Adverse drug reactions related hospitalization identified by discharge ICD-9 codes in a univeristy hospital in Riyadh

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ABSTRACT

الأهداف: تحديد شيوع التنويم في المستشفى نتيجة الأعراض الجانبية للأدوية (ADRs) باستخدام التصنيف الدولي للأمراض النسخة التاسعة (ICD-9).

الطريقة: أُجريت دراسة إستعادية خلال الفترة مابين 1982م وحتى 2005م، في مستشفى الملك خالد الجامعي – الرياض – المملكة العربية السعودية. تم التعرف على المرضى المنومين بسبب الأعراض الجانبية للأدوية باستخدام التصنيف الدولي للأمراض النسخة التاسعة (ICD-9). حُدِدَ العدد الكلي للمرضى اللذين تم تنويمهم في المستشفى للقيام بحساب نسبة شيوع الأعراض الجانبية للأدوية (ADRs) سنوياً. تم تحليل النتائج بطريقة التحليل الوصفي.

النتائج: شملت الدراسة 89 مريضاً. كانت الهرمونات والمكملات الصناعية (14.6%)، ثم المواد الأساسية (13.5%) هي أكثر الأدوية المسببة للأعراض الجانبية (ADR). وجدنا أن نسبة (50%) من المرضى يعانون من أمراض مزمنة ويستخدمون أدوية أخرى. غالبية الأعراض كانت من النوع (أ) (54%) ومن الممكن تجنبها، بينما كان نسبة (39%) من النوع (ب) ومن الصعب تجنبها، أما النوع (ج) فكان بنسبة (6%) أعراض جانبية تظهر على المدى البعيد. معدل شيوع الأعراض الجانبية تراوح ما بين (0.07%) في عام 1993م وحتى (0.003%) في عام 1999م.

خاتمة: كان تحديد الأعراض الجانبية للأدوية (ADRs) والمسببة للتنويم في المستشفى باستخدام التصنيف الدولي للأمراض النسخة التاسعة (ICD-9) سهل وعملي. إلا أنَ عدم الدقة في تسجيل المعلومات في هذا التصنيف قد يكون أحد السلبيات أو المعوقات للاستخدام والاستفادة من هذا النظام.

Objective: To assess the feasibility of using International Classification of Disease code (ICD-9) to ascertain the prevalence, seriousness, and preventability of adverse drug reaction (ADRs).

Methods: A retrospective study between the years 1982 and 2005 was conducted at King Khaled University Hospital (KKUH), Riyadh, Saudi Arabia to examine the ICD-9 codes assigned on discharge to identify ADRs. A list of the ICD-9 codes related to ADRs were identified. These codes were entered into the hospital computer program at the study site to identify corresponding patients' medical records. The total number of patients admitted to the hospital each year was identified to calculate the prevalence of ADRs, and descriptive analysis was also conducted.

Results: A total of 89 patients were identified and included. Drug classes commonly associated with ADR include hormones and synthetic substitutes (14.6%), followed by primary systemic agents (13.5%). Almost 50% of cases had chronic conditions and use other drugs when the ADR had occurred. The majority of the ADRs were type A (54%) "preventable," while 39% were type B "non preventable," and only 6% were type C "occur with long term use." The prevalence per year ranged from 0.07% in 1993 to 0.003% in 1999.

Conclusion: Identifying ADRs causing hospital admission by using ICD-9 coding system is easy and practical. However, under or inaccurate recording of ICD-9 codes may be a limitation to the use of such an important tool.

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The World Health Organization (WHO) defines adverse drug reaction (ADR) as "a response to a drug which is noxious and unintended, and which occur in doses normally used in man for prophylaxis, diagnosis or therapy of disease or for modification of physiological function."[1] The United States Food and Drug Administration (FDA) use the following definition of serious ADR: "a serious adverse events (event relating to drug or device) is one which the patient outcome is death, life threatening (real risk of dying), hospitalization (initial or prolonged), disability (significant, persistent, or permanent), congenital abnormality or require intervention to prevent permanent impairment or damage."[1] In previous studies, it has been estimated that 3-8% of hospital admissions are related to ADRs, and up to 20% of all hospitalized patients experience an ADR.[2-5] In addition to their impact on patient outcome and quality of life, ADRs may also have a significant impact on health costs, in part arising from an increase in length of hospital stay.[6-8] Identification of ADRs on a routine basis has been relatively ineffective. Spontaneous reporting is the most widely used technique but it identifies only 5%[7,10] of events and even as low as 0.1% incidence in one Saudi study.[10] Prospective, manual chart review is more effective but is too costly and labor intensive to be routinely used.[11,12] Retrospective chart review offers the advantage of being effective in identifying ADRs with the use of limited resources. However, the quality of information from retrospective chart review method is inconsistence. One method for detecting ADRs is using the International Classification of Disease code (ICD-9). A number of published studies used the ICD-9 for detecting specific condition such as hyponatremia,[13] complicated peptic ulcer disease,[14] myopathy and rhabdomylosis resulting from the use of lipid-lowering drugs[15] and vaccine related adverse events.[16] The findings of these studies were conflicting. Some suggest that ICD coding could overestimate, or underestimate the presence of certain medical conditions, others found high levels of accuracy comparing hospital medical records with ICD codes and recommended its use for surveillance purposes.[13-21] International Classification of Disease code is designed for classification of morbidity and mortality information for statistical purposes and for indexing of hospital records by disease and operations, for data storage and retrieval. International Classification of Disease code were originally developed to classify and code mortality data, such as from death certificates. In its expanded "clinical modification" (ICD-CM), it has come to be used for morbidity (illness and disease) data in a broad range of settings, such as inpatient and outpatient clinic records, physician offices, and other surveys. The concept of extending the ICD-9 for use in hospital indexing was originally developed in response to a need for a more efficient basis for storage and retrieval of diagnostic data.[20] The aim of this study was to assess the feasibility of using ICD-9 to ascertain the prevalence, seriousness, and preventability of ADRs.

Methods. This is a retrospective study covering the period between the years 1984-2005 conducted at King Khaled University Hospital (KKUH) a tertiary referral center in the Kingdom of Saudi Arabia. The hospital uses ICD-9 for inpatient admission only were each patient episode is coded by coding clerks according to the diagnosis given by the medical staff. If no diagnosis is available, the clerk will examine the notes to establish a suitable code to the case. A list of the ICD-9 codes related to ADRs was identified by one of the researchers using the original book of the ICD-9 CM 4th Edition.[20] The E codes identified (E930.0-E949.9) included correct drug properly administered in therapeutic or prophylactic dosage as the cause of any adverse effect including allergic or hypersensitivity reaction and excluded accidental overdose of drug, wrong drug gave or took in error, accident in technique of administration of drug or biological substance such as accidental puncture during injection or contamination of drug, and administration with suicidal or homicidal intent or intent to harm. In addition, codes 995.0 (other anaphylactic shock), 995.1 (ancioneurotic edema), 995.2 (unspecified ADR due to drug or biological substance), 995.3 (allergy unspecified), 995.4 (shock due to anesthesia), and 995.8 (other specified adverse effect not elsewhere classified) were considered related ADRs and hence identified. These codes were entered by medical records personal into the Health Information Service computer program at the study site to identify corresponding patients' medical records. The study parameters were as follows: 1) Number of patient who were diagnosed to have an ADR, 2) Type of ADR, 3) Drugs involved in an ADR, 4) Seriousness of the ADR (resulting in deaths, hospitalization, resulting in persistent or significant disability, incapacity, or life threatening), and 5) ADR preventability. When judging preventability, ADRs were classified into 4 types.[1] Type A reaction are those that result from an extension of the drug's pharmacological activity and hence considered preventable, Type B reactions are those events that have no relationship to the drug's pharmacological activity and are unpreventable, Type C reaction associated with long term drug use may be considered preventable and they are related to the drug's pharmacological properties such as corticosteroids induced Cushing syndrome, and Type D carcinogenicity and teratogenecity.[1]

A data collection form was designed based on the US Food and Drug Administration ADR reporting

form[22] and the Yellow cards of the British National Formulary.[23] All data collected were checked for accuracy and completeness, coded, and entered into Microsoft Excel and descriptive analysis such as percentage, mean, median were conducted as appropriate.

Results. A total of 193 files were identified, 159 had the E code (E930.0-E949.9), and 34 had unspecified code (995.2). Fifty-eight files were missing and 29 of the E files were not included due to incorrect coding (21 cases) or incorrect code entry 5 cases and 3 cases had no ADRs, and 19 files of the unspecified 995.2 were also not included. Thus, in total 89 files were included in the study 82 had the E-code and 6 had unspecified code 995.2 and one patient had 2 codes so the total number of the reactions were greater than the total number of patient having the reaction. Forty percent of identified cases were men. A high percentage of patients (almost 50%) had chronic conditions and used other medications (other than that causing the ADR) when the ADRs had occurred (**Table 1**).

The median age of the study population was 29 years ranging from one month old to 80 years, 22 (24.7%) of the identified cases were children (under the age of 18). The prevalence per year was calculated as the number of patient admitted due to ADRs divided by the total number of patient admitted per year. The total number of patients admitted to the hospital each year (from 1984-2005) was identified by one of the researchers with the help of computer department at study site. It was possible to collect information on ADRs using the ICD-9 classification back to year 1984. From 1984-1990 the total number of patients admitted was not available. From year, 2000-2005 there was no ADR documentation using the ICD-9 system. Therefore, the prevalence was only estimated from year 1991-1999. It ranges from 0.07-0.003% (**Table 2**).

Drug classes commonly associated with ADRs include hormones and synthetic substitutes (14.6%) especially anterior pituitary hormone then insulin then adrenal cortical steroids, followed by primary systemic agents (13.5%) as anti-allergic and anti-emetic then anti-neoplastic and immunosuppressant then acidifying agents followed by anticonvulsant and anti-parkinson especially hydantion derivatives although the unspecified agents have the higher percentage compared with other agents (**Table 3**). Most common ADR was allergic reaction, followed by CNS disturbance (**Table 4**). Forty-eight (54%) of ADRs were considered preventable type A reactions, 35 (39%) were non-preventable or type B reactions, 5 (6%) were due to long term drug use or type C reactions (all type C reactions were due to long term use of corticosteroids). Type A have been traditionally considered preventable since they are predicted and are an extension from the drug's pharmacological activity and type C although occur with long term use may be considered preventable as it is related to the drug's pharmacological properties (**Table 5**).[1] Serious ADRs according to the FDA definition involved all of the 89 included patients; there were 80 (90.5%) admissions due to serious ADRs. In other cases, serious ADRs had a prolonged hospitalization (n=9, 10.7%), of which 4 cases were life threatening without increase in length of stay. Hospitalization with serious ADRs accounted for a

Table 1 - Characteristics of the study population.

Characteristics	Men	Women	Total
Number	40	49	89
Median age	31.1	27.9	29.36
Mean duration of stay in days (range)	10.5 (1-81)	8.63 (1-43)	9.46 (1-81)
Patient with chronic conditions (%)	22 (24.7)	22 (24.7)	44 (49)
Patients using other medications (%)	19 (21.3)	22 (24.7)	41 (46)

Table 2 - Prevalence of adverse drug reactions cases per year.

Year	Cases	Total admission	Prevalence %
1984	1	No filing	
1985	1	No filing	
1986	5	No filing	
1987	8	No filing	
1988	3	No filing	
1989	8	No filing	
1990	7	No filing	
1991	11	26408	0.04
1992	17	27625	0.06
1993	19	27730	0.07
1994	5	14889	0.03
1995	1	24408	0.005
1996	1	5574	0.02
1997	No case		
1998	No case		
1999	1	34828	0.003
2000	No case		
2001	No case		
2002	No case		
2003	No cases		
2004	No case		
2005	No case		

Table 3 - Drug class commonly associated with adverse drug reactions.

E-Code	Class	No. of cases	(%)	Type of adverse drug reaction
E947*	Other unspecified drug and medical substance.	14	(15.7)	57% allergy, 21% CNS
E932	Hormones and synthetic substitutes	13	(14.6)	31% Cushingoid features, 23 % hypoglycemia, 31% gynoclogical problems
E933	Primary systemic agents	12	(13.5)	42% CNS, 25% allergy
E936	Anticonvulsant and antiparkinson drug	10	(11.2)	36% CNS, 36% Allergy
E934	Agents primarily affecting blood constituents	7	(7.9)	71% GI
E930	Antibiotics	6	(6.7)	50% of reactions are allergy
E935	Analgesia, antipyretic, and antirheumatics	6	(6.7)	40% GI, 40% allergy
995	Unspecified	6	(6.7)	100% allergy
E931	Other anti-infective	3	(3.4)	All are allergic reactions
E939	Psychotropic agents	3	(3.4)	CNS
E942	Agents primarily affecting cardiovascular system	3	(3.4)	Sexual dysfunction, GI, and metabolic
E946	Agents primarily affecting skin and mucous membrane, ophthalmological, otorhinolaryngological, and dental drugs	2	(2.2)	Cushingoid and allergy
E937	Sedative and hypnotics	1	(1.1)	CNS
E943	Agents primarily affecting GI system	1	(1.1)	CNS
E945	Agent primarily acting on smooth and skeletal muscle and respiratory system	1	(1.1)	Urinary retention

*Drug as an exogenous source of injury, CNS - central nerves system, GI - gastrointestinal

Table 4 - Types of adverse drug reactions (ADR).

ADR type	No. of cases	(%)
Allergy	30	(33.7)
General	21	(23.6)
Anaphylactic shock	6	(6.7)
Angiodema	2	(2.25)
Vasculitic drug reaction	1	(1.1)
*CNS disturbance**	16	(19.1)
Abnormal movement	5	(5.6)
Behavioral disturbance and hallucination	3	(3.4)
Psychosis	2	(2.25)
Excessive sleep	2	(2.25)
Tonic clonic convulsion	2	(2.25)
Restlessness	1	(1.1)
Extrapyramidal signs	1	(1.1)
Drug induced cerebral ataxic	1	(1.1)
Hemorrage	9	(10.1)
GI symptoms†	9	(10.1)
Cushing syndrome	4	(4.5)
Hypoglycemia	4	(4.5)
Blood disorders	4	(4.5)
Hyperstimulation syndrome	2	(2.25)
Immunological	2	(2.25)
Others	12	(13.5)

*CNS - central nerves system, †GI - gastrointestinal

Table 5 - Preventability of adverse drug reactions.

Characteristics	Type A	Type B	Type C
Number	48	35	5
Male	23	14	3
Female	25	21	2

Table 6 - Average length of stay per year.

Year	Average length of stay (days)
1984	7
1985	4
1986	8.2
1987	18
1988	3
1989	5.8
1990	7.7
1991	9.4
1992	9.5
1993	11
1994	6
1995	7
1996	17
1999	7

From 2000-2005 the average length of stay data were missing

total length of stay over the study period ranging from 3-209 days per year with average length of stay 56.9 day per year (**Table 6**).

Discussion. Adverse drug reactions are an important cause of hospital admission worldwide and result in a large economic burden on health care costs. In Saudi Arabia, there is a limited research in such an important area which was the main reason for conducting this study as we have a strong belief that our culture and nature may affect the occurrence and type of the ADRs in our population. Many of the results of this study were consistent with published studies and some differ. Our results suggest that drug classes commonly associated with ADR include: hormones and synthetic substitute's especially anterior pituitary hormone then insulin then adrenal cortical steroids. This is consistent with a published study conducted by Moor et al[11] although, others[4] had non-steroidal anti-inflammatory drugs on top of the list. According to the current study, patients experiencing ADRs were mainly adult and fewer were pediatrics or elderly while other studies[11,24] reports that the adverse events populations were elderly. Possible explanation could be that most of the drugs causing ADRs are hormones which are mainly used in the adulthood age rather than pediatrics or geriatrics. Our study was consistent with others that patients took more medications (46%) and are more often female.[11] Hospital admissions resulting from ADR in published trials are of a metabolic, hematologic, or gastrointestinal nature, however, in our study allergy and CNS adverse events are predominant followed by hematologic or gastrointestinal, again possibly due to the nature of the drugs used. Regarding preventability, we found that approximately 60% of identified ADRs are considered preventable. This is in accordance with other publications which found preventability ranging from 3-59%.[4,25] The high rate of prevented ADRs may suggests that not much thought is given to prevention measures at the study site. Simple measures such as regular review of prescriptions, the use of computerised prescribing, and the involvement of pharmacists in assessing prescribing behaviour may all reduce the burden caused by ADRs. The average length of stay associated with ADRs was 9.5 days per year which was comparable to published figures of 11.3 days per year.[11] At the study site, the stay cost per patient per day is 1000-1500 Saudi Riyals (SAR) in the general ward room and SAR 4000-5000 in Intensive Care Unit room (year 2005). Although it was not the main aim of this study to estimate the total cost implications of ADRs, it reasonable to suggest that a substantial amount of money is spent on managing ADRs yearly.

Various studies have been undertaken worldwide to identify prevalence of ADRs, however, the methods of these studies were inconsistent limiting the applicability of their findings. The reported prevalence of ADRs related admission using prospective and retrospective studies ranges from 3-8%.[2-5] The results of this study indicate that ADRs prevalence ranged annually from 0.003-0.07%. A possible explanation could be that using ICD-9 system could results in underestimating of ADRs prevalence because of poor documentation or inappropriate use of ICD-9 coding. There are no ICD-9 codes indicating ADR from year 2000-2005 which also supports our assumption as it is very unlikely that no ADR cases occurred during this period. There is a considerably high prevalence (with respect to the remaining years) in year 1993 and there is almost no documentation after 1999. The differences in prevalence between years could be due to the fact that in certain years there was more emphasis from the administrative authority at the study site to use ICD-9 codes appropriately. Administrative databases have clear advantages in terms of availability, cost- effectiveness, and are often large enough to provide adequate population sizes for measuring drug exposure and rare medical events.[13,14] A study of narcotic drugs at 2 acute hospitals found that non of the 21 cases discovered included an ICD code appropriate to the diagnosis, which was also a problem in our study; as we found that there were ADRs cases with no appropriate ICD-9 coding, which underestimate the prevalence. The reason for that could be as mentioned in Farhan et al[19] study that only 60% of the medical records are of good quality regarding documentation and coding. Thus, main limitations to use ICD codes for identifying ADRs is that the diagnosis may be inaccurate since physicians may believe that ICD codes are used only for administrative purposes, and hence they are less concerned with accurate coding or simply use these codes inappropriately.

As the limitation of any retrospective study design there were many missing information that could not be retrieved or missing files. However, a strong point of this study is that ICD-9 code was narrowed to be more drug oriented, by using E codes related to drug events, and hence the ability to detect incidents that were adverse drug events would be improved as suggested by Cox et al.[26]

In conclusion, the use of IC-9 codes system is practical and has much potential to help in identifying ADRs, however, it is underutilized. Future research should explore how we can increase the efficiency of using administrative databases such as ICD-9 codes. There is a need also to examine the best way for ADRs reporting from the viewpoints of healthcare providers.

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References

1. Ninno SD, Ninno MA. Adverse Drug Events. In: Pharmacotherapy Self-assessment Program. 4th ed. Kansas City (MO): American College Clinical Pharmacy; 2000. p. 113-148.
2. Lundkvist J, Jonsson B. Pharmacoeconomics of adverse drug reactions. ***Fundam Clin Pharmacol*** 2004; 18: 275-280.
3. Howard RL, Avery AJ, Howard PD, Partrige M. Investegation into the reasons for preventable drug related admission to a medical admission unit: observational study. ***BMJ*** 2003; 12: 280-285.
4. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, et al. Adverse drug reaction as a cause of admission to hospital: prospective analysis of 18 820 patients. ***BMJ*** 2004; 329: 15-19.
5. Wasserfallen JB, Livio F, Buclin T. Rate, Type, and Cost of Adverse Drug Reactions in Emergency Department Admissions. ***Eur J Intern Med*** 2001; 12: 442-447.
6. Gautier S, Bachelet H, Bordet R, Caron J. The costs of adverse drug reactions. ***Expert Opin Pharmacother*** 2003; 4: 319-326.
7. Honigman B, Light P, Pulling RM, Bates DW. A computerized method for identifying incidents associated with adverse drug events in outpatients. ***Int J Med Inform*** 2001; 61: 21-32.
8. Janaje Munasinghe TM, Singer DR. Costs and prevention of adverse drug reactions. ***Eur J Intern Med*** 2001; 12: 403-405.
9. Al-Ahdal A. Implementation of an Adverse Drug Reaction Reporting and Monitoring program at Riyadh Armed Forces Hospital. ***Saudi Pharm J*** 2001; 9: 51-57.
10. Lapeyre-Mestre M, Gary M, Machelard-Roumagnae M, Bonhomme C, Bugat R, Montatruc JL. Incidence and cost of adverse drug reactions in a French cancer institute. ***Eur J Clin Pharmacol*** 1997; 53: 19-22.
11. Moore N, Lecointre D, Noblet C, Mabille M. Frequency and cost of serious adverse drug reactions in a department of general medicine. ***Br J Clin Pharmacol*** 1998; 45: 308.
12. Jha AK, Kuperman GJ, Teich JM, Leape L, Shea B, Rittenberg E, et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. ***J Am Med Assoc*** 1998; 5: 305-314.
13. Moviga KLL, Leufkensa HGM, Lenderink AW, Egbertsa ACG. Validity of hospital discharge International Classification of Diseases (ICD) codes for identifying patients with hyponatremia. ***J Clin Epidemiol*** 2003; 56: 530-535.
14. Bright RA, Avorn J, Everitt DE. Medicaid data as a resource for epidemiologic studies: strengths and limitations. ***J Clin Epidemiol*** 1989; 45: 937-945.
15. Andradea, Graham DJ, Staffa JA, Schech SD, Shatin D, Grenade LL, et al. Health plan administrative databases can efficiently identify serious myopathy and rhabdomyolysis. ***J Clin Epidemiol*** 2005; 58: 171-174.
16. Nash JQ, Chandrakumar M, Farrington CP, Williamson S, Miller E. Feasibility study for identifying adverse events attributable to vaccination by record linkage. ***Epidemiol Infect*** 1995; 114: 475-480.
17. Cattaruzzi C, Troncon MG, Agostinis L, Garcia Rodriguez LA. Positive predictive value of ICD-9th codes for upper gastrointestinal bleeding and perforation in the Sistema Informativo Sanitario Regionale database. ***J Clin Epidemiol*** 1999; 52: 499-502.
18. Raiford DS, Perez Gutthann S, Gracia Rodriguez LA. Positive predictive value of ICD-9 codes in the identification of cases of complicated peptic ulcer disease in the Saskatchewan hospital automated database. ***Epidemiol*** 1996; 7: 101-104.
19. Farhan J, Al-Jummaa S, Alrajhi AA, Al-Rayes H, Al-Nasser A. Documentation and coding of medical records in a tertiary care center: a pilot study. ***Ann Saudi Med*** 2005; 25: 46-49.
20. Puckett CD. Post binder of hospital version the educational annotation of ICD-9 CM. Reno, Nevada: Channel Publishing Ltd; 2000.
21. Geraci JM, Ashton CM, Kuykendall DH, Johnson ML, Wu L. International Classification of Diseases, 9th Revision: clinical modification codes in discharge abstracts are poor measures of complication occurrence in medical inpatients. ***Med Care*** 1997; 35: 589-602.
22. MedWatch for Volunteer Reporting of Adverse Events Product Problems and Product Use Errors. Accessed dated 5th May 2007. Available from URL: https://www.accessdata.fda.gov/scripts/medwatch
23. Joint Formulary Committee. British National Formulary. 42nd ed. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; 2001.
24. Hafner JW Jr, Belknap SM, Squillante MD, Bucheit KA. Adverse drug events in emergency department patients. ***Ann Emerg Med*** 2002; 39: 258-267.
25. Beijer HJ, de Baeny CJ. Hospitalization caused by adverse drug reaction: a meta-analysis of observational studies. ***Pharm World Sci*** 2002; 24: 46-54.
26. Cox AR, Anton C, Goh CHF, Easter M, Langford NJ, Ferner RE. Adverse drug reactions in patient admitted to hospital identified by discharge ICD-10 codes and by spontaneous reporting. ***Br J Clin Pharmacol*** 2001; 52: 337-339.