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Research

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Analysis of post-authorisation safety studies in developing countries: the Middle Eastern and North African experience

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Abstract

Introduction: *post-authorization safety studies (PASS) play a vital role in pharmacovigilance. However, there is a notable gap in experience and knowledge regarding PASS practices in developing countries. This study aimed to review the PASS implementation status in the region, identify the gaps and challenges and suggest actionable insights for enhancing the understanding and implementation of PASS in the Middle East and North African region (MENA).* ***Methods:*** *the study utilized a three-pronged approach: reviewing regional and national PASS legislations, analyzing PASS studies conducted in the MENA region and registered in the European Union Post-authorization studies register (EU PAS) and ClinicalTrials.com databases for the years 2020-2022, and circulating a questionnaire among MENA pharmacovigilance professionals.* ***Results:*** *despite the regional initiative, national implementation of Pharmacovigilance (PV) legislation remains inconsistent across the region, with significant variations in adherence and an entire lack of PASS guidance in some countries. Only 21 PASS studies were identified over three years on the EU PAS register. Low numbers of PASS studies in MENA reflect a broader issue of inconsistent execution. This inconsistency is compounded by absence of imposition of PASS by health authorities, and reliance on the studies conducted in the EU. Key challenges include difficulties in initiating and obtaining approval for PASS studies, illustrating further complexities and variances of conducting these studies in MENA.* ***Conclusion:*** *the adoption and enforcement of PASS regulations vary widely across countries, with Saudi Arabia, Egypt, United Arab Emirates (UAE), and Israel leading in implementation. By adopting comprehensive PASS frameworks and advocating their enforcement by the health authorities, as well as application and facilitation of initiation, the region can improve pharmacovigilance and patient safety, whereby addressing the unique healthcare needs and genetic diversity of its populations. Encouraging joint PASS studies can be a way forward to overcome resource limitations. Addressing these challenges will be crucial for advancing medication safety surveillance and post-marketing evaluations in developing countries.*

Introduction

When assessing the safety and effectiveness of a new drug, randomised controlled trials (RCT) are regarded as the most reliable method. However, despite their advantages in providing measures of the safety and efficacy of the new medications, it is often uncertain how applicable they are to real-world patients, especially when drugs developed in one region are registered and used in others with different patient demographics and characteristics. Enforcing strict eligibility criteria that exclude patients with comorbidities or those above a certain age usually results in trial respondents being different from the overall clinical population [1]. Therefore, upon placing the medicine on the market, to gain a better understanding of the safety profile of the new drug in real-world clinical settings, post-authorisation safety studies are often conducted. These studies are particularly crucial in emerging markets, regions like the MENA, where diverse patient demographics and developing PV systems present a unique blend of challenges and opportunities for drug safety evaluation.

The pharmacovigilance system in MENA is developing at various paces in different countries of the region; there is a lack of standardization and implementation of documents describing individual PV activities on a regional as well as local level [2-5]. The lack of awareness among healthcare professionals about reporting in MENA leads to poor adverse drug reaction (ADR) reporting practices, which in turn leads to a lack of real-world data in the local population [6-9]. Several authors [10-12] further highlight that the MENA region is characterised by high rates of diabetes, genetic disorders, and increasing cancer incidence. These challenges provide a compelling rationale for conducting post-authorisation safety

studies to evaluate the safety of medications in the region and to gather comprehensive safety data on the local population [13-15]. The study aimed to closely examine the degree of implementation and prevalence of PASS in the MENA region, identify existing operational gaps and challenges in the process of PASS conduct, and offer practical recommendations to improve the understanding and implementation of PASS. By doing so, the study seeks to enhance drug safety within the unique and varied healthcare landscape of the MENA region.

Methods

Study design: this study utilized a mixed methods design. The approach included a review of good pharmacovigilance practices (GVP) for Arab countries and available national guidelines. Good pharmacovigilance practices for Arab countries were additionally compared with the European Medicines Agency (EMA) GVP guidelines, which were taken as a benchmark and also used as the foundation when preparing GVPs for Arab countries. Furthermore, the study included examination of data from public registries, where the majority of the PASS and observational studies (phase IV) have been found: PASS studies registered in the EU PAS Register (currently found under The European Network of Centres for Pharmacoepidemiology & Pharmacovigilance (ENCePP) website) and ClinicalTrials.gov. This phase involved analysis of the studies by country and possible trends, which helped provide an overview of the current state and progression of PASS studies in the MENA region. Lastly, the methodology incorporated the analysis of responses to a specifically designed questionnaire, which consisted of 22 questions. This questionnaire was prepared to obtain responses from professionals working in the PV field in the region and to gather insights into the application of guidelines and challenges with PASS studies conducted within the MENA region. The responses helped identify gaps and areas of opportunity to enhance pharmacovigilance practices.

Study setting: the study was conducted in the MENA region, covering countries with varying levels of pharmacovigilance maturity and national guidelines availability. Review of the registries included data from January 2020 to November 2022. The designed questionnaire was distributed in October 2022, with the data lock point for the responses collection of 30th November 2022.

Study participants: additionally, a survey was sent to pharmacovigilance professionals in the region to gather insights into the practical challenges of conducting PASS studies. Eligibility criteria for survey participants included professionals actively engaged in pharmacovigilance and patient safety activities in the MENA region.

Variables: the primary variables examined were the number and characteristics of PASS studies in the MENA region, adherence to regulatory guidelines, and the barriers to study initiation and approval. Survey responses were used to further identify operational challenges and the actual extent of guidelines application.

Data sources/measurement: based on the data extracted from the registries, the study specifically analyzed the number, type, and geographic distribution of these studies within the MENA region, highlighting the involvement of different countries and any observable trends over the three years. Data extraction included study identifiers, study design, status (ongoing, planned, completed), and whether the studies were voluntary or imposed by regulatory authorities. The survey consisted of 22 questions designed to gather qualitative data on the actual application of PASS guidelines and challenges encountered in the execution of these studies.

Bias: to address selection bias, the survey was distributed targeting a diverse range of pharmacovigilance professionals working in different sectors, including regulatory bodies, pharmaceutical companies, and distributors who provide PV services. This approach aimed to ensure a broad representation of perspectives on

PASS implementation. Cross-referencing data from the EU PAS Register and ClinicalTrials.gov helped to validate the findings and mitigate information bias. Additionally, the use of publicly available registries ensured transparency and consistency in data collection, reducing the likelihood of reporting bias. However, a limitation remains due to the reliance on publicly registered data, which may not capture all PASS activities, particularly those not registered in international databases.

Study size: twelve national publicly available guidelines were examined. The study reviewed a total of 31 PASS studies and 922 observational studies from the specified registries. A total of 64 responses were collected from the survey, with 19 responses analyzed from MENA professionals.

Quantitative variables: quantitative data included the number of studies, types of PASS (voluntary vs. imposed), and study status (ongoing, planned, or completed). Statistical comparisons were made between the number of studies in MENA and the EU to highlight the disparities.

Statistical methods: given the descriptive nature of the study, no advanced statistical modeling was applied. The focus remained on providing a clear, factual presentation of the current state of PASS in the MENA region, drawing on both quantitative registry data and qualitative survey insights to inform recommendations for improving pharmacovigilance practices in the region.

Ethics approval: the questionnaire used for this article is approved by the Health, Science, Engineering and Technology Ethics committee of the University of Hertfordshire (United Kingdom) and Protocol number is LMS/PGR/UH/05125.

Results

Participants: the study identified and reviewed 31 PASS studies and 922 observational studies registered in the EU PAS Register and ClinicalTrials.gov databases from January 2020 to November 2022. After removing duplicates, only 21 unique PASS studies were conducted in the MENA region within the three years. The designed questionnaire included 22 questions, contacted 206 people from LinkedIn connections and received 64 responses, which is approximately 31% of those contacted. Fifteen connections informed that they are not involved with PASS studies in their organizations and, therefore, couldn't provide the answers (11 respondents were from MENA). Eight other connections provided various answers on why they could not fill in the questionnaire; seven of them were from the MENA region (Table 1). One person started the questionnaire but skipped the majority of the questions. In total, 40 connections answered the questionnaire. This accounts for only a 23% response rate. Nineteen respondents were from the MENA region whose answers were used for analysis.

Descriptive data: Figure 1 further provides an overview of the respondents` demographics in terms of location of their current job.

Outcome data: given the nature of the study, there are no data to present here.

Analysis of legislations

Good pharmacovigilance practices guidelines for Arab countries and national guidelines: to align with global standards, the GVP guidelines for Arab Countries were established in 2015, drawing inspiration from the European GVP model [9]. This adoption aimed to standardize pharmacovigilance practices across the region without the necessity of developing entirely new guidelines. However, not all the countries in the region follow it (Table 2). While the GVP for Arab Countries serves as the primary guideline, national variations tailored to each country's healthcare system are encouraged, and many countries in the region have their own guidelines. The implementation of these guidelines, however, varies significantly. A few countries, such as Tunisia, Israel, Jordan and Morocco, have established local comprehensive legal frameworks for pharmacovigilance. Kuwait,

Qatar and Bahrain follow GVP for Arab Countries as they lack national GVP guidelines. The Kingdom of Saudi Arabia (KSA) and Egypt have extensive national guidelines closely resembling GVP for Arab Countries and also include chapters focusing on adaptation to local requirements [16-35].

PASS chapter: good pharmacovigilance practices for Arab Countries guidelines for PASS studies (Module VIII) is a copy of EMA GVP Module VIII on PASS, with minor differences, such as the timing of the protocol approval and to some extent the categorization of PASS studies. However, as with the guidelines, the availability of guidance on PASS also varies from country to country (Table 2). Countries following GVP for Arab Countries have the PASS chapter in full, as outlined in the EMA GVP Module VIII. Some countries, such as Yemen, Algeria, Sudan, and Morocco, have national guidelines but lack PASS study chapters. The United Arab Emirates and Oman guidelines include PASS chapters, but they only provide a short description of what PASS studies are, lacking guidance on initiating, conducting, and concluding studies.

Databases analysis: good pharmacovigilance practices guidelines for Arab countries outline the requirements for non-interventional PASS studies to be included in local PASS registries, promoting transparency and exchange of safety information; however, no national publicly available registry for PASS studies has been found in the region. Therefore, the international public registries were examined. The number of studies found in the EU PAS Register and Clinicaltrials.com database for the period starting on 01.01.2020 and ending on 30.11.2022 was 31 and 922 respectively (Table 3, section A). The number of PASS studies conducted in the EU region for the same period was added for comparison to see the difference between developed and developing regions. There are also 24 ongoing and 23 studies planned in the MENA region (Table 3, section B).

When the duplicates were removed from the numbers (the studies conducted in several countries were counted as 1 study), only 21 PASS studies were conducted in MENA within 3 years. The breakdown of studies by year showed no apparent trend of increasing or decreasing numbers (Table 3, section C). Out of 21 completed or ongoing PASS studies, the majority, 15 studies, were voluntary (72%), and 6 were imposed (28%). Out of 6 imposed studies, 4 studies were category 3, that were initiated by the companies themselves; 1 study was of category 1, that was imposed as a condition for marketing registration; and 1 study category was not specified. Out of all the PASS studies conducted in MENA, 20 studies were also conducted in the EU region, and only 1 study was a national study in Lebanon. The number of planned studies without duplicates is 17, which represents a considerable increase in the number of studies. Further analysis of PASS study data for the MENA region reveals a significant difference in the number of studies conducted in each country. Figure 2 illustrates the number of PASS studies found on the EU PAS Register by country, while Figure 3 reflects the number of observational studies by country.

PASS studies in the MENA region show a distinct distribution among the countries, with most countries not conducting any studies. Israel, KSA, and UAE emerged as the leading countries based on the number of PASS studies conducted over the three years of analysis. When compared the numbers of observational studies in the MENA region, the number of studies is low in most countries as well, with Egypt being the standout leader and Israel and KSA following with 44 and 24 studies.

Questionnaire analysis: seven respondents (37%) reported an increase in the number of PASS studies. Two respondents attributed this increase to new safety concerns involving high-risk molecules, such as Ranitidine (UAE, Qatar), or to stricter regulatory requirements reflecting a strengthened regulatory system in the country (Iraq). However, 6 respondents (31%) did not notice any change (Figure 4). The remaining respondents pointed out that in the MENA region,

there have been hardly any PASS studies conducted by their companies. Based on the answers of 12 respondents (63%), three main reasons emerged as justification for the absence of PASS in the region: the use of generic medicines which do not require PASS, reliance on limited PASS studies from the EU and lack of clear regulations. When the survey respondents were asked to detail their main challenges in the process of PASS studies, their responses, summarised in Table 1 (answers 8-13), highlight that in the MENA region, the primary difficulties revolve around the initiation and approval stages of PASS studies. Another respondent highlighted that conducting the studies is often time and resource-consuming, therefore, making it difficult for MAHs to initiate a study promptly, and, as a result, rely on EU-based studies.

Discussion

Legislation: the legislative framework governing PASS in the Middle East and North Africa region presents a fragmented landscape, largely attributed to the absence of a unified legal foundation (Table 2). The adoption of GVP for Arab Countries, inspired by the European model, marks an attempt to standardise pharmacovigilance practices. Despite this effort, the adherence to these guidelines is inconsistent across the region. This discrepancy underscores the challenges in establishing a regulatory environment conducive to the effective conduct of PASS. The situation is further complicated by national variations, where countries like Tunisia, Israel, and Morocco have developed comprehensive local frameworks, contrasting sharply with those relying on the regional GVP for Arab countries due to a lack of national guidelines. The GVP for Arab Countries' approach to PASS studies is mirroring the EMA GVP Module VIII with minor adjustments. This reliance may limit the guidelines' adaptability to local healthcare system nuances and patient demographics, potentially hindering the applicability and effectiveness of PASS in addressing regional safety concerns. Furthermore, the variability in the inclusion and detail of PASS chapters across national guidelines highlights a significant gap in regulatory support for these critical studies. The absence of comprehensive PASS guidance in several countries' national guidelines reflects a broader issue of insufficient regulatory infrastructure to support the robust conduct of PASS activities in the region.

Databases analysis: as seen from the analysis of the studies found in public registries, Israel, the Kingdom of Saudi Arabia, and the United Arab Emirates have emerged as the frontrunners in the conduct of PASS studies, with Kuwait trailing closely behind. Egypt, Israel, and KSA are the leaders in observational studies, followed by the UAE and Tunisia, who have participated in a considerable number of studies as well. This pattern highlights the pivotal role of regulatory guidance in fostering pharmacovigilance research. The evident correlation between the volume of studies and the existence of comprehensive GVP guidelines, particularly detailed chapters on PASS, suggests that the regulatory environment significantly influences the pursuit and implementation of such studies. As Egypt, Israel and KSA have the most extensive and detailed GVP guidelines and PASS chapters, they are also leading in the number of performed studies. Kuwait, Tunisia and UAE either follow GVP for Arab countries or have their own national GVP guidelines, which provide detailed guidance and allow them to conduct PASS studies, which also points to the ability to conduct studies better.

An analysis aimed at discerning trends in the registry data revealed a stable count of studies over the analysed three-year span without apparent increase or decrease in numbers. However, the registries showed a significant increase in ongoing and planned studies (Table 3, section B). The upcoming increase in planned PASS studies, particularly in leading countries like Israel, KSA, and UAE, is a positive sign. Additionally, Kuwait is joining the leading group with a higher number of studies planned, that draws it closer to

the leading group of countries. Iran is set to participate in one PASS study (Figure 2). On one hand, it indicates a very slow but growing recognition of the importance of such studies in ensuring drug safety. It may be an early indication that as PV systems evolve in MENA countries, more countries will participate in PASS studies, and the trend will continue to grow.

On the other hand, no other countries have studies planned, which also indicates that the progress in the region is very slow and potentially may point to a stagnant situation where certain conditions in the countries prevent initiation and conduct of PASS studies. Therefore, it is essential to monitor these trends, as well as any contributing factors, to better understand the dynamics of PASS studies in these regions and to identify areas for further improvement and collaboration, as the importance of PASS studies in MENA cannot be overstated. The majority of the studies were voluntary, with only 1 study imposed as a condition to marketing authorisation for EU risk management plan. There was no study that was imposed by the MENA health authorities. In addition, all the studies conducted in the MENA region were also conducted in the EU region. Only one study was a National study in Lebanon. This points to the fact that the health authorities in the MENA do not impose PASS studies in the region.

Compounding the challenges is the absence of a dedicated regional registry for non-interventional PASS studies, which poses a significant barrier to transparency and data sharing within the MENA region. This reliance on external registries like the EU PAS Register and Clinicaltrials.gov not only suggests a deficiency in the region's capacity to autonomously oversee PASS studies, potentially, due to limited resources, but also risks the underrepresentation of the actual volume of research conducted. This is also supported by Zeeneldin and Taha [36], who argued in their work that the number of trials conducted in Egypt and registered on clinicaltrials.gov is low and does not reflect the actual work being carried out.

Questionnaire analysis: in discussing the findings from the questionnaire analysis, several key themes emerged that reflect the challenges and the current state of PASS studies in the region and confirm the findings from the registries and legislation analysis. Out of 37 connections contacted for MENA region only 19 participants (51%) from the region were able to answer the questions. This underscores the difficulty of finding professionals who are involved in the PASS studies in the region. According to Alshammari [37], although GVP guidelines for Arab Countries say that national health authorities can impose PASS in case of a particular safety concern, this is rarely done in practice. This observation is supported by informal discussions with health authority representatives from various countries within the region during the annual summit. These conversations revealed that, although regulations permit the imposition of PASS studies to address safety concerns, it is not currently a common practice. One of the reasons is the limitation of financial and infrastructural resources that restricts the ability to conduct PASS studies locally, therefore, many regulators prefer to rely on data from the studies conducted in other regions [38-42]. This was also confirmed by the survey respondents, who indicated the absence of PASS and lack of their imposition (Table 1).

The finding that 37% of respondents from the MENA region reported an increase in PASS studies is indicative of a growing recognition of the importance of these studies. The increase attributed to new safety concerns and stricter regulatory requirements suggests an evolving landscape where patient safety and regulatory compliance are becoming increasingly prioritised. This reflects a positive trend towards strengthening the pharmacovigilance systems in these countries, aligning with global standards for drug safety and monitoring.

Conversely, the fact that 31% of respondents did not notice any change and a significant portion pointed out the absence of PASS studies due to various reasons, highlights significant challenges.

The reliance on PASS studies from the European Union, the prevalence of generic medicines which may not require PASS, and a lack of clear regulations cited as primary reasons for this absence underscores a critical gap in the regional pharmacovigilance framework, suggesting that while some countries are making strides, the region as a whole, faces hurdles in implementing comprehensive PASS studies. Even though the region has many generic medications, the PASS studies could be helpful in understanding how these medications work in a specific MENA population.

The challenges detailed by respondents, particularly in the initiation and approval stages of PASS studies, are telling of the broader difficulties faced in the MENA region (Table 3). These challenges reflect a need for enhanced regulatory clarity, improved stakeholder engagement, and increased resources dedicated to pharmacovigilance activities. Addressing these challenges by facilitating the initiation process would be a step towards improving PASS culture and practice in the region [40-42].

Conclusion

A significant gap has been identified between the existing regulatory frameworks and their actual implementation within the region, indicating a pressing need for a more unified and proactive approach to strengthen drug safety monitoring. The implementation and availability of PASS regulations vary significantly from country to country in the region, underscoring a difficult environment to promote the increase in PASS studies. A limited number of countries, including Saudi Arabia, Egypt, the United Arab Emirates, and Israel, have emerged as pioneers in the adoption of PASS, showcasing a relatively sophisticated and advanced regulatory milieu. Nevertheless, a considerable segment of the region remains disengaged from conducting such essential studies, primarily due to a lack of standardization and insufficient guidance on PASS. The PASS studies analysed within the MENA region are predominantly characterized by voluntary studies, often undertaken within the broader scope of European Union (EU) PASS investigations, with only one national study discovered over a three-year evaluation period. This trend underscores a minimal engagement in PASS studies within the MENA region, with a consequential overreliance on European outcomes. This reliance risks missing out on capturing the critical differences between the MENA and EU populations, which could be pivotal in understanding drug safety and efficacy in the region's unique demographic and health contexts.

The scarcity of PASS studies in the MENA region can be attributed to three main factors: the absence of clear, unified guidance; the widespread use of generic medications, which are often exempt from PASS; and the acceptance of results from studies approved by Stringent Regulatory Authorities (SRAs) conducted outside the region. These challenges are exacerbated by often incomplete or missing PASS chapters in the guidelines, revealing a fundamental issue with the initiation and approval processes for PASS studies in the region. The feedback obtained through questionnaires further highlights the fact that, despite the presence of regulations, their practical enforcement or application by health authorities remains largely absent.

To bridge the gap between the current regulatory frameworks and their practical application in the MENA region, it's essential to adopt a more unified approach in the regulations establishment and implementation, taking into account differences in the local healthcare system. Strengthening the conduct of PASS also requires encouraging the undertaking of local, national studies to capture the unique demographic and health contexts of the MENA population, thus addressing the critical differences overlooked by relying heavily on EU-conducted studies. Expanding the scope of PASS to include generic medications, which constitute a significant portion of the region's healthcare, could significantly enhance the understanding of

drug safety and efficacy in the unique population of the region. With the anticipated development of pharmacovigilance systems across MENA, the imposition of PASS studies by health authorities might be a good way towards promoting the conduct of studies in the region. This approach will elevate the total number of studies conducted in the region. However, at the same time it is also crucial to foster an environment that supports and facilitates initiation, approval and participation in PASS studies.

As the PV systems across MENA countries continue to develop, an increase in participation in PASS studies is anticipated, potentially elevating the total number of studies conducted in the region. It is crucial to monitor these trends and underlying factors to gain a deeper understanding of the PASS studies' dynamics in the region and to identify opportunities for enhancement and collaboration. A potential way forward to overcome financial and operational constraints could be the adoption of joint PASS studies between countries in the region. These collaborative studies, conducted by multiple pharmaceutical companies under regulatory supervision, could help share costs, streamline regulatory approvals, and encourage better participation. Encouraging such collaborations would not only reduce financial strain but also ensure better safety data collection tailored to the population in the MENA region. Furthermore, a national or regional registry for PASS studies will help in promoting transparency and methodological robustness in such studies, as well as collecting important real-world data for the unique population in each country and the region as a whole. The accessibility and completeness of PASS study registries could, in turn, help address the concerns of underreporting and lack of transparency, leading to a more robust pharmacovigilance system.

Disclaimer: the views expressed in this article are the personal views of the author(s) and may not be understood or quoted as being made on behalf of or reflecting the position of the organizations with which the author(s) are employed/affiliated. The work was done in partial fulfilment of the requirements of the University of Hertfordshire for the degree of Master of Science.

What is known about this topic

- *Post-authorization safety studies are critical for understanding the real-world safety of medications, especially in regions with diverse patient demographics;*
- *The MENA region faces unique challenges in pharmacovigilance due to diverse healthcare systems, genetic variances and a lack of standardization in PASS practices;*
- *PASS studies are essential in regions like MENA, where randomised controlled trials may not adequately represent the local population, leading to potential gaps in drug safety data.*

What this study adds

- *This study highlights the discrepancy between pharmacovigilance guidelines and their operationalization in the MENA region, revealing a critical deficit in the enforcement of PASS by local health authorities;*
- *The research systematically identifies and analyzes the primary barriers to the initiation and regulatory approval of PASS within the region, including legislative ambiguities and insufficient engagement of key stakeholders;*
- *Through an examination of healthcare system heterogeneity across MENA countries, this study highlights how these structural differences influence the design, conduct and effectiveness of PASS, advocating for the development of context-specific pharmacovigilance frameworks.*

Competing interests

The authors declare no competing interests.

Authors' contributions

All authors contributed to the development of the study, as well as to the writing and approval of the final version of this manuscript. John Talbot is now deceased.

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Tables and figures

Table 1: responses given by the connections on LinkedIn who did not proceed to answer the questionnaire (answers 1-7) and challenges faced with PASS studies conducted in the MENA Region (answers 8-13)

Table 2: available national GVP guidelines and PASS chapters by country

Table 3: analysis of the studies found in registries

Figure 1: number of respondents by country in MENA

Figure 2: PASS studies distribution by country, MENA region (PASS studies found on EU PAS Register)

Figure 3: observational studies distribution by country, MENA region

Figure 4: perceived trends in PASS studies by survey respondents

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Table 1: responses given by the connections on LinkedIn who did not proceed to answer the questionnaire (answers 1-7) and challenges faced with PASS studies conducted in the MENA Region (answers 8-13)

	Area responsible for	**Response**
1	UAE	I went through the questionnaire, and I found that most of the questions are not applicable to my region, as most of the multinational companies, when performing a PASS studies, select some other countries to perform it, and most probably, the MENA countries are not selected (as per my experience)
2	UAE	In my region, there has been no PASS for years
3	Jordan	We don't perform PASS studies at all
4	Levant area (Israel, Lebanon, Jordan, Syria)	No PASS in the region, as our medicines are imported; we don't manufacture them here. So, all registrations are based on data generated from studies in the EU mostly. Unless there is a special request by the local authorities, but so far, no requests at all
5	Algeria	PASS is not mandatory in North Africa, nor are interventional studies for registration purposes
6	UAE	Most of the products in the region are generics, so not much has been done on the PASS study part
7	Jordan	No PASS, as we manufacture generics
	Area responsible for	**Response**
8	Oman	Initiation and conduct
9	Qatar	Initiation: as MAH incurs costs to conduct such studies, it is difficult to start promptly
10	UAE	Initiation
11	Egypt	Approval stage: follow up with patients
12	Iraq	Approval of such studies takes time; patients and doctors are not aware of PASS studies and are not supportive
13	UAE	Mostly approvals

PASS-Post-authorisation safety study; MENA- Middle East and North Africa; MAH- Marketing Authorisation Holder; UAE- United Arab Emirates

Table 2: available national GVP guidelines and PASS chapters by country		
Country	**National guideline**	**Chapter on PASS**
Algeria	Yes	No
Bahrain	No, follows GVP for Arab countries	No
Egypt	Yes	Yes
Iran	Yes	Yes
Iraq	Yes	Yes
Israel	Yes	Yes
Jordan	Yes	Yes
Kuwait	No, follows GVP for Arab countries.	Yes
Lebanon	Yes	No
Libya	No, follows GVP for Arab countries	Yes
Morocco	Yes	No
Oman	Yes	Yes
Palestine	Yes	No
Qatar	No, follows GVP for Arab countries	Yes
KSA	Yes	Yes
Sudan	Yes	No
Syria	No information	No information
Tunisia	Yes	Yes
UAE	Yes	Yes
Yemen	Yes	No
GVP-good pharmacovigilance practices; PASS- post-authorisation safety study		

Table 3: analysis of the studies found in registries				
A - The breakdown of the studies found in the analysed databases				
	PASS from EU PAS Register	**Observational studies from ClinicalTrials**		
MENA	31	922		
EU				
B - The breakdown by study status in MENA	1103	8189		
	Number of PASS studies ongoing or completed within a 3-year-period	**Ongoing**		**Planned**
PASS from EU PAS Register				23 (17*)
C - The breakdown of PASS studies in the region by year	31 (21*)	24 (12*)		
	2020	**2021**	**2022**	**Total**
MENA PASS studies (EU PAS)	8	5	8	**21**
*-number of studies without duplicates, PASS: post-authorisation safety study, EU PAS: European Union Post-autorisation studies, MEN:Middle East and North Africa				

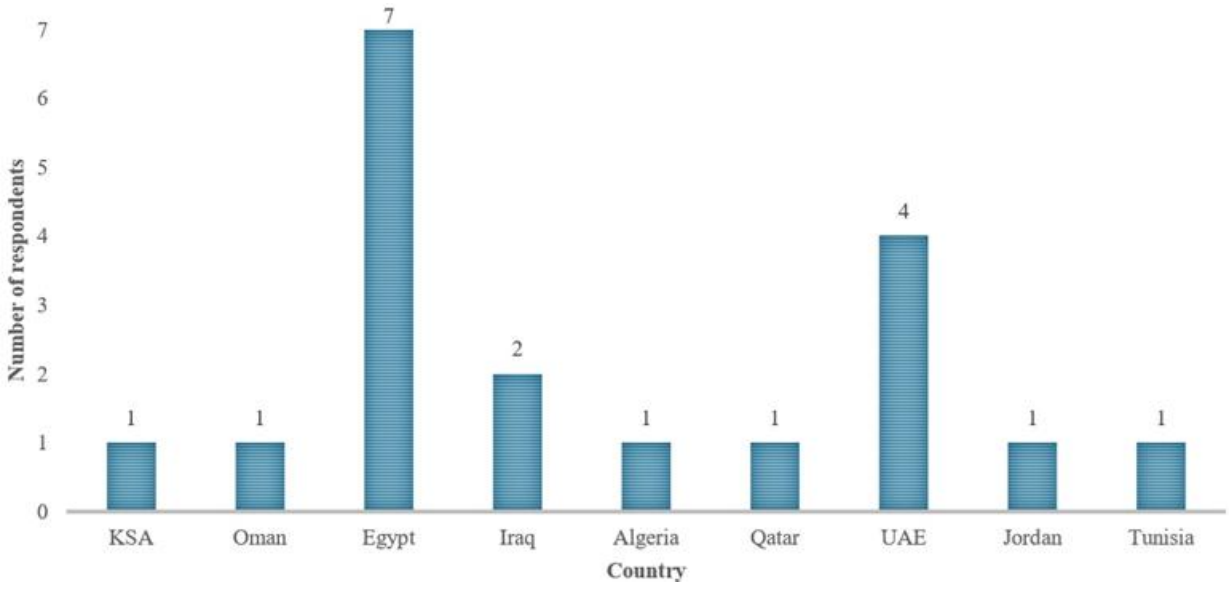

Figure 1: number of respondents by country in MENA

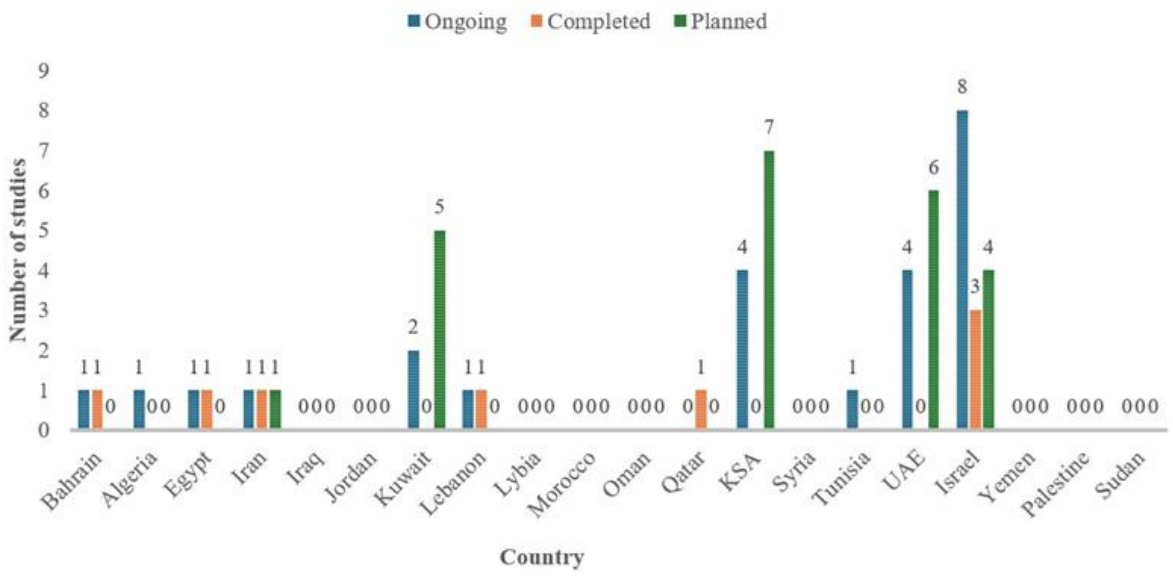

Figure 2: PASS studies distribution by country, MENA region (PASS studies found on EU PAS Register)

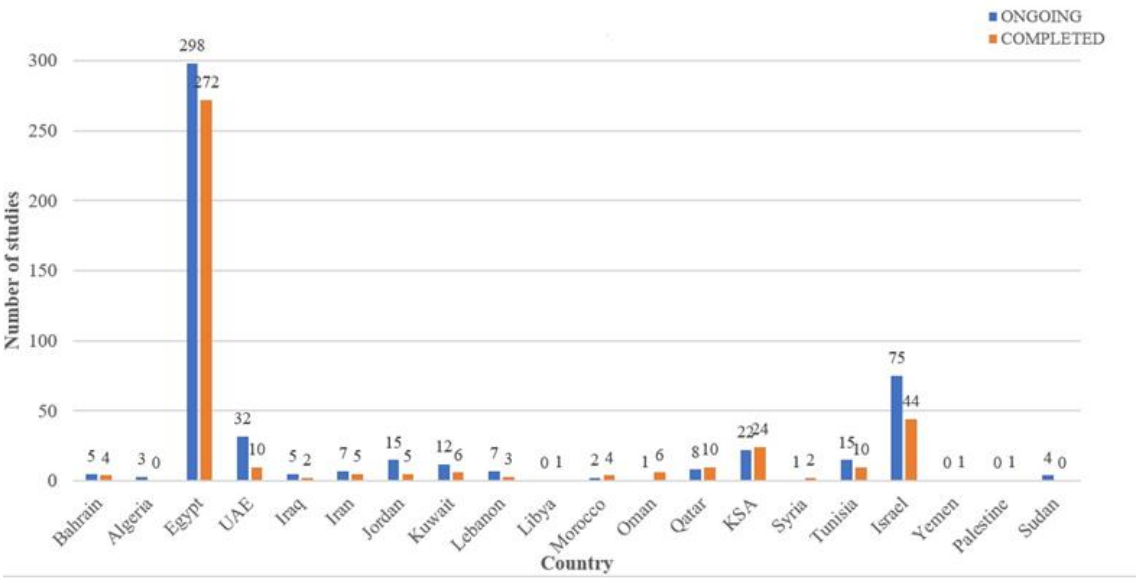

Figure 3: observational studies distribution by country, MENA region

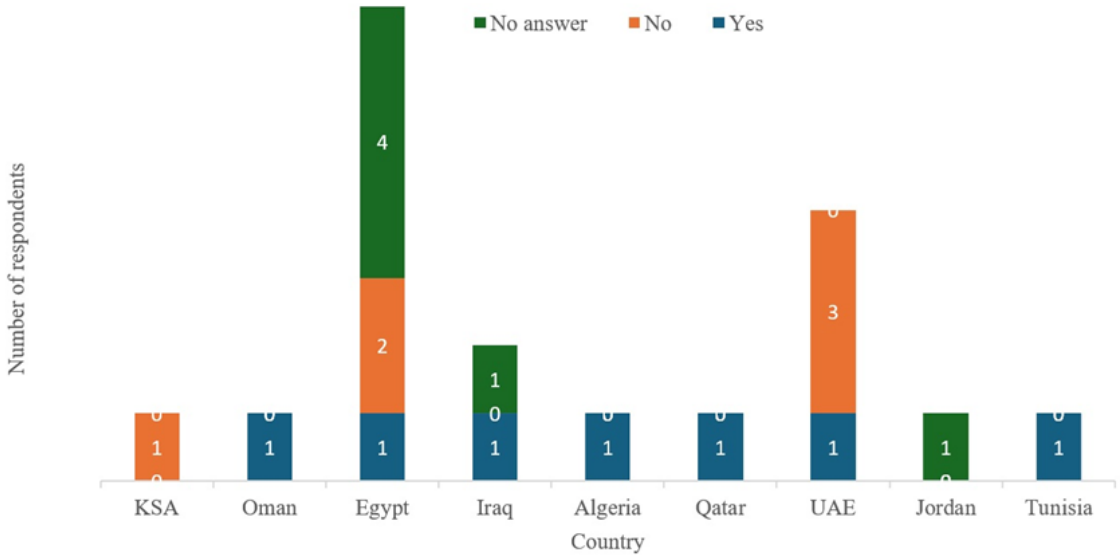

Figure 4: perceived trends in PASS studies by survey respondents