Chapter 25

Epidemiology of Patients Diagnosed with Prescription and Non-Prescription Drug Overdose at the Riyadh Security Forces Hospital Between January 2007 and December 2011

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Additional information is available at the end of the chapter

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1. Introduction

There is global concern concerning the higher rate of drug overdose morbidity and mortality, particularly from opioid medicines.[1] Drug overdose is one of the leading causes of death in many countries.[2] In the US, prescription drug mortality rate is higher than the death rate from illicit drugs, and drug overdose mortality currently exceeds mortality from motor vehicle accidents.[3] Moreover, there has been a tenfold increase in painkiller prescriptions in the US over the past 15 years.[4] In Saudi Arabia, there has been a significant increase in the use of prescription drugs compared with the previous decade, as the Ministry of Health stated in its 2009 annual report.[5] A number of studies have been conducted that investigate the epidemiology of drug overdose in Saudi Arabia. However, most of these studies were conducted in the late twentieth century.[6,7]

The purpose of this research is to investigate prescription and non-prescription overdose cases admitted to the emergency department of the Security Forces Hospital, Riyadh, from 2007 to 2011. The study sought to identify demographic characteristics of patients who were admitted to the emergency department with drug overdose, including age, gender, income and occupation.

The findings of this study have a number of implications for the Security Forces Hospital and drug overdoses in Saudi Arabia, particularly for elderly patients who take Warfarin continuously. Further, it appears that parents leave their medications unsecured and unpro-

tected from children; thus, preventive and awareness programs are needed to address these issues.

2. Literature review

An Adverse Drug Event (ADE) is defined as an injury resulting from medical intervention related to a drug.[8] It is considered a major problem in medicine because it results in hospital admissions. ADEs include harm caused by the drug, such as adverse drug reactions and overdoses, and harm resulting from using the drug, such as dose reductions and discontinuation of drug therapies.[9] Previous studies have found that ADEs account for 3.9–6.2 per cent of hospital admissions. Further, drug overdoses account for a higher hospital admission rate of ADEs.[10,11]

Drug overdose can be defined as intentionally or unintentionally administering a higher dose of prescription or non-prescription drugs than recommended.[12] Drug overdose is considered a major health problem, particularly in developed countries. In the United States (US), the Centers for Disease Control and Prevention (CDC) recently reported that fatal overdoses from opiate painkillers currently exceed those from cocaine and heroin combined.[12] The rate of prescription drug use is increasing globally.[13] In Saudi Arabia, there has been a significant increase in prescription drug use since 2000 compared with the previous decades; however, there is a dearth of information relating to drug use and overdoses.[5]

In many Asian countries, drug overdose mortality is considered a major problem. For example, a study in northern Thailand which investigated the overdose mortality rate of injecting drug users between 1999 and 2002 found a death rate of 8.97 per 1,000 people among 861 drug users who were Human Immunodeficiency Virus (HIV)-negative.[14] A study in Xichang City, China, found a heroin overdose mortality rate of 4.7 per 100 people among 379 people who injected drugs during 2002 to 2003.[15] Further, in a review conducted in several central Asian countries, emergency medical services stated that there were 21 drug overdose deaths in Tajikistan and 57 in Kyrgyzstan in 2006.[1]

Many European countries also consider drug overdose a major concern, and it is considered one of the leading causes of death. The average mortality rate is 21 deaths per 1 million people aged 15–64.[16] Drug overdose in Europeans aged 15–39 accounted for 4 per cent of all deaths. Males were at a greater risk than females in all countries, with males accounting for 81 per cent of all drug-related deaths reported in European countries. The male to female ratio varied across countries, with the lowest rate in Poland (4:1) and the highest rate in Romania (31:1). The most common drugs used in almost all countries were opioids, which accounted for 90 per cent of drugs used in five countries and 80–90 per cent in 12 countries.[16]

Drug overdose is also considered a major public health threat in the US. There, the drug overdose mortality rate among adults increased from 4 per 100,000 people in 1999 to 8.8 per 100,000 in 2006. Moreover, deaths from drug overdose increased from 11,155 in 1999 to

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22,448 in 2005, which can be attributed mainly to prescription drugs rather than illicit drugs.[3] Drug overdose is the second leading cause of death among all unintentional deaths in the US. The most common drugs that caused death by overdose were heroin, cocaine and pain-killers. The use of prescription medicines has increased, thus contributing to the death rate.[4] According to the CDC, from 2005 to 2007, prescription drugs such as benzodiazepine, anti-depressants and opioid medicines were found in 79 per cent (2,165 cases) of all substance overdoses.[17]

In Australia, there appears to be a lower risk of drug overdose than in other countries. For instance, the rate of death from opioids was 101.9 per 1 million people in 1999 and 31.3 deaths per 1 million in 2004.[18] Moreover, in 2005, the Illicit Drug Reporting System distributed a survey among intravenous drug users and found that 46 per cent had experienced an overdose.[18] It was also found that 357 deaths were caused by opioid overdose and 40 per cent of deaths occurred in New South Wales. Males accounted for 75 per cent of overdose deaths, and those aged 25–34 were most at risk, accounting for 40 per cent of deaths.[19] Recently released Australian prisoners are at significantly increased risks of illicit drug overdose and deaths.[20]

In Saudi Arabia, studies have noted an increase in drug overdoses in localised cohorts over the past several decades. However, there are no significant statistics for drug overdose morbidity and mortality in Saudi Arabia as a whole.[6,21] Several studies have been undertaken in Saudi Arabia to investigate the drug overdose in hospitals. Moazzam's and Aljahdali's studies found that paracetamol accounted for 24.1 per cent of 170 drug overdose cases and 30 per cent of 79 cases, respectively.[21,22] Ahmed's study found that mefenamic acid accounted for 20 per cent of 50 cases investigated.[6] The rate of death amongst drug overdose was investigated in some studies in Saudi Arabia. Ahmed stated that there was one death among 106 drug overdoses admitted between 1992 and 1994.[6] Elfawal investigated 249 deaths from substance overdose between 1990 and 1997, and found 20 per cent of cases related to medically prescribed drugs.[7] Aljahdali and Ahmed found females accounted for a higher percentage of drug overdose cases.[6,22] Moazzam and Elfawal found males were represented in a higher percentage of cases.[7,21]

Drug overdoses could result from non-prescription substances such as herbal medicines.[23] The problem with herbal remedies relates to limited control and regulation among stores that provide them.[24] Many people believe that herbal substances are harmless and that it is safe to administer excessive amounts because they come from natural sources.[25] Although the rate of usage has increased, fewer than half of patients consult their physicians before administrating herbal remedies.[26] Further, the accurate dosage of herbal medicines is variable, and there are no guidelines to determine correct dosage.[25]

Drug overdoses could result from administering illicit drugs such as heroin and hashish.[27,28] As Saudi Arabia is a strict Islamic country, and Islam prohibits the use of illicit drugs, overdose cases involving illicit drugs are rare.[22] However, according to a world drug report, Saudi Arabia is considered a major market of phenethylline (Captagon) in the Middle East. The Saudi government confiscated more than 10 million pills in one seizure in 2010. However, the prevalence of amphetamines in Saudi Arabia is low compared with other

western countries: in 2006, the prevalence of amphetamines in Saudi Arabia was 0.4 per 100,000 people, whereas in Australia and the US, the prevalence was 2.7 and 1.5 per 100,000 people respectively. Further, the prevalence of opioids and cannabis was 0.06 and 0.3 per 100,000 respectively in Saudi Arabia, 0.4 and 10.6 per 100,000 respectively in Australia and 5.9 and 13.7 per 100,000 respectively in the US. Therefore, the prevalence of opioids and cannabis are markedly lower in Saudi Arabia than in Australia and the US.[13]

Suicide is one of the major motivations and outcomes of intentional drug overdose.[29] Suicide accounts for 2 per cent of all deaths in the world. In 2005, there were about 800,000 deaths from suicide, and about 56 million deaths globally.[30] Drugs cause 11 per cent of suicides in Australia.[30] A study found that suicide is a greater risk among people who had a history of drug overdoses compared with people who did not.[31] Another study found a positive correlation between suicide and drug overdose.[32] Moreover, research has found that committing suicide by administering drugs is common among adolescents.[33] One study found suicide was associated with both prescription and non-prescription drugs, with a strong association between opiates and suicide, and opioid users were 14 times more likely to attempt suicide compared with non-opioid users.[34]

The excessive availability of medicines in households is due to the relative affordability of drugs, which can be bought from a range of places including markets, internet pharmacies and cosmetic stores. For instance, patients can purchase prescription drugs from an internet pharmacy without a prescription.[35] One survey investigated how easy it was for adolescents to acquire prescription medications. The question asked was 'which is easiest for someone your age to buy: cigarettes, beer, marijuana or prescription drugs without prescription?' Nineteen per cent of respondents said it was easier to buy prescription drugs compared to 13 per cent in the previous year.[36]

Two main factors contribute to the excessive availability of medicines: physicians and patients. Physicians appear to prescribe more medicines than in the past. For example, there was a 300 per cent increase in the prescription of painkillers in the US in 1999.[35,37] According to the National Institute on Drug Abuse (NIDA), the number of potentially addictive drug prescriptions for pain rose to 200 million in 2011.[38] There is also an association between patient death and physicians who frequently prescribe painkillers. Dhalla published a study in Ontario in 2011 that investigated the opioid prescription rate in family physicians and their relation to opioid-related deaths. He found that 20 per cent of physicians have a prescription rate that is 55 times higher than the 20 per cent of physicians who prescribed the lowest. The top 20 per cent of physicians were responsible for 64 per cent of patient deaths caused by painkillers.[39] In addition, many people falsely reporting symptoms in order to obtain a prescription and this is defined as drug seeking behaviour. The most drugs associated with drug seeking behaviour are benzodiazepine and opioids.[40]

Alcoholism is considered a major risk factor for intentional overdoses. Several studies state that the risk of drug overdose from prescription medicines is higher among people who drink alcohol.[41-43] A study by Li in 2011 investigated trends of paracetamol overdose in US emergency departments from 1993 to 2007 using data from physicians' diagnoses codes and cause of injury codes. The author found those who drank alcohol were 5.48 times more

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likely to overdose compared to people who did not drink alcohol, and the p-values were statistically significant.[41]

A study published by Wazaify in 2005 examined OTC drugs and prescription drug overdoses for three months, as well as the potential risk factors. The study investigated 247 overdose cases, excluding alcohol intoxication and spiked drinks. He found alcohol was a major risk factor for overdoses of both OTC and prescription drugs, and that alcohol contributed more to OTC drug overdoses (32.2 per cent) than prescription drugs combined with OTC drugs (24.7 per cent).[42] Moreover, the prescription drug overdose death rate increased with alcohol consumption. West Virginia found 32.9 per cent of overdose deaths were associated with alcohol consumption.[43] Another study on paracetamol overdose found more than one-third of drug overdoses were associated with alcohol consumption at the time of overdose, and it was slightly higher in males (12 per cent) than females (11 per cent).[44] In addition, people who consumed alcohol could overdose on lower doses of paracetamol compared with those who did not consume alcohol.[45] Paulozzi conducted a study on methadone overdose and found that the concentration of methadone was lower when alcohol was involved.[28] Mixing drugs with alcohol is therefore considered a risk factor for drug overdose.[46]

Violence involving sex and family could also be associated to intentional drug overdose.[33,47] A study by Budnitz investigated the pattern of acetaminophen overdoses in the emergency department from two components of the National Electronic Injury Surveillance System. Of the 2,717 annual acetaminophen overdose cases, 69.8 per cent were related to self-directed violence. Further, females had a greater rate of self-directed violence (27.2 per 100,000) compared with males (14.4 per 100,000).[33] Violence and strife have also contributed to the increased rate of illicit drug use in the US.[47]

Drug overdoses can be associated with people who take drugs for recreational purposes. According to the Centers for Disease Control and Prevention (CDC), opioids are involved in more overdose deaths than heroin and cocaine combined, and they are often associated with recreational use.[4] Further, several studies found that recreational use contributed to many of the drug overdoses presenting to emergency departments. For example, a study found that 15.4 per cent of 500 overdose cases presented to emergency departments resulted from recreational use.[48] Further, a survey of 975 students found that 16 per cent abused medicine for recreational purposes.[49]

Buykx found that many people overdose on drugs after they experience interpersonal conflicts.[31] Britton's 2010 study investigated the risk factors of non-fatal overdoses over 12 months. The author recruited 2,966 participants and found that 23.5 per cent of all overdose cases had experienced sexual abuse. Moreover, victims of sexual abuse were 2.02 times more likely to overdose, and the result was statistically significant.[50] Other forms of physical abuse were also addressed in the study: 33.4 per cent of all overdose cases had experienced physical abuse, and they were 1.91 times more likely to overdose, which was statistically significant.[50]

The level of a medicine's purity could lead to a drug overdose, particularly for people using non-prescription medicines. Previous studies have found the fluctuation of heroin purity contributed to the overdose rate.[51] Moreover, in a survey of healthcare providers that asked about risk factors for opioid overdose, approximately 90 per cent mentioned the fluctuation of opioid purity.[52] Of 855 heroin users, 29 per cent split the tablets in half when the purity was unknown.[53] In addition, a study stated that many heroin users believed that purity fluctuation contributed to drug overdose.[54] Conversely, several studies on heroin (e.g. Toprak and Risser) found no association between drug overdose and purity.[55,56]

Other factors that contribute to intentional drug overdose include psychiatric illness, marital problems and family size.[6] Ahmed found that psychiatric illness was a greater risk among males than females, and it was a risk factor in 10 of the 50 cases he investigated. Further, five cases had experienced marital problems.[6] Family size could be a major factor in drug overdose. Large families are common in Saudi culture. A 2011 study by Bani found that 43 per cent of participants had six to eight family members.[57] A study by TNS Middle East of demographic characteristics in Saudi Arabia in 2006 found that 40 per cent of Saudi families are considered large, with six or more members.[58] Aljahdali found that large family size was a risk factor in drug overdoses: 59 per cent of the 79 cases in his study had more than five family members This could indicate that because large families have more children, parental supervision amongst the children is lowered, potentially increasing the chance of the unsupervised ingestion of drugs.[22]

A previous drug overdose might also be a risk factor for another drug overdose, as many studies have attested.[59],[60],[46] For example, Kinner's study in 2012 investigated the risk factors of non-fatal overdoses among illicit drug users, recruiting 2,515 illicit drug users in Vancouver, Canada. The author found an association between drug overdoses and previous drug experiences; people with previous overdoses were four times more likely to overdose compared with people who had no previous experience.[59] This finding is similar to that of a study by Hall in 2008, which investigated the pattern of unintentional drug overdose caused by prescription drugs, recruiting 295 participants. The author found that people who had experienced a previous overdose had a 30.2 per cent chance of overdose compared with 14.4 per cent of people who had not.[60] In addition, a New York study that investigated the risk factors of heroin users found that participants who had overdosed were 28 times more likely to overdose than those who had not experienced a previous overdose.[46] In contrast, some previous studies found no associations between drug overdose and previous overdose experience.[59]

Doctor shopping is considered the most common method of obtaining prescription drugs for legal and illegal use.[61-64] It is defined as patients visiting several doctors to obtain prescription medicines without medical need, and it is considered one of the major mechanisms of diversion.[35] Several studies have found that doctor shopping contributes to drug overdose. For example, the author Hall found that doctor shopping contributed to 21.4 per cent of 259 overdose cases.[65] Further, it found that 19 per cent of participants who overdosed acquired their medicines through doctor shopping.[49] Moreover, doctor shopping is attrib-

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uted to a higher rate of drug overdose death.[65,66] Several studies have stated that controlling doctor shopping would assist in preventing drug overdoses.[35,67]

The consumption of prescription drugs, especially opioids, has increased due to their euphoric and energising effects.[4] For example, methamphetamine and alprazolam users tend to redose every three-to-eight hours to maintain the euphoric effect.[46] Further, drug users tend to abuse cocaine to feel euphoric and increase a feeling of sexual desirability.[68] Some medicines do not enhance euphoria until taken in higher doses. For example, drug users take higher doses of benzodiazepine to experience the euphoria effect.[24] Many fatal overdoses occur when larger doses of medicines have been taken to achieve the euphoric effect.[37]

Long-term therapy could be related to overdoses, especially in patients suffering from chronic pain. Further, such patients have easy access to painkillers in the home, which increases the chance of a fatal overdose.[69] Previously, long-term therapy was restricted to cancer patients; however, currently, it is commonly used for chronic pain in non-cancer patients. Unfortunately, the latter have been associated with higher overdose rates.[70] One of the reasons for drug overdose in chronic patients is inadequate pain management.[69,70] The critical issue with chronic pain is pain management, and inadequate pain management could lead to increased doses of painkillers and consequently, an increased rate of drug overdoses.[71]

Calculating the dose is an important factor, and miscalculated doses could lead to unintentional overdoses.[72] Many parents have difficulty measuring and calculating the appropriate dose of paracetamol for their children.[73] One survey asked 100 caregivers if they were able to determine the appropriate dose for their children; only 30 per cent were able to do so.[73] Hixson conducted a study in 2010 to compare the ability of parents to calculate the appropriate dose of acetaminophen using product information leaflets or the Parental Analgesia Slide. Participants were divided into two groups, and a questionnaire was distributed to each group. The author found that caregivers using the Parental Analgesia Slide had fewer dosing errors than caregivers using product information leaflets, but the difference was not statistically significant.[74] Limited literacy and numeracy skills are also associated with poor clinical outcomes and overdoses. Many people with limited numeracy skills are confused with dosing instructions and warning labels. Moreover, people could be confused with the information on the labels of prescription medicines.[75]

Mental states could be a major risk factor of drug overdose, as patients with mental disorders and drug addictions are more vulnerable.[76] For example, Hasin's study found that 15–20 per cent of patients with mental disorders overdosed on drugs at least once in their lives, and patients with depressive disorders were 3.7 times more likely to overdose.[76] Fischer's study found that people with mental problems were 1.51 times more likely to overdose than people without mental problems, but this result was not statistically significant.[77]

Children are considered at greater risk of drug overdose for several reasons. Inappropriate storage and disposal of medicines can contribute to this risk.[78] For example, according to

the CDC and Prevention, one of the main causes of drug overdose reported to emergency departments is the unsupervised ingestion of OTC and prescription medicines. Further, the CDC stated that of the 72,000 overdose cases presented to emergency departments in 2004, more than 26,000 were caused by OTC drugs.[79] Additionally, Li's study found that children under the age of five accounted for a higher percentage of drug overdose cases in emergency departments,[41] while another study which investigated 3,034 overdose cases among children found 97 per cent of the cases resulted from the unsupervised ingestion of drugs.[80]

Older age is associated with a higher drug overdose rate for several reasons. First, elderly people aged 65 years and over tend to have more medical problems; thus, they may take many medicines that might interact with each other and cause an overdose.[79] Second, many elderly people live independently and might find it difficult to calculate the correct dose. In addition, they may not recognise the symptoms of drug overdose when it occurs.[81] Suicide attempts are common among elderly people by taking an excessive amount of a drug. Several factors contribute to suicide attempts, such as old age, failing physical and mental health, reduced income and social support.[82]

Maintaining a dose is an important factor in preventing intentional overdoses among chronic patients.[83,84] When medicines such as Warfarin have a narrow therapeutic index, it is critical to adjust the appropriate dose.[83] Physicians prefer not to dispense Warfarin because of the uncertainty of patient compliance with monitoring, dietary implications and the fear of haemorrhagic complications.[85] The initial dose is challengeable, which could result in bleeding, and many patients might overdose at the beginning because they might have Warfarin sensitivity or a poor metabolism, thus requiring reduced dose. The maintenance of the dose depends on several factors, such as weight, diet, disease state and concomitant use of other medications, as well as genetic factors.[84] Genetic variability is considered a major factor in determining Warfarin overdose. There are two genes which are cytochrome P450, family 2, subfamily C, polypeptide 9 (CYP2C9), and vitamin K epoxide reductase complex, subunit 1 (VKORC1) contributing significantly to the variability among patients in dose requirements for Warfarin.[84],[86]

Misunderstanding and misreading the abbreviation of prescriptions can lead to medication errors and overdoses. One report demonstrated that a woman had a severe digoxin overdose because her nurse misread the pharmacist's instructions. The pharmacist had used the abbreviation (=), which was unclear because the pen had trailed ink.[87] Maged conducted a study in Saudi Arabia in 2010 to investigate medication errors in prescription medicines. Of the 529 dosing errors, the author found that 46 per cent caused overdoses. The two main errors were the route and frequency of the medicines.[88] Further, many parents have difficulty understanding the instructions to administer appropriate doses for their children. A study in 2008 examined caregivers' understandings of the age indication of OTC drugs and cough medications. Of the 182 participants whose misunderstood dose instruction, the author found that more than 80 per cent had given medicine to their infants when they should have consulted a physician first.[75]

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Many people believe that using excessive amounts of OTC medicines is safe and effective. Some people believe that if a medicine is OTC, it is safe to consume in large quantities.[33], [44] For example, paracetamol is considered a safe medication. However, it has a narrow therapeutic index, so the dangerous dose is close to the recommended dose, and an excessive dose could lead to liver toxicity.[33] Simkin's study found that 20 per cent of the 60 participants did not know the dose that could cause death, and 15 per cent believed that 100 tablets or more would cause death.[44] Advertising and media could contribute to the excessive amounts of OTC drugs administered; for example, advertisements could suggest that the consumption of large amounts is effective before seeing a doctor.[89] Wazaify claims that there is aggressive marketing and advertising for OTC medicines.[42]

There is a higher risk of drug-related deaths among recently released prisoners,[20,90] who are associated with overdoses in the first few weeks after release.[90,91] Many studies state that the leading cause of death for recently released prisoners is accidental drug overdose.[92] For example, a study found that recently released prisoners have an overdose rate that is 12 times higher than the general population.[91] In addition, another study found that the overdose mortality rate is three-to-eight times higher in the first two weeks after release compared to the subsequent 10 weeks.[20] The reasons for higher overdose rates are not understood; however, previous studies have suggested that possible reasons include poor housing, unemployment, psychosocial problems and barriers to health care.[93-95]

Another major factor related to the increase in drug overdose rates is the lack of education, which includes the education of healthcare providers, miscalculation of doses, and limited literacy and numeracy.[35,45,67] Manchikant states that many healthcare providers, such as physicians and pharmacists, do not have adequate education regarding drug misuse.[35] In 2012, Taylor investigated the pattern of acetaminophen overdose in the military and found that a lack of education was a risk factor.[45] The CDC stated that the majority of healthcare providers have the minimum education background regarding prescription drug misuse, and they could prescribe addictive medicines without being aware of the risks involved.[67] Wallace demonstrated that physicians have limited knowledge in detecting, investigating and managing acetaminophen overdoses. Further, Wallace's study proved that the management of overdoses improved when physicians had more knowledge. A management flowchart for paracetamol poisoning was introduced to help physicians treat overdose cases.[96]

Income could be a major factor in drug overdose. People with low incomes could have lower education and numeracy levels compared to those with higher incomes. This is supported by Lokker's study of parental misinterpretations of OTC medication labels, which found that 42 per cent of parents who misinterpreted the labels had an income of less than $20,000 per annum.[75] Further, people with low incomes had more motivation to misuse prescription medicines compared to those with higher incomes.[97] In addition, low-income people were six times more likely to overdose on prescription painkillers, and a US study found that low-income people accounted for 45 per cent of prescription overdose deaths.[37] The CDC also noted that low-income people are at a greater risk of drug overdose.[67]

In contrast, Yu's study in 2005 investigated drug misuse admissions to the emergency department in a large metropolitan teaching hospital in Taipei, Taiwan. The author found that

those on high-incomes were more likely to misuse drugs than low and medium income people, and the result was statistically significant.[98] Another study by Hall, which examined the pattern of unintentional drug overdoses, categorised participants' incomes into four quartiles. He found that the higher-quartile income had a greater risk of drug overdose (24.7 per 100,000 people) than the other quartiles. Further, doctor shopping is related to the higher quartile; 58 per cent of doctor shoppers were represented by the higher-quartile income.[60] Paulozzi's study also categorised income into four quartiles and found that the higher-quartile income was at a greater risk of death from methadone overdose (29.9 per cent) and other opioid analgesics (33.1 per cent).[28]

Adverse Drug Reaction (ADR) consider as the fifth leading cause of death and illness in the developed world with direct medical costs estimated to be US$30–130 billion annually in the US and claiming 100,000-218,000 lives annually.[99] Despite this, health-related associations estimate that 95 per cent of all ADRs in Canada and the US are not reported.[100] Many drugs have caused adverse drug reactions after there have been proved, and this were attributed to the drug safety issue. For example in Canada, 3–4 per cent of drugs approved will eventually be withdrawn from the market because of safety issues, Faster approval of new drugs has the potential to produce more safety problems once drugs are on the market. Many agencies have launched post marketing surveillance and pharmacosurveillance systems, and these are aimed to generate safety signals for marketed drugs.[101]

Identifying patterns of drug overdose will help to implement evidence-based policies. In a study in the UK on the effects of the withdrawal of Distalgesic (a prescription-only analgesic compound) from the market, the author found an 84 per cent reduction in intentional drug overdoses presenting to emergency departments in hospitals compared with the three years before the drug was withdrawn. Further, there was a marked reduction in tablet sales after the medicine was withdrawn, from 40 million in 2005 to 500,000 in 2006. Thus, identifying drugs that are commonly involved in overdoses will help in reducing the overdose rate.[102]

3. Methodology

An emergency department visit for drug overdose was the primary outcome measure, including unintentional and intentional overdoses. Drug overdoses are identified by physicians in the emergency department using the terms overdose, poisoning and drug relayed problem. Secondary measures include the patient's age, gender, interior personal occupation, Length of Stay (LOS) in the emergency department, patient type, drug level, previous admission, previous overdose and measurement outcome.

In this research, participants are categorised into three groups. First, interior personnel are identified as people who work in the Ministry of Interior. The second group is interior personnel relatives, where each employee has the right to have his family treated in the hospital. The third group is called exceptional people; many people do not belong to the Ministry

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of Interior, but they seek treatment in the hospital because they have acquired an exceptional letter, as they require special health intervention.

Overdose cases obtained in the study are divided according to prescription and non- prescription drugs in order to test the hypothesis of the study. Moreover, the number of medicines involved in the cases is addressed and the drugs are categorised into three groups: single, double and triple. In addition, drug level is addressed in the study and it is standardised to moderate or severe according to the level of drug in the body. The LOS of patients was determined by calculating the period between the time of admission and the time of discharge from the emergency department, or the time when admitted to the inpatient management is included in the study and all cases are divided into two categories: discharged from the emergency department and admitted to the inpatient department.

Descriptive statistics such as frequencies and cross-tabulations were obtained to describe the various motives reported by the sample. All drugs involved in overdoses were obtained, as well as their frequency, to identify the medicine that accounted for the highest percentage. Further, the medicines used in overdoses were tabulated according to their medical indication of use and then each medicine was categorised according to their medical indication group. Fisher and chi-square tests were conducted to test the differences between categorical variables. As the chi-square prefers two-by-two tables and each cell must have at least five cells, the patients' type needed to be re-categorised into two groups: interior and non-interior. Although the patients' type was allocated to two groups, one of the cells had less than five, so a Fisher exact test was used.

The data was obtained from medical records, which raises the issue of confidentiality. However, the anonymity of participants will be protected, and only de-identified data was accessed. A letter was obtained from the hospital to ensure the anonymity of the research. The data was obtained only from files that were considered essential for the research. No patient was contacted as part of this study. Each participant will have a unique three-digit code. The data collection complies with the National Health and Medical Research Council's National Statement on Ethical Conduct in Human Research. Further, the study has been approved by the Security Forces Hospital's Research Committee. In addition, the UWA's Human Research Ethics Committee has approved this study.

4. Results

4.1. Demographic characteristics

One hundred and forty drug overdose cases were admitted to the emergency department of the Riyadh Security Forces Hospital between 1 January 2007 and 31 December 2011. Table 1 describes the demographic characteristics of patients associated with drug overdose, and the findings are discussed below. Females accounted for 57.90 per cent of cases and males accounted for 42.10 per cent. In this study, there is a variety in age distribution, with patients aged between 11 months and 86 years. The patients' ages were divided into seven groups:

(0.01–1.12), (2.00–9.12), (10.00–19.12), (20.00–29.12), (30.00–44.12), (45.00–59.12) and (over 60 years). This study demonstrates that groups (2.00–9.12 years) and (over 60 years) accounted for the highest percentage of drug overdose cases (22.9 per cent).

Characteristics	Number	Per cent
Gender:		
Male	59	42.1
Female	81	57.9
Age groups:		
0.01–1.12 years	8	5.7
2.00–9.12 years	32	22.9
10.00–19.12 years	9	6.4
20.00–29.12 years	25	17.9
30.00–44.12 years	19	13.6
45.00–59.12 years	15	10.7
Over 60 years	32	22.9
Type:		
Interior Personnel	30	21.4
Relatives	105	75.0
Exceptional people	5	3.60
Income groups:		
Less than 22,000 USD	37	27.4
22,001–45,000USD	69	51.1
45,001–67,001USD	18	13.3
More than 67,001 USD	11	8.1

Table 1. Socio-demographic characteristics of drug overdose cases.

The interior personnel relatives group accounted for the highest percentage of cases (n=105, 75 per cent), and interior personnel and exceptional people accounted for 21.4 and 3.60 per cent respectively. Income was divided into four groups that were represented by United State Dollar (USD) per annum: (less than 22,000 USD), (22,001–45,000USD), 3 (45,001–

67,001USD) and (more than 67,001 USD). The study showed that (22,001–45,000USD) group represents the highest percentage of participants.

According to Table 2, 96.4 per cent of all drug overdose cases reported to the emergency department between January 2007 and December 2011 were caused by prescription medicines. Previous overdoses were addressed in the study, and only eight patients were found to have previous overdose experiences. Further, the study found that 53.6 per cent of cases were associated with previous admission, and patients with one previous admission represented 20 per cent of all participants who had been admitted previously. In the study, some patients used more than one drug to overdose. It found that 91.4 per cent of patients were taking one drug, while double and triple drugs accounted for 7.9 per cent and 0.7 per cent respectively. In addition, 67.5 per cent of the cases were found to have moderate drug levels, while severe drug levels accounted for 26.4 per cent of cases.

LOS groups were categorised into the following: (less than five hours), (5.01–10.01 hours), (10.01–15.00 hours), (15.01–20.00 hours), (20.01–35.00 hours) and (over 40 hours). It found that 50.0 per cent of all cases reported to the emergency department stayed for less than five hours, and these cases were either discharged or transferred to the inpatient admission department. The study found that 106 drug overdose cases were referred to the inpatient admission department.

Interior relatives accounted for 75 per cent of all overdose cases in the study. It found that 28.6 per cent of the cases were aged 2–9.12 years. Further, 54 per cent of the participants' income was between (22,001–45,000USD) per annum. Eight cases were associated with previous overdose cases, and seven of them were relatives. Moreover, 49.5 per cent of cases stayed in the emergency department for less than five hours. Further, there were 34 discharged cases in the study, 28 of which were relative cases.

The outcome of a drug overdose is statistically different between patients' type (one-sided p-value = 0.007). It found that the inpatient admission department accounted for 93.3 per cent for all interior personnel cases, while non-interior people who were relatives and exceptional people accounted for 78 per cent of the cases, and the difference of outcome management among patient type is significant. By using the Fisher exact test, previous admission is statistically relevant to patient type (one-sided p-value = 0.033). It found that 70 and 50.1 per cent of interior and non interior cases were associated with previous admission; thus, the difference is significant. The difference between drug level and outcome management was tested using a chi-square test, and a significant difference was found. It found that 72.6 per cent of moderate-level cases were admitted to the inpatient department and 91.9 per cent of severe-level cases were admitted to the inpatient department. The management outcome from admission is statistically relevant to the level of drug (one-sided p-value = 0.008). The difference between gender and patients' type was tested using the Fisher exact test; thus, gender is statistically relevant to patients' type (one-sided p-value = 0.000).

Characteristics	Number	Per cent
Previous overdose:		
Yes	8	5.7
No	132	94.3
Previous admission:		
Yes	75	53.6
No	65	46.4
Number of previous admissions:		
0	65	46.4
1	28	20.0
2	21	15.0
3	8	5.7
4	6	4.3
5	4	2.9
7 and more	8	5.6
Drug kind:		
Prescription	135	96.4
Non-prescription	5	3.6
Drug combination:		
Single drug	128	91.4
Double drugs	11	7.9
Triple drugs	1	0.7
Drug level:		
Moderate	95	67.9
Severe	37	26.4
LOS groups:		
Less than five hours	70	50.0
5.01–10.01 hours	24	17.1
10.01–15.00 hours	12	8.6
15.01–20.00 hours	13	9.3
20.01–35.00 hours	10	7.1
Over 40 hours	11	7.9
Outcome management:		
Discharge	34	24.3
Inpatient admission	106	75.7

Table 2. Characteristics of drug overdose cases

4.2. Drug overdose percentages and rates

The means of LOS age and income per annum of patients in the emergency department are addressed, and it was found that the average LOS was around 11 hours, average age was 33 years and four months, and average income was around 35,951 USD.

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The number of drug overdose cases was calculated for each year of the study. The annual number of emergency admissions was requested from the medical records department to identify the rate of drug overdose cases among all emergency cases. All results are shown in Table 3. According to the results, the rate of drug overdose reduced between 2007 and 2011.

Year	Number of cases	Number of emergency cases	Rate
2007	33	9576	3.45 per 1,000
2008	30	9131	3.26 per 1,000
2009	26	8707	2.99 per 1,000
2010	26	8209	3.17 per 1,000
2011	25	7883	3.17 per 1,000

Table 3. Number and rate of drug overdose for each year in the study

Most patients overdosed on one drug. Fifty-eight prescription and non-prescription medicines were included in the study. These medicines were categorised in terms of medical indication purpose. Seven drug categories were found in the study, and each one involved more than seven cases. Further, anti-coagulants and analgesics accounted for 35.3 per cent of drug overdose cases. These categories were investigated in terms of age groups. The findings show that 55 per cent of anti-coagulant overdose cases occurred in patients aged over 60 years, while 41 per cent of analgesic overdose cases occurred in patients aged 20–30 years. According to the findings, Warfarin accounted for the highest percentage of drug overdoses. Warfarin accounted for 85 per cent of overdoses in patients aged over 50 years, while two cases occurred in children and middle-aged people respectively. Further, people in lower and middle-income groups accounted for 85.7 per cent of anti-coagulant cases.

The results show that four patients from age (20.00–29.12 years), had a previous overdose, and this age group represented 50 per cent of patients associated with previous overdoses. Moreover, two patients overdosed on OTC medicines twice, and one patient overdosed twice on Warfarin. Two deaths occurred from drug overdoses: one death was a patient who overdosed on paracetamol twice, and the other was attributed to amphetamine. In addition, there were 18 overdose cases aged from 15 to 25 years. It found that analgesics and antipsychotics accounted for 38.8 and 22.2 per cent of the cases respectively. Cholesterol-lowering and diabetic medicines were involved in two cases and antihistamine and antiepileptic drugs were involved in one case each.

As the hospital belongs to the Ministry of Interior, it is important to identify the occupations that are more involved in drug overdoses. There were 30 interior personnel cases, and eleven positions represented all interior personnel drug overdose cases. The system of occupation in the Ministry of Interior has two major categories: officer and non-officer. Non-officer personnel presented at a higher rate in drug overdoses than non-officer personnel. In this study, five of 30 cases belong to officers and the rest belong to non-officers.

Position name	Frequency
Soldier	7
First soldier	5
Captain	4
First Sargent	3
Sargent	2
Staff-Sargent	2
Unknown	2
Colonel	1
Corporal	1
Chief-Sargent	1
Porter	1
Senior-Sargent	1

Table 4. Occupations of interior personnel cases and their frequency

5. Discussion

We found that females accounted for a higher percentage of drug overdose cases than males, which is similar to findings in previous studies.[6,22,103,104] In contrast, Alfawal's study found that males accounted for 88 per cent of the cases.[7] Further, it found that (2.00–9.12 years) and (over 60 years) patients accounted for the highest percentage, at 22.9 per cent of cases. Previous studies associated the elderly with a higher percentage of drug overdoses, and this study had a similar result.[79,82] Further, the CDC found that the highest risk group of drug overdose among children was amongst those aged two years.[80] This research reached the same conclusion. Thus, most cases might have occurred unintentionally because previous studies demonstrated that children and the elderly are at a higher risk of unintentional overdose.[80]

The finding stated that 75.7 per cent of cases were referred to the inpatients admission department. According to the medical records department supervisor, this high percentage is not because most cases were severe; rather, many cases that were presented and discharged from the emergency department were missing and did not register to the medical files. There are two possible reasons for missing drug overdose cases. First, there is a higher load on emergency physicians; so many diagnostic forms are not fully completed. Second, many cases present to the emergency department have not been registered in the patients' medical records, so some overdose cases may have been missed and not caught by the ICD-9-CM. This explains why there were only 140 drug overdose cases in the five-year period. A study conducted in the National Guard Hospital in Riyadh, which is considered larger than the

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Security Force Hospital, found nine drug overdose cases per month,[105] compared to this study, which found around three cases per month. This is further evidence that there might be missing cases.

Fifty-eight medicines were involved in the drug overdose cases, and the most common drug was Warfarin, which caused 29 overdose cases. This finding differs from previous studies conducted in Saudi Arabia, which found that OTC medicines accounted for a large percentage of drug overdoses. Moazzam's and Aljahdali's studies found that paracetamol accounted for 24.1 per cent of 170 drug overdose cases and 30 per cent of 79 cases, respectively. [21,22]Ahmed's study found that mefenamic acid accounted for 20 per cent of 50 cases investigated.[6] Moreover, Malik's study found that the most common drugs used were analgesics and non-steroid anti- inflammatory drugs.[104] AbuMadini's study found that 80 per cent of cases were caused by paracetamol,[103] which was the second most common medicine in this study (12 cases).

According to the findings, children aged 2–9 years accounted for 22.4 per cent of drug overdose cases. This might indicate that many parents leave medicines unprotected from children, so children might administer excessive amounts of drugs accidentally. Education and awareness campaigns should be conducted to educate people about the risk of leaving medicines unprotected, as well as how to store their medicines correctly.[1,75,106, 107] Further, leaving medicines unsecured from children can contribute to an increase in the rate of drug overdose.[78,108,109] According to the American Association of Poison Control Centers, in 2009, prescription and OTC drugs caused more than 30 per cent of children's death in the US.[110]

Many policy and prevention measures can be implemented to protect children from drug overdoses, such as child-resistant packaging (CRP), product reformulations and heightened parental awareness. CRP reduced the drug overdose mortality rate of children by 45 per cent between 1974 and 1992.[22,80] Medication packaging will not protect children from overdose, and it becomes ineffective if the medication is not re-secured correctly.[109] Further, packaging has not proved to be effective, as young children have the dexterity to open these containers.[111] Some prevention programs have been conducted to educate parents about storing medicine in safe places. The Preventing Overdoses and Treatment Exposures Task Force (PROTECT) launched a program called 'Up and Away', which aims to educate parents about effectively storing medicines, and it emphasises the need to return medicines to a safe storage location immediately after every use to prevent children from reaching them.[109]

Other strategies might be helpful in preventing drug overdoses in children. For example, the use of adaptors on bottles of liquid medication so that the medication can be accessed only with a needleless syringe; parents should not allow children to drink medicine directly from the bottle; and using unit dose packaging might reduce the amount of accidental drug ingestion. These strategies are highly recommended for common medicines such as OTC drugs.[80]

As children account for a higher percentage of drug overdose cases, parents' misunderstanding and miscalculation of doses can contribute to a higher percentage of overdoses. Contributing factors include limited literacy and numeracy, particularly in age indication. This problem is emphasised in terms of OTC medicines, as no instructions are provided directly by healthcare providers.[28,112] Applying simple language instructions and warning labels in the leaflets of medicines might be helpful in terms of calculating correct doses.[75] Further, healthcare providers should request that parents with low literacy levels use one product for all children in the family, which might help to prevent dose miscalculation.[73]

Another major factor contributing to drug overdoses in children is the availability of unused drugs in homes.[113] The solution for this problem is medication disposal. Campaigns for the disposal of medications have been used in many countries, which would help to reduce accidental drug overdoses in children, intentional drug abuse and the accumulation of drugs by elderly people, as well as protect the physical environment and eliminate waste in the healthcare system.[113,114] The government of Ireland launched a campaign called Dispose of Unused Medicines Properly (DUMP), which encouraged the public to return unused or expired medicines to community pharmacies. The project was launched in 2005, and 9,608 items were returned in the first year and 2,951 kilograms were returned in 2006. The most common medicine group returned was the nervous system class, which accounted for 26.3 per cent.[115]

A study conducted in Saudi Arabia in 2003 identified the issue of unused and expired medicines in Saudi dwellings. The study recruited 1,641 households in 22 cities. The study found that more than 80 per cent of Saudi families had more than five medicines, with an average of more than two medicines that were expired or unused. The most common drugs found in the participants' houses were respiratory drugs (16.8 per cent), followed by central nervous system (CNS) agents (16.4 per cent) and antibiotics (14.3 per cent). Of the 2,050 CNS medications, OTC analgesics (including non-steroidal anti-inflammatory agents) constituted 49.9 per cent of the total (n = 1,023). Further, 51 per cent of all medicines found were not currently used and, of these, 40 per cent were expired. So medication wastage can provide greater opportunity to access prescription drugs in Saudi Arabia. The study recommended disposal medication campaigns to reduce the danger of available unused and expired medicines.[116]

According to the results a large number of medicines were involved in drug overdose, and thus might indicated that many patients have excessive amount of medicines in there dwelling. One reason might contribute to the excessive amount of medicines is drug seeking behaviour. Warfarin accounted for the highest percentage of drug overdoses. Eighty-five per cent of all Warfarin overdoses occurred in patients aged over 50 years, while two cases occurred in children and the middle-aged, respectively. This might indicate that the overdoses occurred unintentionally. One of major reasons for Warfarin overdoses is that it has a narrow therapeutic index; thus, administrating a larger dose would easily lead to overdoses.[117] Further, Warfarin is associated with complex pharmacology and inherent risk of outcome. As it is used continuously, maintaining the dose is critical to ensure safe and effective therapy.[117]

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According to the results, females accounted for a higher percentage of drug overdoses. Several factors might contribute to this. First, family conflict was stated as a higher-risk factor of drug overdoses in women. Aljahdali's study found that 80 per cent of the 79 overdose cases investigated were female, and 60 per cent had family conflicts.[22] Further, a study was conducted in the King Fahd Hospital of the University (KFHU) to investigate cases of deliberate self-harm presented to the emergency department of the hospital. The study recruited 362 cases, and the female to male ratio was 1.8:1. The study found that 71 per cent of cases were drug overdoses, of which 50.3 per cent were caused by family problems.[103] Moreover, a study was conducted in Saudi Arabia in KFHU to investigate non-fatal, deliberate self-harm cases. There were 55 cases investigated over nine months, and 80 per cent of them were female. The most common method used was self-poisoning (drug and chemical). The study found that family conflict was the main factor, contributing to 50.9 per cent of cases.[118]

The rate of drug overdose for each year of the study period was reduced from 3.45 to 3.17 per 1,000. However, the number of emergency admissions also reduced annually. This result contrasts with previous studies. For example, Moazzam found an increased rate of drug poisoning in the alQassim region in Saudi Arabia, from 6.6 per 100,000 in 1999 to 10.7 per 100,000.[21] Further, Malik found that the number of drug overdose cases presented in Asir Center Hospital increased from two cases in 1989 to 22 cases in 1993.[104] This indicates that there were perhaps more preventive and awareness programs in Saudi Arabia in the previous years.

There are several pharmacyosurveillance implications; one of them is collecting data regarding motivations and causes of drug overdose. According to the finding most of the cases occurred in elderly and children, so targeting these groups of people would help in reducing the rate of drug overdose cases.[119] Further, another implication would be the use of Electronic prescription. It is defined as a tool for prescribers to electronically prepare and send an accurate, error-free and understandable prescription directly to a pharmacy. Previous study found that electronic prescription system reduced medical errors by 55 per cent - from 10.7 to 4.9 per 1000 patient-days.[120] According to the results the rate of drug overdose cases in the emergency department decreased between 2007 and 2011, and this was attributed for using electronic prescription system in the hospital.

Drug related problems account for large amount of money in hospital cost. For example, in US a probability model in 2002 estimated that morbidity and mortality associated with DRPs account for $76.6 billion in hospital cost. Further, a study conducted in Saudi Arabia in 2008 found that the estimate cost of one day admission for drug related problem is 666$. So Implementing preventable measures such as pharmacosurveillance system would be a cost effective.[105]

Some policies might be implemented to reduce the risk of drug overdose cases. As Warfarin accounted for the highest percentage of drug overdoses, particularly in elderly people, further dose instruction should be given to elderly patients to ensure they have understood the instructions correctly.[85] Further, patients acquired Warfarin from hospital; thus, if the quantity of medicine dispensed is reduced, drug overdose cases might be prevented. In addition, children accounted for the highest percentage of drug overdose cases, so policymak-

ers should implement awareness courses to educate parents to secure and protect medicines from children.[80] There was a wide range of medicines involved in drug overdose cases, so further dose instruction is needed. Moreover, patients must be educated regarding the dangers of overdosing.

6. Conclusion

Despite religious, cultural and legal deterrents, occasional cases of drug overdoses occur in the Saudi population.

The main limitations of this study mainly in relate to the quality of data available in patients' medical records, as many files might not be fully documented, and some variables related to research are not found in the medical records (e.g. education level). Moreover, as the income level is identified based on the household occupation, a number of files did not document the household occupation; thus, some patients' incomes were not available. The sample size is considered small, as there are few statistically significant associations between variables. Thus, the findings relating to associations between variables might not represent the actual validity of the associations between the independent and outcome variables. In addition, the data in this study was collected from a single institution, and the patients of drug overdoses have special characteristics that might not be similar to the general Saudi population. For example, all people treated in the hospital obtain medicines from the pharmacy without any charge. Further, One of the limitations of this study is that it does not state the reasons for drug overdoses, and it does not identify if overdoses occurred intentionally or accidentally.

Some significant findings were made, such as Warfarin causing 29 overdose cases, and patients aged over 50 accounting for 85 per cent of all Warfarin cases. This finding signifies a problem with Warfarin in elderly patients, and further research is needed to identify the major cause of this high percentage and to assist in implementing preventive measures to protect the elderly from the risk of overdosing. Further, children accounted for a high percentage of drug overdoses, and the study stated that 66.6 of anti-hypertensive overdoses were children. Thus, further research should be conducted to identify the reasons why children overdose so they can be protected from drug overdoses.

These findings could help the hospital to implement preventive strategies and policies. As many cases occur accidentally, education and awareness programs are required regarding dose instructions and the storage and disposal of medicines. Further, many patients keep excessive amounts of medicines in their dwellings, so reducing the amount of medicines provided to chronic patients would help to reduce drug overdose cases. Education of physicians on drug-seeking behaviour of patients is important. Further, special courses in dose instructions could be implemented for elderly patients, as well as programs that target parents regarding dose calculations for their children and the safe storage of medicines. In addition, clinical guidelines for overdose management need to be standardised, and the surveillance and recording of overdose information should be improved. Lastly, improved edu-

cation is required for the public and for health workers in order to prevent drug interactions that might precipitate overdoses.

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