Importance Of Rare Diseases Awareness For Medical And Nursing Students At KSA

Dr. Selvia Mary Amalanathan Arokiya[1*], Dr. Abdulaziz Asiri[2], Dr. Eman Elsayed Hussein Mohammad[3]

Abstract

Consequently, there is a need to increase the standards of medical education in the field of Rare Diseases and to revise the undergraduate and postgraduate training programs. However, while studies on medical education in the field of RDs has been conducted in various countries across the both Americas, Asia or the European Union, still little is known about the awareness of RDs among healthcare professionals in the kingdom of Saudi Arabia. Thus, we conducted a survey among 200 medical students and 200 nursing students from the college of applied medical sciences at aseer region. The questionnaire assessed their knowledge about the number, examples, aetiology and estimated frequency of RDs. It also evaluated respondents' self-assessment of competence in RDs. Although the majority of respondents agreed that RDs constitute a serious public health issue both medical students and nursing students showed insufficient knowledge on the aetiology, epidemiology and prevalence of RDs, and many had problems with separating RDs from more common disorders. Moreover, they also lacked knowledge about and the central register of RD patients and reimbursement of orphan drugs in Saudi Arabia. Finally, while almost half respondents declared having had classes about RDs during their studies most perceived their knowledge about RDs as insufficient or poor and felt unprepared for caring for RD patients. Additionally, although majority of respondents in both groups believed that all physicians, regardless of their specialization, should possess knowledge on RDs many respondents did not look for such information at all. While genetics constitutes an important part of medical education, one can observe a lack of knowledge about rare diseases (RD) among medical students and healthcare professionals. Meanwhile, many RD are life threatening and chronically debilitating conditions that significantly reduce patients' quality of life. Most RD patients experience various psychiatric symptoms, behavioural changes and mental retardation. Consequently, physicians should be educated on RD. Thus, the aim of this paper is to assess the knowledge about RD among future medical professionals.

[1*]Asst prof, College of medical sciences University of Bisha
[2]Dean , College of applied medical sciences ,university of Bisha
[3]Asst prof, College of medical sciences University of Bisha

***Corresponding Author:** Dr. Selvia Mary Amalanathan Arokiya
*Asst prof, College of medical sciences University of Bisha

Introduction:

The standards of medical education in the field of Rare Diseases (RDs) need to be increased, and the undergraduate and postgraduate training programs should be revised. While studies on medical education in the field of RDs have been conducted in various countries across the Americas, Asia, and the European Union, there is little known about the awareness of RDs among healthcare professionals in the Kingdom of Saudi Arabia. Therefore, a survey was conducted among 200 medical students and 200 nursing students from the College of Applied Medical Sciences in the Aseer region. The survey aimed to assess their knowledge about RDs, including the number, examples, etiology, and estimated frequency of RDs, as well as their self-assessment of competence in RD s.

There is no single generally accepted definition of rare diseases. Richter et al. [1] identified 296 definitions from 1109 organizations, but it is hard to disagree that "RD are numerous, heterogeneous in nature, and geographically disparate" [2]. A rare disease could be defined as a wide and varied set of disorders that are characterized by each one affecting a small number of individuals in the population, being chronic and disabling, having a high morbidity and mortality rate, and for which therapeutic resources are, in general, scarce and ineffective [3]. Although individual rare diseases affect very few people, it is estimated that jointly they concern 6–8% of the world's population [4]. This combined incidence of rare diseases means that a member of the medical personnel might never meet a patient with a specific RD, while patients with one of these diseases are encountered on a daily basis. The problem, however, does not merely regard the health professionals' lack of knowledge of all the diseases, which, considering the fact that their number exceeds 6000, does not seem possible or expedient [5]. What is necessary is to raise the awareness that statistically more than every twentieth patient suffers from one of the rare diseases and therefore may require a specialized, non-standard approach. But in practice patients often face challenges, due to a variety of reasons [6]. According to Black et al. [7], the "diagnostic odyssey" of rare disease patients encompasses three different periods: patient interval (starting from the first time the patient/parent notices what will later be classified as a symptom or sign of the disease); primary care interval (starting with the first patient/parent visit to primary care); and specialist care interval, the time when the diagnosis is finally made. Specialists are able to shorten each of these three periods. But unfortunately, it is unquestionable that patients with rare diseases face diagnostic delays. This issue was for the first time presented in a large-scale survey of eight rare diseases conducted by EURORDIS in 17 European countries – Rare Diseases Europe [8] [Prader-Willi syndrome (PWS), Marfan syndrome (MFS), Crohn's disease (CD), Duchenne muscular dystrophy (DMD), tuberous sclerosis (TS), cystic fibrosis (CF), Ehlers-Danlos syndrome (EDS) and fragile X syndrome (FRX)]. To identify the main causes of diagnostic delay, questionnaires were mailed to patients' organizations dealing with rare diseases, with 5.980 questionnaires answered. Half of the respondents affected by FRX reported a delay of at least 2.8 years between the first appearance of symptoms and obtaining a correct diagnosis. Half of the respondents affected by EDS reported a delay of at least 14 years. Before the final diagnosis, 41% of the patients were diagnosed incorrectly and the others had no diagnosis. Incorrect diagnosis led to futile medical interventions: 16% of the patients had surgery, 33% did not receive appropriate medical treatment, and 10% were given psychological care on the assumption that symptoms were psychosomatic. Patients who initially received a false psychological or psychiatric diagnosis experienced longer delays in diagnosis. Respondents affected by TS and CF reported delays four times longer if they initially received a psychological or psychiatric misdiagnosis, and MFS patients reported delays ten times longer in the same situation. As a result, 19% of all the analysed patients reported a loss of confidence in the healthcare system. Subsequent studies carried out by organizations of patients with rare diseases confirmed these findings [9, 10]. A recent study conducted in the USA on autosomal dominant tubulo-interstitial kidney disease (ADTKD) has shown that 25% of all

parents of children diagnosed in the years 1996–2017 bypassed their children's physicians and established direct contact with an academic centre specializing in ADTKD since they would otherwise have remained without diagnosis [11]. In the case of acromegaly, a meta-analysis conducted in 2017 showed that the median duration of symptoms until diagnosis was 4.5 to 5 years (range 1– 25 years) [12]. There is a consensus that a significant group of patients with Niemann–Pick disease type C remains undiagnosed or misdiagnosed [13]. In a recently published study on patients with vascular Ehlers-Danlos syndrome (vEDS), 25% of patients replied negatively to a question whether their physician explained their condition to them, or instructed them on how to manage it. When they were asked about the frustrating aspects of the vEDS diagnosis, No cure or treatment available was the most frequent response (64.5%), followed by the statement that Emergency rooms do not know what vEDS is (61.8%) [14]. From the point of view of shaping the health care system and training specialists, the key finding, after delays in the diagnosis of RD, was that even diagnosed patients and their families were not provided with enough information on all aspects of their condition, both at first diagnosis and subsequently. Patients and their families are expecting this information to be provided in a range of formats and at various levels of medical and scientific detail to ensure a full understanding and informed decision making. Parents of children with rare diseases are often frustrated by a lack of knowledge exhibited by health professionals [15]. Early diagnosis can lead to the end of the exhausting "diagnostic odyssey", at least in the first stage. It can help inform family planning, especially in the case of inherited diseases where several children in a family may be affected before diagnosis; it informs prognosis; and finally, it assists the patient and family in gaining access to social and educational support [16]. At the same time, it should be stressed that while RDs constitute a serious problem for patients and their families they also affect physicians and the healthcare system in general. While the medical authorities stress that one of the most urgent areas in the health policy toward RDs is improving the medical education of healthcare students and professionals in Saudi Arabia , still many healthcare professionals, including physicians, lack knowledge about RDs and are not prepared for caring for RD patients. The scarcity of knowledge, guidelines, and training on RDs of healthcare practitioners, seriously impede the diagnosis process, access to healthcare facilities and treatment options and management of such diseases. Consequently, RD patients themselves complain over the endless "diagnostic and therapeutic odyssey" (26, 27) and stress that it hampers timely diagnosis and treatment of patients suffering from a rare disease, especially when RD patients experience more common symptoms. This in turn results in the delays in referring patients for treatment, negatively affects their health, reduces patients' quality of life, and increases healthcare costs.

Materials and Methods

Thus, purpose of this article was two fold. Firstly, we aimed to assess the knowledge and awareness of rare diseases among medical and nursing stud ents.

Secondly, we attempted to determine if there are differences in the knowledge of rare diseases between medical stud and nursing students, and what the main sources of information about rare diseases are.

The main working hypotheses were:

1. As a result of inadequate education and formal training on RD of medical and nursing students, their knowledge does not increase during their professional career.
2. Both medical students and nursing students are unprepared for caring for RD patients.

The study was conducted among medical students and nursing students taking their specialization courses at aseer region (college of applied medical sciences) A previously developed questionnaire was used (28, 29), with which we had earlier tested the knowledge of Spanish students and physicians. The questionnaire, (30), On the basis of the results of an online focus group, a provisional questionnaire was assessed by two external reviewers: medical experts. After the acceptance of the final version of the

questionnaire, the survey was made available online. All interns and students invitations were sent to them via social media. In this group, the response rate was 100%. The questionnaire consisted of three sections. The first group of questions comprised the definition, aetiology and estimated prevalence of RDs worldwide and in Saudi Arabia. In this part of the questionnaire respondents were also asked to separate RDs from more common disorders from a list comprising 29 diseases. The second section addressed nursing students education about RDs and their self-assessment of their knowledge and competence in the field of these diseases. The last section referred to medical nursing students demographic data. The questionnaire consisted of 26 questions, of which we eventually used 25.

The data collected in the questionnaires were verified and checked for completeness, quality and consistency. Then they were coded and exported into the statistical packages SPSS (Version). The results were presented as descriptive statistics. Chi-square was used to assess differences in the distribution of answers among the groups. A 5% level of significance was used for all hypothesis tests.

Results

Our study group included 400subjects, 200 (50%) of whom were students and 200 (50%) (Table 1). Women predominated among both medical (89.1%) and students (74.9%). Simultaneously, in both groups very few respondents declared having a family member suffering from such disease (4.8 and 3% respectively).

The majority of respondents agreed that RDs constitute a serious public health issue. However, both medical students and nursing students showed insufficient knowledge on the etiology, epidemiology, and prevalence of RDs. Many of them had difficulty distinguishing RDs from more common disorders. Additionally, the respondents lacked knowledge about the central register of RD patients and reimbursement of orphan drugs in Saudi Arabia. While almost half of the respondents had classes about RDs during their studies, most perceived their knowledge as insufficient or poor and felt unprepared for caring for RD patients. Although the majority of respondents believed that all physicians, regardless of their specialization, should possess knowledge on RDs, many did not actively seek such information.

Table 1

Characteristics	**MD n=200**	**Nursing n=200**
Years of professional experience		
Residents' 1st year	29	
	14.50%	
Residents' 2nd year	48	
	24.00%	
<5	40	
	20.00%	
6–10	12	
	6.00%	
11–15	34	
	17.00%	
16–20	13	
	6.50%	
More than 20	24	
	12.00%	
Year of Study		
4th		39
		19.50%
Interns' 1st year		92
		46.00%
Interns' 2nd year		69
		34.50%
Gender		

Male	200	79
	100.00%	39.50%
Female	0	121
	0.00%	60.50%
Have you ever met a person suffering from RD		
Yes	71	48
	35.50%	24.00%
No	19	113
	9.50%	56.50%
I do not know	110	39
	55.00%	19.50%
Is anyone in your family suffering from RD?		
Yes	54	122
	27.00%	61.00%
No	60	78
	30.00%	39.00%
I do not know	86	0
	43.00%	0.00%

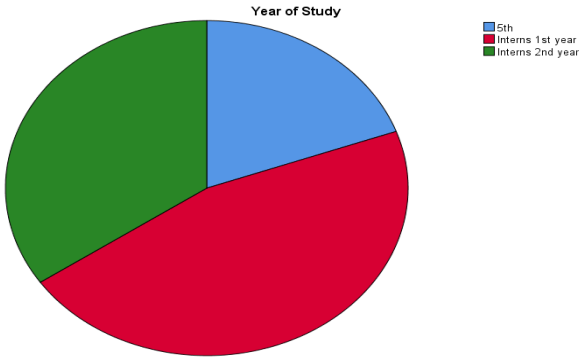

Fig 1.1

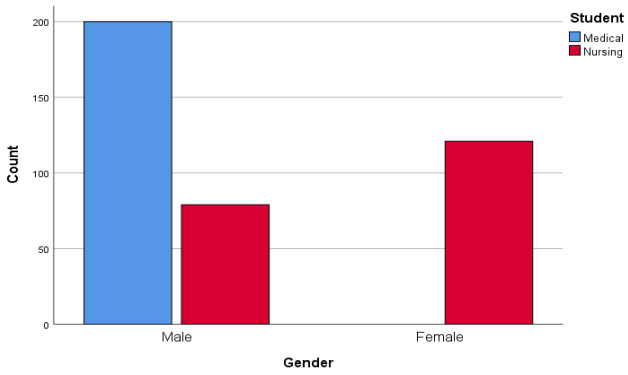

Fig 1.2

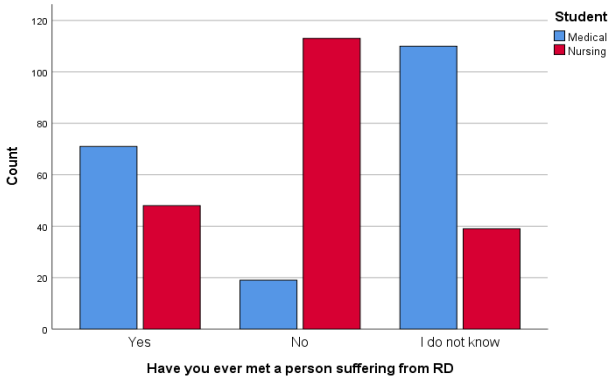

Fig 1.4

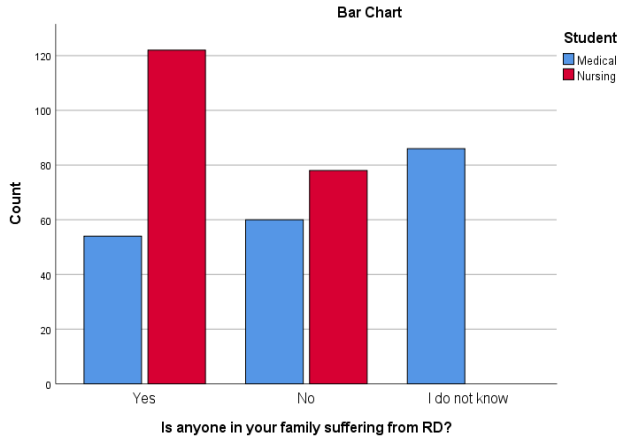

Fig 1.5

TABLE 2 | Respondents' knowledge about rare diseases.		
Characteristics	**MD n=200**	**Nursing n=200**
Have you ever heard the term 'rare diseases?		
Yes	121	65
	60.50%	32.50%
No	79	135
	39.50%	67.50%
A rare disease is the one that affects less than:		
1 person in 1,000	1	48
	0.50%	24.00%
1 person in 2,000	5	127
	2.50%	63.50%
1 person in 3,000	14	25
	7.00%	12.50%
1 person in 5,000	21	0
	10.50%	0.00%
1 person in 10,000	22	0
	11.00%	0.00%
I do not know	137	0
	68.50%	0.00%
What is the estimated number of rare diseases?		
100–500	71	24
	35.50%	12.00%
1,000–2,000	14	68
	7.00%	34.00%
3,000–5,000	85	34
	42.50%	17.00%
6,000–8,000	0	17
	0.00%	8.50%
I do not know	30	57
	15.00%	28.50%
In what age group do rare diseases most frequently appear?		
New-borns	14	80
	7.00%	40.00%
Children	14	14
	7.00%	7.00%
Adolescents	31	25
	15.50%	12.50%
Adults	35	11
	17.50%	5.50%
They are present in all age groups equally	89	1
	44.50%	0.50%
I do not know	6	5

	3.00%	2.50%
How many people suffer from rare diseases worldwide?		
10–15,000,000	14	73
	7.00%	36.50%
50–75,000,000	10	34
	5.00%	17.00%
100–150,000,000	55	18
	27.50%	9.00%
200–250,000,000	38	19
	19.00%	9.50%
300–350,000,000	45	1
	22.50%	0.50%
Over 500,000,000	5	45
	2.50%	22.50%
I do not know	33	10
	16.50%	5.00%
What is the most common cause of rare diseases?		
Infectious and bacterial	5	74
	2.50%	37.00%
Genetic	12	88
	6.00%	44.00%
Autoimmune	9	0
	4.50%	0.00%
Mitochondria	49	0
	24.50%	0.00%
Environmental	114	1
	57.00%	0.50%
I do not know	11	37
	5.50%	18.50%

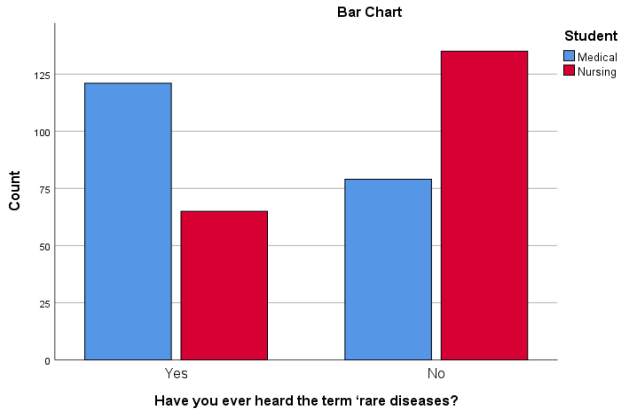

Fig 2.1

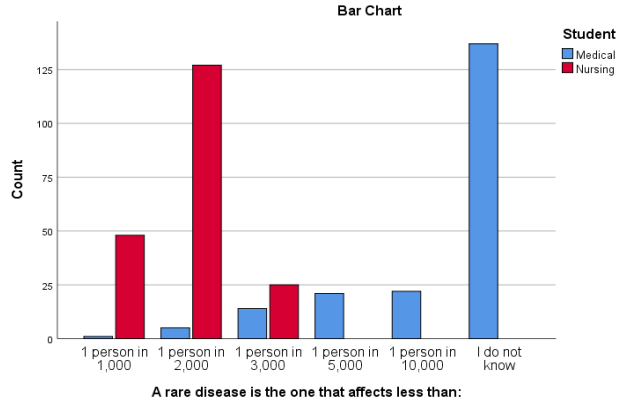

Fig 2.2

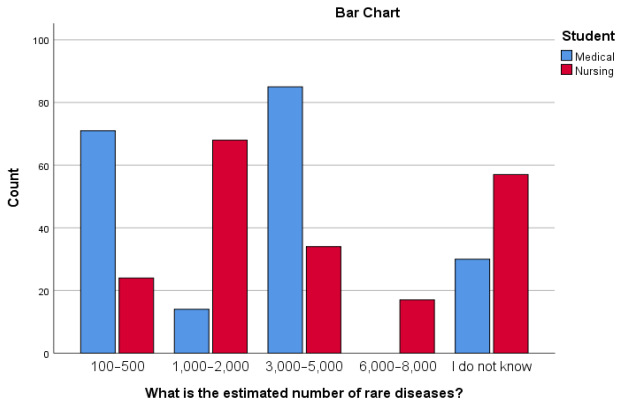

Fig 2.3

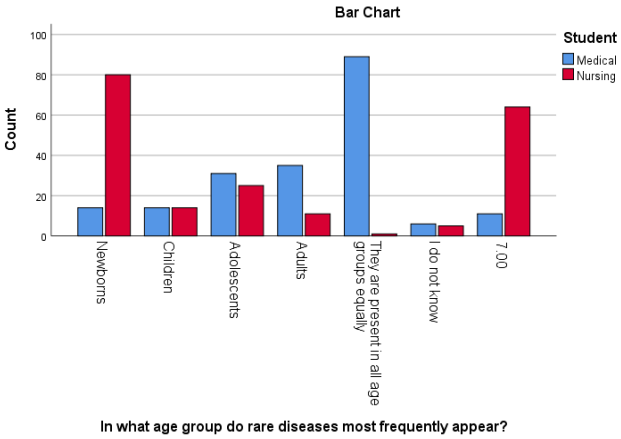

Fig 2.4

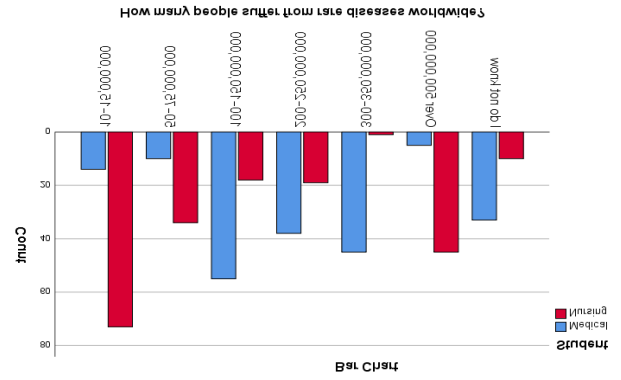

Fig 2.5

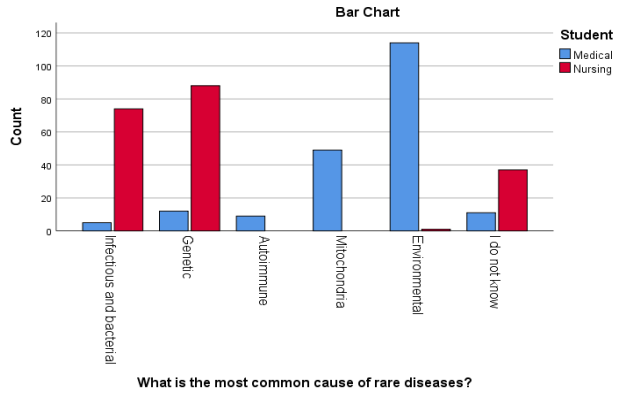

Fig 2.6

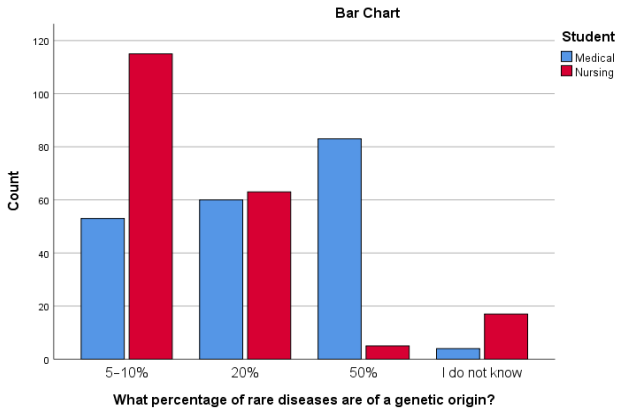

Fig 2.7

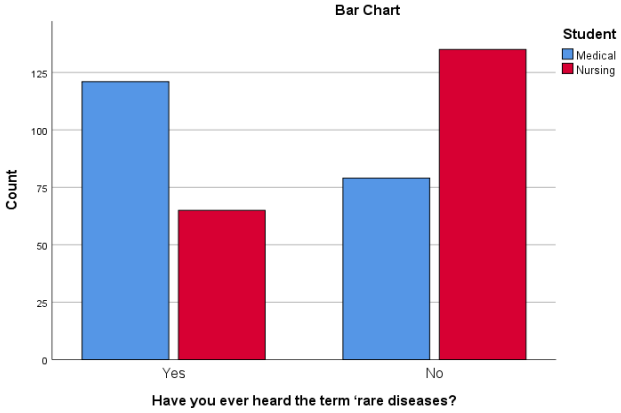

Fig 2.8

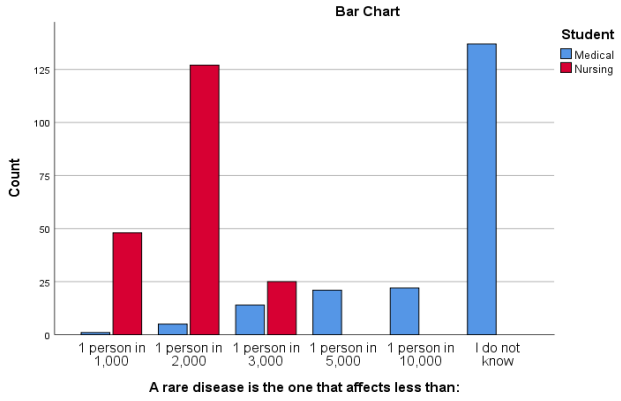

Fig 2.9

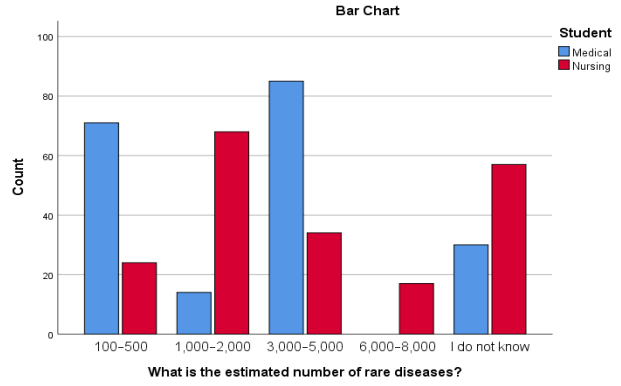

Fig 2.10

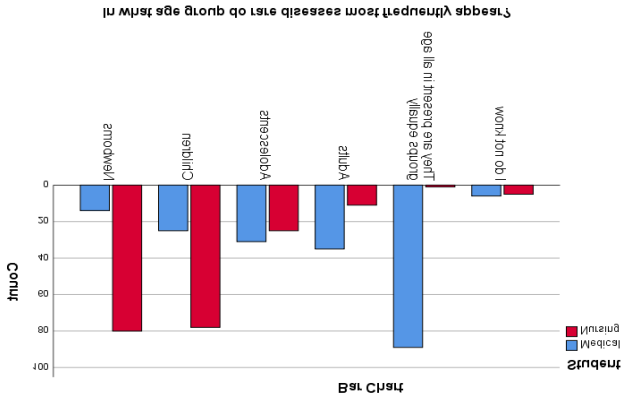

Fig 2.11

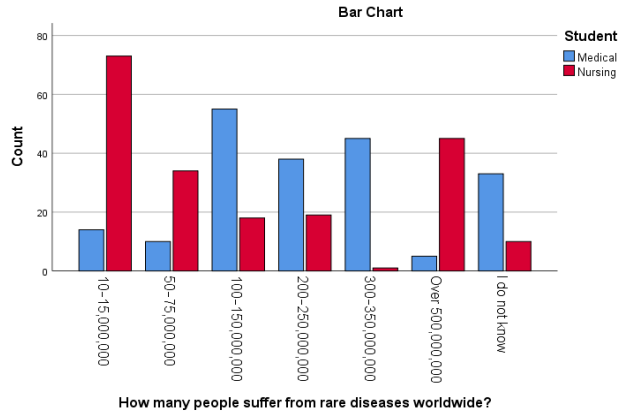

Fig 2.12

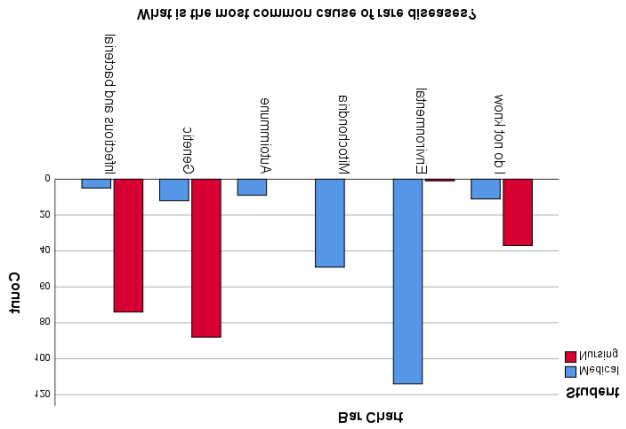

Fig 2.13

Nursing n=200	**p**
26	<0.001
13.00%	
31	<0.001
15.50%	
25	
12.50%	
0	
0.00%	0.002
0	
0.00%	<0.001
0	
0.00%	

1	
0.50%	
1	
0.50%	<0.001
1	
0.50%	
1	
0.50%	
1	
0.50%	
1	
0.50%	
1	
0.50%	
1	
0.50%	
1	
0.50%	
1	
0.50%	
21	
10.50%	
1	
0.50%	
1	
0.50%	
30	<.001
15.00%	
1	
0.50%	
17	
8.50%	
1	
0.50%	
33	.003
16.50%	
1	
0.50%	
2	
1.00%	

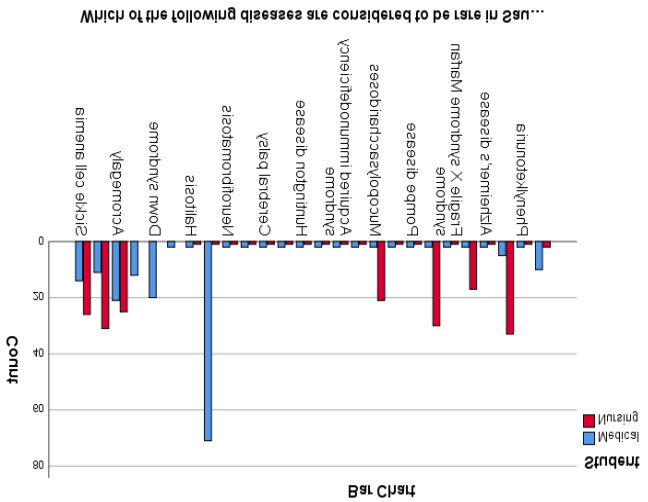

Fig 3.1

TABLE 4 | Respondents' self-assessment of their knowledge about RDs.

	MD n=200	Nursing n=200	p
Do RDs constitute a serious public health issue?			
Definitely yes	19	11	NS
	9.50%	5.50%	
Yes	3	21	<0.001
	1.50%	10.50%	
No	59	80	NS
	29.50%	40.00%	
Definitely not	47	64	NS
	23.50%	32.00%	
I do not know	72	24	<0.001
	36.00%	12.00%	
How would you rate your knowledge about rare diseases?			
Very good	24	30	NS
	12.00%	15.00%	
Fair enough	9	36	<0.001
	4.50%	18.00%	
So, so	49	74	<0.001
	24.50%	37.00%	
Insufficient	45	33	NS
	22.50%	16.50%	
Very poor	73	27	<0.001
	36.50%	13.50%	
Do you feel prepared for caring for a patient with a rare disease?			
Definitely yes	19	27	<0.001
	9.50%	13.50%	
Rather yes	16	32	<0.001
	8.00%	16.00%	
Rather not	45	63	NS
	22.50%	31.50%	
Definitely not	74	34	<0.001
	37.00%	17.00%	
I do not know	46	44	NS
	23.00%	22.00%	
Do you feel prepared for caring for a patient with a rare disease?			
Definitely yes	19	27	<0.001
	9.50%	13.50%	
Rather yes	16	32	<0.001
	8.00%	16.00%	
Rather not	45	63	<0.001
	22.50%	31.50%	
Definitely not	74	34	<0.001
	37.00%	17.00%	
I do not know	46	44	NS
	23.00%	22.00%	
Would you like to broaden your knowledge about rare diseases?			
Yes	14	16	NS
	7.00%	8.00%	
No	76	92	0.012
	38.00%	46.00%	
I do not know	110	92	0.013
	55.00%	46.00%	
Do you think that there should be a mandatory course on rare diseases in the medical and nursing curricula?			
Definitely yes	4	9	NS
	2.00%	4.50%	
Rather yes	22	27	NS
	11.00%	13.50%	
Rather not	48	68	<0.001
	24.00%	34.00%	
Definitely not	58	60	<0.001
	29.00%	30.00%	
I do not know	68	36	<0.001
	34.00%	18.00%	
Did you / do you have any classes about rare disease during your studies?			
Yes	95	18	<0.001
	47.50%	9.00%	
No	12	43	<0.001
	6.00%	21.50%	

I do not know	93	139	<0.001
	46.50%	69.50%	
Where do you / did you get your knowledge about rare diseases from?			
Mandatory courses at the university	27	0	<0.001
	13.50%	0.00%	
Facultative courses at the university	15	20	NS
	7.50%	10.00%	
Scientific literature and research	67	58	<0.001
	33.50%	29.00%	
Scientific conferences, symposia	38	74	<0.001
	19.00%	37.00%	
Internet	39	28	<0.001
	19.50%	14.00%	
Other	5	13	<0.001
	2.50%	6.50%	
I do not search for such information	9	7	
	4.50%	3.50%	
Which physicians should be uniquely trained in RDs?			
Family physician	2	0	NS
	1.00%	0.00%	
Paediatrician	19	19	NS
	9.50%	9.50%	
Neurologist	46	80	<0.001
	23.00%	40.00%	
Geneticist	36	47	NS
	18.00%	23.50%	
Psychiatrist	71	21	<0.001
	35.50%	10.50%	
Other	0	8	NS
	0.00%	4.00%	
Immunologist	9	6	NS
	4.50%	3.00%	
Other	17	19	NS
	8.50%	9.50%	

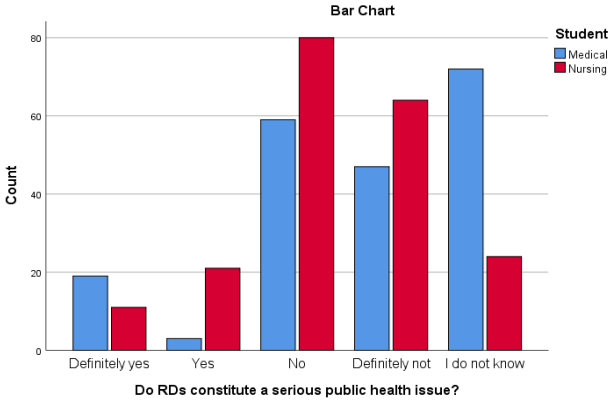

Fig 4.1

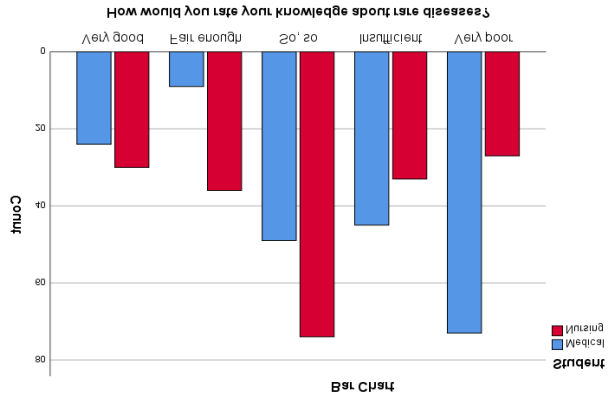

Fig 4.2

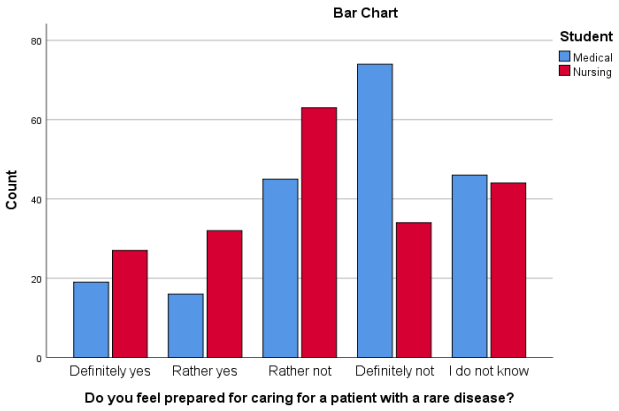

Fig 4.3

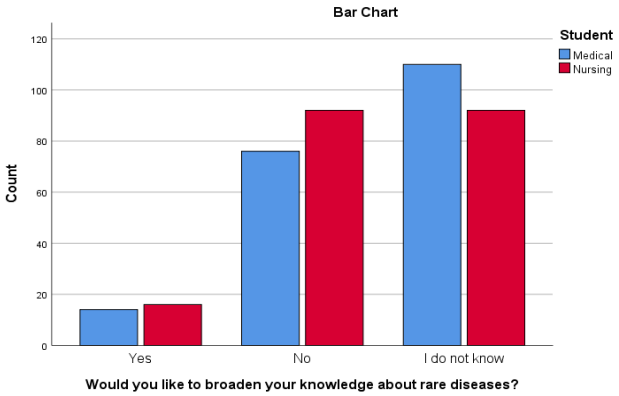

Fig 4.4

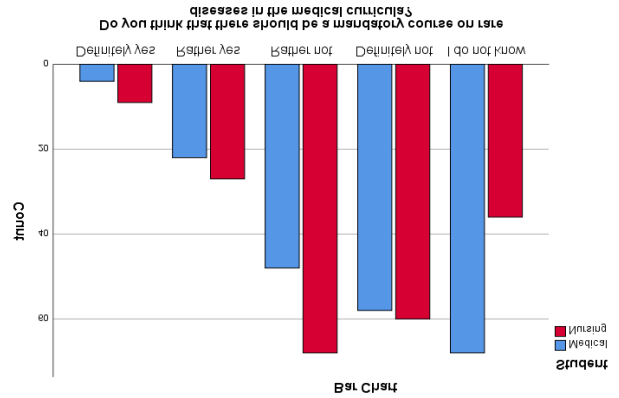

Fig 4.5

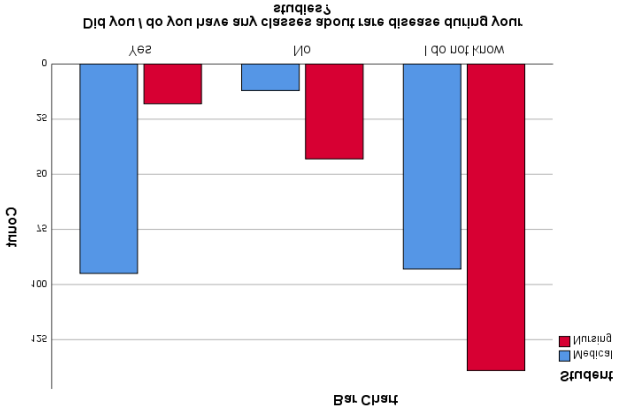

Fig 4.6

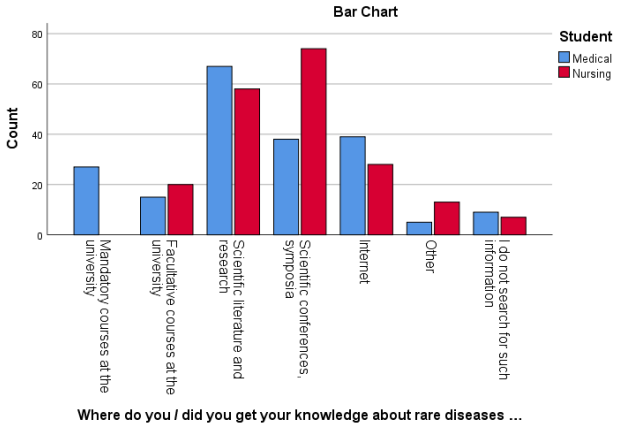

Fig 4.7

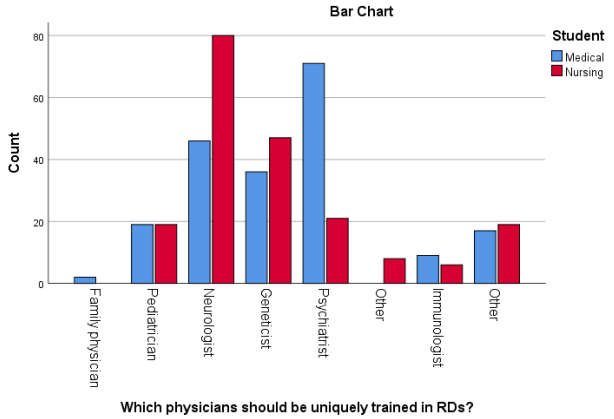

Fig 4.8

Discussion

Genetics is an important part of medical education; however, there is a lack of knowledge about RDs among medical students and healthcare professionals. RDs are life-threatening and chronically debilitating conditions that significantly reduce patients' quality of life. Most RD patients experience psychiatric symptoms, behavioral changes, and mental retardation. Therefore, it is crucial for physicians to be educated on RDs. The aim of the study was to assess the knowledge about RDs among future medical professionals. All in all, we suggest that in order to overcome the educational gap identified, the following guidelines should be implemented:

1. All medical curricula should include an RD module. Additionally, using examples from other European countries, such as Saudi Arabia France, Spain or the UK, Poland should implement teaching programs in RD aiming at increasing knowledge and awareness of all healthcare professionals on RD.
2. All medical and nursing students and healthcare providers should be taught and trained in the basic genetics and new-born screening, including genetic laboratory diagnostics.
3. As the Internet is the main source of information on RD, e-learning programs or courses should be organized. 4. Saudi Arabia web pages with reliable information on RD for healthcare professionals should be available.

Conclusions

The study revealed insufficient knowledge about RDs among medical and nursing students in the Aseer region of Saudi Arabia. The lack of knowledge, guidelines, and training on RDs among healthcare practitioners hampers the diagnosis process, access to healthcare facilities, treatment options, and management of RDs. The study emphasizes the need for improving the medical education of healthcare students and professionals in Saudi Arabia regarding RDs. Early diagnosis of RDs

is crucial to prevent diagnostic delays, inform family planning, provide appropriate treatment and management, and ensure access to social and educational support for patients and their families.

REFERENCES

1. European Parliament and Council. Regulation (Ec) Non141/2000 of the European Parliament and of the Council of 16 December 1999 on Orphan Medicinal Products. Off J Eur Communities. 2000;1. 18/1(January):1-5. https://ec.europa.eu/health/sites/health/files /files/eudralex/
2. vol-1/reg_2000_141_cons-2009-07/reg_2000_141_cons- 2009-07_en.pdf. Accessed June 5, 2019
3. Schey C, Milanova T, Hutchings A. Estimating the budget impact of orphan medicines in Europe: 2010 - 2020. Orphanet J Rare Dis. 2011;6(1):62. doi:10.1186/1750-1172-6-62
4. 3.RareDiseases-Home.Moh.gov.sa.https://www.moh.gov.sa /en/HealthAwareness/EducationalConte nt/Diseases/Rarediseases/Pages/default.asp x. Accessed June 5, 2019.
5. Al-Aqeel A. Common Genetics and Metabolic Diseases in Saudi Arabia. Middle East J Fam Med. 2004;6(6). http://www.mejfm.com/Newarchives2013/ Common Genetics and Meta.pdf. Accessed June 5, 2019
6. 5.Al-Jumah M, Majumdar R, Al-Rajeh S, Awada A, Chaves- Carballo E, Salih M, Al-Shahwan S, Al-Subiey K, Al-Uthaim S. Molecular analysis of the spinal muscular atrophy and neuronal apoptosis inhibitory protein genes in Saudi patients with spinal muscular atrophy. Saudi Med J. 2003;24(10):1052-1054.
7. Richter T, Nestler-Parr S, Babela R, Khan ZM, Tesoro T, Molsen E, Hughes DA. Rare disease terminology and definitions – a systematic global review: report of the ISPOR rare disease special interest group. Value Health. 2015; 18(6):906–14
8. Wakap SN, Lambert DM, Olry A, Rodwell C, Gueydan C, Lanneau V, Murphy D, Cam YL, Rath A. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. Eur J Hum Genet. 2020;28(5):165–73.
9. Palau F. Enfermedades raras, un paradigma emergente en la medicina del siglo XXI. Med Clin. 2010;134(4):161–8. 4. Auvin S, Irwin J, Abi-Aad P, Battersby A. The problem of rarity: estimation of prevalence in rare disease. Value Health. 2018;21(5):501–7. 5. What is a rare disease ? Available online: https://www.eurordis.org/content/ what-rare-disease. Accessed 8 Feb 2020
10. 9.Budych K, Helms TM, Schultz C. How do patients with rare diseases experience the medical encounter? Exploring role behavior and its impact on patient-physician interaction. Health Policy. 2012;105(2–3):154–64.
11. Black N, Martineau F, Manacorda T. Diagnostic odyssey for rare diseases: exploration of potential indicators; policy innovation research unit. London: LSHTM; 2015. 8. EURORDIS. The Voice of Rare Disease Patients in Europe. Available online: https://www.eurordis.org/publication/voice -12000-patients. Accessed 8 Feb 2020.
12. Limb L, Nutt S, Sen A. Experiences of Rare Diseases: An Insight from Patients and Families (2010). Rare Disease UK; 2010. 10. Molster C, Urwin D, Di Pietro L, Fookes M, Petrie D, van der Laan S, Dawkins H. Survey of healthcare experiences of Australian adults living with rare diseases. Orphanet J Rare Dis. 2016;11:30.
13. Bleyer AJ, Kidd K, Robins V, Martin L, Taylor A, Santi A, Tsoumas G, Hunt A, Swain E, Abbas M, et al. Outcomes of patient self-referral for the diagnosis of several rare inherited kidney diseases. Genet Med. 2020;22(1):142–9.
14. Lavrentaki A, Paluzzi A, Wass JAH, Karavitaki N. Epidemiology of acromegaly: review of population studies. Pituitary. 2017;20(1):4–.Evans WRH, Hendriksz CJ. Niemann–pick type C disease – the tip of the iceberg? A review of neuropsychiatric presentation, diagnosis and treatment. BJPsych Bull. 2017;41(2):109–14.
15. Shalhub S, Sage L, Demasi J, Wallace SE, Fulton DS, Bloom L, Driessnack M, Byers PH. Assessment of the information sources

and interest in research collaboration among individuals with vascular Ehlers-Danlos syndrome. Ann Vasc Surg. 2020;62:326–34.
16. Pelentsov LJ, Fielder AL, Esterman AJ. The supportive care needs of parents with a child with a rare disease: a qualitative descriptive study. J Pediatr Nurs. 2016;31(3):e207–18.
17. Evans WR, Rafi I. Rare diseases in general practice: recognising the zebras among the horses. Br J Gen Pract. 2016;66(652):550–1. 17. Kaufmann P, Pariser AR, Austin C. From scientific discovery to treatments for rare diseases – the view from the National Center for Advancing Translational Sciences – Office of Rare Diseases Research. Orphanet J Rare Dis. 2018;13(1):196.
18. Byrne PC. Training medical students on rare disorders. Orphanet J Rare Dis. 2012;7(Suppl 2):A15. 19. Wolyniak MJ, Bemis LT, Prunuske AJ. Improving medical students' knowledge of genetic disease: a review of current and emerging pedagogical practices. Adv Med Educ Pract. 2015;6(6):597–607.
19. Kopeć G, Podolec P. Establishing a curriculum on rare diseases for medical students. J Rare Cardiovasc Dis. 2015;2(3):74–6.
20. Jonas K, Waligóra M, Hołda M, Sulicka-Grodzicka J, Strach M, Podolec P, Kopeć G. Knowledge of rare diseases among health care students – the effect of targeted education. Przegl Epidemiol. 2017;71(1):80–9.
21. Medić B, Divac N, Stopić N, Savić-Vujović K, Glišić A, Cerovac N, Stojanović R, Srebro D, Prostran M. The attitudes of medical students towards rare diseases: a cross-sectional study. Vojnosanit Pregl. 2016;73(8):703–13.
22. Domaradzki J, Walkowiak D. Medical students' knowledge and opinions about rare diseases: a case study from Poland. Intractable Rare Dis Res. 2019;8(4):252–9.
23. Ramalle-Gómara E, Domínguez-Garrido E, Gómez-Eguílaz M, Marzo-Sola ME, Ramón-Trapero JL, Gil-de-Gómez J. Education and information needs for physicians about rare diseases in Spain. Orphanet J Rare Dis. 2020;15(1):18.
24. 24.Miteva T, Jordanova R, Iskrov G, Stefanov R. General knowledge and awareness on rare diseases among general practitioners in Bulgaria. Georgian Med News. 2011;4(193):16–9.
25. Rafferty AM, Busse R, Zander-Jentsch B, Sermeus W, Bruyneel L. Strengthening health systems through nursing: evidence from 14 European countries. Copenhagen: European Observatory on Health Systems and Policies; 2019. https://apps.who.int/iris/bitstream/handle/10665/326183/ 9789289051743-eng.pdf?sequence=1&isAllowed=y. Accessed 11 May 2020.