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Adverse Drug Events and level of harm in Hospitalized Pediatric Patients in Palestine: A retrospective cohort study

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This Thesis was submitted in Partial Fulfillment of the Requirements for the Master's Degree in Health Informatics.

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Dedication

This thesis is dedicated to my family and many friends. I owe a special feeling of gratitude to my beloved parents, Hatem and Nuha, whose words of encouragement and unconditional support inspired me to keep going. My sister Nour, my brothers Ahmed and Abdelwahab, they have always been by my side and offered me advise. To my close friends and colleagues, who supported me in many steps of this work.

I also dedicate this work to my supervisors, Dr. Shahenaz Najjar & Dr. Yousef Mimi who guided and supported me in this process and kept me on track.

Declaration

This thesis was submitted in partial fulfillment of the requirements for the Master's degree in Health Informatics.

I declare that the content of this thesis (or any part of the same) has not been submitted for a higher degree to any other university or institution.

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Date: 04 / 07 / 2022

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Thanks to God, I was able to complete my thesis despite the challenges and difficulties I encountered.

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List of Abbreviations

ADE: Adverse Drug Event;

ADR: Adverse Drug Reaction;

AE: Adverse Event

MOH: Ministry of Health

IHI: Institute for Health care Improvement;

GTT: Global Trigger Tool;

ME: Medication Error

NCC MERP: National Coordinating Council for Medication Error Reporting

MENA: Middle East/North Africa

IOM: The Institute of Medicine

RRR: Retrospective Record Review

IR: Incident Reporting

IRB: Institutional Review Board

PTT: Partial Thromboplastin Time

Abstract

Introduction: Patient safety is a major public health concern around the world. Adverse events increase mortality, morbidity, length of hospital stay and costs. Whereas adverse drug events (ADEs) resulted in higher medical costs, longer hospital stays, morbidity, and ascribable disability all around the world. In Palestine, there is limited data and research on adverse events, precisely medication error. There is an absence of system and tools to detecting the level of harm in terms of hospitalized pediatric patients even with the availability of traditional systems for reporting adverse drug events (ADEs).

Aim of the study: To assess the level of pediatrics adverse drug events (ADE) and harm for pediatric patients during delivering medical treatment and to identify ADE related risk factors in Palestinian hospitals.

Materials and Methods: A quantitative retrospective study conducted using the institute of healthcare improvement (IHI) Global Trigger Tool (GTT) for measuring adverse events (Pediatric ADE Patient Record Review Sheet). The study population comprised patients who had been hospitalized in pediatric wards at each of the six hospitals included in a five-month period from August, 2021 to December, 2021 at each hospital. A total of 600 pediatric patient charts were selected in a systematic random sampling method (100 records per hospital), reviewed, and evaluated according to the IHI GTT instructions.

Results: Among the 600 patients 58.5 % were males and 41.5 % were females with mean age of 2.36 years. Overall, 291 triggers were identified, the most frequently detected trigger across all records was trigger T9 (*Abrupt cessation of medication*, n = 57), followed by trigger T8 (*Rash*, n=55) and trigger T1(*use of anti-allergic drugs*, n=52). The results show that one out of every four pediatric patients suffer harm in

Palestinian hospitals. Harm levels detected showed that 15.2% resulted in temporary harm that required an intervention (category E) followed by 5.5% that resulted in temporary harm that required prolonged hospitalization (category F).

Hospital type, patient age and the length of stay were statistically significant having a correlation to the presence of ADEs and the level of harm with (p-value = 0.000), with regards to area/region the results showed that the occurrence of ADEs gave a statistically significant difference in favor of the south area (p-value = 0.002). Gender was not significantly associated with ADEs.

Conclusion: Our study is the first to assess the adverse drug events occurrence in hospitalized pediatric patients in Palestine showing that one out of every four pediatric patients suffer harm in Palestinian hospitals with most ADEs resulting in temporary harm (Category E and F). Therefore, efforts should be directed towards improving the quality of care and applying policies in health sectors to ensure patient safety.

Keywords: adverse drug events, harm, Global Trigger Tool, patient safety.

Chapter 1: Introduction

1.1 Background

Patient safety is becoming increasingly important worldwide to health and social care providers. The ability to assess obtained patient safety levels, identify areas where improvement is needed, and track the impact of applied actions is an essential component in applying patient safety [1]. Preventing adverse events and/or recognizing them in time so that they can be dealt with and possibly minimized is very beneficial and represent the future direction of growth in patient safety initiatives[1].

Regardless of the exact incidence of errors that result in harm, only one aim is clearly acceptable to every patient and their family, which is zero preventable harm [2]. This can be accomplished in the context of patients living longer with many comorbidities and acute diseases, as well as increasing treatment quality and leading to several measures for enhancing the quality and safety of care to [2].

The healthcare system has become increasingly complicated worldwide, and significant organizational changes are ongoing, showing that human error can be perceived as either created by individuals or due to organizational problems. As a result, errors must be viewed considering the environment in which they occurred[3].

Healthcare professionals are not exempt from errors and misjudgments due to the complexity of today's care[3]. The medical staff is treating patients , nurses and physicians , whose perspectives and experiences are all different however are considered key

groups of healthcare providers[3]. Healthcare providers are responsible and are linked to all levels of the healthcare system, which include patients, teamwork, and the hospital management[3]; leading to discussions regarding the causes of error, and the creation of many patient safety tools, to reduce patient harm[3].That actively demonstrates the acknowledgment of adverse drug events (ADEs) occurrence and measuring them is vital for improving health care and increasing patient safety[4]. Measuring ADEs and levels of harm accurately, on the other hand, is challenging, and the findings of various measurement methods are varying[5].

Adverse drug events are *"the injuries that are either related to the dose of the drugs or the medical interventions"* according to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) [6], they are common in hospitals, occurring either in patients before admission or when being hospitalized, occurrence might also be as a drug reaction or as a consequence of a medication error[7]. They are the fifth greatest cause of death worldwide, accounting for a significant number of hospital admissions[6]. The terms "adverse drug events" and "adverse drug reaction" have been sometimes used interchangeably. However, distinction between definitions is crucial in clinical practice as many have minor variances but plays a role in decision making, for instance an adverse drug reaction (ADR) is "*a response that is noxious and unintended to a medicinal product"*[8] ;therefore, it is agreed upon that all ADRs are referred to as ADEs, although not all ADEs classify as ADRs[6].

Patient safety has become a global concern of healthcare systems[9]. A fragile safety and quality culture, weakens the health care systems' ability to guarantee safe health care[9].

This issue has risen to the top of health-care organizations' priorities in recent years leading to a major rise in research, standards, efforts, and measures focused on patient safety since the publication of the 1999 IOM report *"To Err Is Human: Building a Safer Health System"* and a lot has been learnt about patient safety in pediatrics in particular[10]. Hospitalized pediatric patients are particularly vulnerable to ADEs, are unable to make decisions about their own treatment and have different needs to ensure that their health care is safe, therefore, health practitioners should pay particular attention to them [11,12]. Preventing the occurrence of *"avoidable harm"* is considered as the main purpose in the field of patient safety, particularly, during treatment and care of hospitalized pediatric patients[9]. Even though, there is limited knowledge about overall ADEs in pediatric care[13].

To sum up, assessing the level of adverse drug events will help healthcare providers to highlight areas where adverse drug events occur leading to improve pediatric patient safety. Furthermore, it will serve as a starting point to bringing attention to creating policies to resolve the critical problem of patient safety and quality of pediatrics inpatient care[14].

1.2 **Problem Statement**

Adverse events increase mortality, morbidity, length of hospital stay, and costs[15]. In Palestine, there is limited data and research on adverse events, precisely medication error. There is an absence of systems and tools to detect the level of harm in terms of hospitalized pediatric patients, even with the availability of traditional approaches for reporting adverse drug events (ADEs).

1.3 Significance of the Study

In the Palestinian context, some studies have assessed the level of adverse events rate. However, limited studies have been carried out in the Palestinian context to assess pediatric patients' safety levels. To date, our study is the first study to assess the adverse drug events occurrence in hospitalized pediatric patients[1617].

Therefore, this study will be carried out to fill the knowledge gap and contribute to the existing literature by assessing the adverse drug events using medical records review. This in turn, will help healthcare providers to highlight areas where adverse drug events occur, leading to improve pediatric patient safety. Furthermore , the results of this study will serve as a starting point for achieving the desired outcomes [5,18], bringing attention to creating policies to resolve this critical problem of patient safety and quality of inpatient care[14].

The lack of studies on medication errors in the Palestinian medical system makes this research a pioneer in discovering this issue. Our research will be a baseline study for healthcare providers and healthcare policy in Palestine and Middle East/North Africa (MENA) region. It will be the ground for introducing interventions to improve pediatric patients' services and reducing costs related to having ADEs.

1.4 Aim of the Study

To assess the level of pediatrics adverse drug events (ADE) and harm in Palestinian hospitals when delivering medical treatment and to identify ADE related risk factors.

1.5 Objectives of the Study

The main objectives of this study are to:

1. Describe the incidence of ADEs and their categories in pediatric inpatients
2. Identify ADE related risk factors and levels of harm,

1.6 Thesis Outline

This thesis contains the following chapters:

CHAPTER 1: INTRODUCTION:

This chapter introduces the thesis topics, background, problem statement, significance of the study, purpose of the study and the objectives.

CHAPTER 2: LITERATURE REVIEW:

This chapter includes a general introduction, then a literature review on the patient safety, adverse events (AEs) in which adverse drug events (ADEs), severity of ADEs, incidence and prevalence of ADEs and the detection methods were reviewed from the literature. Moreover, the global trigger tool (GTT), the pediatric patient safety and ADEs, tools to assess ADEs, the trigger tool to measure ADEs, in addition to the levels of harm and pediatric ADE triggers were as well reviewed. Finally, the considerations and limitations of the GTT.

CHAPTER 3: METHODLOGY

In this chapter, the research methodology is presented. The study design, study setting, study population and sampling, inclusion criteria, data collection tool, review process, statistical analysis, and ethical consideration were stated.

CHAPTER 4: RESULTS:

The study findings and illustration of output have been mentioned there.

CHAPTER 5 DISCUSSION & CONCLUSION:

In this chapter, the main study findings, the study's conclusion, recommendations, future work will be presented.

Chapter 2: Literature Review

2.1 Introduction

Two decades ago, the Institute of Medicine published the *To Err Is Human* report that had a revolutionary role in raising patient safety profile, expanding nowadays [14]. According to the World Health Organization (WHO), patient safety is defined as "*the absence of preventable harm to a patient and reduction of risk of unnecessary harm associated with health care to an acceptable minimum*" [19]. The main part of the healthcare organizations' plan is to prevent harm caused by the process of health care itself, mainly hospitalized patients, and reduce the risk of extreme adverse events (harm) to an acceptable minimum [20].

Tools and methodologies were developed and standardized to evaluate and investigate the prevalence of adverse events and detect the level of harm to ensure the preventability of errors during hospitalization of pediatric patients (patients under 18 years of age) as little is known about overall Adverse Drug Events (ADEs) occurrence in pediatric care [11] [21].

2.2 Patient Safety

Despite considerable progress, patient harm continues to be a daily problem in healthcare systems worldwide. The Institute of Medicine's (IOM) study *"To Err is Human"* started a global movement for patient safety in 1999 [22]. Over two decades ago, IOM estimated that 98,000 people die each year as a consequence of preventable harm. [2]. On the other hand, a more recent study (although still debatable and utilizing different

methodology than the IOM) estimated that medical errors cause 250,000 deaths in the United States each year [2].

In most cases, patient harm is avoidable, is caused by unsafe care, and is considered a growing public health challenge leading to death and disability worldwide[23]. To maintain patient safety, healthcare systems should create an environment free of accidental injury by implementing operational processes and procedures that reduce the risk of errors and increase the chances of identifying them before they happen[15].

The WHO established a conceptual framework to provide a uniform understanding of the domain of patient safety with the goal of standardizing definitions and terminology [24]. The International Classification for Patient Safety (ICPS) is a tool for improving patient care by facilitating the description, comparison, measurement, monitoring, analysis, and interpretation of data[24]. ICPS defines patient safety as *"the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available and the context in which care was delivered weighed against the risk of non-treatment or other treatment"*[25]. The goal of the conceptual framework is to provide a thorough understanding of the patient safety area and to demonstrate a continuous learning and improvement cycle that focuses on risk identification, prevention, detection, reduction, and incident handling[26]. All these things can happen at any time and in any place inside the conceptual framework. The concepts developed by the ICPS are the beginning of a long process of continuously improving a uniform international understanding of terms and concepts related to patient safety [25]. A

reportable circumstance, near miss, error, or adverse event are all examples of "*incident types"*[24]. Patient characteristics, incident characteristics, and contributing factors are all important descriptive data for understanding the incident's outcome[24]. The impact on a patient that is entirely or partially due to an incident, as measured by the severity of harm, is referred to as a "*patient outcome"*[24]. On the other hand, the relationship between the type of incident and the relevant elements is complicated; a single incident usually involves more than one contributing cause or hazard, and one incident can be a contributing factor in another[24]. A *harmful incident (adverse event)* is an incident that results in harm to a patient [25]. All healthcare organizations' efforts are now headed towards improving patient safety, especially monitoring in-hospital adverse events (AEs) [27]. On the other hand, improving medication safety and highlighting the importance of quantifying and classifying the occurrence of preventable medication errors (MEs) is crucial[28].

As it is known that MEs and other forms of errors tend to be harmful; however, others cause no harm to the patient and are not classified as AEs [29]. Therefore, improving patient safety must have the main part of monitoring the level of safety and level of harm [18.] The focus on patient safety has emerged the need for an efficient strategy to detect patient harm other than the traditional methods used for reporting adverse reactions, which only focus on spontaneous reporting and tracking of errors, also known as passive AE reporting.

2.3 **Adverse Events (AEs)**

The Institute for Healthcare Improvement (IHI) defines adverse events as follows : *"unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment or hospitalization, or that results in death"* [21]. Other definitions of AEs published by other organizations had the terms that described the adverse outcome that arises from medical care rather than from the patient's underlying condition[24]. Moreover, having those definitions increases the focus on the events for the purpose of implementing and improving the interventions intended for the prevention [4].

Errors and near misses are two more phrases that are commonly used. Any act of commission (doing something wrong) or omission (failing to do the correct thing) that exposes patients to potentially hazardous situations is referred to as an *error*[4]. Errors, unlike AEs, may or may not cause harm to the patient, and not all AEs are necessarily caused by errors[4]. A *near miss* is a potentially dangerous scenario that either resolves independently or is neutralized before it becomes an AE [4]. When using the term *error*, the question of who is to blame frequently arises[4]. Because adverse events have apparent clinical consequences, they are more likely to elicit a complete evaluation of the system factors that led to the adverse event from both physicians and administrators, with a clear focus on improving patient outcomes[21].

The terms adverse drug event (ADE), adverse drug reaction (ADR), and medication error (ME) are currently used to identify medicine-related adverse events[30]. Although these phrases are sometimes confused, they describe events that differ both

"*pharmacologically"* and "*phenomenologically"*; an ADR is a reaction that is usually immediately due to the pharmacology of the triggering drug, whereas this is not always the case with an ADE[30]. An effect that is caused by a drug is considered an ADR; whilst the ADE is how a patient reacts to that effect[30]. Therefore, while all ADRs are ADEs, not all ADEs may be classified as ADRs[30]. Consequently, medication errors are used to divide ADEs and ADRs into preventable and non-preventable; as what is caused by a medication error is considered as preventable, whilst an ADE or ADR that occurred independently is not[30].

2.3.1 **Adverse Drug Events (ADEs)**

The concept of medication-related adverse outcome; points out a problem in the medication process caused by health care professionals while delivering care to patients[31]. This approach encompasses both medication incidents (preventable medication errors and near misses) and medication-related adverse events ; adverse drug events resulting from medication errors or adverse drug reactions resulting from the qualities of the medications provided [31].

Along the lines of having a clear definition of an adverse event for any attempt to identify harm, an adverse drug event (ADE) is defined as follows by the World Health Organization's (WHO) Collaborating Centers for International Drug Monitoring: "*Noxious and unintended and occurs at doses used in man for prophylaxis, diagnosis, therapy, or modification of physiologic functions"*[21]; as an ADE is also known to be a synonym to harm so if an ADE happens without being induced by an error, it is described as an adverse drug reaction (ADR) caused by the drug's properties[31]. Drugs,

blood products, and fluid infusions can all trigger an adverse drug event. One of the most prevalent adverse events in developed countries is drug treatment-related adverse events [4]. An adverse drug event can have significant effects, and it's anticipated that 1 out of every 16 hospitalized patients will experience an ADE , resulting in significant financial losses[4]. Therefore, detecting ADEs and being able to determine the severity and level of harm caused is very important.

2.3.2 **Severity of ADEs**

It is crucial to understand why AEs happen in order to prevent them and remove or reduce risks[31]. Moreover, it is critical to know what can happen and when in order to ensure desired outcomes, plan proper responses, and increase readiness[31]. It is possible to find approaches to improve the safety of care after evaluating the harm and understanding the causes and contributing factors[31].

According to WHO guidelines, ADEs are categorized according to the severity of the harm to the patient (mild, moderate, severe, and death) and their preventability (preventable, not preventable)[32]. It is commonly acknowledged that medication-related adverse effects can cause serious harm to patients, including death. ADEs and MEs, on the other hand, can be relatively harmless, causing only minor adverse effects in the patient[31]. This is particularly true for MEs, which can be detected before reaching the patient and hence cause no actual harm despite creating an intrinsic risk to patient safety. As a result, it is estimated that 25-50 % of ADEs and ADRs cause serious harm to patients[31].

As has been previously reported in the literature, the proportion of MEs that result in severe patient harm ranges from 0.9 % to 9%, moreover, just 2.8 % of all MEs result in real ADEs[31].

Because AEs are prevalent and have a wide range of reported incidence, it's critical to be able to recognize them in order to prevent future AEs and to have an effective method for reducing AEs[33].

2.3.3 **Incidence and Prevalence of AEs**

The goal of categorizing AEs into types is to obtain knowledge about healthcare-related topics to improve patient care. Because the definition of an adverse event focuses on events resulting from medical treatment, AEs should be classified into clinical categories based on the cause of the incident that resulted in the patient's outcome[24].

Adverse drug events are a leading cause of morbidity and mortality worldwide. An ADE is thought to cause one out of every five in-hospital injuries or deaths, with an annual incidence of up to 450,000 injuries in the United States[34].

Because ADEs, ADRs, and MEs can occur in any context involving the use of drugs, they are found in practically every health-care setting[30]. According to Laatikainen & Outi, 2020 several studies on hospital-acquired ADEs, ADRs, and MEs have been done. Depending on the selected specialty, age group, and event definition, the prevalence of ADE and ADR ranges from 1.6 % to 58 % in individual research[30]. Furthermore, the interchangeable use of the terms ADE and ADR in some research increases variability and leads to misreading of the results [30]. Consequently, and according to Laatikainen & Outi, 2020; data abstraction is complicated by a lack of consistency in the use of correct terminology as well as differences in patient demographics between specialties, as

evidenced by estimates from a number of systematic reviews and meta-analyses involving inpatient ADEs and ADRs[30].

According to another study conducted in Palestinian hospitals by Najjar et al. 2013, 70% of the AE's that caused harm might have been avoided for every 1 of the 7 harmed patients (14.2%)[16]. On the other hand, a retrospective study performed in Saudi Arabia by Khan, Al-Harthi et. al 2013 showed an incidence rate of adverse drug reaction of 4.5%[35].

As per the study performed in the USA by Holdsworth et al., 2003 , using a prospective review of medical records as their method; the findings showed a rate of ADEs (6/100 admissions, 7.5/1000 patient days) and potential ADEs rate (8/100 admissions, 9.3/1000 patient-days) in hospitalized children[36]. The incidence of ADE in a study conducted on adults by Zimlichman et al., 2018 showed that 1.54 ADEs were found for every 100 days of hospitalization and 1.81 ADEs for every 1000 doses of medication [34].

2.3.4 **ADE Detection Methods**

There are several approaches for detecting AEs. However, because each of the available methods has its own set of limitations, no approach can be recognized as a definitive standard[37]. ADEs can be detected using various methods, including retrospective patient chart reviews, analysis of hospital incident reports, and direct observation of clinical practice.

Each method has its own set of strengths and limitations, as well as the ability to detect a variety of issues[38].

The following sections will have more details about every method has showing its strengths and limitations in detecting AEs.

2.3.4.1 **Voluntary Incident Reporting (IR)**

Many hospitals worldwide compile data on either mandatory or voluntary reported incidents in their databases[38]. The major goal of reporting occurrences is to learn from them so that they don't happen again, and encourage health-care systems to improve their response to near-misses and errors[38]. Because the data is already available for study, analyzing the data via incident reporting databases is relatively inexpensive and simple[38]. However, a tiny fraction of medication errors is ever recognized and are dependent on estimates, only 10%-20% of them are reported; representing just a small portion of the total number of medication errors[38]. Voluntary incident reporting (IR), is based on information voluntarily collected by personnel directly involved in the incident. To achieve a high level of employee participation, a robust safety culture is required. As a result, IR detects only a small number of AEs, underestimating the true scope of the problem[37].

2.3.4.2 **Direct Observation**

The observation method has been found to be more accurate and efficient than checking patient charts or incident reports in detecting MEs. The Härkänen et al., 2020 study showed that observations had an 11.7 % error rate, chart reviews had a 0.7 % error rate, and incident report reviews had a 0.04 % error rate[38]. When opposed to incident reports or chart reviews, the method is time consuming and consequently resource-intensive. The average cost per studied dose of medication was $4.82 for observations and $0.67 for chart reviews.

On the other hand, direct observation has been found to identify many AEs that are not reported but is too expensive to use in organizations on a regular basis[37]. Furthermore, because the observation method only offers information regarding the observed moment, several factors contributing to errors may go undetected. The observation must be done in a relatively short amount of time. This means that it can't be used to track medication-related problems over time[38].

2.3.4.3 **Retrospective Record Review Methods (RRR)**

Retrospective chart review is a commonly used procedure that is based on the analysis of frequently gathered data. Compared to IR, it provides a more accurate picture of organizational risk. It is, however, both resource and time-intensive[37].

When compared to other methodologies, the retrospective record review method (RRR) has been demonstrated to identify significantly more incidents and according to the study performed by Härkänen et al., 2020 based on a previous study, record reviews were found to be more successful than voluntary incident reporting in identifying errors[3] [38].

The Global Trigger Tool (GTT), the Harvard Medical Practice Study (HMPS), and the Wimmera Clinical Risk Management Model are the three primary types of RRR techniques. All the strategies are aimed at identifying adverse events (AEs) and harm in patients[3]. It is possible to acquire perspective on problem areas that require change through assessment and intervention. This can be achieved by using structured record review to identify AEs[3]. Structured record reviews are frequently conducted on a random sample of admissions and can be done prospectively or retrospectively[3].

2.3.4.4 **The Global Trigger Tool (GTT)**

In the early 1990s, the term "trigger tool" was coined in the United States to describe a strategy for detecting probable adverse drug events[39].The focus on patient safety has emerged the need for an efficient system to detect patient harm other than the traditional methods used for reporting adverse reactions, which only focus on spontaneous reporting and tracking of errors, also known as passive AE reporting. The chart review method as an adopted active retrospective technique for adverse event detection is being used by many hospitals [18,39,40]. The process is done based on the review and analysis of available patient data, showing much promise in increasing detection of adverse events[18].

In late 2003 the Institute for Healthcare Improvement (IHI) developed the Global Trigger Tool (GTT) for measuring adverse events (harm). This tool is used in hundreds of hospitals in multiple countries to detect adverse events rates while improving patient safety [21]. The GTT defines harm as *"an unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment, or hospitalization, or that results in death"* [37]. Tracking adverse events over time is a valuable method to tell if changes being made improve the safety of health care; medical record review allowed rapid examination of medical records by using a set of "triggers" to enable the reviewer to detect and identify possible AEs[21,41]. The tool focuses on harm that occurs during the active delivery of care; events related to substandard care are excluded [29].

The literature showed that the GTT had better results in detecting more AEs than any other methods [15]. Even though the IHI GTT was intended for adults, it was tested on pediatric inpatient records and showed patient damage in more than one-third of

admissions considering that little is known about adverse events (AEs) in pediatric patients [13,42].

According to Kirkendall et al., 2012 the GTT showed the best results in detecting AEs in adult and pediatric populations, with a sensitivity of 94% and a specificity of 100% [18]. Moreover, the review performed by Hibbert, Peter D et al, 2016 shows that if a hospital reviewed 20 records/month as per the GTT protocol, and assuming an AE rate of 30%, 6 AEs would be detected per month[43].

Retrospective patient record review was the common methodology used in the studied literature to identify AEs using the GTT or establish a trigger tool based on the GTT developed by the IHI.

Sam, Lian, Jessica, & Parasuraman, 2015 used a modified version of the Institute for Healthcare Improvement (IHI) Global Trigger Tool to identify the ADEs. The modified version included 24 triggers. They aimed to determine the extent and types of ADEs from patient records and identify the causative factors of medication errors and determine the potentiality and severity [44].

Studies were conducted to detect ADEs using the GTT technique, considering it a proficient method to fulfill their objectives and aims, targeting either adult or pediatric patient population. Hu et al., 2019 conducted the first study to analyze and categorize the AEs of geriatric patients, and they were able to describe the level AEs identified by medical record review [33]. On the other hand, in two different studies conducted by Pierdevara et al., 2016 and Grossmann et al., 2019 the use of GTT allowed the researchers to identify the rate of AEs, and the relation between the length of stay at the hospital and the rate of occurrence of ADEs [20,27].

2.4 Pediatrics Patient Safety and Adverse Drug Events

Many organizations, including the National Quality Forum, Institute for Healthcare Improvement–National Patient Safety Foundation, Agency for Healthcare Research and Quality (AHRQ), the Joint Commission's national patient safety, and others, are involved in patient-safety efforts [10].Despite the multitude of studies on adverse drug events in adults, there are few published studies on pediatric-specific adverse drug events (ADEs) with the suggestion that the rate of harm due to ADEs in pediatrics is higher than that in adults[45]. According to the literature, pediatric ADEs can occur at a rate of 6.6 to 15.7 per 1000 patient days and 1.2 per 1000 medication doses , with a potential ADE rate of 10 per 100 admissions[45].

ADEs are a significant public health issue in the pediatric population. Even with all the efforts to lower the occurrence of medication-related adverse events, the morbidity and death rates from drug-induced reactions, particularly in the pediatric population, remain unacceptably high[46]. On the other hand, it has been observed that ADEs in children result not only in hospital admissions or prolonged hospitalization, but also permanent disability or even death[46].

2.4.1 Tools to Assess ADEs

From another perspective, it was crucial to review studies that targeted the pediatric population. The aim was to estimate the performance of a pediatric trigger tool; designed based on the GTT in detecting harmful medication errors [13,33]. Measuring AEs and levels of harm in pediatric inpatients using the GTT demonstrated utility in the pediatric inpatient setting according to Kirkendall et al., 2012 and MC et al., 2017,

showing a correlation between the number of triggers and the possibility of detecting an AE more significant [18,47].

The two studies conducted by Kirkendall et al., 2012; MC et al., 2017 using the GTT to measure pediatric patients' adverse events showed similar results in terms of the AEs category, mostly E and F (temporary harm). Moreover, there was a positive connection between AEs and medical care triggers, and the more extended stay in the hospital had a considerable effect. The number of triggers and the number of adverse events per patient were found to have a positive correlation [18,47]. Using the GTT regularly has the advantage of characterizing the most common types of AEs aiding in quality improvement, and increasing healthcare professionals' awareness of patient safety by reminding them that one out of every three or four patients is likely to be harmed[43].

2.4.2 Trigger Tool for Measuring Adverse Drug Events

The Idealized Design of the Medication System (IDMS) Group was founded in May 2000 by the Institute for Healthcare Improvement (IHI). This group of 30 physicians, pharmacists, nurses, statisticians, and other experts set out to create a medication system that is ten times safer and more cost effective than present systems. This group created the Trigger Tool for Measuring Adverse Drug Events to assess progress toward this safety goal, and it served as the foundation for the creation of future Trigger Tools[21].

Since medications are the most common source of patient harm, a focus on adverse drug events (ADEs) associated with medication prescribing, dispensing, and administration is needed. The ADE trigger tool is a self-contained tool for detecting medication-related harm. It has the basic GTT medication and laboratory modules[48].

2.4.3 **Levels of Harm**

The trigger tool for measuring adverse events adapts the "*National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Index for Categorizing Errors"* [21]. It brings together all leading health care organizations to address the interdisciplinary causes of errors and promote the safe use of medications [21]. As the IHI GTT counts only AEs, meaning events that cause harm to the patient; the NCC MERP excluded the categories which are classified on a scale from A to D (Table 2.1) [21].

Table 2. 1: Categories That Describe Errors That Do Not Cause Harm From The NCC MERP Index (Categories A-D)

Category A	*"Circumstances or events that have the potential to create error"*
Category B	*"An error that did not reach the patient"*
Category C	*"An error that reached the patient causing no harm"*
Category D	*"An error that reached the patient and needed further monitoring or intervention to ensure that the patient was not harmed"*

The patient harm severity caused by medication errors that "*do cause harm"* is categorized on a scale from E to I as shown in (Table 2.2) below [33].

Table 2. 2 : Classification of Harms Using the NCC MERP index (Categories E–I)

Category E	*"Contributed to or resulted in temporary harm to the patient and required intervention"*
Category F	*"Contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization"*
Category G	*"Contributed to or resulted in permanent patient harm"*
Category H	*"Required intervention to sustain life"*
Category I	*"Contributed to or resulted in the patient's death"*

As per the study performed in the United Stated by Takata et al, 2008 , only 3 (2.8 percent ; 95 % CI: 0.6 % –8 %) of the 107 ADEs identified in their study were classified into *category F:* "*Contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization"*, whereas 104 (97.2 % ; 95 % CI: 92.0 % –99.4 %) were classified into *category E: "Contributed to or resulted in temporary harm to the patient and required intervention"*[49]. On the other hand, 18 (16.8%) of the 107 ADEs identified did not have an associated trigger[49].

2.4.4 **Pediatric ADE Triggers**

AEs are especially common in pediatric patients, with rates as high as 11% reported in some studies[11]. The IHI Global Trigger Tool's triggers relevant to measuring harm from medications were found to be the most useful clues for most healthcare organizations[28]. Focusing on the list of triggers customized for the pediatric population (patients under 18 years of age) as per the IHI trigger tool for measuring adverse events, only nine triggers were customized for the pediatric population, as shown in Table 2.3 below [28].

Table 2. 3 : List of ADE Triggers Based on the IHI Trigger Tool for Measuring Adverse Drug Events Customized for the Pediatric Population.

T1	*Diphenhydramine (Benadryl)*	*"Diphenhydramine is often used to treat drug allergies, it may indicate an ADE, but it's often used as a sleep aid, a pre-operative or pre-procedure drug, or to treat seasonal allergies. If Diphenhydramine was given, check the chart to see if it was given for symptoms of an allergic reaction to a medication given during the hospitalization or prior to it."*
T2	*Anti-emetics*	*"Drug toxicity or overdose can cause nausea and vomiting, particularly in patients with impaired renal*

		function. When theophylline levels reach dangerously high levels, drugs like theophylline preparations frequently cause nausea and vomiting. Anti-emetics are often typically given to patients who have undergone surgery or who are undergoing chemotherapy."
T3	*Naloxone (Narcan)*	*"This is a powerful narcotic antagonist. Narcan use is often associated with narcotic overdosage. Excessive narcotic administration, which is an ADE, is likely to have happened if Narcan was used and the patient's condition changed."*
T4	*Sodium Polystyrene (Kayexalate)*	*"In the treatment of hyperkalemia, sodium polystyrene sulfonate is used. The medication helps in the elimination of excess potassium in the body. Examine the cause of the hyperkalemia and whether the patient was given potassium. Kayexalate may be given in response to a potassium overdose, which would be an ADE."*
T5	*Partial Thromboplastin Time (PTT) > 100 seconds*	*"Check for signs of bleeding, much as with Vitamin K, to see if an ADE has occurred. When patients are taking heparin, a high PTT is not uncommon. If you're giving heparin to a patient with a high PTT during surgery, use professional judgement."*
T6	*Rising Serum Creatinine*	*"Certain medications, especially aminoglycosides, diuretics, and anti-hypertensive drugs, can cause renal toxicity, which can be detected by increasing serum creatinine levels. Examine multiple consecutive findings to see if the levels have risen. If they did, look at whether the patient was given any nephrotoxic drugs. If surgery was required to correct renal problems, an ADE may have occurred."*
T7	*Over-sedation/lethargy/fall/ hypotension*	*"Over-sedation, lethargy, and falls are all signs of over-sedation. Look for a connection between the event and the use of a sedative, analgesic, or muscle relaxant if any*

		of these triggers occur. An ADE has occurred if oversedation, lethargy, or falls occurred as a result of the administration of a sedative, analgesic, or muscle relaxant. Include falls that occurred as a result of an ADE and resulted in admission."
T8	*Rash*	*"A rash can be caused by a variety of factors. Check for signs that the rash is linked to drug administration to see whether an ADE has occurred. A yeast infection, for example, may suggest antibiotic overuse."*
T9	*Abrupt Cessation of Medication*	*"Look for the purpose if "hold" or "stop" prescription orders appear in the order sets.* *These instructions also signify the occurrence of an ADE."*

In Zimlichman et al. 2018 study, a total of 421 triggers were identified in 279 hospitalizations, with 75 ADEs confirmed in 72 hospitalizations (7.5%). The overall sensitivity was 97 %, with a mean positive predictive value of 17.81 %, the study showed 1.54 ADEs per 100 days in the hospital, 7.8 ADEs per 100 admissions, and 1.81 ADEs per 1000 doses of medication. 22.7 % of the 77 ADEs detected were preventable[34]. On the other hand, a study performed in China by Ji et al. 2018, on a total of 1746 pediatric hospitalized patients, showed that triggers found during the chart review, 24 out of the 31 triggers they established were found to be positive (77.4%); 23 of which were linked to ADEs[50]. Positive triggers were found in 1213 (69.5%) of the final 1746 cases. There were a total of 2291 triggers found, with an average of 1.3 triggers per patient with a 13.3% positive predictive value of the triggers list used in this study[50].

2.4.5 **Considerations and Limitations of the GTT**

A limitation agreed on by many researchers was related to the methodology the GTT follows, which is the retrospective review of patient records to identify possible AEs, resulting in bias due to lack of information from medical and nursing records [40]. In addition to not having access to other information from the patients [51]. Another limitation is the lack of international studies, making it hard to perform a comparison of findings [20]. The GTT method was considered time-consuming to some researchers. Other limitations were related to the study's chosen site and the small sample size, limiting generalizing findings.

Previous research has revealed that the GTT detects at least 10 times more incidents than traditional approaches, and that the monitoring results are more accurate than the actual incidence of AEs[33]. The GTT's drawbacks include the relevance of the data generated, the potential for nonspecific results, and the difficulty of comparing hospitals. Previous studies, however, have backed up its ease of use and dependability, as well as its promising capacity to detect prescription errors that damage patients[38].

Pandya et al. claim that the majority of research suggest using " trigger tool" strategies retrospectively, although retrospective record review is based primarily on what physicians document in the clinical record [39]; therefore, their study suggested to add a prospective surveillance strategy that would allow for detailed characterization and identification of elements that contribute to adverse drug events in real time, assisting quality improvement efforts and to overcome any constraints[39]. A hospital can begin to build a culture of safety by focusing on the events that patients actually experience, shifting the focus away from individual blame for errors and toward thorough system reform that decreases patient suffering [39].

2.5 Conceptual Framework

The conceptual framework of our study Figure (1) was designed to describe the relationships between the study variables:

1. Dependent Variables:

In our current study the dependent variables include:

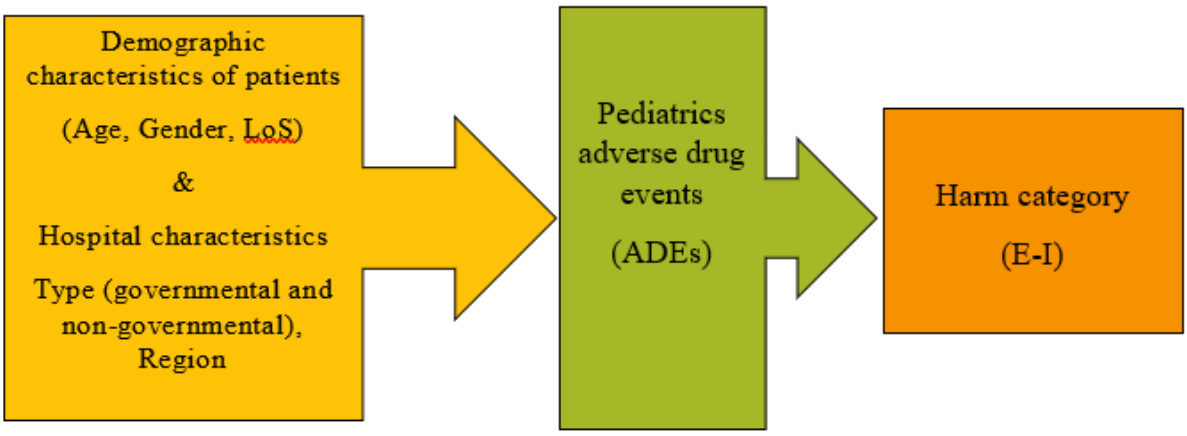
- Level of adverse drug events
- Harm categories (Category E through I) adapted from the NCC MERP Index and listed in the Pediatric ADE Patient Record Review.

2. Independent Variables:

Independent variables include:

- Demographic characteristics: (age, gender, length of stay (LoS) which was identified according to the admission date and the discharge date)
- Hospital characteristics: hospital type (governmental and non-governmental), region

Figure 1 : The conceptual framework



2.6 **Operational Definitions**

- Gender was coded 1 for male and 2 for female.
- Areas in Palestine: (North=1, Middle=2, South=3).
- Age in years: < 1 year =0, and any age above was registered as is in years.
- Triggers found (TRGF): T1=1, T2=2, T3=3, T4=4, T5=5, T6=6, T7=7, T8=8, T9=9); defined in Table (2.3).
- ADE from 1 through 9 based on the trigger causing an ADE or not: (No=0, Yes=1)
- Harm category (HarmC): (category E=1, category F=2, category G=3 category H=4, category I=5), no harm=0)
- Hospital type (HST): (Private (P)=1, Governmental (G)=2)
- Length of Stay (LoS): in days
- Total ADE: Total ADE that occurred for this patient
- TotalMed: Total number of doses of medications for each patient

The following four questions were used to assess the randomly selected patient charts that were included in this study:

Q1: What is the total length of stay (LoS) for this patient?

Q2: Which triggers are detected during patient chart review?

Q3: What proportion of adverse drug events occurred during hospital stay?

Q4: Which harm category should be assigned in accordance to the ADE that was detected?

Chapter 3: Methodology

This chapter illustrates the study's methodology; starting from study design, study site & setting, sampling, study tools, data collection, data analysis and ethical considerations.

3.1 Study Design

A quantitative retrospective study was conducted using the IHI Global Trigger Tool for Measuring Adverse Events ("*Pediatric ADE Patient Record Review Sheet"*). The study tool is a well-established and validated tool used worldwide.

3.2 Site and Settings

The study surveyed six hospitals in Palestine located in three different geographical regions northern, middle, and southern districts in the West Bank. The sample includes three governmental hospitals and three private hospitals. The hospitals participating in the study were as per the following areas in Palestine:

1. In Southern area hospitals located in Hebron city, Al-Ahli private hospital and Alia governmental hospital;
2. In Northern area hospitals located in Nablus city: Specialized Arab Hospital (SAH) and Rafidia governmental hospital.
3. In Middle area hospitals in Ramallah city: Istishari Arab Hospital (IAH) and Palestine Medical Complex (PMC).

The selection of each hospital in each area was primarily based on the fact that each hospital had a pediatric department to serve the study's target population, as well as the ability to compare the outcomes of governmental and private hospitals. The Specialized

Arab Hospital (SAH) in Nablus and the Isishari Arab Hospital (IAH) in Ramallah are part of the Al-Arab Hospitals Group. In many aspects of their operation, both hospitals use computerized and electronic systems. IAH is accredited by the Joint Commission International Accreditation (JCIA), and both hospitals offer a wide range of medical and health services in all departments.[52].

On the other hand, all three governmental hospitals, PMC, Rafidia, and Alia, use the same Avicenna Health Information System provided by the Palestinian Ministry of Health. Al-Ahli private hospital in Hebron, has a 250-bed capacity and holds a fully equipped pediatric & neonatal department. The patient records at this hospital are paper based, which is different than all other five hospitals included in this study.

3.3 **Population and Sampling**

The study population comprised patients who had been hospitalized in pediatric wards at each of the six hospitals included. Following the IHI's procedure, 20 inpatient records were randomly selected every two weeks, in a five-month period from August, 2021 to December, 2021 at each hospital. Six hundred pediatric patient charts were selected in a systematic random sampling method (100 records per hospital), reviewed and evaluated according to the instructions.

3.4 **Inclusion and Exclusion Criteria**

Eligibility criteria were the following:

1. Admission lasting at least 48 hours and formally admitted to the hospital’s pediatric ward.

2. Patients younger than 18 years (0 to 18 years), taking into consideration that according to the Palestinian MOH the pediatric population are of the age under 15 years[53].
3. Completed administrative data that included a discharge summary.

3.5 **Review Teams and Review Process**

The selected reviewing teams throughout the entire duration of the study, included 2 record reviewers with nursing backgrounds and are working as registered nurses (RN) at each hospital. The total number of reviewers members were (6*2=12 reviewers). The researcher gave a one-day training session to the team members at each hospital on how the tool should be used. The training was according to the IHI's instructions in order to focus on understanding the selected triggers and the categories of harm, in addition to understanding all the fields that were to be filled manually in the review sheet (Appendix1).

The two RNs of each team reviewed independently 20 clinical charts per month with a total of 100 charts per the selected period of 5 months. When triggers were detected, the reviewers investigated the chart more thoroughly to decide whether an adverse drug event occurred or not.

The following sampling plan was followed:

(1) The month's list of discharges (minimum 48 hours hospital stay) was retrieved from the hospitals' electronic health records, except for one hospital having paper based patient records.

(2) Twenty patient records at random were selected for each month of the chosen study period.

(3) Each patient file was systematically reviewed over giving special attention to the parts below:

- Discharge summary: by looking for ADEs or suggestions of ADEs in the discharge summary.
- Laboratory reports: looking at lab results that had any triggers.
- Physician orders and Medication Records (MRs): to look for trigger drugs while being hospitalized.
- Nursing notes: to look for any other triggers that might occurred, for example skin rash, nausea and vomiting or any other adverse events.

(4) All triggers found were listed in the "*Pediatric ADE Patient Record Review Sheet"*.

(5) Appropriate parts of the patient's record were reviewed to determine if an ADE has occurred, as even if there was no ADE found but a positive trigger was identified during the review process, this trigger needed to be recorded.

(6) A category of harm was assigned from the categories (E through I) in case an ADE occurred.

(7) After completing the ADE Patient Record Review Sheet for each patient record, triggers found were documented and whether an ADE occurred or not with indicating the level of harm; the total number of ADEs; in addition to the total number of medication doses received.

If a trigger was located, the reviewer referred to the section of the sheet that shows the occurrence of an ADE. Then, the extent of harm was determined using the NCC MERP Index Categories (E through I) if a harmful event was discovered (those that cause harm).

3.6 **Data Collection Tool**

The study used the "*Pediatric ADE Patient Record Review Sheet"* (Appendix1) designed and validated by the Institute for Healthcare Improvement (IHI), and following the instructions of the Trigger Tool for Measuring Adverse Drug Events to conduct the retrospective review of patient records using the listed triggers to identify possible ADEs [21].

3.6.1 ***Pediatric ADE Patient Record Review Sheet and data collection***

The one-page review sheet consists of different parts; 1) a part related to the demographic data of the patient to be taken; 2) the other part where the triggers customized for the pediatric population are listed. On the other hand, 3) there is a section to list all the triggers found, 4) the ADE if found or not, and if the ADE is found a 5) harm category is listed with giving a brief description of the ADE. Then the total number of ADEs that occurred to this patient is registered in another field as well as the total number of medications for this patient.

List of triggers included in this study were customized for the pediatric patient record according to the data collection sheet [21]:

- ***"T1 Diphenhydramine"* or any drug used for allergic reactions:** not necessarily diphenhydramine, this depends on what each hospital uses in their formulary for allergic reactions, as this type of drugs is frequently used for allergic reactions to other drugs which may signal a possible ADE. On the other hand, they can also be ordered as a pre-operative or pre-procedure medication, or for other types of allergies. Therefore, the reviewers examined to see if any of

the medications has been administered, with reviewing the chart to determine the reason of administration.

- ***"T2 Anti-emetics"*:** Chart reviewers used professional judgment in any situation an anti-emetic was given to the patient to determine if an ADE may have occurred, as nausea and vomiting can be the result of drug toxicity or overdose, or as commonly used in patients postoperatively.
- ***"T3 Naloxone (Narcan)":*** the reviewers looked for excessive narcotic administration, which is considered an ADE, and this trigger was listed if naloxone was used and the patient's state changed**.**
- ***"T4 Sodium Polystyrene (Kayexalate)":*** Sodium polystyrene sulfonate is used in the treatment of hyperkalemia. The reason for hyperkalemia was further looked for in the patient's chart to know whether the patient had been receiving potassium, because the administration of Kayexalate may be in response to an overdose of potassium, which would be an ADE.
- ***"T5 PTT > 100 seconds"*:** evidence of bleeding was looked for to determine if an ADE has occurred as high PTT is not an infrequent occurrence when patients are on heparin for example.
- ***"T6 Rising Serum Creatinine"*:** the patients' laboratory results of serum creatinine were reviewed, if the rise was greater than the baseline in each hospital, then the medication administration records were evaluated as certain medications used may have caused this rise, especially aminoglycosides, diuretics, anti-inflammatory drugs, and anti-hypertensive medications which can be nephrotoxic.

- ***"T7 Over-sedation/lethargy/fall/hypotension"*:** If any of these triggers were found, the reviewers looked for a relationship between the event and administration of a sedative, analgesic, or muscle relaxant. If oversedation, lethargy, or falls occurred as a result of administration of a sedative, analgesic, or muscle relaxant, an ADE has occurred.
- ***"T8 Rash"*:** There are many causes for a rash. To determine if an ADE has occurred, the reviewers looked for evidence that the rash is related to drug administration. For example, overuse of antibiotics.
- ***"T9 Abrupt Cessation of Medication"*:** In the order sets, whenever "hold" or "stop" medication orders appear, the reason was looked for as these orders frequently indicate that an ADE has occurred.

Once reviewers have determined that adverse drug events occurred, a harm category was assigned, with the categories of harm followed based on NCC MERP classifications and included in the study are[48 21]:

• "***Category E**: harm that contributed to or resulted in temporary harm to the patient and required intervention."*

• *"**Category F**: harm that contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization."*

• *"**Category G**: harm that contributed to or resulted in permanent patient harm."*

• *"**Category H**: harm that required intervention to sustain life."*

• *"**Category I:** harm that contributed to or resulted in the death of a patient*."

3.6.2 **Review Sheet Reliability and Validity**

This tool adapts the "*National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Index for Categorizing Errors"*. NCC MERP brings together leading health care organizations to meet, collaborate, and cooperate to address the interdisciplinary causes of errors and to promote the safe use of medications[52]. The validity and reliability of the tool were checked by Classen et al. 2011, and the GTT showed a sensitivity of 94.9 % for detecting individuals who had an adverse event and a specificity of 100 % for detecting patients who had no adverse events. They also concluded that the GTT has sufficient criterion-related validity making it a reliable tool for detecting AEs[54].

On the other hand, the inter-rater reliability was performed in a Palestinian context by Najjar et al. 2013, to test the consistency between the reviewers; the two primary reviewers , the primary reviewers and the secondary reviewer , in terms of agreement upon the identified AEs[16]. The two primary reviewers' inter-rater reliability was moderate (κ= 0.58, 95 % CI). The final review by the primary review team (two nurses and a physician) and the secondary reviewer was almost perfect (κ= 0.89; 95 % confidence interval) [16].

3.7 **Statistical Analysis**

All data was entered into Excel. Descriptive statistics was used to summarize the patient characteristics, adverse drug events (ADE) rate/type, ADE level and harm category.

Data cleaning and analysis was done using *IBM SPSS version 26.0* (SPSS Inc., Chicago, IL, USA) and the following statistical analyses was done:

- Descriptive statistics was done for some variables was tested using frequency and percentages.
- Extracting the arithmetical means and standard deviations.
- One-way ANOVA and Independent Samples Test for testing the variance between the variables.
- Spearman correlation test to measure the linear correlation between two variables.
- The independent samples t-test to test the existence of differences within the groups.

3.8 **Ethical Consideration**

Ethical approval was pursued and granted by the faculty of Graduate Studies at the Arab American University of Palestine to conduct this study, in addition to obtaining the consent of the ethical approval to conduct this study from the Helsinki Institutional Review Board (IRB) in Gaza City. Consent forms, which included information about objectives and importance of the study, were submitted to each hospital administration included in this study whom agreed on conducting the study and approved on recruiting the review teams whom were trained to collect the data. Moreover, no personal information was obtained, the information gathered will only be used for the purposes of this study, ensuring patient privacy and confidentiality of information.

3.9 **Summary**

The research methodology was described in this chapter, as this study used a quantitative retrospective method with the "*Pediatric ADE Patient Record Review Sheet"* (Appendix1), which was designed and validated by the Institute for Healthcare Improvement (IHI). With an explanation of the study design, setting, population and sample, inclusion criteria, data collecting method, and review procedure. Data was processed using *IBM SPSS version 26.0* (SPSS Inc., Chicago, IL, USA), and various ethical considerations such as consent forms and confidentiality were discussed. The study findings and results will be discussed in the following chapter.

Chapter 4: Results

4.1 Introduction

This chapter contains detailed presentation of data analysis and the results of this study. The medical records of 600 patients were randomly selected and investigated at six hospitals in three areas across Palestine (North, middle and south areas). Three were private hospitals, and the other three were governmental. A total of 100 patient records per hospital were reviewed to count the triggers found in each patient record in addition to the ADEs and to categorize harm's level for identified ADEs.

4.2 Descriptive Analysis: Demographic And Hospitalization Characteristics Of The Patients

During the study period, 58.8% of the population was < 2 years old (n=351) , the other were ≥ 2 years old (n=249) 41.2%. The mean age was 2.36 years and a median age of 1 year; among which 351 (58.5%) were males and 249 (41.5%) were females. The 600 patients had 2377 total days of hospital stay, with the average being 3.96 days; all had at least two days and at most 26 days. The number of records reviewed per area was equal to 33.3% (n=100). A total of 2313 medication doses were prescribed, with a mean of 3.85 medication doses for all admissions as shown in Table (4.1) below.

Table 4. 1: Demographics Characteristics of Participants

Variables		**No.**	**Percentage**
Gender	Male	351	58.5%
	Female	249	41.5%

Variables		**No.**	**Percentage**
	Total	**600**	**100.0%**
Area	North of West Bank	200	33.3%
	Middle of West Bank	200	33.3%
	South of West Bank	200	33.3%
Hospital Type	Private	300	50.0%
	Government	300	50.0%
	Total	**600**	**100.0%**
Child's age (years)	< 2 years	351	58.5%
	≥ 2 years	249	41.5%
Length of Stay	0-2	225	37.5%

Variables		No.	Percentage
(Nights)	3-5	255	42.5%
	6+	120	20.0%

4.3 **Triggers and ADEs**

Overall, 291 triggers were identified (Table 4.2). The most frequently detected trigger across all records was trigger T9 ("*Abrupt cessation of medication"*, n = 57). Followed by trigger T8 ("*Rash"*, n=55) and trigger T1(*use of anti-allergic drugs*, n=52). Our retrospective review revealed that 155 hospitalized pediatrics patients (25.8%) experienced one or more ADEs. The trigger most frequently connected to the identification of an ADE was trigger T8 ("*Rash"*, n=41). The results show a total of 53.3% ADE's were found per trigger. Overall, 67.0 ADEs rate for every 1000 doses of medication and the rate of adverse drug events per 1000 patient days was 65.2.

It was found that 9 out of 10 of the triggers *T4 "(Sodium Polystyrene)"* found caused an ADE, followed by *T8* "(*Rash*)" where 74.5% of the total 55 triggers found caused an ADE. While *T9 "(Abrupt cessation of medication)"*, out of the 57 triggers found during chart review, only 4 leads to an ADE.

Table 4. 2 :**Characterization of Adverse Drug Events Identified in 600 Patients**

Tr. #	**Trigger Description**	**Total Triggers found**	**Total ADEs found**	**% ADEs per trigger**
T1	*Use of anti-allergic drugs*	52	35	67.3%
T2	*"Anti-emetics"*	41	23	56.1%
T3	*"Naloxone (Narcan)"*	-	-	-
T4	*"Sodium Polystyrene"*	10	9	90.0%
T5	*"PTT > 100 seconds"*	6	4	66.7%
T6	*"Rising Serum*	24	15	62.5%

T7	*"Over-sedation/lethargy /fall/hypotension"*	46	24	52.2%
T8	*"Rash"*	55	41	74.5%
T9	*"Abrupt Cessation of Medication"*	57	4	7.0%
	Total	**291**	**155**	**53.3%**

4.4 **Group Characteristics According to the Presence of ADEs**

One out of every four pediatric patients suffer harm in Palestinian hospitals. In terms of ADEs per area/region the results show that the occurrence of ADEs in south of west bank was 5.0 % which is less than the other areas of the middle (10.3%) and the north area (10.5%) giving a statistically significant difference in favor of the south (p-value = 0.002).

Regarding the type of hospital, a significant difference was found, 18.3% of ADEs were in the private sector, compared to 7.5 % in the public sector (p-value = 0.000). In comparison to government hospitals, patients admitted to private hospitals had nearly twice the likelihood to experience ADEs. There is also a significant difference according to the age of the patients, (p-value = 0.000), the ages ≥2 years old were more likely to have ADEs n=91 (15.2%). Moreover, the length of patient stay resulted in significant difference (p-value = 0.000) showing that patients who stayed at the hospital for 3-5 days had ADEs more frequently n=62 (10.3%). While there are no statistically significant differences according to the gender of the patient.

Table 4. 3 : **Sample Characteristics According to the Presence of ADEs**

Variables		**No ADE**	**%**	**With ADE**	**%**	**p-value**
Hospitalizations		445	74.1%	155	25.8%	-
Gender	Male	261	43.5%	90	15.0%	
	Female	184	30.6%	65	10.8%	0.785
Area	North of West Bank	137	22.8%	63	10.5%	
	Middle of West Bank	137	22.8%	62	10.3%	
	South of West Bank	171	28.5%	30	5.0%	0.002
Hospital Type	Private	190	31.6%	110	18.3%	
	Government	255	42.5%	45	7.5%	0.000
Child's age	< 2 years	185	30.8%	64	10.7%	
	≥ 2 years	260	43.3%	91	15.2%	0.000
Length of Stay (Nights)	0-2	191	31.8%	34	5.7%	
	3-5	193	32.1%	62	10.3%	
	6+	61	10.1%	59	9.8%	0.000

4.5 Severity of Harm

The percentage of harm to inpatients resulting from the ADEs was 21.2%, while the types of harm were distributed according to the category as follows:

• "***Category E**: harm that contributed to or resulted in temporary harm to the patient and required intervention"* with15.2%.

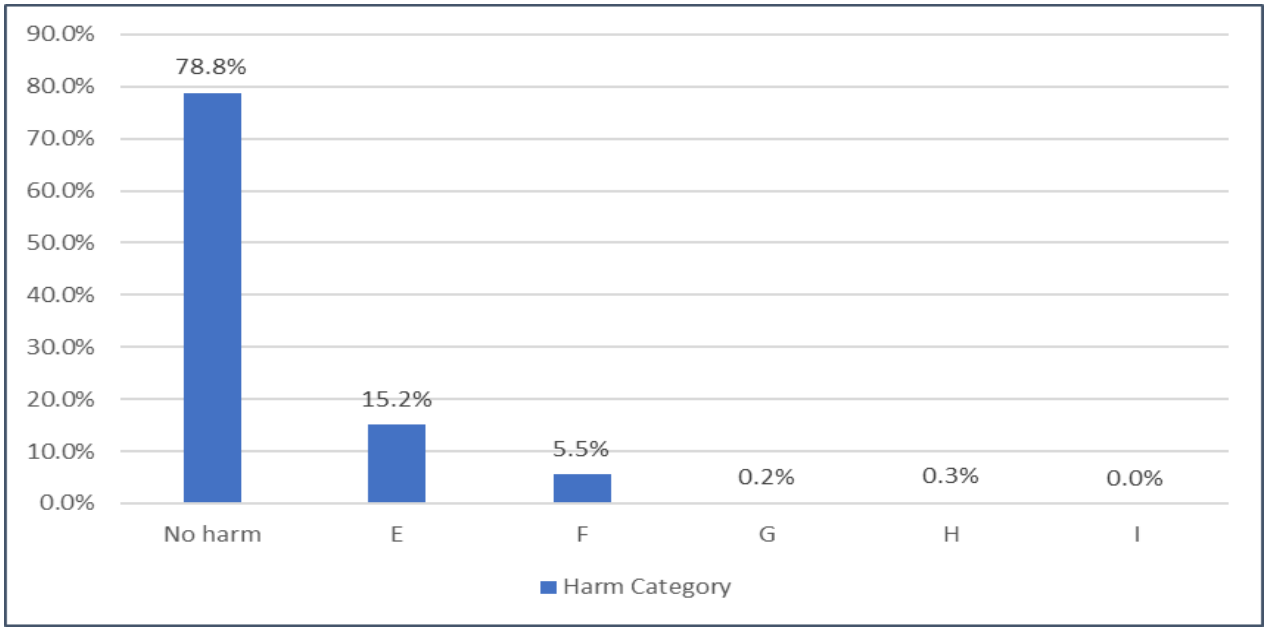
• "***Category F**: harm that contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization"* with 5.5%.

• "***Category G**: harm that contributed to or resulted in permanent patient harm"* with 0.2%.

• "***Category H**: harm that required intervention to sustain life"* with 0.3%.

While "***Category I (**harm that contributed to or resulted in the death of a patient)"* was not identified, meaning that 78.8% of the triggers found did not results in an ADE and without causing any harm.

Figure 2 : Illustrates Percentage Distribution of Harm Category



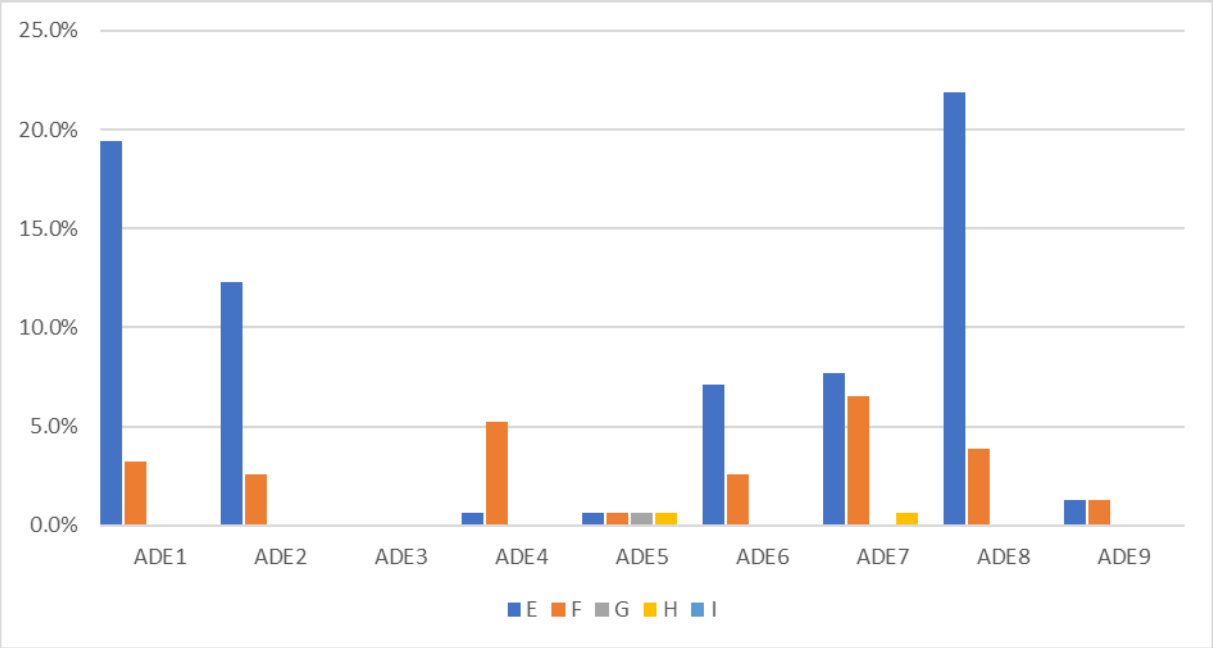
4.6 **Distribution of Harm Category Per ADE Type and Presence**

By using the NCCMERP Index, 111 ADEs (71.0%) were determined to be "*category E (contributed to or resulted in temporary harm to the patient and required intervention)"*, and 41 (25.8%) were "*category F (contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization").* One (0.6%) ADEs resulted in "*permanent harm (category G)"*, 2 (1.3%) "*required intervention to sustain life (category H)"*, and none of the ADEs resulted in death of the patient. More details can be found in (Table 4.4).

Table 4. 4**: Illustrates Percentage Distribution of Harm Category by Type and Presence of ADEs**

Type of ADE	**Harm Category**									
	E		**F**		**G**		**H**		**I**	
	N	%	N	%	N	%	N	%	N	%
Use of Antiallergic drugs	31	19.4%	5	3.2%	0	0.0%	0	0.0%	0	0.0%
Antiemetics	19	12.3%	4	2.6%	0	0.0%	0	0.0%	0	0.0%
Naloxone	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Sodium Polystyrene	1	0.6%	8	5.2%	0	0.0%	0	0.0%	0	0.0%
PTT > 100 seconds	1	0.6%	1	0.6%	1	0.6%	1	0.6%	0	0.0%
Rising Serum Creatinine	11	7.1%	4	2.6%	0	0.0%	0	0.0%	0	0.0%
Over-sedation/lethargy/fall/hypotension	12	7.7%	10	6.5%	0	0.0%	1	0.6%	0	0.0%
Rash	34	21.9%	6	3.9%	0	0.0%	0	0.0%	0	0.0%
Abrupt Cessation of Medication	2	1.3%	3	1.3%	0	0.0%	0	0.0%	0	0.0%
Total	**111**	**71.0%**	**41**	**25.8%**	**1**	**0.6%**	**2**	**1.3%**	**0**	**0.0%**

Figure 3 : Percentage of Harm Category per type of ADE



4.7 Harm Count and Percent of Total Harms By Group Characteristics

This section demonstrates the levels of harm detected by the characteristics of the patients included in the study.

In terms of gender, harm "*category E (contributed to or resulted in temporary harm to the patient and required intervention)"* was the most prevalent in both, with highest percentage of 42.5% in males, and a total harm category of 55.9%. Total harm category per area of the West bank, was most prevalent in the north area n=56 (44.1%), on the other hand harm "*category E (contributed to or resulted in temporary harm to the patient and required intervention)"* was noticed to have the highest prevalence in the middle area of the west bank 35.4%.

Private hospitals showed a noteworthy difference in terms of the presence of harm due to ADE with a percentage of 74.0% in comparison to the governmental hospitals 26.0%. the predominant harm category in private hospitals was "*category E (contributed to or*

resulted in temporary harm to the patient and required intervention)" 50.4%, whilst it contributed to 21.3% of the same category. In private and governmental hospitals, respectively, 22.0 % and 3.9 % of harm "*category F (contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization)"* were found. The length of stay of 3 to 5 days showed to have the most prevalent harm detected n=51 (40.2%).

Table 4. 5: **Group Characteristics According to the Presence of Harm Category**

Variables		**Harm category**						
		E	F	G	H	I	**Total %**	**(n)**
Gender	Male	42.5%	11.0%	0.8%	1.6%	0.0%	**55.9%**	**71**
	Female	29.1%	15.0%	0.0%	0.0%	0.0%	**44.1%**	**56**
Area	North of West Bank	25.2%	18.9%	0.0%	0.0%	0.0%	**44.1%**	**56**
	Middle of West Bank	35.4%	2.4%	0.0%	0.0%	0.0%	**37.8%**	**48**
	South of West Bank	11.0%	4.7%	0.8%	1.6%	0.0%	**18.1%**	**23**
Hospital Type	Private	50.4%	22.0%	0.0%	1.6%	0.0%	**74.0%**	**94**
	Government	21.3%	3.9%	0.8%	0.0%	0.0%	**26.0%**	**33**
Child's age	Less than 2	25.2%	16.5%	0.8%	0.8%	0.0%	**43.3%**	**55**
	2+	46.5%	9.4%	0.0%	0.8%	0.0%	**56.7%**	**127**
Length of Stay (Nights)	0-2	19.7%	3.1%	0.0%	0.0%	0.0%	**22.8%**	**29**
	3-5	29.1%	9.4%	0.8%	0.8%	0.0%	**40.2%**	**51**
	6+	22.8%	13.4%	0.0%	0.8%	0.0%	**37.0%**	**47**

4.8 **Bi-Variable Analysis**

4.8.1 **Relation Between Presence of ADE and Hospital Type and Patient Gender**

According to our data, there is no significant difference between presence of ADEs and hospital type at the level ($\alpha \leq 0.05$) and between presence ADEs and patient's gender at the level ($\alpha \leq 0.05$).

The t-test was performed to show how significant is the differences between group means. The differences in total ADEs (interval scale) were tested by comparing the means between male and female for the variable " Patient's gender" and Private and governmental hospitals for the variable “Hospital Type”. The results showed statistically significant differences as mentioned in the Table (4.6).

Table 4. 6**: Independent samples T-test output, total ADEs for patient**

Dimension	**Independents**		**N**	**Mean**	**Std. Deviation**	**Sig. (2-tailed)**
ADEs for patient	Hospital Type	Private	300	0.37	0.606	0.000
		Gov.	300	0.15	0.449	
	Patient's gender	Male	351	0.26	0.553	0.918
		Female	249	0.26	0.531	

While for the patient's gender there was no significant correlation with the ADEs, p-value >.05 = “0.918”, the findings reveal that the presence of ADEs varies significantly depending on the type of hospital.

4.8.2 **Relation Between Patient Characteristics (Gender, Hospital Type, Hospital Area, Patient Age and the Length of Stay) and the Level of Harm**

A Spearman's rho test was used to measure the association between two variables of each included patient characteristics (gender, hospital type, hospital area, patient age and the length of stay) and the harm category. The results demonstrated in Table (4.7) showed that there is no correlation between patient gender and level of harm (p-value =0.437). While in terms of the relation to other variables in the study the results showed a significant correlation between other patient characteristics and level of harm with a correlation coefficient of -0.253 for the hospital type, -0.169 for the area, 0.176 for the age and 0.227 for the length of stay, with p-value <.01).

Table 4. 7**: Spearman's rho test to show the correlation between the patient characteristics and the harm category**

Characteristics			**Harm**
	Gender	Correlation	0.032
		Sig. (2-tailed)	0.437
		N	600
	Hospital type	Correlation	-0.253**
		Sig. (2-tailed)	0.000
		N	600
	Area	Correlation	-0.169**
		Sig. (2-tailed)	0.000
		N	600
	Age	Correlation	0.176**
		Sig. (2-tailed)	0.000
		N	600
	LoS in days	Correlation	0.227**
		Sig. (2-tailed)	0.000
		N	600

4.8.3 **Relation Between Presence of Ades and the Hospital's Area/Location, Age, and The Length of Stay**

The One-way ANOVA Test for the variables was used to determine the existence of differences within the variables and whether the groups created by the levels of the independent variables (area, age and LoS) are statistically different by calculating whether the means of the variables are different from the overall mean of the dependent variable (ADEs). The results showed that there were statistically significant differences according to the variables mentioned in Table (4.8).

Table 4. 8 **: One-way ANOVA: ADEs and Hospital's Area/Location, Age, and the Length of Stay**

		Sum of Squares	**Df***	**Mean Square**	**F***	**Sig.**
Area	Between Groups	9.937	3	3.312	5.048	.002
	Within Groups	391.062	596	.656		
	Total	400.998	599			
Child's age (years)	Between Groups	32.903	3	10.968	10.171	.000
	Within Groups	642.722	596	1.078		
	Total	675.625	599			
Length of Stay (Nights)	Between Groups	16.287	3	5.429	10.426	.000
	Within Groups	310.338	596	.521		
	Total	326.625	599			

*** Df: degree of freedom, F: variation between sample means / variation within the samples**

4.9 **Summary**

The study's findings were presented in this chapter. Starting with data cleaning and preprocessing, a descriptive analysis of demographic and hospital features, triggers and

ADEs discovered, and harm levels were described, followed by a descriptive analysis of the demographic and hospital characteristics. Relations between the patient characteristics and the presence of ADEs and ham levels were presented. The next chapter discusses the study findings and presenting them in the context of the literature.

Chapter 5: Discussion, Conclusion and Recommendations

5.1 Introduction

This study is the first to assess the incidence of adverse drug events and level of harm in hospitalized pediatric patients in Palestine using the IHI Global Trigger Tool for Measuring Adverse Events. This chapter is structured around our main findings. Moreover, results are compared across the sections in relation to other relevant studies.

5.2 Descriptive Statistics for Participants and Hospitals

The study targeted female and male patients of ages < 15 years old hospitalized in the pediatric wards, where 58.5 % were males and 41.5 % were females. The study showed that most children 58.5% were aged < 2 years old and 41.5% were above 2 years old. According Ministry of Health, Health Annual Report, Palestine 2020, published on May 2021[53] the age group 0-14 years old represented 38.2% of the population, with 19.5% males and 18.6 % females. This explains that the targeted population in this study consists mostly of males. These findings are comparable to those of Ji et al. (2018), who conducted a study in a tertiary teaching children's hospital in China, with 65% of patients included were from males and 35% from females, and the age of the patients ranged from 0.08 to 17.75 years, with a mean of 3.84[50] and their results showed that there were no significant differences in age and gender, and they were not associated with the occurrence of ADEs. Whilst this study showed that there was no significant difference in gender, however, for the age, it was the opposite.

For the selected areas in this study, north, middle, and south of Palestine; an equal number of 2 hospitals were included per area, with an equal percentage of participants of 33.3% for each. A private and governmental hospital was selected in each governorate in order to be able to have comparable results. Similarly, a study conducted in Riyadh, Saudi Arabia by Aljadhey et al. 2016, on adult inpatients, which included four hospitals, one teaching hospital, one private hospital, one large government hospital, and onesmall government hospital, showing that on the contrary to this study, the large government hospital had the highest incidence of ADEs of 32.9 per 100 admissions[55]. Whilst the results of this study, showed higher incidence in private hospitals 74.0%.

5.3 **Adverse Drug Event Related Triggers**

Triggers are utilized as “flags” or “clues” for potential harm while evaluating a medical record allowing a more efficient record review process. Those may be found as a laboratory result that is outside of the normal range, a drug that has been administered or abruptly stopped or requiring a higher or prolonged level of care, could all be considered as triggers[29]. Moreover, not all positive triggers indicate that an ADE has occurred, but when identified they give a lead to harm that may have occurred[29].

In our study, the most frequent triggers found were T9 “abrupt cessation of medication” n=57 followed by, *T8 “rash”, T1 “use of anti-allergic drugs”,* then *T7 “over-sedation /lethargy/fall/hypotension”*. Whilst, *T8 “Rash”*, was most frequently connected to the identification of an ADE. According to literature, "Abrupt cessation of medication " was the most frequent trigger that gave a lead to detect ADEs, while *"diphenhydramine,"* and *"Over sedation/lethargy/fall/hypotension"* indicated ADE whenever present [56].

On the other hand Ji et al. 2018 stated in their study, trigger *T1 "diphenhydramine"*, should be further specified; either for usage in therapeutic strategies or ADEs, as these drugs i.e. anti-allergic drugs, were commonly used for medical treatment as well as in cases of an ADE, leading to false positive results[50].

5.4 **Adverse Drug Events**

The general findings of this study identified an adverse drug event rate of 25.8%. By comparing our findings with international data we found the incidence of adverse events, which include ADEs, in mature patient groups ranges from 2.9 % to 16.6 %, according to international data[57]. Matlow et al. 2012, on the other hand, observed a 15% adverse event rate (including the drug module) in their study on pediatric patients in Canada, while other studies in Europe revealed rates of between 9% and 12%[57,58]. These findings should not lead us to conclude that our result is higher than any of the reviewed studies as the methodology used in these studies are different (e.g., prospective observational method), in addition to the differences in the study population included in each study. Another possible explanation that when the reviewers in our study explored that the patient's medical record contained more than one trigger that caused an ADE, and more than one harm category was selected, they referred the case to an expert (head of the nursing department) at each of the hospitals to determine the level of harm that was most appropriate for this patient, which would count it as one event. It is important to emphasize that reviewers may occasionally discover that each trigger found caused an ADE. So, all the events detected were included in the findings.

According to the IHI Global Trigger Tool for measuring adverse events it is recommended to track the harm rate over time. The goal of doing so is to reduce the percentage of admissions with an ADE by 75% within 1 year [21,29]. In our findings, the ADEs rate per 1000 patient days was 65.2. The range of ADE in international studies was between 24.50 and 80.72[33 59]. Najjar et. al conducted a study in 2013 with an aim to assess the level of adverse events in Palestinian hospitals. The study revealed that 70% of the incidents that caused harm might have been avoided for each of the 7 injured individuals (14.2%)[16]. Another study was done in the United States by Stockwell et al. 2018, New born intensive care unit (NICU) and pediatric intensive care unit patients (PICU) were found to have significant rates of harm in multisite investigations, with 74 and 203 adverse events per 100 patients in NICU and PICU admissions, respectively[60].

Our study, shows that rashes were the most common ADEs induced by triggers, with n=41 (26.5%), followed by use of anti-allergic drugs, oversedation/lethargy, antiemetic, rising serum creatinine, sodium polystyrene, then high PTT and abrupt cessation of medication were the least. These results were not surprising as rash that was detected within patients who were given an antibiotic during their hospitalization period (e.g., vancomycin) which led to the use of an anti-allergic drug and the cessation of the medication that caused the rash. With regards to over-sedation/lethargy (T7), it was recurrently detected in children who underwent surgery, regardless of the type, as the medication used for anesthesia may cause over-sedation and dizziness which is considered an ADE. On the other hand, the use of sedatives and anesthetics were also involved in cases of nausea and vomiting leading to the use of anti-emetics (T2). Therefore, those observations show that more than one trigger could be involved in identifying adverse drug events.

5.5 **Harm**

In our study, the harm levels detected due to occurrence of ADEs showed that around 15.2% "*resulted in temporary harm that required an intervention (category E)"* followed by 5.5% that resulted in *"temporary harm that required prolonged hospitalization (category F)".* Until recently, most research attempted to calculate harm rates for comparison reasons over large populations, with estimates ranging from 3% to 17% of patients experiencing an adverse event during a hospital stay[59]. The majority of these studies relied on retrospective, unstructured case note reviews, which are time-consuming, expensive, and impractical for routine harm monitoring [59]. On the contrary Takata et al. 2008, observed that all the ADEs detected in their study caused temporary harm using the pediatric-focused trigger tool [49].

5.6 **Group Characteristics and ADEs**

Demographic, environmental, and nutritional factors all play a role in the occurrence of ADEs around the world. Differences in health services, pharmaceutical products, and, most significantly, the detection methods used are all possible attributes[35].

MC et al. 2017 found that there was a correlation between the presence of AEs and the number of triggers, hospitalization , and hospital length of stay[47]. In the current study as well, there is a correlation between the hospital type and presence of an ADE, however, there was no correlation between patient gender and presence of ADEs. Our results showed that there is a significant difference between presence ADEs due to, patient's age, and length of hospital stay. Which means a correlation between those variables and the presence of ADEs.

According to Priyadharsini et al., 2011 study which was done on patients of the pediatric age group of less than 12 years, 60% of the ADRs occurred in patients less than 1 year of age. In our study the incidence of ADEs was greater in ages ≥2 years old 15.2%, whilst the incidence in the age < 2 years was 10.7%, this difference could have been due to the diagnosis that led to the hospitalization, which necessitated specific management and the administration of several doses of medications that lead to higher chance of an ADE to occur, taking into consideration that multiple dose regimens expose hospitalized patients to additional encounters in which a potential error might occur [34].A longer length of stay as per the literature was associated with higher incidence of ADEs. In our study it was also found that there is a relation between the longer length of stay and the presence of ADEs, this could be because the greater number of medications resulted in higher incidence ADEs, which required more length of stay to treat the occurred harm[45].

5.7 **Group Characteristics and Level of Harm**

The results of this study showed that there is no correlation between patient gender and level of harm. Whilst in terms of the relation to other patient characteristics (hospital type, the area, age and length of stay), a correlation was found.

In terms of the presence of harm due to ADE according to the hospital type; our findings revealed that private hospitals have a significant difference with a proportion of 74.0% compared to 26.0% in governmental hospitals. Those results were noteworthy, and might be linked to the documentation process followed at each hospital depending on the procedures and protocols set at the hospitals. While, the three governmental hospitals included in our study all use Avicenna Health Information System, two of the

private hospitals used an electronic health information system and one still uses paper based patient record system. Under-documentation might have had an impact on the actual ability of the reviewers to detect the ADEs, this also may be owing to differences in drug products available and used at each hospital, and patient safety initiatives which are related to reporting of events that occur during the hospitalization period.

In "*The Canadian Paediatric Adverse Events Study*" by Matlow et al. 2012 they compared the incidence, type, and severity of adverse events in children admitted to academic pediatric centers which more frequent vs children admitted to community hospitals in Canada and found that this could be owing to the higher number of healthcare providers, trainees in academic hospitals, as well as different documentation standards[61].

5.8 **Study Strengths and Limitations**

Trigger tool technique used in our study is widely recognized as one of the most effective methods to detect harm in a manner that enables for local learning. Moreover, the systematic random sampling way used in this methodology, provides the best strategy to control unknown confounding variables. Using this methodology has also been found to produce consistent, trustworthy, and relevant data at a reasonable cost, even though the cost varies by hospital[59].

Nonetheless, due to the retrospective nature of the study we were unable to assess the preventability of ADEs. However, we collected our data from three main regions; north, central, and south, the results may not be generalizable to all hospitals in Palestine.

5.9 **Conclusion**

In general, our study reported ADE frequency was 25.8% and most ADEs resulted in temporary harm (Category E and F). The age of patient, total hospital length of stay and hospital type were associated to the presence of ADEs. The rates of ADE in our study for inpatient pediatric populations is consistent with studies from literature concluding that the trigger tool methods seem to be more robust than the traditional methods of occurrence reports[49]. The findings of our study could serve as a groundwork for comprehensive, evidence-based preventative initiatives aimed at reducing the significant risk of medication-related harm in our pediatric in-patient population and the GTT was effective in identifying ADEs. Finally, ADEs are a significant public health issue in the pediatric population. Despite efforts to lower the incidence of medication-related adverse events, the morbidity and death rates from drug-induced reactions, particularly in the young population, remain unacceptably high[46].

5.10 **Recommendations**

The following recommendations can be formulated based on the study findings:

- While the results of this study offer a baseline rate of adverse drug events in a Palestinian healthcare context, more investigations are needed to identify the average rate of adverse drug events in Palestine.
- Initiatives on adverse drug events and patient safety should be initiated to increase the awareness among healthcare providers
- To have a specific health data management policy at each hospital in order to improve health outcomes, and to expand the quality of care.

5.11 **Future Research Directions**

Future research should focus on employing the GTT in a prospective and retrospective study across Palestinian health facilities to collect more data for benchmarking and measuring the extent of diversity in harm rates.

Moreover, a cost management study is recommended to be done for each positive trigger, as this will have a positive effect financially due to cutting the expenses and reducing the number of hospitalizations and length of hospital stay

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Appendices

Appendix 1 : Pediatric ADE Patient Record Review Sheet

Trigger Tool for Measuring Adverse Drug Events

Pediatric ADE Patient Record Review Sheet

Patient Identification Number _____

Admission Date _____ **Patient's Age** _____

Discharge Date _____ **Date** _____
(Two-day minimum hospital stay required)

T1 Diphenhydramine (Benadryl)
T2 Anti-emetics
T3 Naloxone (Narcan)
T4 Sodium Polystyrene (Kayexalate)
T5 PTT > 100 seconds
T6 Rising Serum Creatinine
T7 Over-sedation/lethargy/fall/hypotension
T8 Rash
T9 Abrupt Cessation of Medication

Triggers Found:	ADE Found?		Harm Category*	Description of ADE
	Yes	No		
Total ADEs for this patient:				
Total number of doses of medications for this patient (if available):				

*Harm Category (adapted from NCC MERP Index; Categories A–D do not cause harm):
Category E: Temporary harm to the patient and required intervention
Category F: Temporary harm to the patient and required initial or prolonged hospitalization
Category G: Permanent patient harm
Category H: Intervention required to sustain life
Category I: Patient death

Appendix 2: Arab American University thesis approval

Arab American University

Faculty of Graduate Studies

الجامعـــة العربيـــة الأمريكيـــة

كلية الدراسات العليا

Study title: **"Adverse Drug Events and level of harm in Hospitalized Pediatric Patients in Palestine: A retrospective cohort study"**

Submitted By:

Student's Name: Farah Mattour

Supervisor: Dr. Shahenaz Najjar

Co-advisor: Dr. Yousef Mimi

Date Reviewed:

15 April 2021

Date approved:

1 June 2021

Study titled: "**Adverse Drug Events and level of harm in Hospitalized Pediatric Patients in Palestine: A retrospective cohort study**" was reviewed by AAUP research committee for research and ethical principles and was approved on 1 June 2021.

Dr. Shahenaz Najjar

Dean of Graduate studies

كلية الدراسات العليا
FACULTY OF GRADUATE STUDIES

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E-mail: FGS@aaup.edu ; PGS@aaup.edu Website: www.aaup.edu

Appendix3:Palestinian Health Research Council (PHRC):Helsinki committee approval

المجلس الفلسطيني للبحث الصحي

Palestinian Health Research Council

تعزيز النظام الصحي الفلسطيني من خلال مأسسة استخدام المعلومات البحثية في صنع القرار

Developing the Palestinian health system through institutionalizing the use of information in decision making

Helsinki Committee

For Ethical Approval

Date: 2021/12/13 **Number:** PHRC/HC/1001/21

Name: Farah Hatem Ahmad Mattour الاسم:

We would like to inform you that the committee had discussed the proposal of your study about: نفيدكم علماً بأن اللجنة قد ناقشت مقترح دراستكم حول:

Adverse Drug Events and level of harm in Hospitalized Pediatric Patients in Palestine: A retrospective cohort study

The committee has decided to approve the above mentioned research. Approval number PHRC/HC/1001/21 in its meeting on 2021/12/13 و قد قررت الموافقة على البحث المذكور عاليه بالرقم والتاريخ المذكوران عاليه

Signature

Member Chairman Member

13 12 2021

Genral Conditions:-

1. Valid for 2 years from the date of approval
2. It is necessary to notify the committee of any change in the approved study protocol
3. The committee appreciates receiving a copy of your final research when completed.

Specific Conditions:-

E-Mail:pal.phrc@gmail.com

Gaza - Palestine غزة - فلسطين

Appendix 4 : Istishari Arabi Hospital approval

Arab American University
Faculty of Graduate Studies

الجامعة العربية الأمريكية
كلية الدراسات العليا

2021-10-28

حضرة السادة المستشفى الاستشاري العربي المحترمين

تسهيل مهمة بحثية

تحية طيبة وبعد،

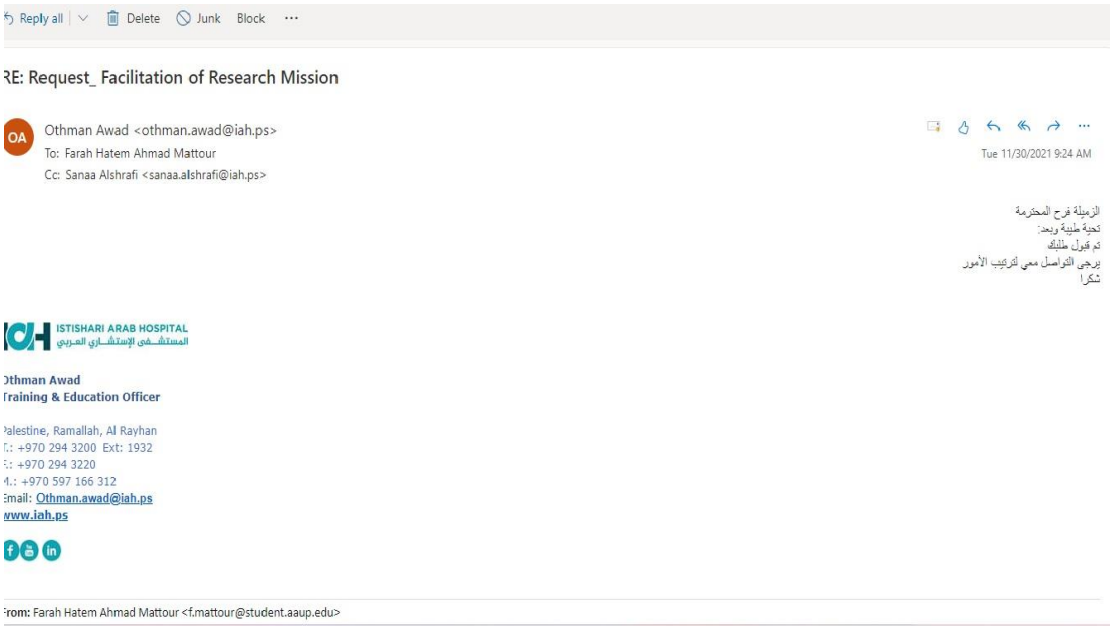
تهديكم كلية الدراسات العليا في الجامعةالعربيةالامريكية اطيبالتحيات، وبالإشارةالى الموضوع أعلاه، تشهد كلية الدراسات العليا في الجامعة بأن الطالبة **فرح حاتم أحمد مطور** والتي تحمل الرقم الجامعي 201912483 هي طالبة ماجستير في الجامعة العربية الامريكيةتخصص المعلوماتية الصحية وتعمل على رسالة بعنوان **"رصدالآثار الجانبية للأدويةومستوى الضرر بينالمرضى نزلاء قسم الاطفال في المستشفيات في فلسطين: دراسة الملفات الطبية بأثر رجعي"** نأمل من حضرتكم لايعاز لمن يلزملمساعدتها في الحصول على المعلومات اللازمة للدراسة وعمل المقابلات اللازمة. علما" ان المعلومات ستستخدم لغاية البحث فقط وسيتم التعامل معها بغاية السرية، وقد أعطيت هذه الرسالة بناء" على طلبها.

وتفضلوا بقبول فائق الاحترام

د. شاهيناز نجار

عميد كلية الدراسات العليا

كلية الدراسات العليا
FACULTY OF GRADUATE STUDIES



Reply all | Delete | Junk | Block | ...

RE: Request_ Facilitation of Research Mission

OA Othman Awad <othman.awad@iah.ps>
To: Farah Hatem Ahmad Mattour
Cc: Sanaa Alshrafi <sanaa.alshrafi@iah.ps>

Tue 11/30/2021 9:24 AM

الزميلة فرح المحترمة
تحية طيبة وبعد:
تم قبول طلبك
يرجى التواصل معي لترتيب الأمور
شكرا

ISTISHARI ARAB HOSPITAL
المستشفى الإستشاري العربي

Othman Awad
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From: Farah Hatem Ahmad Mattour <f.mattour@student.aaup.edu>

Appendix 5: Palestine Medical Complex

Arab American University
Faculty of Graduate Studies

الجامعة العربية الأمريكية
كلية الدراسات العليا

2021-10-28

حضرة السادة مجمع فلسطين الطبي المحترمين

تسهيل مهمة بحثية

تحية طيبة وبعد،

تهديكم كلية الدراسات العليا في الجامعة العربية الامريكية اطيب التحيات، وبالإشارة الى الموضوع أعلاه تشهد كلية الدراسات العليا في الجامعة أن الطالبة **فرح حاتم أحمد مطور** والتي تحمل الرقم الجامعي 201912483 هي طالبة ماجستير في الجامعة العربية الامريكية تتخصص المعلوماتية الصحية، وتعمل على رسالة بعنوان **"رصد الآثار الجانبية للأدوية و مستوى الضرر بين المرضى نزلاء قسم الاطفال في المستشفيات في فلسطين: دراسة الملفات الطبية بأثر رجعي"** نأمل من حضرتكم لا يعاز لمن يلزم لمساعدتها في الحصول على المعلومات اللازمة للدراسة وعمل المقابلات اللازمة. علما" ان المعلومات ستستخدم لغاية البحث فقط وسيتم التعامل معها بغاية السرية، وقد أعطيت هذه الرسالة بناء" على طلبها.

وتفضلوا بقبول فائق الاحترام

د. شاهيناز نجار

عميد كلية الدراسات العليا

كلية الدراسات العليا
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Appendix 6 : Specialized Arab Hospital

Arab American University
Faculty of Graduate Studies

الجامعة العربية الأمريكية
كلية الدراسات العليا

2021-10-28

حضرة السادة المستشفى العربي التخصصي ا لمحتوين

تسهيل مهمة بحثية

تحية طيبة وبعد،

تهديكم كلية الدراسات العليا في الجامعة العربية الامريكيةاطيبالتحيات،و بالإشارةالى الموضوع أعلاه، تشهد كلية الدراسات العليا في الجامعةأن الطالبة **فرح حاتم أحمد مطور** والتي تحمل الرقم الجامعي 201912483 هي طالبة ماجستير في الجامعةالعربية الامريكية تخصص المعلوماتية الصحية،وتعمل على رسالة بعنوان **"رصد الاثار الجانبية للادويةو مستوى الضرر بينالمرضى نزلاء قسم الاطفال في المستشفيات في فلسطين: دراسة الملفات الطبية بأثر رجعي"** نأمل من حضرتكم لا يعاز لمن يلزملمساعدتها في الحصول على المعلومات للازمة للدراسة وعمل المقابلات اللازمة، علما" ان المعلومات ستستخدم لغاية البحث فقط وسيتم التعامل معها بغاية السرية، وقد أعطيت هذه الرسالة بناء" على طلبها.

وتفضلوا بقبول فائق الاحترام

د. شاهيناز نجار

عميد كلية الدراسات العليا

كلية الدراسات العليا
FACULTY OF GRADUATE STUDIES

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Appendix 7: Rafidia and Alia Hospitals approval

State of Palestine **Ministry of Health** **General Directorate of Education in Health and Scientific Research**	دولة فلسطين وزارة الصحة **الإدارة العامة للتعليم الصحي والبحث العلمي**

Ref.: ....
Date:..................

الرقـــم: عتص/٢٢٦٩/٢٠٢١
التــاريخ: ٢٣/٤/٢٠٢١

الأخ مدير عام الادارة العامة للمستشفيات المحترم،،،

تحية واحترام...

<u>الموضـــوع: تسهيل مهمة بحث</u>

يرجى التكرم بتسهيل مهمة الطالبة: **فرح حاتم احمد مطور، ماجستير معلوماتية صحية- الجامعة العربية الامريكية**، لعمل بحث بعنوان:

"رصد الاثار الجانبية للأدوية ومستوى الضرر بين المرضى نزلاء قسم الاطفال في المستشفيات في فلسطين"

حيث ستقوم الطالبة بجمع معلومات من خلال مراجعة ملفات المرضى، وبوجود المسؤول عن الملفات، ودون التعرض للمعلومات التعريفية للمرضى وتحت طائلة المسؤولية، مع العلم أن مشرف الدراسة: د. شهناز نجار، ود. يوسف الميمي.

وذلك في: **- مستشفى عاليه - مستشفى رفيديا**

على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا، وتحت طائلة المسؤولية.

على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، التعهد بعدم النشر الا بعد الحصول على موافقة وزارة الصحة على النتائج.

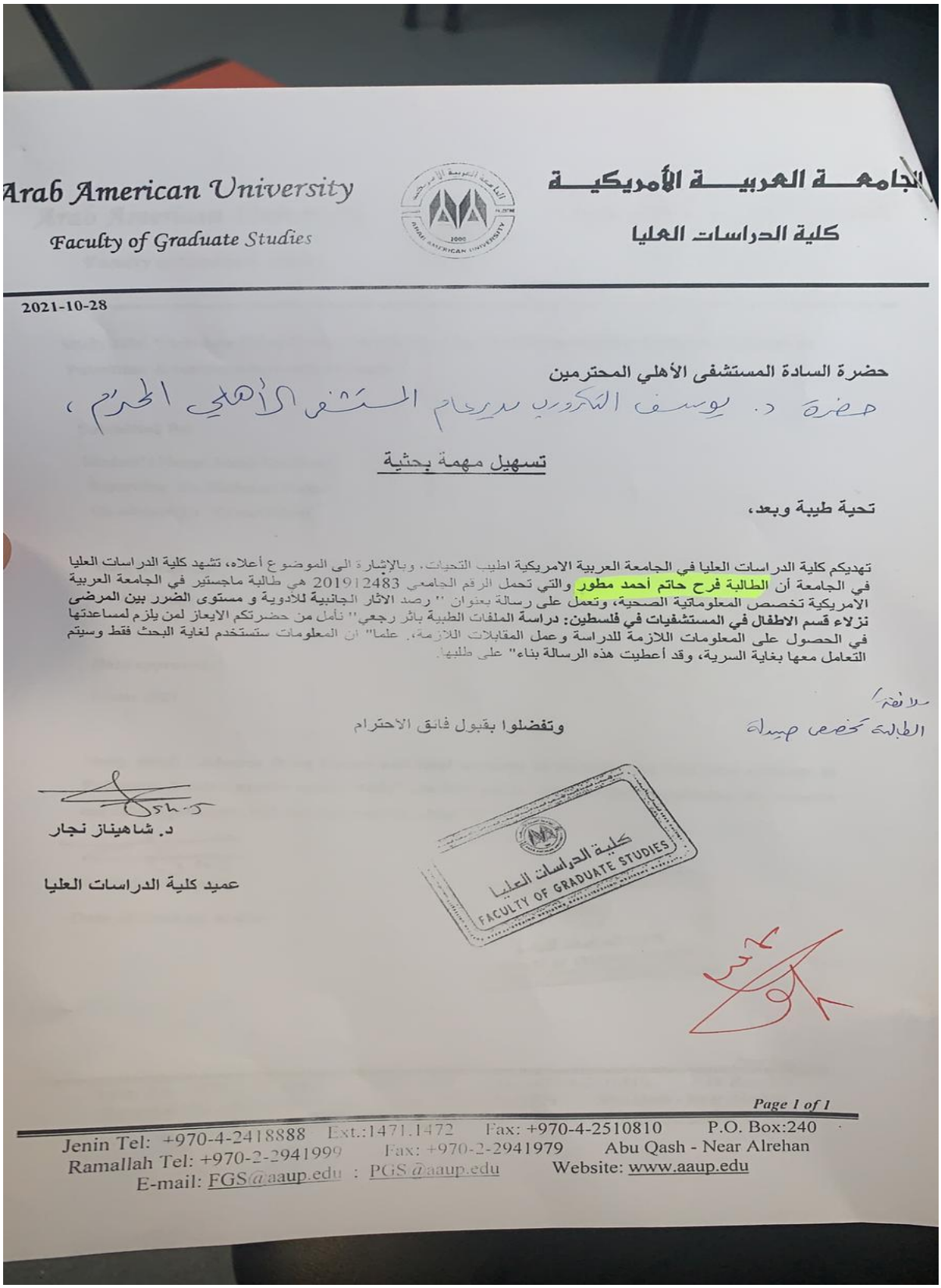
مع الاحترام...

د. عبد الله القواسمي
مدير التعليم الصحي والبحث العلمي

نسخة: عميد كلية الدراسات العليا المحترم/ الجامعة العربية الامريكية

P.O .Box: 14 | scientificresearch.dep@gmail.com | ص.ب. 14
Telfax.:09-2333901 | تلفاكس: 09-2333901

Appendix 8: AlAhli hospital approval



Arab American University

Faculty of Graduate Studies

الجامعة العربية الأمريكية

كلية الدراسات العليا

2021-10-28

حضرة السادة المستشفى الأهلي المحترمين

حضرة د. يوسف الكردي مدير عام المستشفى الأهلي المحترم ،

تسهيل مهمة بحثية

تحية طيبة وبعد،

تهديكم كلية الدراسات العليا في الجامعة العربية الامريكية اطيب التحيات. وبالإشارة الى الموضوع أعلاه، تشهد كلية الدراسات العليا في الجامعة أن الطالبة فرح حاتم أحمد مطور والتي تحمل الرقم الجامعي 201912483 هي طالبة ماجستير في الجامعة العربية الامريكية تخصص المعلوماتية الصحية، وتعمل على رسالة بعنوان " رصد الاثار الجانبية للادوية و مستوى الضرر بين المرضى نزلاء قسم الاطفال في المستشفيات في فلسطين: دراسة الملفات الطبية باثر رجعي" نأمل من حضرتكم الايعاز لمن يلزم لمساعدتها في الحصول على المعلومات اللازمة للدراسة وعمل المقابلات اللازمة، علما" ان المعلومات ستستخدم لغاية البحث فقط وسيتم التعامل معها بغاية السرية، وقد أعطيت هذه الرسالة بناء" على طلبها.

وتفضلوا بقبول فائق الاحترام

الطالبة فرح حاتم مطور

د. شاهيناز نجار

عميد كلية الدراسات العليا

كلية الدراسات العليا
FACULTY OF GRADUATE STUDIES

Page 1 of 1

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E-mail: FGS@aaup.edu ; PGS@aaup.edu Website: www.aaup.edu

الملخص

مقدمة: تعد سلامة المرضى مصدر قلق رئيسي للصحة العامة في جميع أنحاء العالم. وتزيد الاثار الجانبية الضائرة من الوفيات والمراضة وطول مدة الإقامة في المستشفى والتكاليف. في حين أن الاحداث الدوائية الضارة (ADEs) أدت إلى ارتفاع التكاليف الطبية ، والإقامة الطويلة في المستشفى ، والمراضة ، والعجز الذي يمكن نسبه في جميع أنحاء العالم.

هناك بيانات وأبحاث محدودة حول الأحداث السلبية في فلسطين ، وتحديدا الأخطاء الطبية. هناك غياب للنظام والأدوات اللازمة للكشف عن مستوى الضرر المتعلق بالمرضى الأطفال في المستشفيات حتى مع وجود الأنظمة التقليدية للإبلاغ عن الاحداث الدوائية الضارة (ADEs).

هدف الدراسة: رصد الاحداث الدوائية الضارة (ADEs) بين المرضى نزلاء قسم الاطفال و رصد مستوى الضرر الذي لحق بالمرضى أثناء تلقي العلاج وتحديد عوامل الخطر المتعلقة بالاحداث الدوائية الضارة في المستشفيات الفلسطينية.

منهجية البحث : دراسة كمية بأثر رجعي أجريت باستخدام أداة (GTT) التابعة لمعهد (IHI) لرصد الاحداث الدوائية الضارة (Pediatric ADE Patient Record Review Sheet). وشملت الدراسة على المجموعة المستهدفة من المرضى الذين تم إدخالهم إلى المستشفى في أقسام الأطفال في كل مستشفى من المستشفيات الستة المدرجة في الدراسة في فترة خمسة أشهر، من أغسطس 2021 إلى ديسمبر 2021. تم اختيار ما مجموعه 600 سجل للمرضى الأطفال بطريقة عشوائية منهجية (100 سجل لكل مستشفى) ، وتمت مراجعتها وتقييمها وفقا لتعليمات اداة البحث.

النتائج: من بين 600 ملف مريض تمت مراجعته ، كان 58.5 % من الذكور و 41.5 % من الإناث الذين يبلغ متوسط أعمارهم 2.36 سنة. بشكل عام ، تم تحديد 291 دليلا ، وكان الدليل الأكثر اكتشافا في جميع السجلات هو T9 (التوقف المفاجئ عن تناول الدواء ، n = 57) ، يليه T8 (الطفح الجلدي ، n = 55) و T1 (استخدام الأدوية المضادة للحساسية ، n = 52). وتظهر النتائج أن واحدا من كل أربعة مرضى أطفال يعاني من الضرر في المستشفيات الفلسطينية. وأظهرت مستويات الضرر المكتشفة أن 15.2 % أدت إلى ضرر مؤقت تطلب تدخلا (الفئة E) يليه 5.5 % أدى إلى ضرر مؤقت تطلب دخول المستشفى لفترات طويلة (الفئة F).

كان لنوع المستشفى وعمر المريض ومدة الإقامة دلالة إحصائية لارتباطهم بوجود الاحداث الدوائية الضارة ومستوى الضرر (p-value = 0.000) ، وفيما يتعلق بالمنطقة الجغرافية أظهرت النتائج أن وقوع الاحداث الدوائية الضارة أعطى فرقا ذا دلالة إحصائية لصالح منطقة الجنوب (p-value = 0.002). ولم يكن نوع الجنس مرتبطا بوجود الاحداث الدوائية الضارة.

الخلاصة: هذه الدراسة هي الأولى لتقييم و رصد الاثار الجانبية للأدوية و مستوى الضرر بين المرضى نزلاء قسم الاطفال في المستشفيات في فلسطين مما اظهر على أن واحدا من كل أربعة مرضى أطفال يعانون من ضرر في المستشفيات الفلسطينية في معظم الاثار الجانبية للأدوية مما يؤدي إلى ضرر مؤقت (الفئة E و F). ولذلك، ينبغي توجيه الجهود نحو تحسين نوعية الرعاية وتطبيق السياسات في القطاعات الصحية لضمان سلامة المرضى.