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Clinical pharmacists' knowledge, attitude, perception, and beliefs about the role of pharmacogenetic testing for genes polymorphisms when prescribing mercaptopurine

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ABSTRACT

Background: Single nucleotide polymorphisms in the gene encoding proteins involved in mercaptopurine metabolism can influence drug efficacy and safety. This study aims to assess clinical pharmacists' knowledge about mercaptopurine-related genes and their polymorphisms and investigate their attitudes, perceptions, and beliefs about the need for and importance of pharmacogenetic testing for mercaptopurine.

Methods: A cross-sectional descriptive study was conducted among oncology/hematology clinical pharmacists in Saudi Arabia using an online-questionnaire developed by experts in the field. The questionnaire consists of four-sections exploring clinical pharmacists' knowledge, attitudes, perceptions, and beliefs about the importance of gene testing and genes polymorphism when prescribing mercaptopurine. Descriptive statistics were used to analyze the data in the study.

Results: A total of 41 oncology/hematology clinical pharmacists responded to the survey invitation. Almost half of them had more than 10 years of work experience, but only 17 % of them received formal training in pharmacogenetics. The overall level of knowledge about pharmacogenetics among participants was low, with a mean score of 2.8 points (1.7) out of 8 items. However, around 76 % agreed that it is important to perform pharmacogenetic screening prior to prescribing mercaptopurine, and almost 93 % state that it will influence their dosage recommendation. Most of the participants had a good perception (95.1 %) of their role in genetic testing for medication selection, dosing, and monitoring; however, about 10 % of surveyed pharmacists reported not being completely responsible about recommending pharmacogenetic testing. The surveyed pharmacists had a good belief in the importance of pharmacogenetic testing and their overall attitude was positive toward the use of pharmacogenetic testing, with emphasis on the importance of training on the proper assessment and interpretation of pharmacogenetic tests.

Conclusions: Pharmacists demonstrated good perception and positive attitude toward pharmacogenetic testing, despite the low level of knowledge and limited formal training. Thus, more attention to developing national guidelines on pharmacogenetic testing is warranted to ensure successful pharmacogenetic testing implementation.

1. Background

Pharmacogenetics and precision medicine aid in delivering safe and effective treatment based on patients' specific gene variation (Munindra, 2019). They help identify genetic factors that may influence the patient's pharmacokinetics and pharmacodynamics and help personalize medication and treatment planning according to the patient's own genetics (Rodríguez-Antona & Taron, 2015). Clinical providers, especially pharmacists, play a crucial role in driving the successful integration of genomic medicine into practice (Raheem et al., 2020).

Thiopurine drugs are hazardous medications that are mostly used as immunosuppressive and anticancer therapy for hematological malignancies, inflammatory bowel disease, and renal transplant patients (Abaji & Krajinovic, 2017). Mercaptopurine is one of the most important thiopurines and is a key element in the therapy protocols for childhood acute lymphoblastic leukemia, which is considered one of the most

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common types of cancer, accounting for approximately 25%-30% of all childhood malignancies (Dean & Kane, 2012; Abaji & Krajinovic, 2017).

Thiopurine S-methyltransferase (TPMT) and Nudix hydrolase 15 (NUDT15) are enzymes involved in the metabolism of mercaptopurine into its major active metabolite: 6-thioguanine triphosphate (6-TGTP) (Dean & Kane, 2012). Single nucleotide polymorphisms in the genes encoding these proteins can contribute to either a poor or rapid metabolism, resulting in serious toxicities or sub-therapeutic effects that significantly influence the drug's efficacy and safety (Hawwa et al., 2008; Dean & Kane, 2012; Zhang et al., 2016). Individuals with certain variant alleles of TPMT and NUDT15 will be either poor or rapid metabolizers. Poor metabolizers will suffer from severe life-threatening reactions such as myelosuppression, severe hematotoxicity, and hepatotoxicity, while rapid metabolizers will have sub-therapeutic effects. Both effects can lead to longer hospitalization, drug discontinuation, and increased financial burden. Therefore, deciding on the optimum treatment plan for each patient based on the patient's genetic characteristics is recommended for some types of medications (Zhang et al., 2016). This approach will improve patient outcomes by minimizing the adverse events and toxicities associated with gene polymorphism, especially with cancer therapy since it uses highly toxic medications (Hawwa et al., 2008).

There is a need for pharmacists who understand pharmacogenetic changes and develop guidelines for medications that require pharmacogenetic testing and dosage adjustment (Haidar et al., 2022). Pharmacists are encouraged to be a knowledgeable in clinical pharmacogenetics to collaborate effectively with medical teams by ordering pharmacogenetic tests, interpreting its results, and optimizing therapy (Crews et al., 2011; Owusu-Obeng et al., 2014). Moreover, the involvement of pharmacists in pharmacogenetic testing was reported to have positive impact on patient's therapy. A pharmacogenomic program that was implemented by pharmacogenetic-certified ambulatory care pharmacists leads to enhancement of medication safety and efficacy (Wick et al., 2023). In addition, a pharmacist-provided pharmacogenetic service that was established at the University of Colorado Hospital worked well and patients benefited from its implementation (Liko et al., 2021). Moreover, the existence of pharmacogenetic testing offered a medication improvement opportunity for commonly used medications in more than 50% of tested patients (Matey et al., 2022).

Researchers have been investigating pharmacists' knowledge, perceptions, and beliefs about and attitudes toward pharmacogenetics since 2013 or earlier; however, the amount of research remains limited. A finding from a recent systematic review in 2022 that only included 15 articles indicates that pharmacists, especially clinical pharmacists, possess interest in implementing pharmacogenetic services. However, knowledge, training, and clinical guidelines are still not well established in this area (Hansen et al., 2022).

The perspectives of and knowledge about pharmacogenetics in Saudi Arabia have been studied before, and pharmacists' knowledge of pharmacogenetics was found to be limited; however, the pharmacists displayed passion about learning more and implementing such services in their daily practice (Algahtani, 2020; Bagher et al., 2021; Alhaddad et al., 2022). Clinical pharmacists are now more involved in inpatient care and in medication dosage adjustment and monitoring. We aimed for more specificity in this study and targeted clinical pharmacists practicing in oncology/hematology departments. Since gene polymorphism is an important aspect of mercaptopurine dosing, this study seeks to assess clinical pharmacists' knowledge, perceptions, attitudes, and beliefs about the importance of pharmacogenetic testing, taking mercaptopurine as an example case.

2. Methods

2.1. Study design

A questionnaire-based, online, cross-sectional study was conducted in Saudi Arabia between December 2021 and March 2022. The study targeted clinical pharmacists in Saudi Arabia practicing in the oncology/hematology field. The Institutional Review Board (IRB) for Research on Human Subjects at King Saud University Medical City approved this study (IRB# E-21–6202), and consent was obtained electronically from the participants. To qualify for inclusion in this study, participants had to be oncology/hematology clinical pharmacists who practice in Saudi Arabia.

The survey was distributed through the Saudi Commission For Health Specialists (SCFHS) to only target oncology/hematology clinical pharmacists. However, a limited number of pharmacists specialize in this field; thus, the snowball sampling technique was employed later on to collect data from all clinical pharmacists providing care to cancer patients. Consequently, personal communications with oncology/hematology clinical pharmacists' colleagues was done and those were requested to distribute the survey to other clinical pharmacists working in this filed to request their participation. Participation in the study was voluntary, responses were completely anonymous, and participants were allowed to stop the survey whenever they wanted.

2.2. Questionnaire development

The questionnaire was developed by the authors based on expert opinions from research and practice, as well as on previous studies on this topic (Hartzler et al., 2013; Munindra, 2019; Przybylski et al., 2020). The drafted questionnaire was reviewed for its content validity and amended over three rounds of revisions by two experts in the field; one is a clinical pharmacy consultant in the oncology/hematology field who is one of the leaders and mentor for many practicing clinical pharmacists in this field at the national level and the other is a pharmacy consultant/researcher in the field of pharmacogenetics and pharmacogenomics. Furthermore, it was piloted to ten pharmacists who practice in the oncology/hematology field based for revision to ensure the completeness and comprehensiveness of the survey, and no changes were made at this stage. The survey was developed and deployed on a Google form and sent electronically with an invitation letter to clinical pharmacists in this field in Saudi Arabia (n=100), followed by a reminder within 2 weeks.

In addition to questions about demographic characteristics, the online questionnaire included 38 questions that explore four dimensions: pharmacists' knowledge about polymorphisms in metabolic pathway genes and their potential role in treatment adjustment with mercaptopurine; pharmacists' perception of their role in genetic testing for medication selection, dosing, and monitoring; the importance of pharmacogenetic testing for mercaptopurine from pharmacists' perspective; and the pharmacists' attitudes toward the use of pharmacogenetic testing in practice. A 5-point Likert scale (5, strongly agree; 4, agree; 3, neutral; 2, disagree; 1, strongly disagree) was used to score the pharmacists' perceptions, attitudes, and beliefs about the importance of pharmacogenetic testing in practice. Participants with total points that are equivalent to more than 70% of the points in the domain were considered to have positive outcome, namely positive perception, belief, and attitude. Besides that, the knowledge section consisted of 8 statements that can be answered by stating "correct," "incorrect," or "I do not know." The total score for the knowledge item is out of 8, and anyone with more than 5 correct answers (>60%) were considered to have good knowledge. Conversely, participants with 3–5 correct answers or fewer than 3 were considered to have moderate or low-level knowledge, respectively.

2.3. Statistical analysis

Descriptive statistics, mainly frequency with percentages or mean with standard deviation (SD), were used to summarize the participants' knowledge, perception, attitude, and beliefs about the importance of pharmacogenetics. In addition, Chi-square or Fisher-exact tests were

used as appropriate to investigate the effect of demographics on the participants responses. The inter-items reliability was assessed for each domain using the Cronbach's alpha statistics. Data were stored and managed using Microsoft excel. Data were analyzed using the SAS statistical analytics software version 9.4 (SAS Institute, Inc., Cary, NC).

3. Results

A total of 41 clinical pharmacist responded out of 100 pharmacists approached (~40.0% response rate). The responses came from four out of the five largest regions in the country. Almost half of the participants had more than 10 years of work experience, 46% had at least a PGY-2 training, and only 17% of them indicated receiving formal training in pharmacogenetics (Table 1).

The overall level of knowledge among the participants was moderate to low, with only 4 participants (9.8%) having good level of knowledge. The knowledge was high in only one item related to pharmacogenetic testing—severe myelosuppression (80.5% answered correctly). However, going deeper into more specific items, the participants' answers reflected a low level of knowledge, where the least level of knowledge was observed in the item related to genetic variation in the ATIC gene (4.9% answered correctly). The items on the questionnaire for the knowledge domain had a moderate inter-item reliability level with a Cronbach's alpha of 0.61. The items asked and the participants correct or incorrect responses are presented in Table 2.

When we examined the pharmacists' perceptions about their role in genetic testing for medication selection, dosing, and monitoring, all pharmacists agreed or strongly agreed that the clinical adoption of pharmacogenetic testing did not yet reach its potential. In addition, the majority of pharmacists (97.6%) agreed or strongly agreed that pharmacogenetic data are helpful in tailoring an appropriate treatment plan.

Table 1
Demographic characteristics for the participants.

Characteristic	Number (%)
Age	
20–30 years	14 (34.1)
31–40 years	17 (41.5)
41–50 years	5 (12.2)
> 50 years	5 (12.2)
Gender	
Male	23 (56.1)
Female	18 (43.9)
Highest level of education or training	
Bachelor's degree in pharmaceutical sciences	3 (7.3)
Pharm D	4 (9.8)
PGY-1 training or Master's degree	15 (36.6)
PGY-2 training or fellowship	19 (46.3)
Nationality	
Saudi	34 (82.9)
Non-Saudi	7 (17.1)
Level of care provided at your institution	
Primary care	2 (4.9)
Secondary care	7 (17.1)
Tertiary care	32 (78.0)
Work setting	
Ministry of health hospitals	15 (36.6)
Other governmental hospitals	21 (51.2)
Private hospitals	5 (12.2)
Years of experience	
Less than 5 years	9 (22.0)
5–10 years	15 (36.6)
More than 10 years	17 (41.5)
Received formal training or certification on PGx	
No	34 (82.9)
Yes	7 (17.1)
Work region	
Central region	28 (68.3)
Eastern region	2 (4.8)
Western region	10 (24.4)
Northern region	1 (2.4)

Table 2
Pharmacists' knowledge about polymorphisms of the metabolic pathway genes and its potential role in treatment.

Knowledge items	Correct response n (%)	Incorrect response or don't know n (%)
Pharmacogenetic testing is recommended if a patient using mercaptopurine experiences recurrent severe myelosuppression.	33 (80.5)	8 (19.5)
Mercaptopurine should be avoided in patients who are homozygous mutants or who have extremely low or absent thiopurine S-methyltransferase (TPMT).*	6 (14.6)	35 (85.4)
Patients with homozygous deficiency due to nudix hydrolase 15 (NUDT15) mutation may suffer exacerbation of severe myelosuppression toxicity with a standard dose of mercaptopurine.	26 (63.4)	15 (36.6)
Previous studies have shown that TPMT and NUDT15 polymorphisms are commonly present among the Saudi population.*	5 (12.2)	36 (87.8)
Patients with TPMT homozygous deficiency require 10 % or less of the standard dose of mercaptopurine.	22 (53.7)	19 (46.3)
Genetic variation in the ATIC gene may affect the metabolism of mercaptopurine.*	2 (4.9)	39 (95.1)
Patients with NUDT15 heterozygous deficiency require 50 % of the standard dose of mercaptopurine.*	4 (9.8)	37 (90.2)
Patients with very high levels of TPMT activity are less likely to respond to mercaptopurine and may delay the treatment outcomes.	18 (43.9)	23 (56.1)
Average number of correct responses for the knowledge items (SD)	2.8 (1.7) /8 items	

Note:
*These items represent incorrect statments on the knowledge scale.
Participants who answer "don't know" are counted toward the incorrect responses.

However, the item that attracted the most disagreement (9.8%) asked about the pharmacists' responsibility to recommend pharmacogenetic testing for drug therapy selection, dosing, and monitoring (Fig. 1). The clinical pharmacists' overall perception of their role in genetic testing was positive; 95.1% of the participants had a total score of more than 25 points (out of 35 points) on the Likert scale (≥70%) for the perception domain (Table 3). The items on the questionnaire for the perception domain had a high inter-item reliability level with a Cronbach's alpha of 0.78.

When asked about the importance of pharmacogenetic testing for mercaptopurine use from their perspective, 92.7% stated that it will influence their dosage recommendation, and approximately 83% of the participating pharmacists indicated that having results from pharmacogenetic testing prior to dispensing mercaptopurine will enhance their confidence in their recommendation. However, the only item that received a disagreement response (12.2%) was about the decrease in the need for frequent monitoring when preemptive pharmacogenetic testing for mercaptopurine is applied (Fig. 2). The clinical pharmacists' overall belief in the importance of pharmacogenetic testing for mercaptopurine use was mostly positive; 85.4% of the participants had a total score of more than 18 points (out of 25 points) on the Likert scale (≥70%) for this domain (Table 3). The items on the questionnaire for the belief domain had a high inter-item reliability level with a Cronbach's alpha of 0.82.

The majority of pharmacists (95.1%) agreed or strongly agreed that training is essential when interpreting the results of pharmacogenetic tests, while 85.4% of them agreed or strongly agreed that when needed, they actually recommend pharmacogenetic testing for their patients. Moreover, 80.5% of pharmacists agreed that they are capable of using pharmacogenetic tests for drug therapy selection, dosing, or monitoring

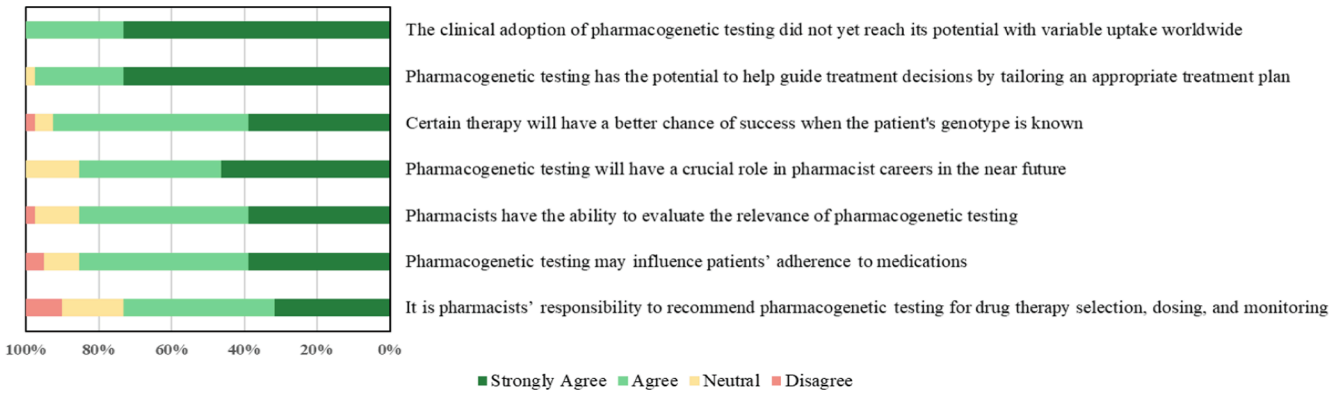

Fig. 1. Pharmacists' perception of their role in genetic testing for medication selection, dosing, and monitoring.

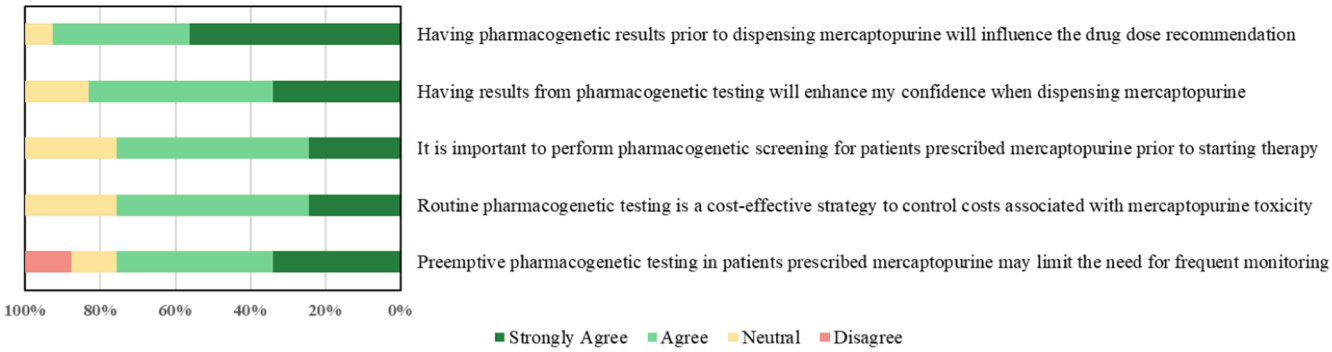

Fig. 2. The importance of pharmacogenetics for mercaptopurine from pharmacists' perspective.

and for dosage adjustments. Conversely, only 56.1% of pharmacists agreed or strongly agreed that they avoid reading the results of pharmacogenetic tests, tend to search for information about pharmacogenetics, or tend to advise treatment with certain medication despite the pharmacogenetic test showing it would be ineffective or toxic (Fig. 3). The clinical pharmacists' overall attitude toward the use of pharmacogenetic testing in practice was mostly positive, 82.9% of the participants had a total score of at least 28 points (out of 40 points) on the Likert scale (≥70%) for the attitude domain (Table 3). The items on the questionnaire for the attitude domain had a moderate inter-item reliability level with a Cronbach's alpha of 0.63.

Besides that, multiple inferential statistics were conducted to investigate the effect of different demographics on the study domains. However, none of these analyses or comparisons was significant (Table 3).

4. Discussion

The study was conducted to assess the current level of knowledge, perceptions, attitudes, and beliefs about the importance of pharmacogenetic testing for mercaptopurine among clinical pharmacists providing care to oncology/hematology patients in Saudi Arabia. The study found that the level of knowledge about genetic polymorphisms in the metabolic pathway for mercaptopurine among clinical pharmacists providing care to these patients was medium to low. However, the results indicate that the surveyed clinical pharmacists held positive perceptions of their role in genetic testing for medication selection, dosing, and monitoring. In addition, their attitudes toward the use of pharmacogenetic testing in practice are positive, and they belief that pharmacogenetic testing is very important. In regards to the effect of demographics on the participants' responses to the items on the study domains, no significant differences were observed among the

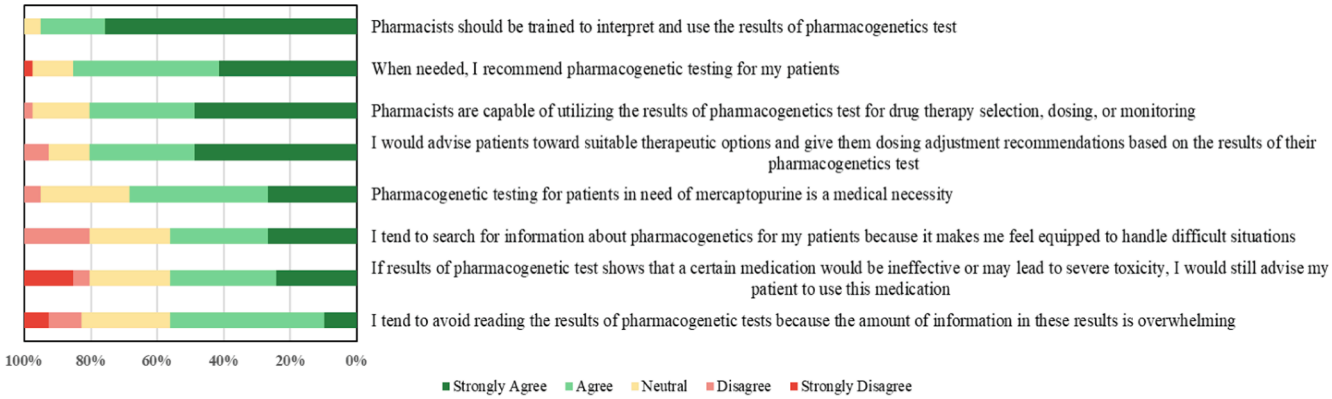

Fig. 3. Pharmacists' attitude toward the use of pharmacogenetic testing in practice.

Table 3
Overall response to the knowledge, perception, belief of importance, and attitude domains based on demographic characteristics for the participants.

	Knowledge			Perception			Belief of importance			Attitude		
	Low to moderate	Good	*p*-value	Negative	Positive	*p*-value	Negative	Positive	*p*-value	Negative	Positive	*p*-value
Overall response	37 (90.2)	4 (9.8)		2 (4.9)	39 (95.1)		6 (14.6)	35 (85.4)		7 (17.1)	34 (82.9)	
Age			0.6616			0.2901			0.0535			0.1273
20–30 years	13 (92.9)	1 (7.1)		1 (7.1)	13 (92.9)		0 (0.0)	14 (100.0)		4 (28.6)	10 (71.4)	
31–40 years	16 (94.1)	1 (5.9)		0 (0.0)	17 (100.0)		2 (11.8)	15 (88.2)		1 (5.9)	16 (94.1)	
41–50 years	4 (80.0)	1 (20.0)		0 (0.0)	5 (100.0)		2 (40.0)	3 (60.0)		0 (0.0)	5 (100.0)	
> 50 years	4 (80.0)	1 (20.0)		1 (20.0)	4 (80.0)		2 (40.0)	3 (60.0)		2 (40.0)	3 (60.0)	
Gender			0.6178			0.8586			0.2239			0.9512
Male	20 (87.0)	3 (13.0)		1 (4.3)	22 (95.7)		2 (8.7)	21 (91.3)		4 (17.4)	19 (82.6)	
Female	17 (94.4)	1 (5.6)		1 (5.6)	17 (94.4)		4 (22.2)	14 (77.8)		3 (16.7)	15 (83.3)	
Education			0.5654			0.0890			0.6914			0.6271
Bachelor's degree in pharmaceutical sciences	3 (100.0)	0 (0.0)		1 (33.3)	2 (66.7)		1 (33.3)	2 (66.7)		1 (33.3)	2 (66.7)	
Pharm D	3 (75.0)	1 (25.0)		0 (0.0)	4 (100.0)		1 (25.0)	3 (75.0)		0 (0.0)	4 (100.0)	
PGY-1 training or Master's degree	18 (94.7)	1 (5.3)		0 (0.0)	19 (100.0)		2 (10.5)	17 (89.5)		4 (21.1)	15 (78.9)	
PGY-2 training or fellowship	13 (86.7)	2 (13.3)		1 (6.7)	14 (93.3)		2 (13.3)	13 (86.7)		2 (13.3)	13 (86.7)	
Nationality			0.3394			0.5106			0.9772			0.8296
Saudi	30 (88.2)	4 (11.8)		2 (5.9)	32 (94.1)		5 (14.7)	29 (85.3)		6 (17.6)	28 (82.4)	
Non-Saudi	7 (100.0)	0 (0.0)		0 (0.0)	7 (100.0)		1 (14.3)	6 (85.7)		1 (14.3)	6 (85.7)	
Level of care provided at your institution			0.8251			0.4383			0.8317			0.7735
Primary care	2 (100.0)	0 (0.0)		0 (0.0)	2 (100.0)		0 (0.0)	2 (100.0)		0 (0.0)	2 (100.0)	
Secondary care	6 (85.7)	1 (14.3)		1 (14.3)	6 (85.7)		1 (14.3)	6 (85.7)		1 (14.3)	6 (85.7)	
Tertiary care	29 (90.6)	3 (9.4)		1 (3.1)	31 (96.9)		5 (15.6)	27 (84.4)		6 (18.8)	26 (81.3)	
Work setting			0.5509			0.8351			0.5475			0.1263
Ministry of health hospitals	14 (93.3)	1 (6.7)		1 (6.7)	14 (93.3)		3 (20.0)	12 (80.0)		1 (6.7)	14 (93.3)	
Other governmental hospitals	18 (85.7)	3 (14.3)		1 (4.8)	20 (95.2)		3 (14.3)	18 (85.7)		6 (28.6)	15 (71.4)	
Private hospitals	5 (100.0)	0 (0.0)		0 (0.0)	5 (100.0)		0 (0.0)	5 (100.0)		0 (0.0)	5 (100.0)	
Years of experience			0.8784			0.7401			0.3813			0.4632
Less than 5 years	8 (88.9)	1 (11.1)		0 (0.0)	9 (100.0)		1 (11.1)	8 (88.9)		1 (11.1)	8 (88.9)	
5–10 years	14 (93.3)	1 (6.7)		1 (6.7)	14 (93.3)		1 (6.7)	14 (93.3)		4 (26.7)	11 (73.3)	
More than 10 years	15 (88.2)	2 (11.8)		1 (5.9)	16 (94.1)		4 (23.5)	13 (76.5)		2 (11.8)	15 (88.2)	
Received formal training			0.6574			0.5106			0.9772			0.1874
No	31 (91.2)	3 (8.8)		2 (5.9)	32 (94.1)		5 (14.7)	29 (85.3)		7 (20.6)	27 (79.4)	
Yes	6 (85.7)	1 (14.3)		0 (0.0)	7 (100.0)		1 (14.3)	6 (85.7)		0 (0.0)	7 (100.0)	

Note: Participants with good knowledge are those who answered correctly to at least 60% of the items on the knowledge about polymorphisms scale; while participants with positive perception, belief of importance, or attitude toward the use of pharmacogenetic testing in practice are those who responded positively to at least 70% of the items on these domains.

participants based on these demographics.

The low level of knowledge among the participants mirror the inadequate formal training that was previously reported in general pharmacogenetics studies (Elewa et al., 2015; Albassam et al., 2018; Algahtani, 2020; Karuna et al., 2020; Hayashi & Bousman, 2022; Nie et al., 2022; Pop et al., 2022), while findings from oncology studies still do not exist. It is well established that knowledge increases with more training and education, which leads to increased confidence in interpreting and applying pharmacogenetic information (Marcinak et al., 2018). Although nearly half of the participants in the study had over 10 years of work experience, only 17% of them had received formal training in pharmacogenetics.

The majority of participants acknowledged the importance of conducting pharmacogenetic screening prior to prescribing mercaptopurine, with more than 75% of participants agreeing that this screening is essential. Furthermore, the majority of surveyed clinical pharmacists stated that having pharmacogenetic testing results prior to dispensing would significantly influence their dosage recommendations and their level of confidence in their decision-making when prescribing mercaptopurine. While studies focusing specifically on mercaptopurine is

lacking, acknowledging the importance of using pharmacogenetic testing in general to provide more personalized and effective patient care was previously reported for pharmacists (Algahtani, 2020; Tsuji et al., 2021; Nie et al., 2022). Algahtani reported that about 32% of surveyed pharmacists indicated that the use of pharmacogenetic results can improve drug selection, dosing, or monitoring (Algahtani, 2020). More recently, Nie et al. reported that 68% of surveyed pharmacists agreed that pharmacogenetic testing could help them choose drugs or optimize dosing (Nie et al., 2022). In addition, Tsuji et al. found that more than 95% of surveyed pharmacists agrees on the role of pharmacogenetic testing in improving treatment efficacy (Tsuji et al., 2021). Our and previous findings highlight the clinical pharmacists' recognition of the value of incorporating pharmacogenetic testing into their practice and acknowledges the importance of using pharmacogenetic testing to provide more personalized and effective patient care.

The findings of this study revealed a strong and positive perception among the participants regarding pharmacogenetics, with the majority (85%) of the participants reporting that pharmacogenetics would play a crucial role in their careers as pharmacists in the near future. Additionally, they show a high sense of responsibility in recommending pharmacogenetic testing when necessary. A Similar findings was previously reported in a study investigating physicians and pharmacists' perceptions toward pharmacogenetic practices which found that around 70% of pharmacists had a positive perception which significantly exceeded the physicians' perception (Albassam et al., 2018). This finding indicates the crucial role of pharmacists in promoting pharmacogenetic practices and their enthusiasm for embracing the potential of pharmacogenetics in optimizing patient care.

The positive attitudes toward pharmacogenetics reported by oncology/hematology clinical pharmacists in this study have been reported previously by clinical pharmacists in China, hospital pharmacists in Thailand, practicing pharmacists in Zimbabwe, and community pharmacists in the USA (Tuteja et al., 2013; Muzoriana et al., 2017; Karuna et al., 2020; Nie et al., 2022). One of the most important parameters in positive attitude is the ability of participants to use pharmacogenetics to improve drug efficacy and reduce the incidence of adverse reaction which was reported by 77% of clinical pharmacists in China (Nie et al., 2022). When warfarin was used as an example to assess pharmacists' attitude towards the application of pharmacogenetic in clinical practice in Zimbabwe, 83% indicated that pharmacogenetic testing will reduce the time to reach the optimal dose and 82% indicated it will help reduce warfarin's adverse drug reactions (Muzoriana et al., 2017). In addition, a noteworthy finding shows that 56% of the participants agreed with the fact that pharmacists avoid reading the results of pharmacogenetic tests due to the overwhelming amount of information. This finding suggests that a significant portion of the surveyed pharmacists may feel challenged by the complexity of handling and interpreting these results to make a proper recommendation. This potential barrier highlights the need for additional support, such as specialized training and accessible resources, to assist pharmacists in navigating and interpreting the result of pharmacogenetic tests. Challenges in the implementation of pharmacogenetic programs within oncology pharmacy practice were assessed in a paper published in 2020, which found that the poor visibility of pharmacogenetic information within the electronic medical record was the most challenging barrier, in addition to the lack of dedicated pharmacogenetic resources and insurance denials for pharmacogenomic-driven medications (Przybylski et al., 2020). By providing the necessary support and resources, pharmacists can overcome the perceived overwhelming nature of pharmacogenetic test results to select an appropriate medication or dose recommendation. Eventually, this approach will enhance their ability to incorporate valuable pharmacogenetics information into their practice to improve patient care.

Moreover, an overwhelming majority of participants (83%) expressed a lack of formal pharmacogenetics education or training during their training and educational programs. To address this gap and enhance knowledge, developing national pharmacogenetic guidelines to ensure successful pharmacogenetic implementation and include pharmacogenetic markers into clinical practice is recommended. In addition, mandatory pharmacogenetics' courses and modules can be offered in the pharmacy curriculum, focusing on the pharmacogenetic principles, applications, and clinical implications. By ensuring that pharmacists receive comprehensive education in this vital field, pharmacists will be better equipped to understand and apply pharmacogenetic principles in their practice, ultimately leading to improved patient care and medication outcomes. This result will help bridge the knowledge gap identified in the study and ensure that pharmacists possess the necessary skills to provide optimal care in the context of pharmacogenetics.

A few limitations in the study should be noted when interpreting its findings. The number of clinical pharmacists specializing in the hematology/oncology field in Saudi Arabia is limited (only 100 clinical pharmacists), which led to a fewer number of participants than expected. Although the response rate was very low, the respondents were a good representation of pharmacists practicing in oncology departments all over Saudi Arabia. Although multiple inferential analyses were conducted to add some comparisons in regards to the study domains based on the participants' demographics, none of these tests came to be significant for any of the demographic variables. This is mainly due to the very small sample in the study and the substantial agreement among the participants in the study domains. Another limitation is that only clinical pharmacists were included in the study. Physicians and other healthcare providers also routinely use pharmacogenetic testing, so they also play a key role in pharmacogenetic implementation in practice. In addition, 66% of the study participants were based in the Riyadh region of Saudi Arabia. Therefore, the findings of this study should be interpreted with caution when applying them to other regions, as they may not offer a comprehensive and accurate representation; indeed, the largest oncology/hematology centers in Saudi Arabia are located in Riyadh.

5. Conclusion

While there is a knowledge gap among clinical pharmacists about pharmacogenetics, in particular mercaptopurine in this case, they demonstrated a positive perception and attitude toward incorporating results from pharmacogenetic testing into their practice as well as the importance of their role in pharmacogenetic testing. Addressing the knowledge gap with lack of formal pharmacogenetic education and training is important to overcome the challenges of overwhelming test results to enhance pharmacists' ability to effectively handle and employ pharmacogenetic tests information in their practice. In doing so, pharmacists can contribute to personalized medication management, improve treatment outcomes, and ultimately deliver better patient care to all patients in Saudi Arabia.

Author contribution

NOA: Conceptualization, Methodology, Investigation, Resources, Validation, Visulization, Supervision, Writing – original draft. **SAA and RKA:** Conceptualization, Investigation, Data curation, Writing – original draft. **OAA:** Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Software, Funding acquisition, Writing – review & editing.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

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