Yazun Jarrar*, Rami Musleh, Anas Hamdan, Mustafa Ghanim, Malik Alqub and Sara Abudahab

Lack of exposure to pharmacogenomics education among the health care providing students in the West Bank of Palestine

https://doi.org/10.1515/dmpt-2022-0180 Received October 29, 2022; accepted January 23, 2023; published online March 13, 2023

Abstract

Objectives: Evaluating the knowledge in pharmacogenomics (PGx) is the first step toward the implementation of PGx testing in clinical practice. This survey aimed to evaluate the knowledge of PGx testing among healthcare providing students at the top-ranked university in the West Bank of Palestine.

Methods: First an online questionnaire consisting of 30 questions regarding the demographic, knowledge, and attitude toward pharmacogenomics testing was structured and validated. Then the questionnaire was distributed to 1,000 current students from different fields.

Results: 696 responses was received. The results showed that almost half of the participants (n=355, 51.1%) have never took any courses about PGx during their university training. Only 81 (11.7%) of the students who took the PGx course stated that it helped them understanding how genetic variations affect drug response. The majority of the students were uncertain (n=352, 50.6%) or disagreed (n=143, 20.6%) that the lectures during university education described the effects of genetic variants on drug response. Although most of the students (70–80%) answered that genetic variants can indeed affect the drug's response, only 162 students (23.3%) responded that *VKORC1* and *CYP2C9* genotypes influence the response to warfarin. In addition, only 94 (13.5%) students

were aware that many medicine labels include clinical information about PGx testing provided by the FDA.

Conclusions: It is concluded from the results of this survey that there is a lack of exposure to PGx education associated with poor knowledge of PGx testing among the healthcare providing students in the West Bank of Palestine. It is recommended to include and improve the lectures and courses regarding PGx as this will have a major impact on precision medicine.

Keywords: education; knowledge; pharmacogenomics (PGx); West Bank of Palestine.

Introduction

The science of pharmacogenomics (PGx) evaluates how human genetic variations can influence drug response. Knowledge of pharmacology and genetics are both required for understanding PGx [1]. The proteins involved in drug targeting and pharmacokinetics, such as drug metabolism, can be influenced by genetic variations, resulting in an alteration of the drug response [2]. PGx testing aims to optimize treatment by maintaining therapeutic efficacy and minimizing side-effects associated with the patient's genetic variants [3]. For example, before administering the anticoagulant warfarin, it is advised to test the genetic variations in the *cytochrome 2C9*, *4F2*, and *vitamin K epoxide reductase* genes [4, 5].

One of the major roles of health care providers is to manage and monitor the patients' drug response. Physicians prescribe, pharmacists dispense, and nurses administrate the drugs to the patients [6]. They must therefore be aware of the factors that can influence drug response, such as patient genetic variations [7]. Currently, the Pharmacogenomics Knowledge Base (PharmGKB) provides information and recommendations based on the functional variants and their clinical impact on the response to medications [8]. Accordingly, PharmGKB is considered one of the primary sources of PGx knowledge. Moreover, PGx recommendations can be found in the drug labels of more than 500 drugs based on the data from the Food and Drug Administration in the USA (www.fda.gov).

Rami Musleh, Department of Pharmacy, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine

Anas Hamdan and Mustafa Ghanim, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine

Malik Alqub, Department of Allied and Applied Medical Sciences, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine

Sara Abudahab, Department of Pharmacotherapy and Outcomes Science, Virginia Commonwealth University, Richmond, VA, USA

^{*}Corresponding author: Yazun Jarrar, PhD, Department of Basic Medical Sciences, Faculty of Medicine, Al-Balqa Applied University, As-Salt, Jordan, Fax: 00962795930283, E-mail: yazan.jarrar@bau.edu.jo

In several countries, including those in the Middle East, the idea of PGx testing was recently included in the curricula of many university programs aimed to increase PGx knowledge in health care providers [9, 10]. Additionally, previous findings assessed the understanding of and attitudes toward PGx testing among students enrolled to become healthcare providers in various Middle Eastern countries [11, 12].

In the West Bank of Palestine, we previously evaluated the knowledge and attitude of pharmacy students toward PGx testing [9]. It was found that most pharmacy students know the basics and aims of PGx testing, however, they have poor knowledge regarding the clinical implementations of PGx [9]. The knowledge of other healthcare provider students was not evaluated; therefore, the present study aims to assess the exposure to PGx education and the knowledge and attitude of the health care providing students toward PGx testing in the West Bank of Palestine.

Materials and methods

This study is a cross-sectional questionnaire-based online survey, and was conducted from October 1 to November 1, 2021. It was sent to students who study medicine, pharmacy, nursing, and paramedical sciences including medical analysis, physiotherapy, and optics at An-Najah National University in the West Bank of Palestine. The questionnaire was to 1,000 students, asking them to complete it, and clearly stated that participation in the study is voluntary.

The Daniel formula was used to calculate the sample size [13], and the significance threshold was set at 0.05, and the confidence at 95%. In 2022, An-Najah University had around 7,500 students in the aforementioned colleges, therefore, a sample size of 380 was determined to adequately representative.

The previous study was utilized as the base for the present study [9], where the questionnaire about the knowledge, attitude, and exposure to PGx education was developed and validated [9]. The questionnaire used in this study consisted of 30 close-ended questions with answers of (Yes/No/I am not sure) and was divided into four sections: (1) collecting demographic characteristics of the student; (2) information about their exposure to PGx education; (3) assessing their basic and clinical PGx knowledge; and (4) evaluating their attitudes towards PGx testing. The Cronbach alpha (measures reliability, or internal consistency) of the PGx knowledge questionnaire was 0.72 [14].

To compare the knowledge of PGx testing between the students at different medical colleges, scores were calculated for each participant as followings: +1 for "I know", 0 for "I am not sure" and -1 for "I do not know". This study used frequencies and percentages to express the categorical variables and used the ANOVA test to compare the responses between the groups. Any missing data was excluded from the analysis. The SPSS V25 statistical software was used for performing the analyses (IBM, Armonk, NY, USA).

An-Najah National University's ethical committee approved the study's protocol, and the Institutional Review Board number of this study is 16-02-2019.

Results

Demographic data of participants

In this study, 696 responses (69.6%): 250 (35.9%) were received from Medical Doctor students, 122 (17.5%) from Medical Analysis students, 104 (14.9%) from Nursing students, 116 (16.7%) from Pharmacy students, 47 (6.8%) from Doctor of Pharmacy students, and 47 (6.8%) from Physiotherapy students, and 10 (1.4%) from Optics students. Most of the participants were 20–24 years of age (n=361, 51.9%) or younger than 20 years (n=316, 45.4%), while only 19 students (2.7%) were older than 24. Majority of the students were females (n=498, 71.6%) and only 198 (28.4%) were males. The participants who provided the most responses were from Nablus city (n=226, 32.5%). The majority of the students were from An-Najah University (n=643, 92.4%).

Exposure to pharmacogenomics education

Less than half of the students (n=283, 40.7%) learned about PGx through their university's didactic courses, while 309 (44.5%) learned about PGx through social media (Table 1). Moreover, 368 (55.5%) students reported that they were never taught about PGx in any of their university courses. Only 81 (11.7%) of the students responded that learning about PGx had helped them understand how genetic variations can affect drug response, while most students disagreed (n=143, 20.5%) or were unsure (n=353, 50.7%) that the effects of genetic variations on medication response were discussed in lectures during their university education.

Basic knowledge of pharmacogenomics

A total of 614 (88.2%) respondents answered that they were aware that human genetics can influence drug response (Table 2). The majority of students (n=615, 88.4%) responded that they were aware that hereditary factors may contribute to inter-individual variation in drug response. In addition, 453 (65.1%) responded were aware that there is an ethnic variation in the response of the drugs.

Most medical students (n=496, 71.2%) were aware that genetic variants can influence the pharmacokinetic characteristics of the drug, and 531 (76.3%) students were aware that variations in drug-target genes may have an impact on how a drug interacts with its target. In addition, 518 (74.4%) of participant students responded that some patients have a

Table 1: Educational exposure to pharmacogenomics.

Question	Frequency (percentage)		
Did you study, during your university education, that there are inter- individual and inter-ethnic variations in the drug response?			
Yes	310 (44.6%)		
I am not sure	164 (23.6%)		
No	222 (31.9%)		
Total	696 (100%)		
How did you learn about pharma	cogenomics?		
University lectures	283 (40.7%)		
Scientific conferences	54 (7.8%)		
Social media	310 (44.5%)		
Television programs	49 (7%)		
Total	696 (100%)		
How many courses mentioned an	d described pharmacogenomics?		
0	356 (51.1%)		
1	192 (27.6%)		
2	106 (15.2%)		
More than 2	42 (6%)		
Total	696 (100%)		

How many lectures, from different courses, mentioned and described the effect of genetic variants on the drug response?

0	349 (50.1%)
1–3	226 (32.5%)
3-5	79 (11.4%)
6–10	27 (3.9%)
>10	15 (2.2%)
Total	696 (100%)

Did the pharmacogenomics information you received during educational courses enable you to understand the effect of genetic variants on the drug response?

Yes	81 (11.6%)
I am not sure	204 (29.3%)
No	411 (59.1%)
Total	696 (100%)

Did the lecturers describe the effect of genetic variants on the drug response clearly?

Yes	200 (28.7%)
I am not sure	353 (50.7%)
No	143 (20.5%)
Total	696 (100%)

significant high risk of drug-induced toxicity due to inherited genetic variations, and 539 (77.4%) students responded that certain patients' responses to medication are caused by specific genetic variations. Finally, 426 students (61.2%) answered that the drug response can be predicted through PGx testing.

Table 2: Pharmacogenomics knowledge among health-providing students in the West Bank of Palestine.

Question	I know	I am not	I do not know
Table with all are actions as in the control of the	C14		
Inherited genetic variants may influ-	614	66 (9.5%)	14 (2.2%)
ence drug response	(88.2%)	66 (0.50()	42 (4 00()
Inter-individual variation in response to	614	66 (9.5%)	13 (1.9%)
drugs and toxicity may be due to	(88.4%)		
inherited genetic variants			
There is an inter-ethnic variation in the	453	150	93
drug response	(65.1%)	(21.6%)	(13.4%)
Inter-individual variation in pharmaco-	496	147	52 (7.2%)
kinetic parameters may be due to ge-	(71.2%)	(21.1%)	
netic variations			
Inter-individual variation in pharmaco-	531	114	51 (7.3%)
dynamics, and the interaction between	(76.3%)	(16.4%)	
the drugs and molecular targets, may			
be due to genetic variations			
Some patients have a high risk of drug	518	123	s
toxicity due to inherited genetic variants	(74.4%)	(17.7%)	
Some patients do not respond to med-	538	132 (19%)	25 (3.6%)
icines due to some inherited variants	(77.4%)	(,	_= (====,
The drug response can be predicted	426	201	69 (9.9%)
using genetic biomarkers	(61.2%)	(28.9%)	05 (5.570)

The effect of the medical study program on the pharmacogenomics knowledge

The responder students' levels of PGx knowledge was analyzed according to the participants' medical colleges. It was found that nursing and paramedical science students had considerably less understanding of PGx (p 0.05, ANOVA) than other students who work in the health care industry (Table 3).

Knowledge about commonly known pharmacogenomic tests used clinically

Only 137 (19.7%) students knew that the gene for the endothelial growth factor receptor influences the effectiveness of the anticancer kinase inhibitors, and only 23.3% (n=162) of students knew that CYP2C9 and VKORC1 variations alter the response to warfarin (Table 4). In addition, 94 (13.5%) students were aware that the FDA includes clinical evidence for PGx testing in the labeling of more than 500 medications (Table 4).

Attitudes towards pharmacogenomics education

Table 5 illustrates the responses of students' attitudes towards PGx testing. A total of 584 students (83.9%) think that PGx

Table 3: Comparison of basic pharmacogenomics knowledge of participating students among different medical programs.

College	Average of PGx knowledge ^a	n	SD	p-Value
Medicine	6.80	250	2.07	0.001
Doctor of pharmacy	7.68	47	1.74	
Pharmaceutical	7.85	116	1.83	
sciences				
Nursing	5.33	104	1.25	
Paramedical sciences	5.45	179	1.71	

The score of PGx knowledge was calculated based on the Likert scale: +1 for "I know", 0 for "I am not sure" and -1 for "I do not know". ANOVA was used to compare between the scores of the groups. p-Value was considered significant when it is less than 0.05.

Table 4: Investigation of awareness of commonly known pharmacogenomic tests.

Question	I know	I am not sure	I do not know
CYP2C9 variants may affect metabolism	162	27 (3.9%)	507
and, hence, the warfarin response	(23.3%)		(72.8%)
VKORC1 variants may affect the phar-	162	33 (4.7%)	501
macodynamics and, hence, the warfarin response	(23.3%)		(71.9%)
Genetic variants in endothelial growth	137	32 (4.6%)	527
factor receptors affects the response to erlotinib	(19.7%)		(75.7%)
FDA provides clinical evidence for	94	296	306 (44%)
pharmacogenomics testing in the la- beling of many drugs	(13.5%)	(42.6%)	

CYP2C9, cytochrome 2C9 gene; VKORC1, vitamin K epoxide reductase complex 1 gene.

 Table 5: Attitudes towards pharmacogenomics testing.

Question	Yes	I am not sure	No
Do you think that pharmacogenomics	584	90	22
testing can improve your future work in	(83.9%)	(12.9%)	(3.2%)
choosing the right drug and dose? Do you want to know more about	580	73	43
pharmacogenomics?	(83.3%)	(10.5%)	(6.2%)
Do you want to apply pharmacogenomics	503	144	49 (7%)
testing in your future work?	(72.3%)	(20.7%)	
Do you want to study the postgraduate	110	259	327
program in pharmacogenomics	(15.8%)	(37.2%)	(47%)

testing is a useful tool in determining the right medications and right dosage for patients. Most of the students (n=580, 83.3%) are interested in learning more about PGx testing and are willing to use PGx testing in clinical practice 72.3% (n=503). While only 15.8% (n=110) had plans to study the science underlying PGx in any of their postgraduate degrees.

Discussion

All members of the health care team should be involved in pharmacotherapy, as this increases the safety and efficacy of medication use [15]. Pharmacogenomics testing aims to optimize pharmacotherapy and reduce the adverse drug response [16]. Consequently, many countries have increased the exposure of medical students to PGx education through workshops, lectures, and postgraduate studies [17]. This study evaluated the current knowledge and educational exposure to PGx testing among medical and paramedical students in the West Bank of Palestine. It found a trend of limited knowledge of certain common PGx tests used clinically. It is believed that this is the result of the current syllabi, as they lack lectures and courses about PGx.

PGx testing is recommended in the labeling of many prescribed drugs and is implemented in pharmacotherapy in numerous countries [18, 19]. The lack of understanding of the PGx knowledge is one of the main barriers against implementing PGx testing in clinical practice [20]. It was previously found that the knowledge of PGx testing is limited among physicians and pharmacists in the West Bank of Palestine [21, 22]. In this study, it is found similar results among medical doctor, medical analysis, nursing, pharmacy, Doctor of Pharmacy, physiotherapy, optics students. This poor knowledge of PGx testing in the medical society, could be due to the absence of educational courses geared towards PGx. Accordingly, we are currently far away from implementing PGx testing in the medical practice in the West Bank of Palestine. Therefore, based on the results of this research. it is recommended to include lectures, courses, and workshops concerning PGx in the syllabi of medical and paramedical students which can improve, at least partly, their pharmacotherapy knowledge.

When the survey of this study was designed, the example of the anticoagulant warfarin was used, since its PGx test can be considered as one of the most common PGx tests used in clinical practice [23]. Moreover, some research about the PGx of warfarin was conducted in Palestine [24, 25]. However, it is found in thus study that most of the respondents do not know about the PGx testing of warfarin. The results of this study showed that pharmacy and doctoral pharmacy students scored the highest in the knowledge of PGx than medical students, on the other hand, the lowest scores among the respondents were reported among nursing and paramedical students (physiotherapy and medical analysis). This was expected as pharmacy and doctoral pharmacy students are taught more pharmacology and pharmacotherapy courses and lectures than nursing

and paramedical students, which introduce the interindividual variation and the influence of genetic variants on the drugs response.

Most of the respondent students were female. This was expected as the records of An-Najah University indicate that the percentage frequency of male and female students in the medical colleges is 29 and 71%, respectively. Furthermore, some previous studies reported similar frequencies of male and female medical students in the Middle East [9, 26]. Accordingly, the sample of medical students used in this study represents the actual distribution of male and female students in the medical colleges.

Most of the respondents (93%) were students at An-Najah University, the biggest and top-ranked university in the West Bank of Palestine which has a variety of medical and paramedical educational programs. Nevertheless, it is a drawback as this study did not include other universities and regions inside Palestine.

Other limitation in this study that the number of students from sub-specialties in the paramedical sciences, optic students, was relatively small.

In this study, the results showed that most of the respondent students have a positive attitude toward PGx testing. This positive attitude toward PGx testing is also reported previously among medical students in other countries [27, 28]. However, this attitude does not bring us toward the clinical implementation of PGx testing without a sufficient required knowledge of PGx.

Conclusions

In conclusion, this study investigated the educational exposure and current knowledge of medical and paramedical students in the West Bank of Palestine toward PGx testing and found that there is a lack of educational exposure toward it and the students have poor knowledge of common clinically used PGx test. It is strongly recommended to enhance their PGx education in university medical programs as a first step toward clinical implementation of PGx testing and personalized therapy in the clinical practice in the West Bank of Palestine.

Acknowledgments: Authors would like to thank An-Najah University (Nablus, the West Bank of Palestine) for supporting this research.

Research funding: No fund was received for this research. Author contribution: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Authors state no conflict of interest. **Informed consent:** Informed consent was obtained from all individuals included in this study.

Ethical approval: An-Najah National University's ethical committee approved the study's protocol, and the Institutional Review Board number of this study is 16-02-2019.

References

- 1. Roden DM, Wilke RA, Kroemer HK, Stein CM. Pharmacogenomics: the genetics of variable drug responses. Circulation 2011;123:1661-70.
- 2. Alhawari H, Jarrar Y, AlKhatib MA, Alhawari H, Momani M, Zayed A, et al. The association of 3-hydroxy-3-methylglutaryl-CoA reductase, apolipoprotein E, and solute carrier organic anion genetic variants with atorvastatin response among Jordanian patients with type 2 diabetes. Life 2020;10:232.
- 3. Malsagova KA, Butkova TV, Kopylov AT, Izotov AA, Potoldykova NV, Enikeev DV, et al. Pharmacogenetic testing: a tool for personalized drug therapy optimization. Pharmaceutics 2020:12:1240.
- 4. Caldwell MD, Awad T, Johnson JA, Gage BF, Falkowski M, Gardina P, et al. CYP4F2 genetic variant alters required warfarin dose. Blood 2008; 111:4106-12.
- 5. Jarrar YB, Lee SJ. Molecular functionality of CYP2C9 polymorphisms and their influence on drug therapy. Drug Metabol Drug Interact 2014;29:
- 6. Tariq RA, Vashisht R, Sinha A, Scherbak Y. Medication dispensing errors and prevention. Treasure Island (FL): StatPearls; 2022.
- 7. Scharfe CPI, Tremmel R, Schwab M, Kohlbacher O, Marks DS. Genetic variation in human drug-related genes. Genome Med 2017;
- 8. Whirl-Carrillo M, Huddart R, Gong L, Sangkuhl K, Thorn CF, Whaley R, et al. An evidence-based framework for evaluating pharmacogenomics knowledge for personalized medicine. Clin Pharmacol Ther 2021;110:
- 9. Jarrar Y, Mosleh R, Hawash M, Jarrar Q. Knowledge and attitudes of pharmacy students towards pharmacogenomics among universities in Jordan and West Bank of Palestine. Pharmgenomics Pers Med 2019;12: 247-55.
- 10. Murphy JE, Green JS, Adams LA, Squire RB, Kuo GM, McKay A. Pharmacogenomics in the curricula of colleges and schools of pharmacy in the United States. Am J Pharmaceut Educ 2010;74:7.
- 11. Rahma AT, Elsheik M, Elbarazi I, Ali BR, Patrinos GP, Kazim MA, et al. Knowledge and attitudes of medical and health science students in the United Arab Emirates toward genomic medicine and pharmacogenomics: a cross-sectional study. J Pers Med 2020;10:191.
- 12. Arafah A, Rehman MU, Syed W, Babelghaith SD, Alwhaibi A, Al Arifi MN. Knowledge, attitude and perception of pharmacy students towards pharmacogenomics and genetics: an observational study from King Saud University. Genes 2022;13:269.
- 13. Daniel WW. Biostatistics, a foundation for analysis in the health sciences, 4th ed. New York: Wiley; 1987, vol xiii:733 p.
- 14. Tavakol M, Dennick R. Making sense of Cronbach's alpha. Int J Med
- 15. Turner RM, Park BK, Pirmohamed M. Parsing interindividual drug variability: an emerging role for systems pharmacology. Wiley Interdiscip Rev Syst Biol Med 2015;7:221-41.

- 16. Aneesh T, Sekhar S, Jose A, Chandran L, Zachariah SM. Pharmacogenomics: the right drug to the right person. J Clin Med Res 2009;1:191-4.
- 17. Bishop JR, Huang RS, Brown JT, Mroz P, Johnson SG, Allen JD, et al. Pharmacogenomics education, research and clinical implementation in the state of Minnesota. Pharmacogenomics 2021;22:681-91.
- 18. Hippman C, Nislow C. Pharmacogenomic testing: clinical evidence and implementation challenges. J Pers Med 2019;9:40.
- 19. Wang B, Canestaro WJ, Choudhry NK. Clinical evidence supporting pharmacogenomic biomarker testing provided in US Food and Drug Administration drug labels. JAMA Intern Med 2014;174:1938-44.
- 20. Tata E, Ambele M, Pepper M. Barriers to implementing clinical pharmacogenetics testing in sub-Saharan Africa. A critical review. Pharmaceutics 2020;12:809.
- 21. Iarrar Y. Musleh R. Ghanim M. AbuKhader I. Iarrar O. Assessment of the need for pharmacogenomics education among pharmacists in the West Bank of Palestine. Int J Clin Pract 2021;75:e14435.
- 22. Jarrar Y, Musleh R, Hamdan A, Ghanim M. Evaluation of the need for pharmacogenomics testing among physicians in the West Bank of Palestine. Drug Metab Pers Ther 2021;36:289-94.

- 23. Grossniklaus D. Testing of VKORC1 and CYP2C9 alleles to guide warfarin dosing. Test category: pharmacogenomic (treatment). PLoS Curr 2010;2:RRN1155.
- 24. Al-Eitan LN, Almasri AY, Khasawneh RH. Impact of CYP2C9 and VKORC1 polymorphisms on warfarin sensitivity and responsiveness in Jordanian cardiovascular patients during the initiation therapy. Genes 2018;9:578.
- 25. Ayesh BM, Abu Shaaban AS, Abed AA. Evaluation of CYP2C9- and VKORC1-based pharmacogenetic algorithm for warfarin dose in Gaza-Palestine. Future Sci OA 2018;4:FSO276.
- 26. Jarab AS, Al-Qerem W, Mukattash TL, Al-Hajjeh DM. Pharmacy and Pharm. D students' knowledge and information needs about COVID-19. Int | Clin Pract 2021;75:e13696.
- 27. Abubakar U, Subramaniam L, Ayinla A, Ambali MN, Mohamed Noor DA, Daud NAA, et al. Knowledge, attitude and perception of community pharmacists towards pharmacogenomics services in northern Nigeria: a cross-sectional study. J Pharm Policy Pract 2022;15:39.
- 28. Koufaki MI, Siamoglou S, Patrinos GP, Vasileiou K. Examining key factors impact on health science students' intentions to adopt genetic and pharmacogenomics testing: a comparative path analysis in two different healthcare settings. Hum Genom 2022;16:9.