022), and liver

transplant units (Mulder et al 2021) revealed substantial medication-related problems.

Several factors can contribute to MEs in these clinical settings, including human error due to miscommunication or lack of knowledge or training (Palojoki et al 2016), heavy workload due to inadequate staffing (Ehsani et al 2013), incorrect or incomplete information in the healthcare system (Velo and Minuz, 2009), poor health literacy and language barrier among patients (Khan et al 2020), complex medication regimens (Wimmer et al 2016), or because of technical issues (Samaranayake et al 2012). MEs can also occur due to a combination of all these factors. Currently, most healthcare organizations use electronic prescribing systems to facilitate communications and reduce errors caused by illegible handwriting, incorrect prescriptions, and drug interactions. However, several studies have failed to report significant reductions in error events due to just using such electronic systems (Sittig and Singh, 2012, Palojoki et al 2016). Therefore, other strategies should be meticulously implemented to prevent or at least minimize MEs in any clinical setting. Having updated healthcare professionals on medication safety by providing regular education and training sessions helps reduce the incidence of medication errors and improve patient safety (Patel et al 2008), Bressers et al 2021). The causes of medication errors were discussed in few previous studies and many different populations. A study in lung transplant cohort which is definitely different than liver transplantation patients concluded that non-adherence to medication in an outpatient setting would be a reasonable cause, however, our study is strictly dealt with in patient transplant which made this factor irrelevant. (Irani et al 2007; Friedman et al 2007).

Rigorous regulations should also be adopted to ensure medication use revisions to identify and address potential errors before they occur promptly. Moreover, it is pivotal to encourage the active participation of all healthcare professionals in the unprejudiced reporting of all medication-related problems in addition to direct communication between healthcare providers and their patients (Berman & Chutka 2016). Appropriate medication reconciliation processes are also necessary to ensure patients are fully aware of any potential adverse effects or interactions related to their medications (Mekonnen et al 2016). Furthermore, a study showed that the pharmacist working in multidisciplinary teams had the capability to identify and resolve and may reduce many medication errors that improved medication safety. (Ho et al 2013). It is crucial to remember that some MEs may go unreported or unrecognized, making it challenging to avoid or manage their deleterious effects.

The role of clinical pharmacist in the detection, reporting and prevention of medication errors (MEs) in a pediatric surgery, emergency department, and primary care units was investigated and proved to have an essential role in reducing MEs and it was found that voluntary reporting is a major strategy to prevent MEs by learning from reported errors (Jaam et al 2021, Ahmed et al 2019). Moreover, a random sample of 254 HCPs were surveyed to assess their awareness of Direct Healthcare Professional Communication (DHPC), where multiple barriers were identified (Faied et al 2019). In another study, hospital pharmacists received training on ME reporting using the national reporting system, there are common problems among different healthcare systems, so that sharing experiences on the national level is essential to enable learning from MEs. Internationally, there is a great need for standardizing ME terminology, to facilitate knowledge transfer (Shehata et al 2016).

One of the limitations that our study did not investigate the relation between the potential to harm and clinical outcome. This is a retrospective evaluation that is multifactorial and may be further prospective studies will be carried out for root cause analysis as well as cost effectiveness of early interventions will be warranted. In addition, under-reporting of medication errors that lead to small sample size can be addressed by enforcing the clinical pharmacist vital role in this important issue.

6. Conclusion

The current report has revealed a substantial incidence rate of errors with liver transplant patients, particularly type-C errors that inopportunely reached the patient but did not cause harm. However, most of the identified errors are related to medications that do not directly concern the management of liver transplant-related problems, such as antimicrobials and analgesics. This could be primarily due to different causes that were not answered in this research. Further prospective root cause studies may provide some solid answers.

Disclaimer

This study was approved by the Institutional Review Board at King Abdullah International Medical Research Center (KAIMRC), Riyadh, Saudi Arabia (#IRB/1172/22).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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