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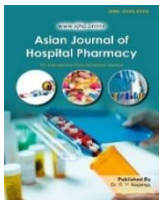

PHARMACOGENETICS IN A TERTIARY CARE CENTER; KNOWLEDGE, ATTITUDE AND PRACTICE AMONG PHYSICIAN AND CLINICAL PHARMACIST

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Abstract

Background**:** Pharmacogenetics is "the study of how genetics influence an individual's response to medicines". Use of Pharmacogenetics in routine health-care remains limited, mainly due to the barriers like lack of knowledge, guidelines and skilled personals. Therefore, assessing the current knowledge level and attitude reveals the significant gap that hinders the effective integration of pharmacogenetics into clinical practice.

Materials and Methods: A cross-sectional survey was conducted among physicians and clinical pharmacists practicing in a tertiary care center, using a self-administered questionnaire. The data were analyzed using SPSS version 25.

Results**:** A total of 80 individuals participated in the study. The overall knowledge score calculated showed that 36 (66.7%) doctors and 20 (76.9%) CPs had good knowledge regarding pharmacogenetics. 39 (72.2%) doctors and 25 (96.2%) CPs had a positive attitude towards pharmacogenetics. A significant number of participants among them 12 (22.2%) physicians and 20 (76.9%) CPs expressed that all the factors like the time & cost, lack of clinical guidelines & knowledge, lack of personnel were the major impediments in practicing pharmacogenetics.

Conclusion**:** The participants had good knowledge regarding pharmacogenetics, with CPs expressing a positive attitude than physicians. Both groups were ready to practice pharmacogenetics, but a significant number of participants expressed their concern regarding the potentials barriers involved in it.

***Keywords*:** *Pharmacogenetics, Precision medicine, Physician, Clinical Pharmacist, Tertiary care center.*

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Introduction

Pharmacogenetics is defined as "the study of how genetics influence an individual's response to medicines". It integrates pharmacology (the science of drugs) with genomics (the study of genes) to produce safe and effective medicines together with precisely tailored dosages based on an individual's genetic makeup [1]. Lately, the health-care approach has been evolving from "one size fits all" model to a more personalized strategy. Modern medicine advocates for the clinical application of "the right drug, right dose, right time, and right technique" [2]. Several studies, including randomized controlled trials, have shown that individualizing drug therapy based on pharmacogenetic testing led to improved patient outcomes for specific drug–gene combinations [3,4]. The recent PREPARE study conducted across seven European countries, investigated the clinical utility of preemptively conducting pharmacogenetic testing for specific drug-gene combinations. The primary reported outcomes of the study suggested an impressive reduction in clinically relevant Adverse Drug Reactions (ADRs) among the participants [5]. The advantages of pharmacogenetics include the reduction of health care costs by reducing adverse drug reactions,the number of failed trials, less time required for drug approval, and less need for testing several medications to find the one with the best results for an individual [6]. Regulatory agencies, like the Health Canada or the US Food and Drug Administration (FDA), have included

pharmacogenetic information on the label of more than 100 drugs, making it available for the prescribers and patients. Moreover, several international consortia, for instance the Canadian Pharmacogenomics Network for Drug Safety and the Clinical Pharmacogenetics Implementation Consortium (CPIC), have been established with the focus of developing clinical practice guidelines and to provide recommendations to the prescribers [7].

In the contemporary world pharmacogenetics has gained the interest of academia and industry, whereby health care personnel have tried to use personalized medicine [8]. Despite the high level of scientific evidence and recognized clinical benefits of applying pharmacogenetics to improve drug therapy outcomes and enhance treatment safety, the process of promoting its adoption by prescribing physicians remain challenging. The use of pharmacogenetic testing in routine health-care remains limited and is primarily seen in large academic medical centres. Deficit knowledge, lack of awareness or confidence, availability of skilled personals and appropriate guidelines are few of the major barriers that averts the implementation of pharmacogenetics [9, 10]. Therefore, assessing the current knowledge level and attitude among major stakeholders like physicians and pharmacists reveals the significant gap that hinders the effective integration of pharmacogenetics into clinical practice. Widely, pharmacists have been recognized as among the most qualified health-care professional to interpret pharmacogenetic test results due to their knowledge in the field of pharmacokinetics and pharmacodynamics of medicines. They are also well positioned to lead inter professional efforts to practice pharmacogenetic testing due to their availability [11]. A clinical pharmacist works directly with physicians and other health professionals to ensure that the medications advised for patients results in the best possible health outcomes. The American Society of Health System Pharmacists (ASHP) recognizes the fundamental role played by a pharmacist in ensuring optimal medication therapy selection based on the pharmacogenetic results, and a pharmacist's involvement as an underlying factor to the successful implementation of pharmacogenetics within a primary care center [12].

Several studies have been conducted worldwide to assess the level of knowledge, attitude and practice regarding pharmacogenetics among health-care providers like physicians, hospital, community and clinical pharmacists, nurses, etc. 1,5,10 Whereas, there are only few studies done to compare the knowledge, attitude and practice of pharmacogenetics among physicians and clinical pharmacists in a tertiary care center in South India, mainly because the field of clinical pharmacy is still under dormancy in developing countries like India. The objective of the current study was to infer and compare the level of knowledge, attitude, and practice of pharmacogenetics among physicians and clinical pharmacists in a tertiary care hospital in South India.

Materials and Methods

Study Design and Population

A cross-sectional survey was conducted in a 570 bedded tertiary care hospital in South India, among 80 medical professionals mainly Physicians and Clinical Pharmacists (CP). Convenience sampling method was followed. Only Physicians belonging to the departments that uses the drugs having the Pharmacogenetic associations listed by the Food and Drug Administration (FDA) were selected. These includes the department of Anaesthesiology, Cardiology, Oncology, Clinical Immunology & Rheumatology, Clinical Pharmacology, Dermatology, Endocrinology, General medicine, Gastroenterology, Nephrology, Neurology, Paediatrics, Obstetrics & Gynaecology, Pulmonology, Psychiatry, Pain and Palliative Medicine, Infectious disease and Urology. The selected physicians and CP were approached and provided with the self-administered survey form containing the survey questions. The participants were explained regarding the objectives of the study and were free to decline participation.

Study Questionnaire

The study survey was adapted from similar studies through literature review, followed by which it was discussed and revised by a panel of experts. The questionnaire consists of four sections with both open and close-ended questions. The section A encompassed questions regarding the demographic and professional information of the participants. The remaining sections B, C and D comprised of four questions each based on the knowledge, attitude and practice regarding pharmacogenetics respectively. For each section, the correct response received a score of one, and zero for the incorrect response. Participants were classified to perceive good or poor level of knowledge based on the total score they received. The attitude section was assessed using a three-point Likert scale (Agree, Disagree, and Neutral). All agree responses received a score of one, while neutral or disagree received a score of zero. If the score was greater than or equal to three, it was regarded as an overall positive attitude. The final section also contained four practice based questions. All participants were allowed to choose one option and all the questions were mandatory. The items of the questionnaire and their quantified responses are presented in tables and figures in the results section.

Statistical Analysis

Data was entered into Microsoft excel and analyzed using the SPSS version 25 (IBM Chicago). Quantitative data was expressed as mean ± standard deviation. Whilst qualitative data was expressed as percentage. A p-value < 0.05 was considered to be statistically significant.

Results

Section A: Demographics, professional and educational information

As depicted in Table. 01 a total of 80 individuals participated in the study, among which 54 (67.5%) were Physicians and

26 (32.5%) were Clinical Pharmacists(CPs). The ages of the participating physicians varied from 27 to 71 years, with an average age of 37.91 ± 9.87 and the ages of the CP ranged from 24 to 39 years, with an average age of 29.46 ± 5.44. Among Physicians, 31 (57.4%) were males, while 23 (42.6%) were females. While, there were only 9 (34.6%) male CPs and the remaining 17 (65.4%) were female CPs. The Physicians who participated in the study were drawn from various departments, mainly Anaesthesiology [9 (16.7%)], Paediatrics [7 (13%)], Neurology [7 (13%)], Oncology [5 (9.3%)], Pulmonology [4 (7.4%)], General Medicine [3 (5.6%)], Cardiology [3 (5.6%)], Dermatology [2 (3.7%)], Endocrinology [2 (3.7%)],, Gastroenterology [2 (3.7%)], Nephrology [2 (3.7%)], Obstetrics & Gynaecology [2 (3.7%)], Psychiatry [1 (1.9%)], Pain and Palliative Medicine [1(1.9%)], Infectious Disease [1 (1.9%)], and Urology [1 (1.9%)], Clinical Immunology and Rheumatology [1 (1.9%)] (Figure. 1). Whereas all the CPs involved in the study belonged to the department of Clinical Pharmacology. Among the physicians, 27 (50%) held post-graduate degrees (DM/MD/DNB), while the remaining 27 (50%) also had post-professional qualifications like any degree after masters such as diploma, fellowship or PhD. All of the clinical pharmacists, totaling 26 (100%), were Doctor of Pharmacy (Pharm D) graduates.

Table 01: Demographic characteristics, professional and educational information of the participants (n=80).

	Clinical Pharmacist	**Physician**	**P-value**
Age	29.46 ± 5.44	37.91 ± 9.87	**<0.001**
Gender			
Male	9 (34.6%)	31 (57.4%)	0.056
Female	17 (65.4%)	23 (42.6%)	
Total	**26 (100%)**	**54 (100%)**	
Years of Experience			
0 to 5 years	24 (92.3%)	30 (55.6%)	**0.034**
5 to 10 years	2 (7.7%)	8 (14.8%)	
>10 years	0(0.0%)	16 (29.6%)	
Total	26 (100%)	54 (100%)	
Educational Qualification			
Post-graduation	26 (100%)	27 (50%)	**0.004**
Post professional degree	0 (100%)	27 (50%)	
Total	26 (100%)	54 (100%)	

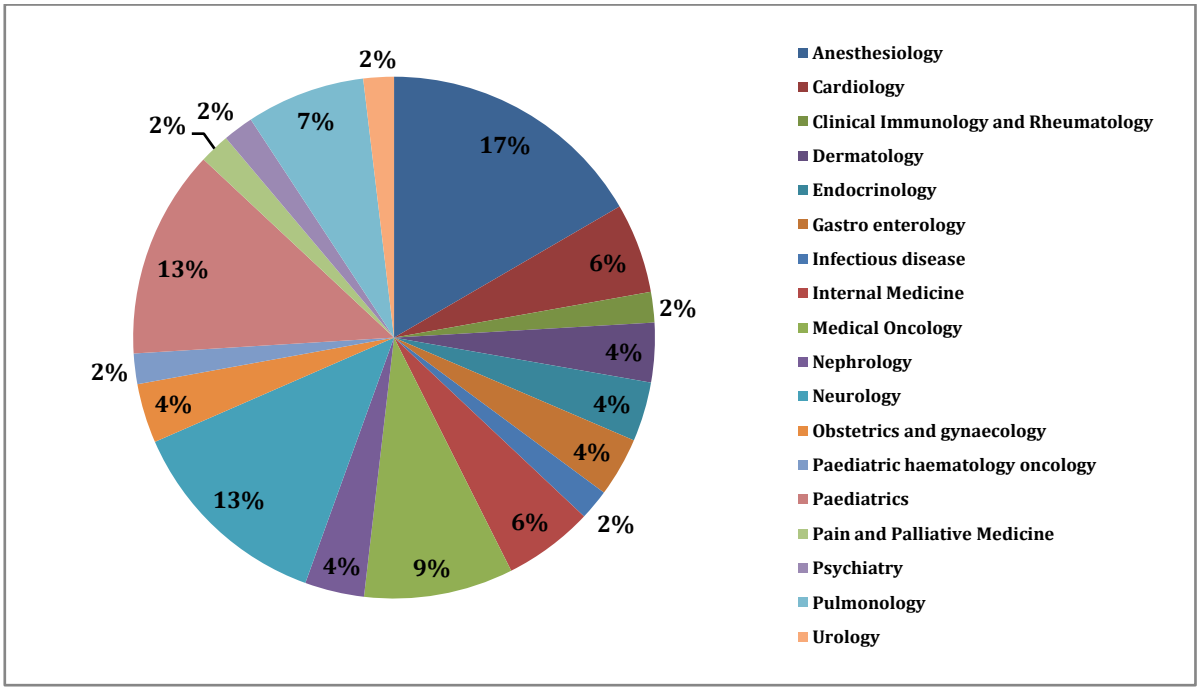

Figure 01: Areas of specialization

Section B: Participants knowledge level regarding Pharmacogenetics

The participant's response towards the questions regarding the knowledge of pharmacogenetics is depicted in the Table 02. It was found that there was no significant difference in the proportion of correct responses given by the Physicians and Clinical Pharmacists for each questions. Among the participants 22 (40.7%) doctors and 8 (30.8%) clinical pharmacists scored the maximum possible score (4/4) for the knowledge section. Whereas the overall knowledge score calculated showed that 36 (66.7%) doctors and 20 (76.9%) CPs had an overall good knowledge (scored≧3), while the remaining 18 (33.3%) doctors and 6 (23.1%) CPs scored less than 3 points, thereby having a poor knowledge. Interestingly, participants with the least years of experience (0 to 5 years) had sound knowledge regarding pharmacogenetics (Table 03).

Table 02: Knowledge based questions

		Clinical Pharmacist	Physician	P-value
1. What is Pharmacogenetics?				
a. Study of how genetic differences cause varied drug response. b. A method to detect genetic abnormalities. c. Study of individual differences in drug metabolism or response. d. Study of hereditary and the variation of inherited characteristics.	Correct (Option 1)	23 (85.5%)	39 (72.2%)	0.103
	Wrong	3 (11.5%)	15 (27.8%)	
Total		26 (100%)	54 (100%)	
2. Which among these drugs ideally require a Pharmacogenetic testing before prescribing?				
a. 5-Fluorouracil (5-FU) b. 2. Paracetamol c. Clopidogrel d. Both 1 and 3	Correct (Option 4)	19 (73.1%)	43 (79.6%)	0.511
	Wrong	7 (26.9%)	11 (20.4%)	
Total		26 (100%)	54 (100%)	
3. The package insert for Clopidogrel has a warning regarding the impaired metabolism in individuals with a specific genetic variant?				
a. Yes b. No	Correct (Option 1)	20 (76.9%)	47 (87%)	0.251
	Wrong	6 (23.1%)	7 (13%)	
Total		26 (100%)	54 (100%)	
4. The Result Of Pharmacogenetic Tests Changes Over A Person's Lifetime?				
a.Yes b.No	Correct (Option 2)	16 (61.5%)	32 (59.3%)	0.845
	Wrong	10 (38.5%)	22 (40.7%)	
Total		26 (100%)	54 (100%)	
Individual scoring for knowledge session.				
1 point		2 (7.7%)	5 (9.3%)	0.341
2 points		4 (15.4%)	13 (24.1%)	
3 points		12 (46.2%)	14 (25.9%)	
4 points		8 (30.8%)	22 (40.7%)	
Total		26 (100%)	54 (100%)	
Overall knowledge score				
Good knowledge(≧3points)		20 (76.9%)	36 (66.7%)	0.348
Poor knowledge(≦2points)		6 (23.1%)	18 (33.3%)	
Total		26 (100%)	54 (100%)	

Table 03: Comparison of knowledge level based on the years of experience

		KNOWLEDGE LEVEL		Total	P value
	Years of experience	**Good knowledge**	**Poor knowledge**		
Clinical Pharmacist	0 to 5	18 (75%)	6 (25%)	24 (100%)	0.420
	5 to 10	2 (100%)	0 (0.0%)	2 (100%)	
Doctor	0 to 5	16 (57.1%)	12 (42.9%)	28 (100%)	0.178
	5 to 10	5 (62.5%)	3 (37.5%)	8 (100%)	
	> 10	15 (83.3%)	3 (16.7%)	18 (100%)	

Section C: Participants attitude towards Pharmacogenetics

As illustrated in Table 04 both the participating groups exhibited a largely positive attitude. Notably, 53 (98.1%) physicians and all 26 (100%) clinical pharmacists agreed that, it is their responsibility as health care professionals to identify medications that require pharmacogenetic testing. Only a single physician expressed a neutral opinion on this matter. When compared to 39 (72.2%) physicians, a significant number of CPs 24 (92.3%) were ready to be part of a multidisciplinary team for implementing pharmacogenetics (P-value=0.040). 51 (94.4%) physicians and all 26 (100%) CPs believed that a trained Clinical Pharmacist in the medical team for implementing pharmacogenetics can be beneficial, while only 3 (5.6%) physicians had a neutral opinion on this. A significant number of participants with 27 (50%) physicians and 20 (76.9%) CPs were interested in attending pharmacogenetic training or courses. While 27 (50%) physicians and 6 (23.1%) CPs had a neutral opinion on it (P-value=0.022). Notably a single physician presented a highly unfavorable attitude towards pharmacogenetics. Appealingly, more than half of the participants, in which 39 (72.2%) doctors and 25 (96.2%) CPs had a very positive attitude (scored≧3) towards pharmacogenetics. An overall positive attitude was observed among the study contributors. (P-value=0.012)

Table 04: Attitude based questions

	Clinical Pharmacist	**Physician**	**P value**
1. It is my responsibility as a health care provider to identify drugs that require Pharmacogenetic testing?			
Agree	26 (100%)	53 (98.1%)	0.485
Neutral	0 (0%)	1 (1.9%)	
Total	26 (100%)	54 100%)	
2. I am ready to be part of a multidisciplinary team for implementing pharmacogenetics.			
Agree	24 (92.3%)	39 (72.2%)	**0.040**
Neutral	2 (7.7%)	15 (27.8%)	
Total	26 (100%)	54 100%)	
3. I believe a trained Clinical Pharmacist in the medical team for implementing pharmacogenetics can be beneficial.			
Agree	26 100%)	51 (94.4%)	0.221
Neutral	0 (0%)	3 (5.6%)	
Total	26 (100%)	54 100%)	
4. I am interested in attending pharmacogenetic courses/trainings?			
Agree	20 (76.9%)	27 (50%)	**0.022**
Neutral	6 (23.1%)	27 (50%)	
Total	26 (100%)	54 (100%)	
Individual scoring for attitude.			
0 point	0 (0.0%)	1 (1.9%)	0.106
1 point	1 (3.8%)	2 (3.7%)	
2 points	0 (0.0%)	12 (22.2%)	
3 points	8 (30.8%)	14 (25.9%)	
4 points	17 (65.4%)	25 (46.3%)	

Total	26 (100%)	54 (100%)	
Overall attitude score.			
Positive attitude	25 (96.2%)	39 (72.2%)	**0.012**
Negative attitude	1 (3.8%)	15 (27.8%)	
Total	26 (100%)	54 (100%)	

Section D: Practice of pharmacogenetics among participants

The participants were asked regarding the major hindering factors for implementing pharmacogenetics. Wherein, a significant number of participants among them 12 (22.2%) physicians and 20 (76.9%) CPs expressed that all the factors like time & cost involved, lack of clinical guidelines & knowledge, lack of personnel were the major impediments. However, 21 (38.9%) doctors and only 2 (7.7%) CPs believed that the only major obstacle was the time and cost involved in conducting pharmacogenetic tests. 14 (25.9%) physicians and 4 (15.4%) CPs suggested that lack of established guidelines hinders them from incorporating pharmacogenetics in their daily clinical practice. Only 5 (9.3 %) participating doctors responded that, their reluctance to recommend pharmacogenetics was mainly due to the lack of knowledge in this field. Lastly, 2 (3.7%) physicians voiced their concern regarding the shortage of personnel to conduct genetic testing for medications. (P-value<0.001) (Table 05).

Table 05: Practice based questions

	Clinical Pharmacist	Physician	P value
1. When I have a patient not responding to medicines or developing side effects I will advise to			
a. Choose another medicine	8 (30.8%)	29 (53.7%)	0.054
b. Run a pharmacogenetic test	18 (69.2%)	25 (46.3%)	
Total	26 (100%)	54 (100%)	
2. I do discuss pharmacogenetic information with other health care providers.			
Yes	17 (65.4%)	34 (63%)	0.833
No	9 (34.6%)	20 (37%)	
Total	26 (100%)	54 (100%)	
3. **I will look for the Pharmacogenetic information on drug label?**			
Yes	21 (80.8%)	40 (74.1%)	0.510
No	5 (19.2%)	14 (25.9%)	
Total	26 (100%)	54 (100%)	
4. In my opinion the major hindering factor in implementing pharmacogenetic testing in clinical practice is			
a. All of the above	20 (76.9%)	12 (22.2%)	**<0.001**
b. Cost and Time	2 (7.7%)	21 (38.9%)	
c. Lack of clinical guidelines	4 (15.4%)	14 (25.9%)	
d. Lack of Knowledge	0 (0.0%)	5 (9.3%)	
e. Shortage of Personnel	0 (0.0%)	2 (3.7%)	
Total	26 (100%)	54 100%)	

Discussion

To the best of our understanding this is the first known study to be conducted in a tertiary care center in South India to assess the knowledge, attitude and practice among practicing Physicians and Clinical Pharmacists. Hence the present study findings may contribute to the limited existing literature in developing countries regarding the implementation of precision medicine and pharmacogenetics in clinical practice. Such study results might be utilized by policy-makers in educational and health care systems to redesign future multifaceted interventions to promote precision medicine in developing countries. Four distinct questions were used to assess the knowledge regarding pharmacogenetics among

the participants. Wherein, majority of the participants proved to have a good knowledge. Compared to doctors, clinical pharmacists scored the highest possible score in the knowledge section. However, it was observed that there was no significant difference in the level of knowledge among the participating groups. The current study results are in contrast with the similar studies conducted in Kuwait and Qatar, wherein, the total knowledge score among the participating physicians and pharmacists were low with no statistical significance [13, 14]. Within the participants, more than half of them were able to rightly identify the pair of drug that ideally require a pre-emptive pharmacogenetic testing. Approximately, a similar percentage of participants were also aware about the impaired metabolism of Clopidogrel in specific genetic variants. It is a common misconception that the pharmacogenetic study results of an individual changes over the lifetime. Whereas, in the current study around sixty percentage of participants were aware that the results of pharmacogenetic studies remain unchanged throughout an individual's lifetime. Meanwhile, in the study conducted in Kuwait most of the respondents believed that the genetic determinants of drug response vary over time [13]. In the current study, physicians and young CPs with the least experience (less than 5 years) had good knowledge regarding pharmacogenetics. In a similar study conducted in Malaysia, those 30 years old or younger and those practicing for four years or less scored the highest in knowledge section. This is probably due to the fact that pharmacogenetics is relatively a new field and that it was only recently incorporated into the curricula of medical and pharmacy schools, which gives those who graduated more recently an advantage [15].

Health care providers generally have a positive attitude towards pharmacogenetics, acknowledging its potential to improve patient outcomes by optimizing drug therapy. However, there's a notable gap between positive attitude and practical implementation, often due to factors like lack of education and training, and perceived barriers such as cost and limited guidelines. Meanwhile, in the present study the participating clinical pharmacists had a significantly positive attitude than physicians towards pharmacogenetics. Interestingly, only a single physician expressed a very negative attitude towards pharmacogenetics. Majority of the participants in the present study agreed that it was their responsibility as a health care provider to identify those medicines that require pharmacogenetic testing, because understanding how genetic variations influence drug response allows for better prediction of individual patient outcomes, potentially leading to fewer adverse drug reactions, more effective treatments, and reduced health care costs. In a survey conducted by McCullough KB.et.al among the inpatient and outpatient pharmacists, more than half of the participants agreed that they should be capable of providing information on pharmacogenomics testing and, if presented with test results, they should be able to provide therapy recommendations [16]. It is well known that an interdisciplinary team is crucial for successfully implementing pharmacogenetics due to the complexity of the field, requiring expertise across various disciplines can help to overcome barriers and improve patient outcomes. In the current study a significantly high number of participants were ready to be part of a team comprising of multidisciplinary members to implement pharmacogenetics. A study conducted by Caraballo.et.al mainly to evaluate how a comprehensive operational model can support pharmacogenetics implementation in routine prescribing concluded that, a coordinated and dedicated multidisciplinary team (physicians, residents/fellows, physician assistants, nurse practitioners, and pharmacists from multiple clinical areas) were critical for successfully facilitating the clinical adoption of this model and to ensure the technical feasibility of pharmacogenetics guided therapy [17]. In this study physicians,when compared to CPs had a significantly positive attitude towards attending pharmacogenetics training or courses. A similar conclusion was also observed in the study conducted in Qatar, wherein, pharmacists expressed more willingness to participate in pharmacogenetic training sessions and workshops [14]. Continuing education on pharmacogenetics for health care professionals in practice will be required to ensure that they are fully prepared to adopt pharmacogenetic testing. Personalized pharmacogenetics training, tailored to the health care professionals, their setting and context should be offered [18].

In the current study majority of the participants believed that a trained clinical pharmacist in the medical team for implementing pharmacogenetics can be beneficial. While both pharmacists and clinical pharmacists can contribute to pharmacogenetic programs, clinical pharmacists are often in a better position to lead and implement them. Their expertise in clinical pharmacology, drug-gene interactions, and patient-specific drug therapy makes them well-suited to manage the complexities of pharmacogenetic testing and application [19].

Although, in the present study center pharmacogenetic testing was only conducted in a few departments like psychiatry and oncology, the response of the participants towards the practice based questions were positively overwhelming. Majority of the participants replied that they will recommend to run a pharmacogenetic test for a patient not responding to the medicines or experiencing adverse effects. Similarly, majority of the participants have discussed matters regarding pharmacogenetics with their colleagues and were also ready to read the drug inserts or labels to check for information regarding pharmacogenetics. Although, it is relatively simple to enumerate the potential barriers in implementing pharmacogenetics in clinical practice, it is very difficult to determine which barrier presents the most significant

problem. Many of these barriers are sufficient in isolation to stall implementation [20]. In the current study a significant number of participants believed that the following were the major barriers in implementing pharmacogenetics at the study site, primarily the cost and time involved in conducting a pharmacogenetic test, the lack of proper guidelines, knowledge and personals. Whereas, in the study conducted to assess the pharmacist's knowledge and insights in implementing pharmacogenetics in Saudi Arabia, concluded that the primary barrier was the lack of availability of testing devices, followed by the lack of guidelines, knowledge and shortage of personnel [21]. The findings from the studies conducted in Qatar and Kuwait also states that it was the lack of knowledge and skills that hinders them from applying pharmacogenetics in the daily practice [13,14].

Conclusion

In the current study majority of the participants have good knowledge regarding pharmacogenetics. Moreover, clinical pharmacists expressed a positive attitude towards pharmacogenetics than physicians. Albeit, both the participating groups were ready to practice pharmacogenetics in their daily clinical practice, a significant number of participants expressed their concern regarding the potentials barriers involved in it. Therefore, it is the peak time to initiate educational interventions and continuing educational programs among health care providers to ease the implementation of pharmacogenetics into clinical practice.

Strength and Limitations

The potential strength of the study is that, it is the first study to the best of our knowledge to be conducted in South India focusing clinical pharmacists and consultants. Our study has limitations as it was conducted in a tertiary care hospital and participants were selected based on the fact that they might have come across drug-gene interaction, therefore, study results may not be generalized. The study was limited only to clinical pharmacists and doctors, other health care providers were not approached.

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Conflict of Interest

Nil

Informed Consent

Not applicable

Ethical Statement

The study was approved by the Rajagiri hospital's institutional ethics committee with the ethical approval number.

Author Contribution

All authors contributed equally towards the process.

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