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Pharmacovigilance and Ranitidine Withdrawal Awareness among Libyan Private Pharmacies (Gharyan): A Cross-Sectional Study

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ABSTRACT

INTRODUCTION. Pharmacovigilance ensures drug safety through continuous monitoring, yet awareness remains limited in low-resource settings. Ranitidine, a widely used antacid, was withdrawn globally in 2020 due to contamination with N-nitrosodimethylamine (NDMA), a suspected carcinogen. Despite an official withdrawal from drug circulation, ranitidine is still at risk of being used unreasonably; the conditions given make it a relevant goal to assess professional awareness of pharmaceutical employees.

AIM. This study aimed to detect pharmacovigilance challenges among Lybian pharmacies and explore the new growth vectors using awareness of ranitidine withdrawal reasons and safety issues among pharmacy employees as an example.

MATERIALS AND METHODS. A cross-sectional study was conducted engaging 130 pharmacy employees of Gharyan city, Libya, in January-March 2023. A structured questionnaire with three sections was used, including: 1) demographics (age, gender, education, and experience); 2) basic pharmacovigilance knowledge of participants (six questions with Yes/No answers); 3) awareness of ranitidine withdrawal (six questions with Yes/No answers). Data were analysed using descriptive statistics.

RESULTS. The survey showed that almost a third of participants (36.2%) were not familiar with the term "pharmacovigilance"; more than two-thirds (63.8%) did not know that Libya's national pharmacovigilance centre existed. This contradicts the responses regarding pharmacovigilance measures: 78.5% stated they were trained in pharmacovigilance; 81.5% knew about special report forms to be filled out for any adverse drug reactions, while 16.2% previously made reports on adverse reactions. 55.4% of participants were familiar with the cases where drugs were withdrawn due to related risks. At the same time, 79.2% thought that ranitidine was still dispensed from the pharmacies; and 30.8% misclassified ranitidine, a H2-blocker, as an antihistamine. 61.5% of participants thought carcinogenic impurities were caused by manufacturing contamination; moreover, only another 36.1% associated the impurities also with the improper storage.

CONCLUSIONS. The identified critical gaps in pharmacovigilance knowledge and ranitidine safety highlight the need for targeted educational interventions among Gharyan pharmacy employees and regulatory enforcement of drug withdrawals from the circulation.

Keywords: pharmacovigilance; drug safety; ranitidine; H2-histamine antagonists; anti-ulcer drugs; nitrosodimethylamine; NDMA; awareness; withdrawal

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Осведомленность о фармаконадзоре и изъятии ранитидина из обращения среди сотрудников ливийских частных аптек (г. Гарьян): поперечное исследование

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РЕЗЮМЕ

ВВЕДЕНИЕ. Фармаконадзор обеспечивает безопасность препаратов благодаря постоянному мониторингу, и все же осведомленность фармацевтических работников остается недостаточной. Широко применяемый антацид ранитидин был изъят из обращения во всем мире в 2020 г. из-за примеси N-нитрозодиметиламина (НДМА), потенциального канцерогена. Несмотря на официальное изъятие ранитидина из обращения, сохраняется вероятность его необоснованного применения в практике. В этих условиях актуальной задачей становится оценка уровня профессиональной осведомленности фармацевтических работников.

ЦЕЛЬ. Выявление проблем системы фармаконадзора аптечных организаций Ливии и направлений ее совершенствования на примере оценки осведомленности работников аптек о безопасности ранитидина и причинах его изъятия из обращения.

МАТЕРИАЛЫ И МЕТОДЫ. Поперечное исследование проводили с января по март 2023 г. среди 130 сотрудников аптек г. Гарьян (Ливия). Использовали структурированный опросник, имеющий три раздела: 1) демографические данные (возраст, пол, специализация, стаж); 2) базовые знания о фармаконадзоре (6 вопросов с ответами «Да/Нет»); 3) осведомленность об изъятии ранитидина из обращения (6 вопросов «Да/Нет»). Данные анализировали с помощью описательной статистики.

РЕЗУЛЬТАТЫ. Результаты проведенного опроса показали, что почти треть участников (36,2%) не знакомы с термином «фармаконадзор», более двух третей (63,8%) не знали о существовании Центра фармаконадзора в Ливии. Это противоречит ответам респондентов о фармаконадзорных мероприятиях: 78,5% указали, что проходили обучение по фармаконадзору, 81,5% знали о специальных бланках отчетности, которые нужно заполнять при выявлении побочного действия лекарственных препаратов, а 16,2% ранее готовили такие отчеты. О случаях отзыва лекарственных препаратов из-за связанных с ними рисков были осведомлены 55,4% участников. В то же время 79,2% респондентов указали, что ранитидин можно приобрести в аптеке, 30,8% неверно относили ранитидин, блокатор H2-гистаминовых рецепторов, к антигистаминным препаратам. Источником канцерогенных примесей в препарате 61,5% респондентов считали загрязнения при производстве, и только 36,1% ответили, что примеси также могут образоваться вследствие неправильного хранения.

ВЫВОДЫ. Выявленные критические пробелы в знаниях о системе фармаконадзора и безопасности ранитидина обусловливают необходимость целенаправленного обучения сотрудников ливийских аптек и более активного законодательного урегулирования процедуры изъятия лекарственных препаратов из обращения.

Ключевые слова: фармаконадзор; безопасность лекарственных средств; ранитидин; H2-гистаминоблокатор; противоязвенные препараты; нитрозодиметиламин; изъятие из обращения; осведомленность

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INTRODUCTION

Drug safety is linked to the term pharmacovigilance (PV), which identifies adverse drug reactions (ADRs) after their use and marketing. PV infrastructure in low- and middle-income countries remains underdeveloped [1]. Ranitidine, a histamine-2 blocker, was withdrawn in 2020, after N-nitrosodimethylamine (NDMA) — a potent carcinogen — was detected in formulations [2, 3]. Libya's PV framework is only being initiated, with limited infrastructure for drug safety monitoring. Ranitidine remains available in some pharmacies, causing public health risks [4].

Study aim — to detect pharmacovigilance challenges among Gharyan pharmacies and explore the new growth areas based on awareness of ranitidine withdrawal and safety issues among pharmacy employees.

MATERIALS AND METHODS

Study design and participants. A descriptive cross-sectional study was conducted from January to March 2023, involving 130 employees from 58 private pharmacies in Gharyan City, Aljabal Algharbi area — Libya. Participants included pharmacists, trainees, physicians, and non-medical staff.

Sample size. Calculated using Lemeshow and Lwanga's formula (1991)[1] according to the equation of Steven K. Thompson as follows:

$$(N\text{-}1)\ (d\times d/z\times z)] + p(1-p), \qquad (1)$$

where: *n*, sample size; *N*, population size; *P*, probability (50%); *d*, error proportion (0.05); *z*: *T*-value confidence level 95%.

Questionnaire development. A structured questionnaire was designed in collaboration with faculty experts specialising in medical and applied statistics. This tool was based on validated surveys from prior studies and peer-reviewed literature to ensure robustness. The first section captured essential demographic characteristics of the participants. These included age (categorised as 19–24, 25–30, 31–36, 37–42, 43–48), sex (male/female), professional specialisation (trainee student, intermediate institute pharmacy diploma, advanced institute pharmacy diploma, pharmacy bachelor's degree, dentist, general physician, non-medical profession), distinguishing between private and public sector practice where applicable for trainee student, intermediate institute pharmacy diploma, advanced institute pharmacy diploma, and pharmacy bachelor's degree, and years of professional experience (grouped as 1–5, 6–10, 11–15, 16 and above). The second section focuses on the concept of PV and contains six questions about the PV fundamentals that can be answered with "Yes" or "No". Meanwhile, the third section relates to knowledge about ranitidine and the reasons for its withdrawal from the pharmaceutical market. It also includes six questions that can be answered with "Yes" or "No".

Data collection. Surveys were conducted in person at participating pharmacies during both morning and evening shifts to provide diverse staff availability. Participation was fully voluntary, and informed consent was secured before the questionnaires were distributed. Researchers were on hand to clarify any questions immediately, ensuring everything was understood. Ethical practices were prioritised by anonymising responses and underscoring the importance of respondent choice. This approach effectively combined comprehensive questionnaire design with a systematic and ethically responsible method of data collection, aimed at identifying gaps in knowledge regarding PV and drug safety practices.

Statistical analysis. Frequencies and percentages were computed using IBM SPSS Statistics Version No. 23.

RESULTS

To study the demographic factors, the researchers worked with a total of 130 employees. The largest age group was 25–30 years, with a total number of participants 45 (34.6%), and the smallest age groups were 37–42 and 43–48 years, 8 employees each (6.2%). The workforce was relatively young, with the majority (67.7%) being 30 years old or younger. The *Figure 1* shows the age distribution of the employees in private pharmacies in Gharyan city.

Regarding gender distribution, there were 46 (35.4%) male employees, while the female employees made 84 (64.6%). Otherwise, *Table 1* provides a clear overview of the educational background of the participants.

The most common qualification was "higher diploma in pharmacy (private)", with 38 (29.2%) employees. "General medicine", a slightly lower qualification, was reported in 37 employees (28.5%). While the least common qualifications were "intermediate diploma in pharmacy (private)" and "non-medical profession", each held by 2 employees, or 1.5% of the total. As for the number of pharmacists who held bachelor's degrees, they represent-

[1] Lwanga S, Lemeshow S. Sample Size Determination in Health Studies. A Practical Manual. WHO; 1991.

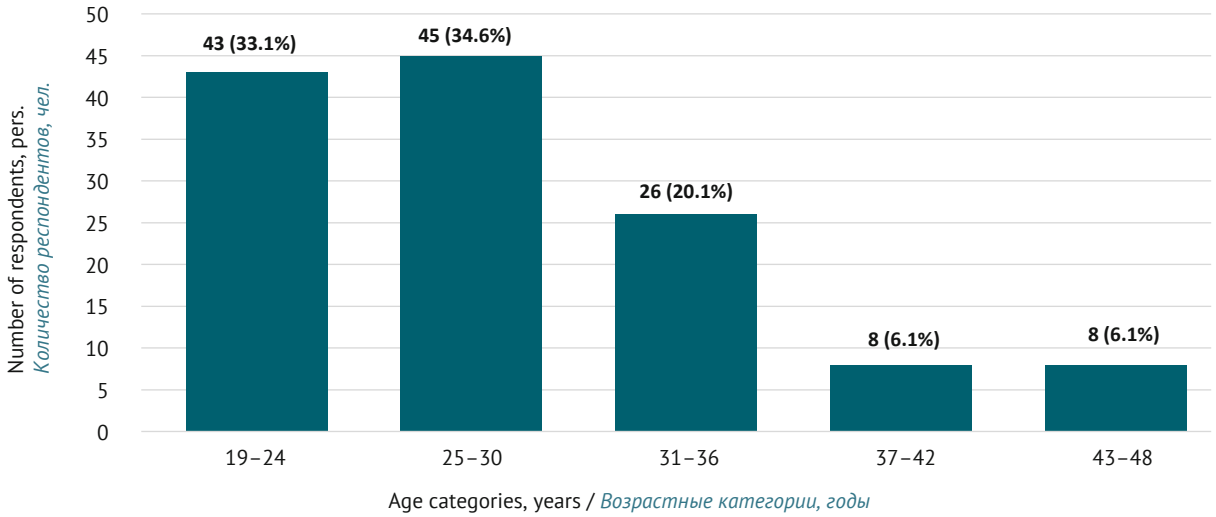

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Fig. 1. Age categories of employees in private pharmacies, Gharyan city, Lybia, *n*=130
Рис. 1. Возрастные категории опрошенных сотрудников частных аптек г. Гарьян, Ливия, *n*=130

Table 1. Education level of employees in private pharmacies, Gharyan city, Lybia, *n*=130
Таблица 1. Уровень образования опрошенных сотрудников частных аптек г. Гарьян, Ливия, *n*=130

Education level *Уровень образования*	Number of participants *Количество участников*	
	n	%
Trained student *Студент-стажер*	18	13.8
Intermediate diploma in pharmacy (private) *Диплом о неполном высшем фармацевтическом образовании (частное учебное заведение)*	2	1.5
Higher diploma in pharmacy (private) *Диплом о высшем фармацевтическом образовании (частное учебное заведение)*	38	29.2
Intermediate diploma in pharmacy (public) *Диплом о неполном высшем фармацевтическом образовании (государственное учебное заведение)*	8	6.2
Bachelor in pharmacy (private) *Бакалавр по специальности «Фармация» (частное учебное заведение)*	7	5.4
Bachelor in pharmacy (public) *Бакалавр по специальности «Фармация» (государственное учебное заведение)*	10	7.7
Dentist *Стоматолог*	8	6.2
General medicine *Диплом по специальности «Лечебное дело»*	37	28.5
Non-medical *Немедицинское образование*	2	1.5

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ed only 10 (7.7%) of the total number. Meanwhile, according to the years of experience of the study sample, it was found that most employees had 1–5 years of experience, with 84 (64.6%) sampled. As the experience increased, the percentage of participants decreased, so we found that only 7 (5.4%) employees had an experience of 16 years or more, which constitutes the lowest percentage *(Fig. 2)*.

For the PV concepts, nearly a third of participants (36.2%) did not know the term “pharmacovigilance”, and more than two-thirds of participants (63.8%) did not know that there was a PV center in Libya. This contradicts the participants’ answers about the center’s distribution of reports on drug side effects, as approximately (82%) answered “Yes”, and a small percentage

of participants (16.2%) had previously prepared reports on drug side effects. Regarding the participants' awareness about previous drug withdrawals due to their risks, less than two-thirds of the participants (55.4%) were aware of drug withdrawals by the Food and Drug Administration (FDA), while 44.6% were not aware of withdrawals (see *Table 2*).

Concerning ranitidine withdrawal variables, the majority of responses (79.2%) are "Yes" for prescription of ranitidine recently in pharmacy, which indicates a lack of vigilance regarding withdrawing ranitidine by FDA[2]. 69.2% of respondents did not know that ranitidine is a H2 blocker and misclassified it as an antihistamine, 61.5% of respondents answer "Yes" for that ranitidine causes carcinogenic impurity due to manufacturing, suggesting that most respondents are not aware of cancer risk due to improper storage or expired manufacturing dates exactly *(Table 3)*.

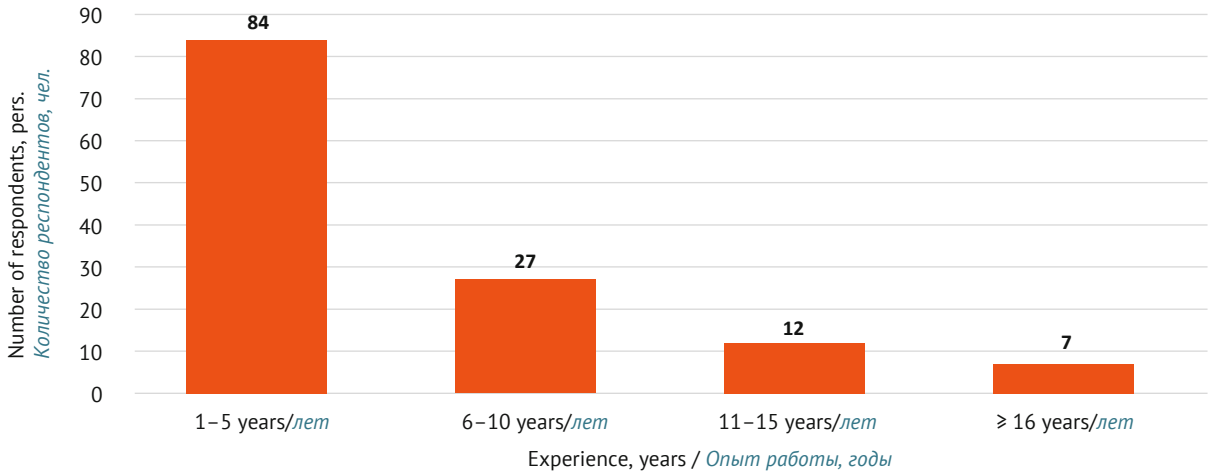

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Fig. 2. Participant's distribution according to experience, experience as private pharmacy employees, Gharyan city, Lybia, *n*=130

Рис. 2. Опыт работы опрошенных сотрудников частных аптек г. Гарьян, Ливия, *n*=130

Table 2. Awareness of employees surveyed in private pharmacies, Gharyan city, Libya, of pharmacovigilance principles

Таблица 2. Информированность опрошенных сотрудников частных аптек г. Гарьян, Ливия, об основных принципах фармаконадзора

Question *Вопрос*	**Frequency, abs. (%)** *Количество ответов респондентов, абс. (%)*	
	Yes / *Да*	**No / *Нет***
Are you familiar with pharmacovigilance? *Знаете ли вы, что такое фармаконадзор?*	83 (63.8)	47 (36.2)
Do you know if there is a pharmacovigilance Centre in Libya? *Известно ли вам о существовании Центра фармаконадзора в Ливии?*	47 (36.2)	83 (63.8)
Does the Centre distribute specialised forms for reporting drug side effects if they occur? *Рассылает ли Центр фармаконадзора специальные бланки, которые заполняются для выявленных побочного действия препаратов?*	106 (81.5)	24 (18.5)
Have you received training on pharmacovigilance before? *Проходили ли вы раньше обучение по фармаконадзору?*	102 (78.5)	28 (21.5)
Have you prepared a report on the side effects before? *Составляли ли вы раньше отчеты о побочном действии препарата?*	109 (83.8)	21 (16.2)
Have you heard of the medicine being withdrawn from the market due to safety concerns? *Слышали ли вы об отзыве препарата с рынка из-за проблем с безопасностью?*	58 (55.4)	72 (44.6)

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[2] FDA requests removal of all ranitidine products (Zantac) from the market. 01.04.2020. https://www.fda.gov/news-events/press-announcements/fda-requests-removal-all-ranitidine-products-zantac-market

DISCUSSION

This study reveals significant gaps in PV awareness and knowledge regarding ranitidine withdrawal among private pharmacy employees in Gharyan City, Libya. Although 63.8% of surveyed individuals reported familiarity with PV concepts, only previously filled out ADR reporting protocols (see *Table 2*). This notable disparity between theoretical awareness of the participants and practical knowledge points to systemic challenges observed in other low-resource settings, such as Morocco and Egypt, with fragmented PV systems and insufficient training regarding effective drug safety practices [1, 5].

A concerning revelation is that 79.2% of respondents continued dispensing ranitidine despite its global withdrawal in 2020. This regulatory noncompliance underscores gaps in both policy enforcement and availability of updated drug safety information. For instance, ranitidine is not a typical antihistamine. While it is classified as an H2 receptor antagonist, 30.8% responded that ranitidine is an antihistamine, which indicates a lack of understanding of the drug's classification by employees. Similar misclassifications have been documented in Saudi Arabia, where even licensed pharmacists struggled with drug categorisation, indicating broader regional educational deficiencies [6].

Notably, a survey revealed that while 61.5% of respondents linked NDMA impurities with manufacturing, only 36.1% understood its association with improper storage. This observation supports existing research indicating that high temperatures can lead to increased NDMA levels in ranitidine — a detail that is often overlooked in discussions of drug safety [2, 7]. The emphasis on manufacturing over storage risks may reflect a broader oversight in PV training programs, which rarely address real-world drug-handling scenarios. Such gaps highlight the urgent need for context-specific educational interventions that bridge theoretical knowledge and practical application.

The study's cross-sectional design limits causal inferences, and self-reported data may introduce recall bias. Geographic restriction to Gharyan City also affects generalisability, though the predominantly young, female workforce mirror demographic trends in Libyan urban pharmacies [4]. Despite these limitations, the findings underscore actionable priorities: integrating PV modules into pharmacy education, enforcing drug withdrawal protocols, and launching community initiatives stimulating public activity to emphasise NDMA risks. Collaborative efforts between policymakers and educators, as seen in Tunisia's successful PV reforms, could serve as a model for Libya [8].

CONCLUSION

This study reveals critical gaps in PV awareness and ranitidine-related knowledge among Gharyan City's private pharmacy employees. In particular, low PV awareness goes with ranitidine being dispensed from the pharmacies and pharmacy em-

Table 3. Awareness of employees surveyed in private pharmacies, Gharyan city, Libya, of ranitidine safety and its withdrawal from the circulation

Таблица 3. Информированность опрошенных сотрудников частных аптек г. Гарьян, Ливия, о безопасности ранитидина и его изъятии из обращения

Question *Вопрос*	Frequency, abs. (%) *Количество ответов респондентов, абс. (%)*	
	Yes / *Да*	No / *Нет*
Have you been dispensed or recently purchased ranitidine to your pharmacy? *Продавали ли вам в аптеке / закупали ли вы ранитидин для своей аптеки в последнее время?*	103 (79.2)	27 (20.8)
Is ranitidine an antihistamine? *Относится ли ранитидин к антигистаминным препаратам?*	40 (30.8)	90 (69.2)
Do you have information that ranitidine causes a carcinogenic impurity due to storage at high temperatures? *Считаете ли вы на основе известных вам данных, что хранение ранитидина при высокой температуре вызывает образование канцерогенной примеси?*	47 (36.1)	83 (63.9)
Do you have information that ranitidine causes carcinogenic impurities due to manufacturing? *Считаете ли вы на основе известных вам данных, что при производстве ранитидина образуются канцерогенные примеси?*	80 (61.5)	50 (38.5)
Do you know the possible side effects associated with the use of ranitidine? *Знаете ли вы о возможных побочных эффектах, связанных с применением ранитидина?*	77 (59.2)	53 (40.8)

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ployees misclassifying the drug / underestimating its risks. Persistent dispensing of withdrawn medications, coupled with pharmacological misclassifications, points out the need for urgent systemic reforms. To mitigate public health risks, Libya's Ministry of Health must prioritise standardised PV training, stringent regulatory oversight, and multidisciplinary collaborations to enhance drug safety guidelines. Future research should evaluate the long-term impact of educational interventions and assess NDMA contamination levels in retained ranitidine stocks. By addressing these gaps, Libya has the opportunity to enhance its PV practices in line with global standards, ensuring the health and safety of patients within the changing pharmaceutical vision.

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