Knowledge and Perception of Iraqi Pharmacists Towards Biosimilar Medicines

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Abstract

Biosimilars are non-innovative versions of biologic medicines which are proven to be clinically equivalent to, as effective, and as safe as their reference biologics. Biosimilars create opportunities for cost savings for payers, governments, and patients compared to the reference products. Pharmacists play an essential role in developing biosimilars from manufacturing to post-marketing pharmacovigilance monitoring. The aim of the current study was to explore the level of knowledge and perception of a sample of Iraqi pharmacists towards biosimilars. The current study was a cross sectional and was carried out during May 2020. A total of 264 pharmacists (143 male, 121 female) were involved in this study. A web-based self-administered questionnaire was used for data collection. Regarding pharmacists' knowledge of biosimilar medicines, the results showed that two questions received the highest percentages of adequate answers: biosimilar medicine requires preclinical and clinical studies (58.0%) and biosimilar medicines require more comprehensive data compared to generic drugs (56.1%). In contrast, marketing authorization of biosimilar medicines is granted on the sole investigation of pharmacokinetic bioequivalence received the lowest percentage of adequate answers (21.6%). In addition, the current study showed that more years of experience and male gender were associated with better knowledge. With respect to perceptions of pharmacists to biosimilars, two statements received the highest percentage of pharmacist agreements: biosimilar medicines are tested in terms of efficacy and safety (64.4%) and biosimilar prescription allows for reducing costs (64.4%). At the same time, 40.2% of the participating pharmacists agreed with pharmacist replacing a reference biologic medicines with its biosimilar product. In conclusion, the majority of the pharmacists included in the survey had insufficient knowledge about biosimilars. The study highlighted that Iraqi pharmacists needed more accurate and comprehensive information about biosimilars.

Keywords: Biosimilars, Pharmacists, Iraq, Knowledge, Perception.

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معرفة وتصور الصيادلة العراقيين تجاه المشابهات الحيوية

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الخلاصة

المشابهات الحيوية هي نسخ غير مبتكرة من الأدوية الاحيائية التي ثبت علميًا أنها مكافئة سريريًا ، وفعالة وآمنة مثل الأدوية الاحيائية المرجعية. تخلق المشابهات الحيوية فرصًا لتحقيق توفير في التكاليف للدافعين والحكومات والمرضى ، مقارنة بالمنتجات المرجعية. يلعب الصيدلي دورًا مهمًا في تطوير المشابهات الحيوية بدءًا من التصنيع حتى دراسات اليقظة الدوائية وما بعد التسويق.

كان الهدف من الدراسة الحالية هو استكشاف مستوى المعرفة والتصورات لعينة من الصيادلة العراقيين تجاه المشابهات الحيوية. الدراسة الحالية عبارة عن دراسة مقطعية أجريت خلال شهر ايار ٢٠٢٠. شارك في هذه الدراسة ٢٦٤ صيدليًا (١٤٣ ذكرًا و ١٢١ أنثى). تم استخدام استبيان عبر الإنترنت لجمع البيانات المتعلقة بالدراسة. فيما يتعلق بمعرفة الصيادلة بالمشابهات الحيوية ، أظهرت النتائج أن سؤالين تلقيا أعلى النسب المئوية للإجابات الكافية: المشابهات الحيوية تتطلب دراسات ما قبل السريرية والسريرية (٥٨,٠٪) و المشابهات الحيوية تتطلب بيانات أكثر شمولاً مقارنة بالأدوية الجنيسة (٥٦,١٪) . في المقابل ، يُمنح ترخيص تسويق المشابهات الحيوية بناءً على تحقيق وحيد للتكافؤ الحيوي الدوائي حصل على أقل نسبة من الإجابات الكافية (٢١,٦٪). بالإضافة إلى ذلك ، أظهرت الدراسة الحالية أن المزيد من سنوات الخبرة وجنس الذكور مرتبطان بمعرفة أفضل. فيما يتعلق بتصورات الصيادلة حول المشابهات الحيوية ، حصل بيانان على أعلى نسبة من اتفاق الصيادلة: تم اختبار المشابهات الحيوية من حيث الفعالية والأمان (٦٤,٤٪) ووصف المشابهات الحيوية يسمح بخفض التكاليف (٦٤,٤٪). في الوقت نفسه، اتفق ٤٠,٢٪ من الصيادلة المشاركين على امكانية قيام الصيدلاني باستبدال الأدوية الاحيائية المرجعية بمنتج من المشابهات الحيوية. كنتيجة فأن غالبية الصيادلة الذين شملهم الاستطلاع لم تكن لديهم معرفة كافية بالمشابهات الحيوية. سلط المسح الضوء على الحاجة إلى تزويد الصيادلة العراقيين بمعلومات دقيقة وشاملة عن المشابهات الحيوية.

الكلمات المفتاحية: المشابهات الحيوية ، الصيادلة، العراق، معرفة ، تصور.

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Introduction

The introduction of biologic medicines represented a significant development in therapy for many serious diseases. [1] Despite their important value, biologic medicines have become a big financial problem to the health care systems. [2] Therefore, availability of "generic" copy of biological medicines would be essential as this could save billions of dollars yearly. [3] The U.S. Food and Drug Administration (FDA) defines a biosimilar product as highly similar but not identical to an already licensed biologic product in terms of quality, safety, and efficacy. [4]

Costs of biosimilars are about 15–30% less than the originator prices so their use creates opportunities for cost savings for payers, governments, and patients compared with the reference products since. [5]

Biologic medicines are big molecules that are mostly proteins. The manufacturing of biologic medicines is very complex which required living cells; so variation in the final product is a concern. Post-translational modifications such as oxidation and glycosylation and even a small variation in the manufacturing process can change the structure of biologic medicines, with possible changing in pharmacological activity, safety profile, efficacy, and immunogenicity.

Accordingly, the manufacturing of biologic medicines must be closely monitored so that consistency of batch to batch will be ensured. Consequently, it is almost difficult to synthesize a biologic medicine that is identical to its originator. [6] In Iraq, a specialized committee called the "Biologics and Biosimilars Registration Committee (BBRC)" to register biosimilars was established by the National Regulatory Authority (NRA). The BBRC established the first version of guideline for biosimilars and submitted it to the Medicines Policy Committee for approval on April 28th of 2019. The Iraqi biosimilars guidelines were adapted mainly from the European Medicines Agency (EMA) guidelines, since EMA was the pioneer in the biosimilars' field. [7]

Pharmacist plays an important role in developing biosimilars medicines from synthesis to dispensing to post-marketing pharmacovigilance monitoring. In many countries, pharmacists must be well educated about any new regulations concerning biosimilars. In addition, pharmacists are involved in educating physicians and patients about similarity, efficacy and safety of biosimilar medicines. [8]

The aim of the current study was to explore the level of knowledge, behaviors and practices of a sample of Iraqi pharmacists towards biosimilar medicines.

Subjects and Method

Study population

The current study was a cross sectional study carried out during May 2020. A total of 264 Iraqi pharmacists)143 males, 121 females) were involved in this study.

Inclusion criteria

Any Iraqi pharmacist willing to participate in the study were included.

Data collection

A web-based, self-administered, questionnaire was used for data collection. The questionnaire investigates knowledge, behaviors and practices of pharmacists regarding biosimilar medicines. It consisted of three parts, the first part was about the sociodemographic and background characteristics of the participants. The second part addressed the knowledge of pharmacists about biosimilar medicines, this included 9 statements about quality, safety, efficacy and marketing authorization. Knowledge domain have response categories of (Yes, No, and Don't know). The third part (6 questions) were used to investigate pharmacists perceptions about biosimilar medicines, implementation of biosimilar medicines, substitution, and cost saving. The agreement of participants and attitude domains have five Likert scale response categories. [9]

Ethical consideration

The current study gained its approval from the ethical and scientific committee at the College of Pharmacy/University of Baghdad. All participants were informed about the study objectives and confidentiality of their answers.

Statistical analysis

Analyses were conducted using the Statistical Package for the Social Science (SPSS, version 22, IBM, New York, USA). Descriptive statistics (Categorical variable) were described using frequencies and percentages while, mean and standard deviation (SD) were used to describe (continuous variables) of the participants. Independent T-test was used to measure the difference between the means of accurate answer scores according to gender. We excluded "not sure" group from the analysis.

The total score of correct answers for each participants was calculated by giving one point for each correct answer. Spearman correlation was used to measure the correlation between the pharmacist experience years and the mean of total score of correct answers to questions about biosimilar medicines. A p-value of less than 0.05 was considered to be statistically significant.

Results

The study recruited 264 pharmacists with average age of (30.16 ±6.94 years) and more than half (54.2%) were men. The average years of pharmacists' experience in field of pharmacy were (6.38±6.04 years).

Approximately, three-quarters (75.0%) of participants had bachelor's degree in pharmacy (BSc). Most of them lived in Baghdad (58.7) as shown (Table 1).

Table 1. Demographic characteristics of participating pharmacists

Item		Subcategory	Frequency (N)	%
Gender		Female	121	45.8
		Male	143	54.2
Degree		Bachelor	198	75.0
		Diploma	18	6.8
		Master	40	15.2
		Ph.D.	8	3.0
Province		Baghdad	155	58.7
		Anbar	28	10.6
		Diyala	16	6.1
		Karbala	12	4.5
		Najaf	11	4.2
		others	42	15.9
Item	Minimum	Maximum	Mean	Std. Deviation
Age	22	68	30.16	6.94
Experience years	0	33	6.38	6.04

When the respondents were asked about the basic information regarding biosimilar medicines, the results showed that two questions received the highest percentages of adequate answers: The requirement of biosimilar medicine for preclinical and clinical studies (58.0%) and the requirement for more comprehensive data compared to generic drugs (56.1%)" . In contrast, the lowest percentage of adequate answers (21.6%) was for question regarding the role of bioequivalence study in marketing authorization of biosimilar medicines (Table 2 and Figure 1).

Table 2. Pharmacists' knowledge about biosimilar medicines

|	Statement	Adequate	N	%
1	«A biosimilar medicine is structurally identical to its reference medicinal product»	No	106	40.2
2	«A biosimilar medicine is similar to a reference medicinal product that has gone off-patent»	Yes	114	43.2
3	«A biosimilar medicine has no meaningful differences from a reference medicinal product in terms of quality»	Yes	117	44.3
4	«A biosimilar medicine has no meaningful differences from a reference medicinal product in terms of safety»	Yes	142	53.8
5	«A biosimilar medicine has no meaningful differences from a reference medicinal product in terms of efficacy»	Yes	137	51.9
6	«A biosimilar medicine has the same dosage and route of administration compared to its reference medicine»	Yes	146	55.3
7	«A biosimilar medicine is a drug for which marketing authorization is granted on the sole investigation of pharmacokinetic bioequivalence with its reference medicine»	No	57	21.6
8	«A biosimilar medicine is a drug for which assessment of biosimilarity requires more comprehensive data compared to generic drugs»	Yes	148	56.1
9	«A biosimilar medicine requires preclinical and clinical studies»	Yes	153	58.0
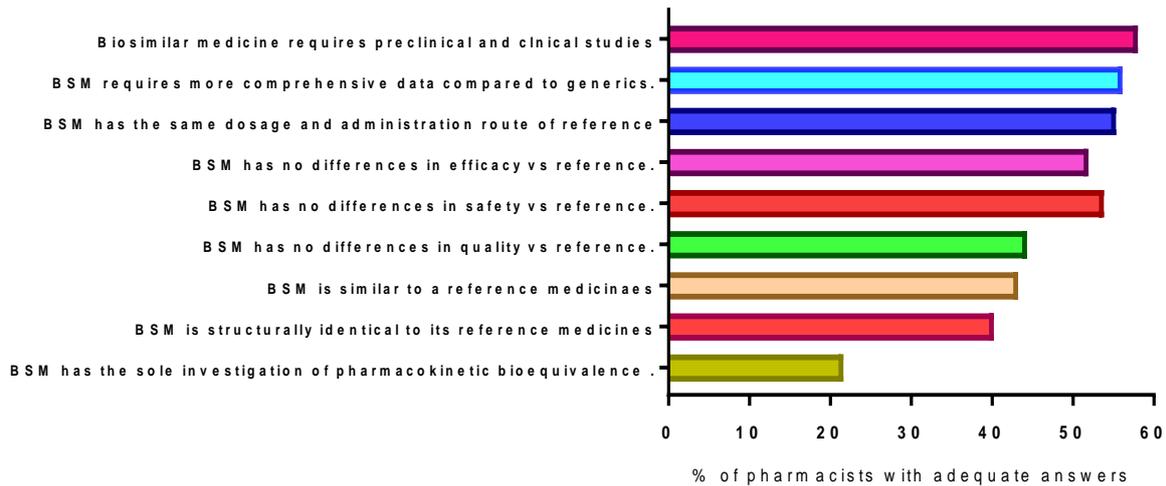
Figure 1. The percentage of pharmacist with correct answers about biosimilar medicines (BSM).

The number of participants who adequately answered to the questions about biosimilar medicines is normally distributed. Approximately 41% of the pharmacist answered half of the questions adequately, 60 (22.7%) and 48 (18.2%)

participants correctly answered five and four questions respectively. Only 14 (5.3%) had all wrong answers, while eight (3.0%) had all nine correct answers (Table 3).

Table 3. Frequency distribution of participants according to number of correct answers with respect to knowledge.

	Correct answers	***n***	**%**
1	Nine correct answers	8	3.0
2	Eight correct answers	10	3.8
3	Seven correct answers	25	9.5
4	Six correct answers	36	13.6
5	Five correct answers	60	22.7
6	Four correct answers	48	18.2
7	Three correct answers	31	11.7
8	Two correct answers	23	8.7
9	One correct answer	9	3.4
10	No correct answer	14	5.3

The Spearman correlation shows there is significant (P< 0.05) positive correlation between the pharmacist years of experience and total score of the correct answers (Table 4). In other words, longer experience years gives more correct answers.
According to the independent samples T-Test, male pharmacists had significantly higher mean of total score of correct answers compared to female pharmacists (Table 5).

Table 4. Correlation between the score of adequate answer and pharmacist experience years

Correlation Coefficient (r)	**0.138**
P-value	**0.025***
N	**264**

* Correlation is significant at the 0.05 level (2-tailed). Significant positive correlation using Spearman correlation

Table 5. The difference between the means of accurate answer scores according to gender.

	Gender	N	Mean	Std. Dev.	Mean Difference	P-value
Total score	**Female**	121	3.926	2.122	-1.025	.0001*
	Male	143	4.951	1.962		

* Significant difference (P-value < 0.05 level).

A total of 6 questions were used to investigate pharmacists' perceptions about biosimilar medicines, and the results were outlined in (Table 6). Two statements received the highest percentage of pharmacist agreements: Biosimilar medicines are tested in terms of efficacy and safety (64.4%) and biosimilar prescription allows for reducing costs (64.4%). At the same time, 40.2% of the participating pharmacists agreed replacing a reference biologic medicines with its biosimilar product by pharmacist.

Table 6. Pharmacists' perceptions about biosimilar medicines

Item	Strongly disagree N (%)	Disagree N (%)	Neutral N (%)	Agree N (%)	Strongly Agree N (%)
«I am in favor with the implementation of biosimilar medicines»	24 (9.1)	14 (5.3)	**114 (43.2)**	90 (34.1)	22 (8.3)
«Biosimilar medicines are tried and tested in terms of efficacy and safety»	19 (7.2)	31 (11.7)	44 (16.7)	**123 (46.6)**	**47 (17.8)**
«Biosimilar medicines are not only pharmacist's concern»	33 (12.5)	27 (10.2)	50 (18.9)	**107 (40.5)**	**47 (17.8)**
«I approve a pharmacist substitution of a reference biological medicine to its biosimilar product»	33 (12.5)	54 (20.5)	81 (30.7)	**73 (27.7)**	**33 (12.5)**
«I approve a pharmacist substitution of a reference medicine product to its generic product»	31 (11.7)	34 (12.9)	79 (29.9)	**80 (30.3)**	**40 (15.2)**
«Biosimilar medicines prescription allows for reducing healthcare costs»	25 (9.5)	22 (8.3)	47 (17.8)	**99 (37.5)**	**71 (26.9)**

Discussion

The current study provided a snapshot of Iraqi pharmacists' knowledge, and perceptions about biosimilars.

Regarding pharmacists' knowledge of biosimilars, about half of respondents (52.6%) have answered 5 or more questions (out of 10 questions) correctly. Comparing the results of the current study with that of one French study revealed a significant gap. For example, more than 90% of French pharmacists answered adequately regarding the statements " A biosimilar has no meaningful differences from a reference in terms of quality" and " A biosimilar medicine has no meaningful differences from a reference in terms of efficacy " compared to (44.3%) and (51.9%) in the current study, respectively. All French pharmacist adequate answers for the remaining of the nine questions were more than 70.0% except for the first one " A biosimilar medicine is structurally identical to its reference medicinal product" which was (59.4%). [9] In Europe Union, France is the first country establishing a regulation for biosimilar substitution and creation of a French directory for biosimilars. [10] Although the exact means of biosimilar education were not stated, van Overbeeke *et al*. suggested a positive relationship between biosimilar education and biosimilar knowledge. [11] The current finding showed that there is a strong need for pharmacist-directed education to enhance knowledge about biosimilars which might increase acceptance of biosimilars as safe and effective therapeutic options. In addition, the current study showed that more experience years associated with better knowledge. When there is little education about biosimilars in the undergraduate study, it is expected that practical experience will be an influential factor. Also, the current study showed that male gender was associated with better knowledge. Possible explanation may be that, compared to female, male Iraqi pharmacists are more involved in drug promotion and marketing where the term " biosimilars" frequently encountered.

A total of 6 questions were used to investigate pharmacists' perceptions about biosimilars. Two statements received the highest

percentage of pharmacist agreements: Biosimilar are tested in terms of efficacy and safety (64.4%) and biosimilar prescription allows for reducing costs (64.4%). Regarding efficacy and safety, various clinical trials gave evidence-based results to confirm that there are no essential differences between a reference biological medicines and their biosimilars in terms of efficacy, and safety. [12, 13] Concerning cost reduction, biosimilars are not only lower in cost to biologic therapies, but also introduce price competition leading to a decrease in the price of reference product. [6]

Pharmacist-led biosimilar substitution was another main issues raised in current survey where about 40.0% of pharmacists have approved a pharmacist substitution of a reference biologic medicine to its biosimilar counterpart. This proportion is relatively comparable with the rate of pharmacists who agreed with the substitution of a reference chemical medicines by its generic one (about 45.0%). However; it is lower than that reported in French study where about 53.0% of pharmacists approved pharmacist substitution of a reference biologic medicine to its biosimilar. [9]

Iga Pawłowska *et al.* in their study detected that most Polish pharmacists (about three-quarters) were worried about pharmacist-led substitution and only 23% of pharmacists thought that the reference medicine could be substituted by a biosimilar during therapy [14]. In Ireland, Joan Ocallagan *et al.* found that more than half of Irish pharmacists (58%) were comfortable in changing patients from reference medicine to biosimilars in agreement with the prescriber and only (14%) preferred to make their own decision regarding suitable substitution. [15]

Pharmacists must be included in any policy making or regulations concerning biosimilars since they have close contact with both physicians and patients. There are continuous debates about the right of interchangeability, substitution and extrapolation of indications. While the innovative manufacturers are interested to keep their market share large and avoid any competition, biosimilar advocates are more interested in increasing share of biosimilars in the biologic market. Pharmacists are in a good position to keep the balance between the two groups by looking for this issue from the patients' side to provide biologic products readily accessible and at acceptable prices. [8]

Conclusions

The majority of the surveyed pharmacists had insufficient knowledge towards biosimilar medicines. The study highlighted that Iraqi pharmacists needed more comprehensive information concerning biosimilar medicines.

Limitation of the study

The study had some limitations. First, a small sample size of the participants. Hence, the results of the current study cannot be generalized to the whole Iraqi pharmacists. Second, the survey was short and detailed information was not obtained. Nevertheless, the short form of the questionnaire may increase the willingness of pharmacists to complete the survey. Third, the study was cross-sectional done at a particular time point, and the perceptions of pharmacists may change over time. So, it will be valuable to repeat a similar survey several years later to know whether perceptions have changed or not.

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