The South African Nurse’s Knowledge of Occupational Human Immunodeficiency Virus Postexposure Prophylaxis in the Era of Controlled and Stable HIV Prevalence

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Featured Application: The paper contributes to the understanding of the challenges that occupational health and safety practice are facing regarding HIV in the era of controlled and stable HIV prevalence.

Abstract: Knowledge is a crucial aspect of nursing. Nurses, just like any other healthcare workers (HCWs), are empowered with the knowledge of Human Immunodeficiency Virus (HIV) Postexposure Prophylaxis (PEP) protocol to be followed, including post-exposure to blood and body fluids (BBFs). The utilization of HIV PEP demonstrated its capabilities to prevent HCWs from HIV infections. However, the practice in healthcare settings remains a challenge, as many HCWs do not adhere to the protocol. This study investigated how knowledgeable nurses are about HIV PEP in the era of controlled and stable HIV prevalence. Ninety-four nurses completed a self-administered questionnaire to provide information. A biostatistician assisted with data analysis, using Microsoft Excel converted to the STATA 13 format. Most (77.0%) were female with a mean age of 30 ± 9 years. The degree of knowledge was low, although the results showed that 90.43% of nurses had been informed about HIV PEP. Eighty (84%) did not know where to access HIV PEP, and (55.32%) were unaware of HIV PEP guidelines. A comparison between knowledge and work experience revealed that those with five years and less experience are less knowledgeable. There is a need to improve nurses’ knowledge of HIV PEP to reduce the risk of HIV acquisition from work-related activities.

Keywords: HIV; knowledge; nurses; occupational exposure; postexposure prophylaxis

1. Introduction

It is well known that knowledge is power [1–3]. The power in knowledge gives one confidence to practice without fear. Nurses, just like any other people, need knowledge to be empowered in performing procedures and activities within their practice. In nursing, knowledge is drawn from a range of sources, which are embedded in theory and practice. Nurses use their acquired knowledge to justify actions or stop unsafe practices to protect and prevent occupational infections such as Human Immunodeficiency Virus (HIV). South African nurses are at risk of occupational exposure, since the country is still heavily affected by HIV infections. Antiretroviral Therapy (ART) has converted HIV infection to a manageable chronic disease that is frequently treated at health care facilities [4]. Moreover, the World Health Organization (WHO) has recognized, recommended, and circulated HIV Postexposure Prophylaxis (PEP) guidelines as a valuable tool for preventing occupational HIV
infection [5]. Occupational HIV PEP emerged as an effective and ethical method with which to prevent HIV infection among healthcare workers (HCWs) [6,7].

Prophylactic PEP is designed for use as a preventative intervention which includes following a protocol and completing a program of postexposure management to prevent HIV infection after experiencing occupational exposure [8]. Additionally, PEP intervention recognizes the need to improve uptake and completion rates without differentiating between exposure sources but rather provides recommendations across all exposures [7]. The utilization of HIV PEP demonstrated its capabilities to protect and prevent HCWs from the transmission of occupational infections. While HIV PEP is recognized and highly recommended as a cornerstone and the only means of reducing the risk of HIV infection after accidental exposure in the healthcare setting, there is evidence that some HCWs, including frontline nurses, lack knowledge about PEP. Some studies have reported favorable knowledge of HIV PEP among HCWs, including nurses [9–11], while several others have found important knowledge gaps in PEP among healthcare workers [12–14].

Drawing from the above background, it is evident that poor knowledge of HIV PEP remains a challenge among HCWs, including nurses. The evidence shows that HCWs are reluctant to use and adhere to the reporting procedure and take precautionary treatment. For instance, a study that was conducted in the Hiwot Fana specialized university hospital in eastern Ethiopia on the knowledge of, attitude to, and practice of PEP against HIV infection among HCWs indicated that all the respondents had heard about HIV PEP and 83% of the participants had adequate knowledge of HIV PEP. However, 43.4% had an unfavorable attitude towards PEP, because they failed to report incidents of exposure and follow PEP protocol [15]. A study in southwestern Nigeria also showed that, among 181 HCWs who had heard about PEP and were aware of the national PEP guidelines, only 2.7% had good mean knowledge scores, while 57.3% and 40.0% had moderate and poor mean knowledge scores for PEP, respectively [16].

In South Africa, a study on the knowledge and uptake of occupational post-exposure prophylaxis amongst nurses caring for people living with HIV showed that 40% did not know what PEP is and 22% did not know or were not sure if it was available in the hospital where they were working. As such, poor knowledge made them not seek PEP when the need arose [17]. Failure to seek PEP placed them at risk of being infected with HIV and bloodborne infections. Similarly, inadequate knowledge of HIV PEP in South Africa has been reported among medical doctors in a tertiary hospital [18]. Hence, [5] argued that it is essential to provide relevant information on HIV PEP to nurses to help prevent the transmission of HIV. In support, [19] reported that HIV PEP knowledge “provides epidemiological data, identify unsafe practices, and reduce anxiety, and/or increase staff retention and productivity”.

With evidence from studies suggesting that nurses are at higher risk of the occupational acquisition of HIV in the healthcare setting, the dissemination of HIV PEP information was discussed and evaluated. The researchers argued that health care students should be provided with information related to HIV and PEP as soon as they enroll in a health care course in order for them to be knowledgeable and familiar with the correct measures and practices. Studies have suggested that information on HIV PEP should be shared repeatedly, evaluated, and updated among HCWs to identify the gaps existing in the knowledge of HIV PEP protocol among nurses. Lack of information sharing increases the shortage of knowledge, adding to the risk of acquiring HIV infections in the healthcare setting. Determining the knowledge and practice of PEP among nurses would identify their needs and the next line of PEP action. Therefore, this study assessed nurses’ knowledge regarding the HIV PEP protocol and guidelines for preventing occupational HIV infection. The results will highlight participants’ HIV PEP knowledge and the level of awareness that can be offered to nurses regarding HIV PEP services to prevent poor practices post-exposure to BBFs. Thus, the nurse’s knowledge level of HIV PEP may have an impact on the efficiency and effectiveness of occupational PEP services provided in healthcare settings. The results will further inform the development of interventions that may improve the knowledge of HIV PEP and the uptake of PEP services among nurses and other HCWs to reduce
the risk of occupational HIV infection transmission. The paper contributes to the understanding of the challenges that occupational health and safety practice are facing regarding HIV in the era of controlled and stable HIV prevalence. This paper is part of a larger data set collected for the research required for the completion of a master’s degree.

2. Materials and Methods

2.1. Study Area

This study was carried out in Tshwane district, Gauteng province of South Africa at a tertiary hospital. The HIV epidemic continues to be a major challenge in developing countries such as South Africa despite the availability of information on how to prevent the transmission of HIV infection. This tertiary hospital is one of the clinical facilities for health care students including nurses from different colleges in the Tshwane district. The hospital was selected for this study because it is a public health care facility providing specialized clinical inpatient and outpatient services. The hospital has a large volume of patients receiving ARTs. Several sickbays and clinics refer patients to this facility, and their HIV status is not known. The researchers assumed that the same patients receive medical and surgical treatment from this hospital, which places HCWs at risk of exposure to bloodborne infections if they accidentally come into contact with BBFs. It is also well documented in the literature that health care workers are exposed to needle stick injuries and percutaneous exposures to fluids of suspected and confirmed HIV cases while at work [20].

2.2. Study Design

This study adopted a quantitative non-experimental, descriptive survey because the researchers sought to systematically study and explain the nurses’ knowledge of HIV PEP through the generation of numerical data so that the results can be projected to a larger population. The study participants were male and female nurses aged between the ages of 18 and 59 years who had been working in an operating room, emergency room, intensive care unit, or maternity ward in the selected hospital for more than three months. The reason for the selection of the clinical areas was that nurses are most vulnerable to accidental occupational exposure as most of the time they are actively dealing with emergency and very sick patients. The study sample was selected using a systematic sampling method so that every person in the targeted population has a chance of being selected [21]. The study selected 100 nurses \((n = 100)\) from a population of 312 nurses to participate in the study by selecting every third name from a combined list of all nurses working in the selected clinical departments in Tshwane district hospital. Approval for the study was obtained from the university ethics committee and permission was obtained from the selected hospital. All the selected nurses were invited to complete a questionnaire. They were assured that the information provided would remain anonymous and confidential. They all signed a consent form to voluntarily complete a questionnaire. Student nurses and other HCWs were excluded from the study.

2.3. Data Collection

A structured, pre-tested, self-administered questionnaire was used to collect data. A questionnaire was developed by the authors in English from the relevant literature to address the objectives of this study. The biostatistician and HIV experts reviewed the questionnaire, and it was piloted in nurses working at sickbays and clinics that are affiliated with the selected hospital. A pilot study was conducted to assess the content and face validity of the questionnaire. Eight questions were used to assess the level of knowledge about HIV PEP. Closed-ended questions were multiple choice or answered by yes or no, true or false. Open-ended questions asked them to define or explain HIV PEP items as indicated. The researcher, in consultation with the biostatistician, used Cronbach’s alpha co-efficient to test the reliability. The reliability coefficient was 0.65, proving the reliability and acceptability of the instrument. The researchers distributed 100 questionnaires to the selected nurses.
The completed questionnaires were posted into sealed boxes with small openings left at each selected ward. The principal researcher collected the boxes weekly for four weeks.

2.4. Data Analysis

Data analysis was conducted in collaboration with a biostatistician using the STATA 13 statistical software. All the collected questionnaires were sequentially numbered before data collection, making it easier to go back to each questionnaire during the data cleaning process. Different items and responses in the questionnaire were assigned codes for easy capturing and analysis. An Excel spreadsheet was used to capture the data and converted to STATA 13. Both descriptive and inferential statistics were applied during the data analysis. A Z-score test was applied to determine the level of respondents’ HIV PEP knowledge and compared to a critical z-score of 1.96, and a Chi-square test was conducted to determine the association between the biographical characteristics and knowledge of HIV PEP of the participants. A p-value of 0.05 was used as the level of significance of the study. The results were summarized in frequencies and percentages. A scoring system was generated manually, and the respondents were given a score on each correct answer provided. The overall knowledge score was determined based on the sum of correct answers to the eight knowledge-based questions. A correct response to each question received one point. Respondents who scored greater or equal to seven correct answers out of eight were considered to have “good knowledge”. Those who scored less than seven but above five were considered to have “average knowledge”, while those who scored less than five were considered to have “poor knowledge”.

3. Results

3.1. Sociodemographic Characteristics

The socio-demographics of the respondents are summarized in Table 1. Out of 100 questionnaires distributed, 94 questionnaires were completed and returned, giving a good response rate of 98%. The majority of respondents were female 72 (77.0%) compared to the 23% of male counterparts. The mean age of the respondents was 30 ± 9 years and ranged between 18 and 59 years. Of the 94 respondents, the majority were 66 (70%) registered nurses, followed by 24 (26%) enrolled nurses, and the number of enrolled assistant nurses in the sample was 4 (4.0%). A clear majority of the respondents (52, 55.0%) had an undergraduate diploma in general nursing science, while 27 (29.0%) had a certificate in nursing, 12 (13.0%) had an undergraduate degree in nursing, while only 3 (3.0%) respondents had a post-graduate degree in nursing. Most of the respondents (36, 38.30%) had 6–15 years’ experience working in their specialized clinical area, and 29 (30.85%) respondents had less than 5 years of working experience in their specific clinical area.

Table 1. Respondents’ socio-demographic characteristics.

| Variables | All N (%) |
|-----------|-----------|
| **Gender** |           |
| Female    | 72 (77)   |
| Male      | 22 (23)   |
| **Age**  |           |
| 23–29     | 20 (21.28) |
| 30–39     | 26 (27.66) |
| 40–49     | 25 (26.60) |
| 50–59     | 16 (17.02) |
| Not indicated | 6 (7.44)  |
Table 1. Cont.

| Variables                  | All N (%) |
|----------------------------|-----------|
| **Nursing category**       |           |
| Registered nurse            | 66 (70)   |
| Enrolled nurse              | 24 (26)   |
| Enrolled assistant nurse    | 4 (4)     |
| **Educational level**       |           |
| Certificate                 | 27 (29)   |
| Diploma                     | 52 (55)   |
| Undergraduate degree        | 12 (13)   |
| Postgraduate degree         | 3 (3)     |
| **Years of experience**     |           |
| 03 months–05 years          | 29 (30.85)|
| 06–15 years                 | 36 (38.30)|
| 16–25 years                 | 23 (24.47)|
| 26–32 years                 | 5 (5.32)  |
| Not indicated               | 1 (1.06)  |

3.2. Knowledge of HIV PEP Protocol and Guideline

Table 2 shows the respondent’s level of knowledge of the HIV PEP protocol and guidelines. Based on the measurement of different variables, and as per scores on the scoring system, the respondents in this study had a poor knowledge of HIV PEP, despite a good proportion of 85 (90.43%; p-value < 0.0001) of respondents who had heard about HIV PEP before. Out of 94 respondents, the majority (71, 75.0%) were informed by their clinical area, whereas 14 (15.0%) were informed by the media (z-score = 7.0; p-value = < 0.0001). Two (2.0%) were informed by friends and family, whilst 7 (8.0%) were informed by unspecified others. Among the 85 (90.43%) who indicated that they were informed, a significant majority (72, 79.79%) knew the basic concept of HIV PEP, 3 (3.19%) gave the incorrect meaning of HIV PEP (z-score = 10.6; p-value = < 0.0001), while 10 (17.02%) respondents left the question unanswered.

Table 2. Respondents’ knowledge of HIV PEP.

| Variable                                      | Response Rate N (%) | z-Score; p-Value |
|-----------------------------------------------|---------------------|-----------------|
| **Ever heard information about HIV PEP**      |                     |                 |
| Yes                                           | 85 (90.43%)         |                 |
| No                                            | 9 (9.57%)           |                 |
| **Source of information about HIV PEP**       |                     |                 |
| Media                                         | 14 (15%)            |                 |
| Clinical area                                 | 71 (75%)            | 7.0015;         |
| Friends and family members                    | 2 (2%)              | 0.00001         |
| Other (specify)                               | 7 (8%)              |                 |
| **Meaning of HIV PEP**                        |                     |                 |
| Correct                                       | 72 (79.79%)         |                 |
| Wrong                                         | 3 (3.19%)           | 10.6581;        |
| Unanswered                                    | 10(17.02%)          | 0.00001         |
| **Knowledge of reporting to the supervisor immediately after occupational exposure** | | |
| Yes                                           | 83 (88.30%)         | 8.95930;        |
| No                                            | 11 (11.07%)         | 0.00001         |
Table 2. Cont.

| Variable                                      | Response Rate N (%) | z-Score; p-Value |
|-----------------------------------------------|---------------------|-----------------|
| Place where PEP services are offered in the facility |
| Correct                                       | 14 (16%)            | -9.6271; 0.0001 |
| Incorrect                                     | 80 (84%)            |                 |
| Availability of HIV PEP guidelines in the hospital |
| Yes                                           | 52 (55.32%)         | 1.45860;        |
| No                                            | 42 (44.68%)         | 0.1443          |
| Maximum time delay to access HIV PEP services after an accidental occupational exposure |
| Within 72 h                                   | 52 (55.32%)         | 4.16330; 0.00001 |
| After 36 h                                    | 26 (27.66%)         |                 |
| Do not know                                   | 13 (13.83%)         |                 |
| Drugs recommended for HIV PEP                 |
| Correct                                       | 37 (39.36%)         | -2.9173; 0.0035 |
| Incorrect                                     | 34 (36.17%),        |                 |
| Unanswered                                    | 23 (24.47%),        |                 |

Out of 94 respondents, the majority of the respondents (83, 88.30%) had knowledge of reporting to the supervisor immediately after occupational exposure, compared to 11 (11.07%) that did not know to do this (z-score = 8.9; p-value < 0.0001). Despite many respondents knowing that they should report first to the supervisor, there were 80 (84%) respondents who did not know a place where PEP services were offered in the facility (z-score = -9.6; p-value < 0.0001), and more than half (52, 55.32%) were unaware of the availability of HIV PEP guidelines in their hospital, although this did not significantly differ from the 42 (44.68%) who knew about the availability of HIV PEP guidelines in the hospital (z-score = 1.45; p-value = 0.1443 > 0.05).

The maximum time delay to access HIV PEP services after an accidental occupational exposure was 72 h, as indicated by the majority of respondents (52, 55.32%), compared to 26 (27.66%) who indicated that it is within 36 h (z-score = 4.16; p-value < 0.0001). Although 55.32% of the nurses knew the best time to initiate PEP regimens for HIV, a significantly lower number of respondents (37, 39.36%) could correctly identify the recommended drugs used as precautionary measures for HIV infection, compared to 34 (36.17%) who indicated the wrong drug(s) used in their hospital for HIV PEP. An alarming percentage (23, 24.47%) of the nurses did not answer this question (z-score = -2.9173; p-value = 0.0035 < 0.05).

Although it was not statistically significant, the variables compared with the knowledge of HIV PEP showed that the nurses who had had above five years of experience were likely to have a better knowledge than those who had had less than five. Nurses whose source of knowledge of HIV PEP was from the clinical setting were more likely to have good knowledge of HIV PEP’s meaning than their counterparts.

3.3. Association between Biographical Characteristics and Knowledge of HIV PEP

Table 3 presents the association between biographical characteristics and knowledge of HIV PEP. The results of the study showed that there is enough evidence to conclude that the biographical characteristics of respondents had an association with their knowledge of HIV PEP, gender, age, professional qualification, and working experience. Gender (Chi-square = 12.27; p-value = 0.0021 < 0.05) and the respondents’ professional qualifications (Chi-square = 13.25; p-value = 0.01101 < 0.05) had an association with their responses to the knowledge question on PEP being started as soon as possible, preferably within 72 h of exposure. Age had a strong association with knowledge and the understanding that precautionary measures should be taken when handling
blood and body fluids (\(\chi^2 = 191.15; p\)-value = 0.00026 < 0.05); after exposure to hazardous blood and body fluids, health care workers can take Post Exposure Prophylaxis to prevent HIV infection (\(\chi^2 = 1632; p\)-value = 0.0117 < 0.05). HIV Post Exposure Prophylaxis is a short-term medical therapy to prevent the spread of HIV infection (\(\chi^2 = 1077.075; p\)-value = 0.0312 < 0.05). The results further showed that being more experienced had a strong association with the knowledge and understanding that HIV PEP is a short-term medical therapy to prevent the spread of HIV infection (\(\chi^2 = 170.0244; p\)-value = 0.0039 < 0.05) and that, as immediate first aid after exposure to hazardous blood and body fluids, health care workers should wash the affected area with clean water and soap (\(\chi^2 = 47.06067; p\)-value = 0.0001 < 0.05).

Table 3. Association between biographical characteristics and knowledge of HIV PEP.

| Biographical Characteristics     | Knowledge and Understanding about HIV/AIDS Infection and PEP                                                                 | Chi-Square | Degrees of Freedom | p-Value |
|---------------------------------|-------------------------------------------------------------------------------------------------------------------------------|------------|--------------------|---------|
| Gender                          | Post Exposure Prophylaxis is started as soon as possible, preferably within 72 h of exposure.                                  | 12.27480   | 2                  | 0.00216 |
| Age                             | Precautionary measures should be taken when handling blood and body fluids.                                                    | 191.1544   | 128                | 0.00026 |
| Professional Qualification      | HIV Post Exposure Prophylaxis is a short-term medical therapy to prevent the spread of HIV infection.                           | 1077.075   | 992                | 0.0312  |
| Working Experience              | HIV Post Exposure Prophylaxis is started as soon as possible, preferably within 72 h of exposure.                               | 13.25414   | 4                  | 0.0101  |
|                                 | As immediate first aid after exposure to hazardous blood and body fluids, health care workers should wash the affected area with clean water and soap. | 47.06067   | 16                 | 0.0001  |

4. Discussion

This study assessed the knowledge of nurses regarding HIV PEP in order to identify the risks of contracting HIV infection in the era of controlled and stable HIV prevalence. The nurses’ working experience in the clinical areas ranged from 4 months to 32 years. The results showed that the hospital from which the respondents operated does have HIV PEP protocol and guidelines in place. A significant majority (90.43%; \(p < 0.0001\)) of the respondents reported to have been informed about HIV PEP protocol, similarly to the study conducted in Nigeria in which 90.4% were informed of HIV PEP [11]. However, this index study has shown that a significantly high proportion of respondents were knowledgeable about the meaning of HIV PEP (79.79%; \(p < 0.0001\)) and informed of the clinical practice, compared to the rates of 22.42% to 69.5% observed in other studies [13,15].

The majority of respondents in this index study had knowledge of reporting to their immediate supervisor prior to seeking HIV PEP (88.30%; \(p < 0.0001\)), although this was low compared to the rates of 95.3% found in a similar study [22]. The poor reporting of occupational exposures has been reported by other studies [5,11]. In line with this index study finding, our study showed that the majority of respondents indicated that the maximum time delay to access HIV PEP services after an accidental occupational exposure is within 72 h. The study found that a lack of knowledge regarding reporting protocol and guidelines increases the lack of reporting occupational exposures over time. Thus, the contact person in the event of occupational exposure should be known by all HCWs at the hospital level. Proper awareness could encourage nurses to protect themselves from exposures to
BBFs, and seeking PEP can prevent contracting the infection. Poor awareness implies poor HIV PEP practices, resulting in the occupational transmission of HIV infection, as the study found that level of professional qualification and working experience had an association with the responses provided by the respondents.

On the other hand, almost half (44.68%; \( p = 0.14 > 0.05 \)) of the respondents did not know if HIV PEP services were available in their own hospital, although this did not significantly differ from the 55% that knew of PEP services’ availability. This finding is lower than 60% of the participants who were unaware of the availability of PEP guidelines [12]. This indicates a poor adherence to reporting procedure and implies that the respondents will not report occupational exposures in time, increasing the risk of HIV infection transmission amongst HCW. Adherence to the reporting protocols and guidelines is fundamental for the prevention of the accidental acquisition of HIV infection in healthcare settings. Furthermore, it assists with the proper immediate management of the exposed individual in the control and prevention of the infection. Among the respondents, 84% did not know a place to seek HIV PEP in their own hospital, which was significantly lower than those who knew (16%) \( (p < 0.0001) \). This result means that when there is a need for PEP service, nurses will experience delays as they do not know the exact place to access PEP services. According to [23], this is a reason why many HCWs are not reporting occupational exposures, as they are not sure where to report. This finding highlights the implications of the increased risk of unknown ongoing HIV transmission among HCWs. Therefore, a need to continuously train, inform. and support HCWs regarding HIV in general to strengthen their practice in managing occupational exposure to HIV infections is recommended. Health care workers who recognize the presence of occupational HIV risk are motivated to practice universal infection control measures.

Comparison between the knowledge of HIV PEP and work experience revealed that those with five years and less experience are less knowledgeable compared to those with higher than 5 years’ experience in responding to the question that HIV Post Exposure Prophylaxis is a short-term medical therapy to prevent the spread of HIV infection (Chi-170.024; \( p=0.0039 \)) and, as immediate first aid after exposure to hazardous blood and body fluids, health care workers should wash the affected area with clean water and soap (Chi-47.06067; \( p<0.0001 \)). On the positive side, most of the study respondents knew the preferred time delay to take PEP (55.32%), and the results found a strong association with gender for this response (Chi-12.27; \( p=0.00216 < 0.05 \)). These results are far better than (5.3%) those reported in eastern Ethiopia [15]. It is advisable to provide HIV PEP within an hour to 72 h following exposure, since the efficacy of HIV PEP depends on the time that it is initiated [24]. Although 39.36% had knowledge of the recommended drugs for HIV PEP, it was disturbing to realize that 24.47% of the nurses left the question unanswered and 36.17% answered incorrectly with a significant difference \( (p = 0.03 < 0.05) \). The HIV PEP involves the use of ART drug combinations with some specific instructions relating to their side effects, use, and route of administration. The poor knowledge of recommended HIV PEP drugs implies that nurses do not have adequate knowledge of the benefits, use, route, and completion of course for the effectiveness and side effects of the drugs, and implies that nurses could stop them when they experience side effects. The literature shows that many HCWs stop taking ARTs before finishing the course and choose not to follow up as they are supposed to.

5. Conclusions

This study assessed nurses’ levels of knowledge and understanding of HIV PEP. The results show that the majority of nurses are not familiar with most of the important information included in the guidelines to prevent the occupational transmission of HIV infection. Given that the majority of nurses had heard information about HIV PEP before and did not know that there were HIV PEP services within their hospital, were unable to identify the place to access HIV PEP in case of exposure, and did not know the recommended drugs for HIV PEP, it can be seen that the HIV PEP knowledge and understanding amongst nurses is a concern and thus more awareness of HIV PEP amongst nurses
is needed. To improve the HIV PEP knowledge among nurses, this study recommends increasing awareness through training and educating HCWs on HIV PEP protocol and guidelines.

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**Data Availability:** The data used to support the findings of this study are available from the corresponding author upon request.

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