Analysis of Adverse Events in Elderly Patients Using High Alert Medications At K.R.M.T. Wongsonegoro Regional Hospital Semarang

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ABSTRACT: High-alert medications (HAM) are drugs that require strict monitoring due to their high potential to cause significant harm if used improperly. Patient safety incidents can lead to adverse outcomes, including suboptimal treatment effectiveness and increased healthcare costs. This study aimed to analyze adverse events (AEs) resulting from the use of HAMs, identify the types of HAMs that contributed to AEs, and determine the average direct medical costs incurred by elderly patients at K.R.M.T. Wongsonegoro Regional Hospital, Semarang. This research employed a retrospective cross-sectional observational design using secondary data. The study population consisted of elderly patients who were administered HAMs. The sample size was determined using the Design Effect (DEFF) statistical method for cluster surveys, resulting in a sample of 318 patients who met the inclusion and exclusion criteria. Descriptive analysis was used to assess HAM utilization, AE incidence, and direct medical costs borne by the hospital. The results showed that 40.88% of elderly patients had a history of diabetes mellitus. The most frequently administered HAM was the prandial insulin analogue, insulin aspart injection 100 IU/mL (7.29%), which also accounted for the highest number of AEs (30%). The average direct medical cost for patients without AEs was IDR 7,020,721.24, while for those who experienced AEs, the cost increased to IDR 9,493,661.29. These findings indicate that hypoglycemia caused by prandial insulin analog—insulin aspart injection 100 IU/mL, penfill—was the most common AE among elderly patients. Moreover, the average direct medical cost was significantly higher in the AE group than in the non-AE group.

Keywords: Elderly ; *high alert medication;* adverse events

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INTRODUCTION

Elderly patients are older adults who experience a decline in organ function, psychological, social, economic, and environmental factors that may contribute to health complaints and illnesses, thereby requiring healthcare services (Ministry of Health, 2014). According to data from the Central Bureau of Statistics (BPS) in 2024, 63.29% of the elderly population is classified as young elderly (aged 60–69 years), 28.11% as middle elderly (70–79 years), and 8.61% as old elderly (80 years and above) (Statistics, 2024). Among them, 41.49% reported health complaints, with a morbidity rate of 19.72%. Physiological decline in elderly patients can result in various diseases. These physiological changes contribute to drug-related problems (Fauziah et al., 2020), leading to longer recovery times, with an average hospital length of stay of 5–6 days (5.52%) among elderly patients (Statistics, 2023). The complexity of pharmacotherapy in elderly patients often leads to irrational drug use and polypharmacy, both of which are key factors associated with adverse events (AEs) in this population (Delara et al., 2022).

High Alert Medications (HAMs) significantly increase the risk of patient harm, with prescription error rates ranging from 0.24% to 89.6%. A study on elderly patients in intensive care units in India reported 160.12 HAM prescribing errors per 1,000 patient-days (Aradhya et al., 2023). Another study at the NHO Tochigi Medical Center in Japan found that 5–10% of emergency hospitalisations were caused by adverse drug reactions, mostly among elderly female patients (47.9%). A total of 494 drugs were identified as contributing to inpatient adverse events, with the most common classes being cardiovascular agents (n = 83, 22.6%), musculoskeletal agents (n = 62, 16.8%), antithrombotic agents (n = 49, 13.3%), psychotropic agents (n = 39, 10.6%), and antidiabetic agents (n = 37, 10.1%) (Junpei, 2024). Among elderly patients receiving HAMs, 20% experienced impaired self-care at the highest level (Santoso et al., 2025).

A study conducted in a South Indian teaching hospital found that 26.88% of patients experienced AEs, resulting in prolonged hospital stays and increased direct medical costs (Venkatasubbaiah et al., 2020). In a previous study of 610,979 hospitalisations, 36,004 (5.9%) resulted in harmful incidents that extended the hospital stay by 0.4 to 24.2 days (p < 0.001), with additional healthcare costs ranging from USD 800 to USD 51,067 (p < 0.001) (Tessier et al., 2019). According to ISMP guidelines, high-risk therapies have a cost-benefit ratio of €3.46 per intervention, with an average additional cost of €20.23 (Miarons et al., 2021).

Healthcare costs consist of direct and indirect costs. Direct costs refer to expenditures directly associated with healthcare services, including medications and medical supplies, physician consultations, nursing care, hospital facilities (inpatient rooms, equipment), laboratory tests, informal care, and other health services. Indirect costs refer to productivity losses (Ministry of Health, 2013).

K.R.M.T. Wongsonegoro Regional Hospital in Semarang is a municipal technical institution that provides comprehensive healthcare services including inpatient, outpatient, and emergency care. Evaluating the use of High Alert Medications in elderly patients is essential to minimise adverse events and treatment costs, thereby supporting efforts in quality control and cost containment. This study aimed to assess the use of HAMs, the incidence of adverse events, and the average direct medical costs in elderly patients at K.R.M.T. Wongsonegoro Regional Hospital in Semarang. The analysis and evaluation of HAM utilisation in the elderly are crucial for achieving optimal healthcare quality and cost-efficiency.

METHODS
Study Design
This study employed an observational method using a retrospective cross-sectional design. The research began by identifying elderly patients who had received High Alert Medications (HAMs) during the period 2021–2023 to determine the occurrence of Adverse Events (AEs) and to analyse direct medical costs.

Population and Sample
The study population consisted of all elderly patients who had been hospitalised at K.R.M.T. Wongsonegoro Regional Hospital, Semarang, and had received HAMs. The sample size was calculated using the Design Effect (DEFF) statistical method for cluster surveys, with the sample size determined through the OpenEpi version 3.01 software, applying a 95% confidence level. A total of 318 patients were included in the study. The formula used is as follows:

$$n = [DEFF*Np(1-p)] / [(d^2/Z^2 1-\alpha/2*(N-1)+p*(1-p)]$$

Samples were selected using purposive sampling. The inclusion criteria were: elderly patients who had been hospitalised, had complete medical records, and had complete cost data related to HAM use for treatment in accordance with the indicated therapy. The exclusion criteria included patients referred to another hospital, patients discharged against medical advice, and deceased patients. Samples were selected through medical record review of elderly inpatients during the period of 2021–2023 who had received HAMs.

Data Analysis
Data collection included information on patient characteristics, medication use, subjective and objective clinical data, and direct medical costs. These costs included prescribed medication, medical devices, laboratory tests, physician consultations, inpatient services, and nursing care. Data were processed by categorising patient characteristics, HAM usage, and AE identification, as well as calculating the average direct medical cost from the hospital's perspective. Descriptive analysis was used to illustrate HAM utilisation, incidence of AEs, and direct medical costs for elderly inpatients from the hospital's perspective.

RESULTS AND DISCUSSION
This study involved a sample of 318 elderly patients, comprising 143 males (44.97%) and 175 females (55.03%). This aligns with a previous study conducted in the outpatient department of Madiun Hospital, where female patients also predominated (57.2%) (Rahmawati, 2019). Women tend to be more health-conscious, undergo routine check-ups, and access healthcare services more frequently than men, particularly for chronic conditions such as diabetes, hypertension, and reproductive health (Hasanah, 2023). In contrast, a study by Sasfi et al. conducted in a hospital in Pontianak found that male patients were the majority (53%) (Sasfi et al., 2022). In elderly men, hormonal decline due to andropause may be associated with low androgen levels and aging, which may in turn increase the risk of cardiovascular events and the development of symptomatic cardiovascular disease (Ernst et al., 2011). Therefore, gender may not be the primary determinant of health status in elderly patients.

As shown in Table 1, the majority of patients were in the 60–69 age group, with a total of 216 patients (69.92%). This reflects the increasing life expectancy of the Indonesian

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population and the growing proportion of elderly individuals each year (Statistics, 2024). Previous studies have indicated that younger elderly individuals (aged 60–69 years) tend to have higher life expectancy and greater potential to improve their quality of life. The characteristics of elderly patients in this study are summarised in Table 1.

Table 1. Characteristics of Elderly Patients Using High Alert Medications at K.R.M.T. Wongsonegoro Regional Hospital, Semarang (2021–2023)

Characteristics	Number of Patients (n = 318)	Percentage (%)
Sex		
Male	143	44.97
Female	175	55.03
Age Group		
60–69 years	216	69.92
70–79 years	77	24.21
80–89 years	24	7.55
90–93 years	1	0.31
Occupation		
Unemployed	211	66.35
Employee	12	3.77
Entrepreneur	95	29.87
Payment Type		
National Health Insurance (BPJS)	315	99.06
Out-of-pocket	3	0.94
Length of Stay		
≤ 4 days	158	49.69
> 4 days	160	50.31

Regarding employment status, the highest proportion of elderly patients—211 individuals (66.35%)—were unemployed. This reflects the loss of independence often experienced in old age, which is associated with decreased functional and cognitive capacity, thus requiring assistance in performing basic daily activities (Soares et al., 2023). Prior research also supports that elderly and unemployed individuals are independent predictors of hospital admission (Bender et al., 2023). Employment status is therefore considered an important factor in evaluating the quality of healthcare services (Rahim et al., 2021).

In terms of payment method, 315 elderly patients (99.06%) used the National Health Insurance (BPJS) scheme for their HAM-related treatments at K.R.M.T. Wongsonegoro Regional Hospital. BPJS, or Badan Penyelenggara Jaminan Sosial, is a public legal entity established to administer the national health insurance program in Indonesia (Ministry of Health, 2023).

The length of hospital stay for elderly patients in this study was ≤4 days for 49.69% of patients and ≥4 days for 50.31%. One of the factors influencing hospital stay is age; the older the patient, the longer the predicted hospitalisation duration (Mitha et al., 2024). This aligns with previous findings that age is a determinant of hospital length of stay (Sari & Alvita, 2022).

Elderly patients typically present with one or more chronic degenerative diseases or multiple morbidities. This results from a reduction in physiological reserves and organ function (Dasopang et al., 2015). As shown in Table 2, this study found that most elderly

inpatients had more than one disease. Patients with 2 to 3 comorbidities accounted for the highest proportion (77.36%).

Table 2. Disease Characteristics of Elderly Patients Using High Alert Medications at K.R.M.T. Wongsonegoro Regional Hospital, Semarang (2021–2023)

Characteristics	Number of Patients (n= 318)	Percentage %
Number of Diagnoses		
1 Diagnosis	21	6.60
2-3 Diagnoses	236	77.36
≥ 4 Diagnoses	51	16.04
Primary Diagnoses	**Number of Patients (n= 318)**	**Percentage %**
Diabetes Mellitus	130	40.88
Hypertension	90	28.30
Congestive Heart Failure (CHF)	32	10.06
Bronchopneumonia	66	20.76
Comorbid Diagnoses	**Number of Occurrences (n= 506)**	**Percentage %**
Diabetes Mellitus	130	25.69
Hypertension	110	21.74
Congestive Heart Failure (CHF)	32	6.32
Bronchopneumonia	48	9.49
Chronic Kidney Disease (CKD)	26	5.14
Anaemia	25	4.94
Non-ST-Elevation Myocardial Infarction (NSTEMI)	19	3.75
Atrial fibrillation	17	3.36
Other Complications	99	19.57

In this study, the highest number of patients suffered from Diabetes Mellitus (DM), accounting for 40.88%. Diabetes mellitus is characterised by elevated blood glucose levels caused by metabolic dysfunction, particularly when the pancreas is unable to produce sufficient insulin for the body's needs (Azwar, 2021). Advancing age increases the risk of impaired insulin secretion and pancreatic function. In elderly individuals, both pancreatic performance and insulin sensitivity gradually decline, which may affect blood glucose regulation (Chia et al., 2018).

The results also showed that 142 elderly patients (44.65%) were prescribed between 6 to 10 medications. This is consistent with previous findings stating that the majority of elderly patients receive polypharmacy prescriptions (Fauziah et al., 2020). The prevalence of potentially inappropriate prescribing among elderly patients often includes the use of High Alert Medications (Tian et al., 2023). A previous study found the overall prevalence of polypharmacy in the elderly population to be 33%, with Potentially Inappropriate Medications (PIMs) prescribed in 37% of cases.

Table 3 presents the characteristics of High Alert Medication (HAM) usage among elderly patients at K.R.M.T. Wongsonegoro Regional Hospital, Semarang.

Table 3. Characteristics of High Alert Medication Usage Among Elderly Patients at K.R.M.T. Wongsonegoro Regional Hospital, Semarang (2021–2023)

Number of HAMs per Patient	Number of Patients (n = 318)	Percentage %
2-5 medications	69	21.70
6-10 medications	142	44.65
≥ 10 medications	107	33.65
Drug Class / Medication Name	**Number of Prescriptions (n= 1153)**	**Percentage %**
Anaesthetic. Sedative. Inhalation. and Intravenous Agents		
Ketamine Injection	9	0.78
Propofol Injection	18	1.56
Bupivacaine Injection	10	0.87
Sevoflurane	18	1.56
Antithrombotic Drugs		
Heparin Injection	45	3.90
Fondaparinux Injection	37	3.21
Enoxaparin Injection	5	0.43
Warfarin Tablet	35	3.04
Tranexamic Acid 500 mg Injection	55	4.77
Cancer Chemotherapy Agents		
Docetaxel Injection	1	0.09
Hydroxyurea	1	0.09
Insulin		
Prandial Insulin Analogue. insulin aspart 100 IU/mL. Penfill	84	7.29
Basal Insulin Analogue. insulin glargine 100 IU/mL	71	6.16
Prandial Insulin Analogue. insulin lispro 100 IU/mL	21	1.82
Lispro and Lispro Protamine Combination	7	0.61
Degludec Analogue. insulin aspart 100 IU/mL. Penfill	3	0.26
Insulin Detemir	11	0.95
Antithrombotic Drugs		
Heparin	45	3.90
Enoxaparin sodium	5	0.43
Fondaparinux	37	3.21
Warfarin	35	3.04
Electrolytes and Intravenous Fluids		
Sodium Chloride (NaCl) 3%	61	5.29
Dextrose 40% (D40%)	42	3.64
Sodium Bicarbonate 84%	32	2.78
Potassium Chloride (KCl) 7.4%	18	1.56
Magnesium Sulfate ($MgSO_4$)	2	0.17
Calsium Gluconate 10%	21	1.82
Parenteral Nutrition		
Futrolit Infusion	48	4.16
Cinimix	2	0.17
Tutofusin Infusion	5	0.43

Drug Class / Medication Name	Number of Prescriptions (n= 1153)	Percentage %
Tutosol Infusion	24	2.08
Mannitol Infusion	7	0.61
Martos Infusion	2	0.17
Gelofusine Infusion	5	0.43
Neuromuscular Blocking Agents		
Rocuronium Injection	18	1.56
Opioids		
Morphine Injection	12	1.04
Cardiovascular Drugs		
Adrenergic Agonists (IV)		
Dopamine Injection	11	0.95
Dobutamine	9	0.78
Epinephrine Injection	1	0.09
Norepinephrine Injection	21	1.82
Antiarrhythmic Agents (IV)		
Lidocain Injeksi	40	3.47
Lidocain Comp Injeksi	2	0.17
Inotropic drug. intravena		
Digoxin Injection	2	0.17
Amiodarone	15	1.3
Vasodilators		
Nitroglycerin Injection	27	2.34
Calcium Channel Blockers		
Nicardipine	24	2.08
Anticholinergics		
Atropine Sulfate Injection	23	1.99
Cancer Chemotherapy		
Hydroxyurea	1	0.09
Docetaxel	1	0.09
Sandimun (Cyclosporine)	9	0.78
MST (Morphine Sulfate Tablets)	6	0.52
Narcotics		
Fentanyl Injection	27	2.34
Pethidine Injection	6	0.52
Psychotropics		
Alprazolam 0.5 mg	44	3.82
Diazepam 5 mg/ml	12	1.04
Midazolam Injection	20	1.73

As shown in Table 3, the most frequently used prandial insulin analogue was insulin aspart injection 100 IU/mL, with a usage rate of 7.29%. This finding is consistent with previous research, which reported that the most commonly used treatment for type 2 diabetes in elderly patients was Novorapid, a prandial insulin analogue (insulin aspart injection 100 IU/mL), at 49% usage (Purwakanthi et al., 2020).

The use of High Alert Medications (HAMs) that resulted in adverse events (AEs) in elderly patients is presented in Table 4.

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Table 4. Use of High Alert Medications Causing Adverse Events in Elderly Patients at K.R.M.T. Wongsonegoro Regional Hospital, Semarang (2021–2023)

Event	Number of Patients (n= 318)		Percentage %
No Adverse Events (No AE)		265	83.33
Adverse Events (AE)		53	16.67
Medication Name	**Total Cases (n= 60)**	**Percentage %**	**Adverse Event**	**Day Occurred**

Medication Name	Total Cases (n= 60)	Percentage %	Adverse Event	Day Occurred
Insulin				
Prandial Insulin Analogue. insulin aspart inj 100 IU/mL. Penfill	18	30.00	Hypoglycaemia	2. 3.4.5.6.8.14
Basal Insulin Analogue. insulin glargine inj 100 IU/mL	9	15.00	Hypoglycaemia	2. 3. 4. 5. 9
Prandial Insulin Analogue. insulin lispro inj 100 IU/mL	3	5.00	Hypoglycaemia	1.8
Mixed Analogue Insulin	1	1.67	Hypoglycaemia	2
Antithrombotic Drugs				
Heparin	16	26.67	Bleeding Risk	2. 4
Warfarin	1	1.67	Bleeding Risk	2. 4
Electrolytes and IV Fluids				
Sodium Chloride (NaCl) 3%	4	6.67	Electrolyte Imbalance	2. 5
Dextrose 40% (D40%)	2	3.33	Hyperglycaemia	2. 5
Sodium Bicarbonate84%	1	1.67	Electrolyte Imbalance	2
Opioids				
Morphine Injection	1	1.67	Dyspnoea	7
Cancer Chemotherapy				
Hydroxyurea	1	1.67	Nausea	1
Docetaxel	1	1.67	Asthenia	1
Psychotropics				
Alprazolam 0.5 mg	1	1.67	Risk of Excessive Sedation	1
Diazepam injection	1	1.67	Risk of Excessive Sedation	1

Table 4 shows that High Alert Medications (HAMs) caused Adverse Events (AEs) in 16.67% of elderly patients. The use of HAMs requires close monitoring and caution in administration (Komagamine, 2024).

Prandial insulin analogue, specifically insulin aspart injection 100 IU/mL, is a rapid-acting insulin used to control postprandial blood glucose levels, typically administered 5–10 minutes before meals (Perkeni, 2021). In elderly patients, a decline in organ function can affect the pharmacokinetics and pharmacodynamics of drugs, increasing the risk of undesired events (Brahma et al., 2013).

Elderly patients with diabetes mellitus are at higher risk of hypoglycaemia, especially when treated with hypoglycaemic agents such as sulfonylureas, meglitinides, and insulin (ElSayed et al., 2025). In this study, 30.00% of patients experienced hypoglycaemia on days 2, 3, 4, 5, 6, 8, and 14. Hypoglycaemia due to insulin aspart use most frequently occurred on day 2, accounting for 27.7% (5 out of 18 AEs related to insulin aspart).

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Regular blood glucose monitoring is necessary to maintain target glycaemic levels and to prevent more serious complications (Cefalu & Rodgers, 2024). Insulin aspart is a short-acting insulin analogue with a faster onset and shorter duration of action than human insulin. It is prescribed to manage both type 1 and type 2 diabetes. The most common side effect associated with insulin aspart is hypoglycaemia (Rubin et al., 2024). When administered via continuous subcutaneous insulin infusion, insulin aspart provides better glycaemic control in type 1 diabetes patients (Reynolds & Wagstaff, 2004).

Table 5. Average Direct Medical Costs of Elderly Patients Using High Alert Medications at K.R.M.T. Wongsonegoro Regional Hospital, Semarang (2021–2023)

Cost Component	Average Cost (IDR)
Non-AE Group (n = 265)	
Prescribed medication costs	1.860.830,30
Medical devices and disposables	936.885,07
Laboratory costs	1.460.816,42
Inpatient care	1.522.101,89
Nursing services	299.754,72
Doctor fees	940,332.85
Total direct medical costs	7,020,721.24
AE Group (n = 53)	
Prescribed medication costs	1.993.155,36
Medical devices and disposables	2.881.452,58
Laboratory costs	2.059.090,85
Inpatient care	1.324.650,94
Nursing services	283.301,89
Doctor fees	952.009,67
Total direct medical costs	9.493.661,29

Hypoglycaemia is defined as a blood glucose level below 70 mg/dL. In older adults, hypoglycaemia should be avoided due to its potentially fatal consequences or risk of significant cognitive decline (Perkeni, 2021). Glucagon promotes glucose production by enhancing glycogenolysis and gluconeogenesis in the liver and distributes glucose to various organs including the brain (Kitamura, 2024). It is a pancreatic hormone that stimulates the liver to release stored glucose into the bloodstream (Rusdi, 2020). In cases of severe hypoglycaemia, treatment may include glucagon injection or high-concentration dextrose (Standards, 2020).

When neuroglycopenic symptoms are observed, 20% dextrose (50 cc) can be administered; if ineffective, 40% dextrose (25 cc) can be given, followed by a D5% or D10% intravenous infusion (Yale et al., 2018). In this study, elderly patients who experienced hypoglycaemia-related AEs were treated using D10% infusion and D40% bolus injection. These findings are consistent with previous research, where dextrose was deemed highly effective in regulating blood glucose levels in hypoglycaemic patients (Febrianti & Hisni, 2024).

Managing these adverse events also affects healthcare costs. The cost components considered include direct medical expenses such as inpatient care, doctor consultations, clinical pharmacist visits, hospital accommodation, laboratory tests, and pharmaceutical costs (Ministry of Health, 2013).

According to Table 5, the average total direct medical cost from the hospital's perspective for elderly inpatients without adverse events was IDR 7,020,721.24, while those with adverse events incurred an average cost of IDR 9,493,661.29. Patients with AEs had higher direct medical costs than those without AEs. The direct medical costs from the healthcare perspective for elderly inpatients at K.R.M.T. Wongsonegoro Regional Hospital are presented in Table 5.

Given the increase in healthcare costs and the significant risks posed by HAM usage, evidence-based management strategies and standardised HAM monitoring protocols must be implemented. Efficacy should be a key consideration in treatment decisions to achieve optimal health outcomes, particularly in the context of limited healthcare resources. This is especially crucial for policymakers in the healthcare sector.

CONCLUSION

Hypoglycaemia (30%) was the most common HAM AE in older patients. In 7.29% of inpatient cases, insulin aspart injection 100 IU/mL, Penfill, was the most commonly prescribed medication. Elderly individuals without adverse events had an average direct medical expenditure of IDR 7,020,721.24, while those with adverse events had IDR 9,493,661.29. HAMs raise healthcare expenditures and pose substantial hazards, thus evidence-based management and monitoring practices are necessary. Treatment efficacy must be prioritised to obtain optimal outcomes within existing healthcare systems, especially by policymakers.

ACKNOWLEDGEMENTS

ETHICAL CLEARANCE

This study received ethical approval from the Ethics Committee of K.R.M.T. Wongsonegoro Regional Hospital, Semarang, under reference number: 112/Kom.Etik RSWN/VIII/2024.

AUTHOR CONTRIBUTIONS:

SS: Conceptual idea, data analysis, data collection
WS: Supervision
ED: Supervision
RBS: Data analysis, data collection

CONFLICT OF INTEREST

None to declare

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