Evaluation of knowledge and practices about administration and regulations of high alert medications among hospital pharmacists in Pakistan: findings and implications

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Background: A death of a nine months old child in Pakistan following the rapid administration of potassium chloride raised serious concerns on the awareness of appropriate use of high alert medications (HAMs) among healthcare professionals (HCPs). This study aimed to ascertain HAMs-related knowledge among hospital pharmacists in Pakistan.

Methodology: A cross-sectional study using exponential non-discriminative snowball sampling was conducted among hospital pharmacists in healthcare settings in Punjab, Pakistan. A validated study tool was used to determine knowledge on administration, regulation, and practices related to the HAMs. Barriers to conducting HAMs training in the hospitals were assessed from an open-ended question. All quantitative data were analyzed using SPSS 22.0 while the content analysis was performed on the qualitative data.

Results: A total of 202 hospital pharmacists were included in the study. The mean knowledge score for HAMs administration and regulation were 5.86 ± 1.89 (95% CI 5.60–6.12) and 7.25 ± 1.70 (95% CI 7.02–7.49), respectively. Approximately half of the respondents (49.5%) achieved scores ≥ 70%, demonstrating sufficient knowledge of HAMs. In the multivariable-adjusted model, increasing age and work experience were found to be the positive predictors of good HAMs knowledge. The mean practice score was 36.42 ± 1.97 (95% CI 34.05–38.77), with 62.4% of pharmacists following good HAMs-related practices. We identified several barriers to conducting HAMs training through qualitative analysis. These barriers included lack of knowledge, poor attitude and behavior of medical and para-medical staff, lack of active support by hospital administration, lack of cooperation between HCPs, lack of opportunities, heavy workload, insufficient human resources, financial constraints, and lack of motivation.

Conclusions: A significant proportion of the hospital pharmacists had unsatisfactory knowledge and practices of HAMs. These findings underscore that training on HAMs should be conducted periodically as part of hospital-based pharmacy education to maximize drug safety.

Introduction

The clinical interventions are aimed to provide relief to patients. However, they are sometimes associated with untoward harmful events. The intricate combination of procedures, technologies and human interactions that involves the present-day health services delivery system undoubtedly improves patients’ well-being. Nonetheless, there is also an unavoidable risk of patient harm that can result in adverse health-related consequences. Adverse events due to unsafe care are reported to be among the top ten leading causes of morbidity and mortality across the globe. One in every ten patients gets harmed during treatment in high-income nations. In low and middle-income nations, approximately 134 million adverse events occur in medical centers due to sub-optimal medical care, causing 2.6 million deaths. Worldwide, 4 in 10 patients are harmed in both primary and ambulatory care. This can be prevented in almost 80% of instances.

All medications have the potential to cause harm but high-alert medications (HAMs) carry a greater risk of causing harm to the patients if used improperly. Even if the errors...
might not be more common with such medications, the ramifications of an error are much more detrimental to patients resulting in either severe injuries or even death. These medications include antineoplastic drugs, cardiovascular medications, anticoagulants, opioids and opioid analogs, neuromuscular blockers, benzodiazepines, and concentrated electrolytes (e.g. 15% KCl)\(^7\).

Pakistan has an underdeveloped health care delivery system due to the limitation of resources. The frequency of medication errors (MEs) is high in the country. However, they are not usually reported due to various factors including lack of required mechanism of reporting, fear of patient’s family reaction and adverse career-related consequences\(^8–10\). Recently, the demise of an infant girl due to a rapid injection of 15% KCl by the nursing staff highlighted the concerns of HAMs-related errors in Pakistan\(^11\). As MEs are multidisciplinary and occur at various stages of pharmacotherapy, awareness of health professionals about HAMs is pivotal to maximizing patient safety. Published data show that nurses’ have inadequate knowledge of HAMs\(^12–15\). To our knowledge, there is no published literature concerning the knowledge of HAMs among hospital pharmacists in Pakistan. In this context, the present study is the first of its own kind to evaluate the HAMs-related knowledge of pharmacists providing services in hospitals in Punjab, Pakistan.

**Methods**

**Design**

We opted for an online cross-sectional study due to the restrictive measures (complete lockdown) imposed to curtail COVID-19 in Pakistan.

**Study setting**

Both public and private healthcare systems exist in Pakistan. National health infrastructure is comprised of 1979 hospitals (public = 1279, private = 700). In addition, there are 5527 basic health units (BHUs), 686 rural health centers (RHC) and 5671 dispensaries. Punjab is the most populous (\(N = 109,989,655\)) province of the country. The public healthcare departments are divided into two categories: “Primary and Secondary Healthcare Departments” (PSHD) and “Specialized Healthcare and Medical Education Department” (SMED). The PSHD includes dispensaries, rural health centers, basic health unit, district headquarters hospitals (DHQ), and tehsil headquarters hospitals (THQ) whereas SMED includes tertiary care institutions\(^16\). The province has a total of 23 teaching hospitals, 34 DHQs, 88 THQs, 293 RHCs and 2461 BHUs. Due to the unavailability of pharmacists in RHCs and BHUs, both public and private hospitals were the primary targets for data collection.

**Population**

The target population was pharmacists providing health care services in DHQs, THQs and teaching hospitals of all nine divisions of the most populous province of Pakistan (Punjab). The pharmacy technicians, non-hospital pharmacists, internee pharmacists and those unwilling to participate in the study were excluded.

**Ethical approval**

The prior approval of the current study was obtained from Research Ethics Committee, Department of Pharmacy Practice at the University of Lahore (REC/DPP/FOP/11). We obtained online informed consent from each participant. No personal information was collected on the study instrument. Furthermore, all study participants were guaranteed the privacy of their data.

**Sampling technique**

There is a severe shortage of pharmacists and only one pharmacist is available per 1200 beds in public hospitals in Pakistan\(^17\). The exact number of pharmacists working in hospitals in the Punjab province is not known. A minimum sample size a-priori was not considered to include maximum participants to enhance the representativeness of the sample. A similar approach has previously been used in various studies\(^18,19\). We used snowball sampling to recruit the study participants between July and September 2020.

**Development of study instrument and validation**

An online self-completed questionnaire (Google Form) was developed based on previous studies related to HAMs\(^12,13,15\). As English is the primary language of higher education in Pakistan, the Urdu translation of the study tool was not considered. For content validation, the questionnaire was evaluated by a panel of pharmacy experts (Four academicians and 3 hospital pharmacists). Each member of the panel indicated the questions as essential or non-essential. The mean item-content validity index was found to be 0.98, indicating satisfactory content validity. The panel gave minor revisions to improve the comprehensibility of some items. The questions were revised based on the suggestions of the panel. The final draft of the study instrument had the following sections to evaluate the knowledge of HAMs.

- **Sections A:** This section collected demographic data e.g. age, gender, education/qualification, rank, experience and name of the hospital.
- **Section B and C:** These sections had ten items each that evaluated the extent of knowledge regarding administration (Section B) and regulation of HAMs (Section C). Each right answer was scored 1, otherwise 0 resulting in a cumulative knowledge score of 10 for each domain of HAMs knowledge.
  - To estimate the overall HAM-related knowledge score, each correct answer in sections B and C was scored 5, with a total score of 100 (20 questions × five scores). The further classification of the knowledge score was made to stratify the study participants with good...
knowledge (score ≥70%), or poor knowledge (score <70%)12,13,15.

• **Section D:** This section consisted of 11 items to evaluate pharmacists’ practices related to HAMs. Similar to the scoring criteria in the above section, each right answer was scored 5 while a wrong or neutral response was scored zero; the total possible score ranged from 0 to 55. Practices scores were classified as good ≥70% or poor <70%. One open-ended question was asked at the end of the questionnaire to determine barriers to conducting HAMs training in the hospitals.

### Statistical analysis

Data from the online database (Google Drive) were downloaded in the Microsoft Excel sheet. Data cleaning and appropriate coding were done in the Excel sheet. The data were transferred to the IBM SPSS version 22 for further analyses. To determine the normality of continuous data, skewness and kurtosis values were examined. In addition, a visual inspection of histograms was also done. The continuous data were expressed as mean±standard deviation, while categorical data was shown as frequencies (n) along with proportions (%). HAMs knowledge and practices scores were compared between the demographic variable using the t-test and one-way ANOVA, where applicable. If data violated the assumption of homogeneity of variance, Welch’s ANOVA was used. Furthermore, we performed binary logistic regression to determine predictors of good HAMs knowledge and practices. Age, gender, level of education, work experience and hospital types were covariates in regression analysis. The covariates that were highly correlated with each other were excluded from the regression analysis. The Hosmer-Lemeshow test was performed to check the predictive capability of the models. A two-sided p-value of less than .05 was taken as significant in all statistical tests. The content analysis was performed on the qualitative data10.

### Results

#### Sample characteristics

A total of 202 pharmacists from 41 hospitals (20 THQs, 11 DHQs, and 10 teaching hospitals) provided consent and completed the study instrument (202/244 = 82.7%). Respondents’ demographic data are given in Table 1. The majority were females (63.9%) between 26 to 30 years of age (75.7%).

#### Knowledge of high alert medications (HAMs) administration

Responses to the items related to HAMs administration are shown in Table 2. The maximum correct response rate was 81.2% for the item enquiring whether “the insulin syringe can be replaced with 1 ml syringe” followed by 74.8% for the item related to the dosage expression of insulin. One item generated the lowest correct response rate (18.8%); a majority of pharmacists did not know that port-a-cath cannot be used for drug injections generally. The mean knowledge score of HAMs administration was 5.86 ± 1.89 (95% CI 5.60–6.12). There was a substantial difference (p < .001) in knowledge scores related to HAMs administration among age, gender, education, and experience categories (Table 3).

#### Knowledge of HAMs regulation

The maximum correct response rate was 92.6% for item-2 and -9 followed by 87.2% for item-1 (Table 2). The mean knowledge score of HAMs regulation was 7.25 ± 1.70 (95% CI 7.02–7.49). We observed a significant difference in knowledge scores related to HAMs regulation among age, gender and experience categories (Table 3).

#### Predictors of adequate HAMs-related knowledge

Regarding the overall HAMs knowledge, 50.5% of pharmacists achieved scores <70%, indicating poor knowledge. The logistic regression model to assess the factors associated with good HAMs knowledge was statistically significant \(\chi^2 (7) = 43.512, p < .001\). Our model explained 25.8% (NegelKerke \(R^2\)) of the variance and correctly classified 70% of the cases. Findings of the goodness-of-fit test showed that our model predicted values were not significantly different from what we observed \(\chi^2 (8) = 12.119, p = .143\). After multivariable adjustment, increasing age and job experience were found to be the positive predictors of good HAMs knowledge (Table 4).

#### HAMs-related practices

The HAMs-related practices of the study participants are described in Table 5. Around 84% reported ensuring cautionary labeling on HAMs storage shelves, 78.7% ensured “high alert medication” labels were placed on their containers or product packages, and 66.3% reported adequately labeling the loose ampule or vials of HAMs, indicating good practices. Only 33.7% pharmacists reported of providing HAMs training...
to other health professionals. Overall, 62.4% of the study population was found to have good HAMs-related practices (score $\geq 70\%$). The mean practice score was $36.42 \pm 1.97$ (95% CI 34.05–38.77). As presented in Table 3, there was a significant difference in practice scores among age ($p = .002$), gender ($p = .005$), experience ($p < .001$) and hospital categories ($p < .001$).

**Predictors of good HAMs-related practices**

Factors significantly associated with good HAMs-related practices are presented in Table 6. The logistic regression model was statistically significant ($\chi^2 (4) = 26.392, p < .001$). It correctly classified 68.3% of the cases. The result of the goodness-of-fit test showed the good predictive capacity of the model ($\chi^2 (4) = 1.217, p = .875$). In the multivariate-adjusted model, increasing work experience was found to be the only positive predictor of good HAMs practices.

**Barriers for conducting HAMs training**

Several barriers to conducting HAMs training were identified through qualitative analysis (Supplementary Table 1). These barriers included lack of knowledge, poor attitude and behaviors of medical and paramedical staff, false beliefs, lack of active support by hospital administration, lack of cooperation between healthcare professionals, lack of opportunities, insufficient human resources (clinical pharmacists), overburdened staff/heavy workload, financial constraints, and lack of motivation.

| Item | Questions | Answer | Correct rate $N$ (%) |
|------|-----------|--------|---------------------|
| 1    | For a patient who has mild allergic reaction, administer 1:1000 epinephrine 1 ampule as a fast intravenous push | False | 149 (73.8) |
| 2    | When an emergency happens, administer 10% calcium chloride (CaCl$_2$) 10 ml as a fast intravenous push (in 1–2 minutes) | False | 110 (54.5) |
| 3    | 10% calcium gluconate and 10% CaCl$_2$ are the same drug and are interchangeable | False | 107 (53.0) |
| 4    | Dosage expression for insulin injection is ‘cc’ or ‘ml’ | False | 151 (74.8) |
| 5    | Accurate chemotherapy dose calculation for adults is based on body weight whereas chemotherapy for pediatric patients is based on body surface area | False | 113 (55.9) |
| 6    | When an emergency such as ventricular fibrillation happens, administer 15% potassium chloride (KCl) 10 ml as a fast IV push | False | 103 (51.0) |
| 7    | 15% KCl is better to be added to Ringer’s solution for rapid infusion | False | 106 (52.5) |
| 8    | Insulin syringe can be replaced by 1ml syringe | False | 164 (81.2) |
| 9    | Give fast IV infusion of 3% NaCl 500 ml for patient who has low sodium level | False | 143 (70.8) |
| 10   | Port-A route can be used for drug injections generally | False | 38 (18.8) |

**Discussion**

Ensuring patients’ safety during the provision of health care is a prerequisite for strengthening health care systems. As HAMs have a higher likelihood of causing serious health injuries if used irrationally, great caution must be exercised while prescribing, dispensing and administering such medications. Healthcare workers’ knowledge related to HAMs is one of the key predictors to avoid errors and enhance patient safety. Hsaio et al. reported that the majority of Taiwanese nurses (70.5%) had insufficient knowledge of HAMs administration and regulation. Likewise, studies conducted among Palestinian (60.7%) as Pakistani (84%) nurses also showed inadequate HAMs knowledge among these health professionals. Furthermore, Mustafa et al. reported that the majority of Pakistani medical doctors possess moderate knowledge about HAMs. There have not been any studies conducted among pharmacists to evaluate their awareness of HAMs. In this context, this is the first study of its kind that underscored the knowledge and practices of pharmacists related to HAMs. Our main findings indicated that 49.5% of hospital pharmacists providing services in health care settings of Punjab Province (Pakistan) had good knowledge of HAMs administration and regulation. Furthermore, around 62% were found to have adequate practices related to HAMs. Epinephrine (1:1000) is the recommended first-line therapy for the reversal of anaphylaxis symptoms and should be considered for patients with suspected anaphylactic reactions without any delay. An intramuscular (IM) dose of 0.01 mg/kg (maximum dose: 0.5 mg) every 5–20 min is recommended for the treatment of anaphylaxis. The IM administration of
Continuous blood pressure and cardiac monitoring. In the health capacity equipped with trained experts, and to mention that such infusions should only be considered in the subcutaneous route. However, intravenous infusions of epinephrine into the lateral thigh has the advantage of rapid absorption and higher plasma concentration as compared to epinephrine solution. Calcium administration of calcium. However, this risk is comparatively lower with calcium gluconate as compared to calcium chloride solution. It is important to note that tissue necrosis following fluid extravasation is a potential risk during the administration of calcium. However, this risk is comparatively lower with calcium gluconate as compared to calcium chloride solution. Our analysis showed that approximately one-half of pharmacists did not know the appropriate way of CaCl2 administration. They believed that CaCl2 can be switched with calcium gluconate.

Rapid administration of potassium chloride (KCl) concentrates causes serious adverse events; risks of arrhythmias, cardiac arrest and even deaths. The amount of elemental calcium in an ampule of calcium gluconate (10 ml of 10% formulation) is 8.9 mg/ml whereas it is 27.2 mg/ml in 10% calcium chloride solution. It is important to note that tissue necrosis following fluid extravasation is a potential risk during the administration of calcium. However, this risk is comparatively lower with calcium gluconate as compared to calcium chloride. Our analysis showed that approximately one-half of pharmacists did not know the appropriate way of CaCl2 administration. They believed that CaCl2 can be switched with calcium gluconate.

Table 3. Association of demographic features with high alert medication knowledge and practice scores.

| Variables           | Subgroups   | Knowledge score | Practices score |
|---------------------|-------------|-----------------|-----------------|
|                     | HAM administration | HAM regulation | HAM administration | HAM regulation |
| Age (years)         | ≤30         | 5.54 ± 1.84     | 7.02 ± 1.78     | 34.87 ± 17.22 |
|                     | >30         | 6.86 ± 1.67     | 7.98 ± 1.16     | 41.22 ± 15.53 |
| Gender              | Male        | 6.48 ± 2.04     | 7.58 ± 1.53     | 40.55 ± 14.06 |
|                     | Female      | 5.51 ± 1.70     | 7.07 ± 1.77     | 34.07 ± 18.11 |
| Qualification       | Bachelor    | 5.25 ± 1.97     | 6.98 ± 1.78     | 34.82 ± 16.92 |
|                     | MPhil/PhD   | 6.29 ± 1.70     | 7.45 ± 1.62     | 37.52 ± 17.06 |
| Experience (years)  | ≤1          | 4.84 ± 1.65     | 6.75 ± 1.81     | 30.65 ± 17.31 |
|                     | >1–3        | 6.43 ± 1.67     | 7.59 ± 1.68     | 39.17 ± 15.77 |
|                     | >3–5        | 6.88 ± 1.41     | 7.63 ± 1.46     | 41.25 ± 16.98 |
|                     | >5          | 7.10 ± 1.59     | 7.82 ± 1.21     | 44.36 ± 13.34 |
| Hospital            | Primary/secondary | 5.74 ± 1.84     | 7.20 ± 1.69     | 34.35 ± 17.61 |
|                     | Tertiary    | 6.28 ± 2.00     | 7.43 ± 1.75     | 43.19 ± 12.87 |

Table 4. Predictors of good knowledge for high alert medications.

| Variables           | Subgroups | Knowledge score | Practices score |
|---------------------|-----------|-----------------|-----------------|
|                     | OR (95% CI) | p-value | OR (95% CI) | p-value |
| Age (years)         | ≤30 Years | 1.00(Reference) | – | 1.00(Reference) | – |
|                     | >30 Years | 5.882(2.733–12.658) | <.001 | 2.989(1.159–7.708) | .024 |
| Gender              | Male      | 1.00(Reference) | – | 1.00(Reference) | – |
|                     | Female    | 0.462(0.257–0.832) | .010 | 0.793(0.395–1.591) | .541 |
| Qualification       | Bachelor  | 1.00(Reference) | – | 1.00(Reference) | – |
|                     | MPhil/PhD | 2.125(1.199–3.765) | .010 | 1.673(0.886–3.159) | .113 |
| Experience (years)  | ≤1 Year   | 1.00(Reference) | – | 1.00(Reference) | – |
|                     | >1–3 Years| 3.556(1.759–7.186) | <.001 | 3.004(1.449–6.230) | .003 |
|                     | >3–5 Years| 7.333(2.172–24.764) | .001 | 3.093(0.752–12.725) | .118 |
|                     | >5 Years  | 7.089(3.040–16.533) | <.001 | 3.214(1.158–8.197) | .025 |
| Hospital            | Primary/Secondary | 1.00(Reference) | – | 1.00(Reference) | – |
|                     | Tertiary   | 2.143(1.092–4.204) | .027 | 1.441(0.671–3.092) | .349 |

Abbreviations. HAM, high alert medication. Bold indicates statistically significant values.

epinephrine into the lateral thigh has the advantage of rapid absorption and higher plasma concentration as compared to the subcutaneous route. However, intravenous infusions of epinephrin should be considered if IM or IV bolus administration does not improve the patients condition. It is pertinent to mention that such infusions should only be considered in the health capacity equipped with trained experts, and continuous blood pressure and cardiac monitoring. In the present study, around 74% of the respondents knew that epinephrine should not be given as a fast IV push for a patient with a mild allergic reaction. Calcium chloride (10% CaCl2) is primarily prescribed to correct electrolyte anomalies and is considered advanced cardiac life support. The too rapid injection can cause hypotension and cardiac syncpe, therefore, it is recommended to be administered by slow (not to exceed 1 ml/min) IV injection. Moreover, calcium gluconate is usually administered to manage the low levels of calcium in patients. It is also used to treat cardiototoxicity due to high levels of potassium and magnesium in the blood. In addition, its beneficial effects on cardiac arrest are also well-recognized. The amount of elemental calcium in an ampule of calcium gluconate (10 ml of 10% formulation) is 8.9 mg/ml whereas it is 27.2 mg/ml in 10% calcium chloride solution. It is important to note that tissue necrosis following fluid extravasation is a potential risk during the administration of calcium. However, this risk is comparatively lower with calcium gluconate as compared to calcium chloride. Our analysis showed that approximately one-half of pharmacists did not know the appropriate way of CaCl2 administration. They believed that CaCl2 can be switched with calcium gluconate.
Table 5. Practices among hospital pharmacists related to high alert medications.

| Item | Statements | Answer | N (%) |
|------|------------|--------|-------|
| 1    | I ensure “High Alert Medication” labels/stickers are put on storage shelves. | Agree 169 (83.7) | 7 (3.5) | 26 (12.9) |
| 2    | I ensure “High Alert Medication” labels/stickers are put/pasted on containers or product packages of such medications. | Agree 159 (78.7) | 11 (5.4) | 32 (15.8) |
| 3    | I ensure “High Alert Medication” labels/stickers are pasted on loose vials or ampoules | Agree 134 (66.3) | 25 (12.4) | 43 (21.3) |
| 4    | I ensure “High Alert Medications” are kept/stored at the correct place | Agree 161 (79.7) | 8 (4.0) | 33 (16.3) |
| 5    | I use TALL-man lettering to emphasize differences in “high alert medication” names (e.g. DOPamine and DOBUTamine) | Agree 107 (53.0) | 53 (26.2) | 40 (20.8) |
| 6    | To avoid errors, I double check before “High Alert Medications” are dispensed | Agree 142 (70.3) | 24 (11.9) | 36 (17.8) |
| 7    | I ensure “High Alert Medications” to be dispensed to patients are NOT labeled as high alert. | Agree 99 (49.0) | 48 (23.8) | 55 (27.2) |
| 8    | Before dispensing, I educate the patient and family members/caregivers on the use of “High alert medication” (purpose of the medication, how much and when to take? Common side effects etc.) | Agree 142 (70.3) | 20 (9.9) | 40 (19.8) |
| 9    | I educate the patient and family members/caregivers on the storage of “High alert medications | Agree 143 (70.8) | 23 (11.4) | 36 (17.8) |
| 10   | I educate the patient and family members/caregivers on the disposal of expired/unused “High alert medications” | Agree 147 (72.8) | 17 (8.4) | 38 (18.8) |
| 11   | I provide “High Alert Medications” trainings to other healthcare workers in my hospital. | Agree 68 (33.7) | 33 (6.3) | 101 (50.0) |

Table 6. Predictors of good practices related to high alert medications.

| Variables | Univariate | Multivariate |
|-----------|------------|--------------|
| **Age (years)** | | |
| ≤30 Years | 1.00(Reference) | – |
| >30 Years | 1.703(0.847–3.426) | .135 |
| **Gender** | | |
| Male | 1.00(Reference) | – |
| Female | 0.543(0.294–1.005) | .052 |
| **Qualification** | | |
| Bachelor | 1.00(Reference) | – |
| MPhil/PhD | 1.387(0.779–2.470) | .266 |
| **Experience (years)** | | |
| ≤1 Year | 1.00(Reference) | – |
| >1–3 Years | 3.157(1.534–6.500) | .002 |
| >3–5 Years | 3.643(1.094–12.131) | .035 |
| >5 Years | 6.679(2.555–17.459) | <.001 |
| **Hospital** | | |
| Primary/Secondary | 1.00(Reference) | – |
| Tertiary | 2.364(1.120–4.988) | .024 |

| Abbreviations. CI, confidence interval; OR, odds ratio. Bold indicates statistically significant values. |

stored in hospital wards or nursing units, and free access of nurses to this drug is not advised. Previous studies among nurses and physicians also highlighted inadequacies in the knowledge of KCl administration necessitating interventions for improvement. To avoid errors, I double check before “High Alert Medications” are dispensed. The death of a nine months old child in Pakistan following the rapid IV administration of KCL indicates that the health professionals are not much aware of the appropriate use of HAMs, necessitating the need for structured training programs in hospitals.

Hypertonic saline is a promising therapeutic modality for patients with severe symptomatic hyponatremia, cerebral edema and increased intracranial pressure. For treatment of severe hyponatremia, 3% saline is either infused at a rate of 1–2 mL/kg/hour to elevate the serum sodium concentration by 6–8 mEq/L (not to exceed 10–12 mEq/L in the first 24 h or 18 mEq/L in 48 h) or infusing one dose of 100–150 mL 3% saline over 10–20 min with aim of increasing serum sodium level by 2–3 mEq/L; may repeat bolus twice if symptoms do not resolve. Although common adverse effects are related to the route of administration and include infection at the IV site, thrombophlebitis, infiltration, extravasation, and hypervolemia but rapid correction of severe hyponatremia can result in osmotic demyelination syndrome/central pontine myelinolysis. Other possible adverse reaction includes hyperchloremic metabolic acidosis. Administration of hypertonic saline through peripheral intravenous access is acceptable if no other access is available, but the central venous site is the preferred route. In our study, around 71% of pharmacists were aware of the correct way of hypertonic saline administration. However, inappropriate awareness among 29% of pharmacists is also a point of concern.

All types of insulin, subcutaneous and IV, are considered high-alert medications. A complete understanding of insulin dosage expression and the use of a dedicated insulin syringe reduces insulin administration errors. Illegible handwriting and inconsistent abbreviations of "units" to be "U" or "IU" may be misunderstood as "0," "10," "11" and even "cc" leading to severe insulin overdose. Only 75% of the study participants knew the right dosage expression of insulin and 81.4% gave correct responses regarding the use of a dedicated insulin syringe for its administration.
around 72% knew it was not right to replace “unit” with “U” or “IU” for dosage expression. Although these findings are slightly better than the ones reported among nurses,21,12,13,15 still, instructive efforts should be made to enhance healthcare professionals’ knowledge about the correct concepts of insulin dosage, dosing expression and use of dedicated insulin syringes to reduce insulin administration errors. It is standard practice to individualize chemotherapy doses in patients of all ages. Chemotherapy dosing is usually based on body surface area (BSA) in adults, however, chemotherapy dose calculation in pediatric patients has many complexities.41 The ratio of BSA to body weight (BW) is significantly higher in infants and drastically reduces as a child grows. Therefore, for infants and young children, BSA greatly overestimates the dose needed to achieve a desired area under the curve, whereas BW is a more accurate predictor of drug exposure. The “rule of 30” can be used to adjust a dose from mg/m² to mg/kg; the mg/m² dose is divided by 30 to get the mg/kg dose to administer.41 We observed deficits (correct rate = 55.6%) in the knowledge of chemotherapy dose calculation for adults and pediatrics among our survey respondents.

HAMS must be stored with special care.42 Atracurium, a neuromuscular blocking agent used during endotracheal intubation and for the relaxation of skeletal muscles during surgery or mechanical ventilation, should be stored in a refrigerator at 2 to 8°C to preserve its potency. However, it must be used within fourteen days, even if re-refrigerated. It was extremely concerning to see that around 27% of the study participants did not know atracurium is a refrigerated drug that should not be stored normally with other drugs. Heparin is stored at room temperature whereas insulin is a refrigerated medication that should be stored at 2 to 8°C.44,45 Only 66.3% of the study responders gave correct answers regarding the storage of insulin and heparin. Opioids (morphine, fentanyl, pethidine) must be stored under the double lock chamber in the pharmacy.42 The drug must be sent with a “High Risk Medication” sticker. Furthermore, all the narcotics issued by the pharmacy should be documented in the narcotics book/register.42 Fortunately, a majority (92.6%) of the study participants were aware of these regulations. Although pharmacists were found to have better knowledge of HAMS regulation (7.25 ± 1.70; 95% CI 7.02–7.49) than administration (5.86 ± 1.89; 95% CI 5.60–6.12), the overall knowledge of HAMS was unsatisfactory (good HAMS knowledge = 49.5%). Taken together, the knowledge of healthcare professionals regarding HAMS administration as well as regulation needs to be improved in order to enhance patient safety.

With regards to HAMS storage, attention should be paid to the labeling of these drugs. A label of “High Alert Medication” should be considered for each and every packaging of these medications. A greater responsibility lies with Pharmacy staff and they should read the instructions for “High Alert Medication” carefully to ensure their appropriate and safe placement or storage. Furthermore, Tall Man lettering should be used to label read-alike or sound-alike medication to avoid errors.46 To ensure safety and accuracy, all HAMS must be counterchecked by another independent staff before dispensing. All healthcare professionals dealing with HAMS should have appropriate education on the standard procedures of HAMS. Findings of the present study revealed suboptimal compliance with the abovementioned standard practices (Table 5).

Implications of study findings

We recommend the inclusion of comprehensive HAMS courses as a part of in-school pharmacy education, as well as hospital-based continuing pharmacy education in Pakistan. In addition, to curb HAMS-related errors (prescribing, dispensing and administration errors) and improve patient outcomes, the professional gap between doctors, nurses and pharmacists need to be bridged through effective communication and collaboration. Since there is a huge deficit of clinical pharmacists in Pakistani healthcare settings, the authorities should take the necessary steps to increase the number of qualified and skillful pharmacists in the hospitals. This study also identified various barriers to conducting training courses related to HAMS that should be considered while initiating any educational program in the hospitals. Last but not least, healthcare institutions must develop and implement standard operating procedures for HAMS along with basic training courses on their appropriate use and regulation.

Strengths and limitations

The current study is accompanied by a few limitations which should be considered while interpreting the results. Firstly, this was a web-based study administered using a non-probability sampling method, thus, the propensities of various errors including coverage error, referral bias and selection bias cannot be disregarded. Secondly, a self-completed questionnaire was used so introspection and reporting bias might be present. Thirdly, our target population was hospital pharmacists working in various hospitals in the Punjab province of Pakistan so the generalizability of the findings is limited to other provinces of the country. Nonetheless, the current study is strengthened by the first of its kind ascertaining the knowledge of pharmacists related to HAMS. We believe our findings will serve to design and implement educational initiatives by the health authorities to improve patient care.

Conclusions

This study indicated unsatisfactory knowledge regarding the administration and regulation of HAMS among hospital pharmacists practicing in Pakistan. However, increasing age and work experience were found to be predictors of good HAMS knowledge. We recommend that pharmacy students should receive extensive HAMS-related education and training during their graduation. Furthermore, HAMS training should also be periodically conducted in hospitals as a part of continuing pharmacy education.
Transparency

Declaration of funding

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Declaration of financial/other relationships

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Author contributions

MS & ZM: Conceived and designed the study idea, NS, THM, YHK: data collection, MS, THM, KH & TMK: analysis of results; YKH, MS, ZM: manuscript drafting, NS, KH, THM: critical revision of manuscript. All the authors agreed with the current version of the manuscript.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author.

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