Knowledge, Attitude, and Practice of Physicians toward Primary Immune Deficiency in Children

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ABSTRACT:

BACKGROUND:

Primary immune deficiency (PID) comprises more than 330 diseases, in which alterations in the immune system cause greater predisposition towards infections, autoimmune phenomena, allergies, and neoplasms. The early diagnosis of PID prevents the development of complications and improves the quality of life in children with PID. The lack of medical knowledge is identified in many countries as the probable cause for late diagnosis and under diagnosis of PID.

SUBJECTS AND METHODS:

This is a cross-sectional study conducted in two platforms, a paper and a Google form questionnaire during the period from Jan 2020 to August 2020. We studied knowledge, attitude, and practice of physicians regarding PID in children. The knowledge questionnaire included 10 clues to PID diseases, 5 questions for each of the diagnosis, syndromes associated with PID as well as vaccination of children with PID. Another 5 questions for each of attitudes and practice of physicians toward PID were also surveyed.

RESULTS:

Out of 203 participants, there were 11 (5.4%) trainee doctors, 68 (33.5%) senior residents, 59 (29.1%) general practitioners, and 65 (32%) specialists. Only 29 (14.3%) of participants believe that all 10 clues for PID are true. While 67 (37.9%) of participants knew 5 clues and less for PID. The knowledge about the clues of PID was significantly higher among trainee doctors, senior residents, and specialist doctors in comparison to general practitioners. Also, trainee doctors and senior residents knew more clues in comparison to specialist doctors. Both specialists and senior residents have an attitude indicator (AI) mean of 3 ± 1 while trainees and general practitioners have AI mean of 2±1, and again general practitioners have a lower attitude for PID. In multiple linear regressions, the effect of independent variables knowledge indicator (KI) and attitude indicator (AI) were significantly affecting the practice.

CONCLUSION AND RECOMMENDATION:

PID is still underestimated by physicians regarding warning signs and diagnosis. General practitioners lack a lot of knowledge for PID and that affects their attitude and practice. We recommend increase awareness among PHCCs physicians especially GP doctors for PID warning signs and diagnostic tips.

KEYWORDS: KAP, Physicians, Children, PID, Baghdad

INTRODUCTION:

Primary immune deficiency which today comprises more than 330 diseases, in which alterations in the immune system cause greater predisposition towards infections, autoimmune phenomena, allergies, and neoplasms.[1,2] Contrary to common perception, PIDs as a group are not rare. Studies in United States have reported the prevalence of PIDs as high as 1 in 1200 population.[3] Over the last decades; studies have allowed a greater understanding of the pathophysiology of PID, which enables greater diagnostic precision, as well as the indication of new treatment strategies. On the other hand, the large diversity of genetic defects and clinical manifestations makes recognition and diagnosis of patients with PID a challenge. [4] Serious immune defects are more frequently recognized, but there are cases in which PID is diagnosed only when the patient is submitted to one or more hospitalizations and may already present with permanent sequelae.[5]The early diagnosis of PID prevents the development of complications and improves the quality of life in children with PID. Therefore, physicians and

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interns' awareness of the early diagnosis of PID is extremely important.[6]

The problem of early PID diagnosis is relevant worldwide, especially in countries with poor access to high-quality immunological and genetic testing.[7]The lack of medical knowledge is identified in many countries as the probable cause for late diagnosis and under diagnosis of PID.[8,9] Assessment of Iraqis physicians' education will give a guide on level of education and required plan for development.

SUBJECTS AND METHODS:

A cross-sectional study conducted in two platforms, a paper and a Google form questionnaire during the period from Jan 2020 to August 2020. We studied the knowledge, attitude, and practice of physician about PID in pediatrics. Both Teaching Institutions (TI) as well as Primary Health Care Centers (PHCCs) in Baghdad Al-Rusafa were included. The questionnaire included 2 parts; the first part refers to: Participant name (optional), Age, gender, graduation year, specialization, place of work. The second part had 3 sections: Section one, data about knowledge which included 25 closed questions with yes and no responses. This section contains 4 divisions: The first (Which of the following can be a clue to PID diseases?) with 10 clues. Second: Which of the following Syndromes is associated with PID? Third: Which of the following directly helps in the diagnosis of PID patients: Fourth: Which of the following vaccines should not be administered in a child with PID? Section two, data about attitude, which had 5 closed questions with strongly agree, agree, neutral, disagree, and strongly disagree responses. Section three, data about practice, which had 5 closed questions with strongly agree, agree, neutral, disagree, and strongly disagree responses. The ethical approval was taken from Iraqi Board for Medical Specialties. An administrative agreement was taken from all participating hospitals and PHCCs. Confidentiality was taken in consideration. Statistical analyses were done with the help of the SPSS version 22. A knowledge indicator (KI) was constructed in the form of number, by the sum of scores of the 25 knowledge questions. One point was attributed for each answer considered adequate and a total of 25 points for knowledge. Attitude indicator (AI) and Practice Indicator (PI) were constructed in same manner, the questions with strongly agree and agree were getting 1 point if participant chose strongly agree or agree, other answers (neutral, disagree, and strongly disagree) given 0 point. ANOVA test was used to compare means among more than two groups and a multiple linear regression model was used to test the association between factors, verify which of the variables chosen influenced the KI and AI on PI.

RESULTS:

Out of 203 participants, there were 169 (83.3%) females physicians, 103 (50.7%) physicians graduated before 2010. For specialty, there were 11 (5.4%) trainee doctors (house officer), 68 (33.5%) senior residents, 59 (29.1%) general practitioners, and 65 (32%) specialist doctors. The number of physicians worked in teaching institutions was 67 (33%) while that for physicians working in PHCCs was 136 (67%). The mean age of the participants was 36.18 ± 7.2 years. The mean age of physicians working at TI was 31 years, while for those working at PHCCs was 39 years. Most of participants194 (95.6%) knew that "recurrent infection is a clue for PID", while 94 (46.3%) knew that "the eczema and subcutaneous bleeding is a clue for PID". The response of the physicians for "which of the following can be a clue to PID diseases" is shown in table -1. Only 29 (14.3%) participants believed that all 10 given clues of PID are true. More than 62% of participants knew more than 5 clues, while 67 (37.9%) knew 5 clues and less for PID. The highest proportion of physicians who knew more than 5 clues was among senior residents, while the lowest proportionof physicians who knew more than 5 clues was among GP as shown in table- 2. Knowing the clues was significantly higher among participants who worked at TIs in comparison to participants working at PHCCs as shown in Table-3. Nearly half of participants knew each syndrome and its association with PID, as shown in table-4. On further analysis there was high frequency of knowledge regarding all syndromes given in question "which of the following is associated with PID?" among senior residents and it was significantly higher among them in comparison to other specialties. Also, physicians who work in TIs had significantly higher knowledge regarding the syndromes in comparison to physicians who work in PHCCs. Trainee doctors, senior residents, and specialist doctors had significantly higher knowledge regarding the diagnosis of PID in comparison to GPs. Also, physicians who work in TIs had significantly higher knowledge regarding

the diagnosis of PID in comparison to physicians who work in PHCCs. For attitudes questions, more than 61% of all participants have disagreed or strongly disagreed that "I believe that PID is not a serious health problem". For the second question in attitude section, "I believe that PID diseases need extensive investigation", 74.8% of responses believed on that, (45.8% agreed and 29% strongly agreed), while 39.4% of physicians disagreed to "I believe that PID prophylactic therapy has many side effects so better to avoid it" and only 21.2% of participants agreed and strongly agreed on that. For question 4, "I believe that PID has an impact on polio eradication program", one third of participants were neutral for that. For the last question in attitude section, "I believe that I know little about PID"; 61.1% of physicians believed that (strongly. agreed and agreed) they know little about that PID as shown in table -5. For practice section; majority of participants (85.7%) are willing to refer suspected cases to specialist. There were 42.8% of participants who disagreed or neutral to prescribe prophylactic antibiotics or antifungal for PID patients. Regarding the sending for investigation question, there were 38 (22.8%) physicians who were neutral, disagreed and strongly disagree for that. There were 41(20.2%) physicians who were neutral or disagreed the question "I don't give live attenuated vaccine to PID patients". Majority of participant were willing to learn more about PID and they are trying to do so as shown in table-6. The Knowledge Indicator (KI) showed a mean of 14.9 ± 6, which indicated the knowledge of 14 out of 25 items by each participant. The mean of KI distribution was not homogenous among the specialties (P=0.001), which shows the highest value (21 ± 3) for senior residents and the lowest value observed (11 ± 5) was for GPs (Figure -1). Also, there was significant difference between the mean of Knowledge Indicator (KI) for TI workers (21 ± 3) in comparison to mean of PHCCs workers (12 ± 5) (P = 0.001). The Attitude Indicator (AI) showed a mean of 2.6 ± 1.29. Both specialists and senior residents have mean of 3 ± 1 while trainees and GPs have mean of 2±1. There was a significant difference between both categorize (P = 0.001). The Practice Indicator (PI) showed a mean of 3.7 ± 1.4. The highest mean (5± 1) went for senior residents followed by specialists (4 ± 1), GPs (3 ± 2), and lastly trainees (2 ± 2). There was a significant difference between mean of senior residents and each group of specialty (P = 0.001). In multiple linear regressions, the effect of independent variables (KI) and (AI) were significantly affecting the practice (P = 0.001).

Table 1: Physician's response to "which of the following can be a clue to PID" .

Clues to PID	Response (YES) No. (%)
Recurrent infection	194 (95.6%)
Lymphoid hypoplasia	105 (51.7%)
Frequent common cold	125 (61.6%)
Frequent oral candidiasis	157 (77.3%)
More than 3 weeks delay in umbilicalcord separation	97 (47.8%)
Simultaneous existence of two internal infections	152 (74.9%)
Pneumocystis jiroveci pneumonia	149 (73.4%)
Poliomyelitis after receiving OPV	116 (57.1%)
History of 3 otitis media during childhood	101 (49.3%)
Eczema and subcutaneous bleeding	94 (46.3%)

Table 2: Association between the number of clues to PID answered and specialty of the participants

Specialty	0-5 Clues	>5 Clues	Total	P value
Trainee Doctor	4 (36.4%)	7 (63.6%)	11	0.2
GP	43 (72.9%)	16 (27.1%)	59	0.0001
Senior Resident	0	68 (100.0%)	68	0.0001
Specialist	30 (46.2%)	35 (53.8%)	65	0.7
Total	77 (37.9%)	126 (62.1%)	203	

Table 3: Association between the working place of physicians and response to clues for PID.

Work Place	0-5 Clues	>5 Clues	Total	P value
PHCC	0 (0%)	67 (100%)	67	0.0001
TI	77 (56.6%)	59 (43.4%)	136	

Table 4: Physician's response to questions about Syndromes, diagnosis and vaccines in children with PID.

Questions	Response (Yes)		
Which of the following is associated with PID?	PHCC No. %	TI No. %	Total No. %
Wiskott Aldrich syndrome	55 (51.4 %)	52 (48.6%)	107 (52.7%)
Ataxia telangiectasia	50 (48.5 %)	53 (51.5%)	103 (50.7%)
Kostman syndrome	38 (40.4 %)	56 (59.6 %)	94 (46.3%)
Jobs syndrome	40 (42.1 %)	55 (57.9%)	95 (46.8%)
Chediac Higashi Syndrome	45 (52.3%)	41 (47.7 %)	86 (42.4%)
Which of the following directly helps us in diagnosis PID patients?			
Antibacterial antibody response to previous vaccines	68 (56.2%)	53 (43.8%)	121 (59.6%)
Determining superficial markers of lymphocyte	69 (53.5 %)	60 (46.5%)	129 (63.5%)
Complete blood count and differential	102 (63.4 %)	59 (36.6%)	161 (79.3%)
Serum immunoglobulin levels	95 (58.6 %)	67 (41.4 %)	162 (79.8%)
Candida and tetanus skin test	44 (42.3%)	60 (57.7 %)	104 (51.2%)
Which of the following vaccines should not be administered in a child with PID:			
BCG	53 (45.3%)	64 (54.7 %)	117 (57.6%)
Influenza A vaccine	53 (46.5%)	61 (53.5 %)	114 (56.2%)
IPV	43 (82.7 %)	9 (17.3 %)	52 (25.6%)
Hepatitis B vaccine	45 (46.9%)	51 (53.1 %)	96 (47.3%)
OPV	65 (71.4 %)	26 (28.6)	91 (44.8%)

Table 5: Physician's response to attitudes questions toward PID in children.

Attitude	S.Agree No. (%)	Agree No. (%)	Neutral No. (%)	Disagree No. (%)	S.Disagree No. (%)
I believe that PID diseases is not a serious health problem	34 (16.7)	21 (10.3)	24 (11.8)	73 (35.9)	51 (25.1)
I believe that PID diseases need extensive investigation	59 (29.0)	95 (45.8)	45 (22.1)	4 (1.9)	0
I believe that PID prophylactic therapy has many side effects so better to avoid it	8 (3.9)	35 (17.2)	71 (34.9)	80 (39.4)	9 (4.4)
I believe that PID has an impact on polio eradication program	7 (3.4)	80 (39.4)	68 (33.5)	38 (18.7)	10 (4.9)
I believe that I know little about PID question	19 (9.3)	106 (52.2)	66 (32.5)	12 (5.9)	0

Table 6: Physician's response to Practice questions.

Practice	S.Agree N. (%)	Agree N. (%)	Neutral N. (%)	Disagree N. (%)	S.disagree N. (%)
I refer suspected cases of PID to specialist	103 (50.7)	71 (35)	24 (11.8)	5 (2.5)	0
I prescribe prophylactic Antibiotics and antifungal to PID patients	18 (8.9)	98 (48.3)	49 (24.1)	28 (13.8)	10 (4.9)
I send suspected cases of PID for investigation	20 (9.9)	145 (71.4)	31 (15.3)	4 (2)	3 (1.5)
I don't give live attenuated vaccine to PID patients	41 (20.2)	121 (59.6)	24 (11.8)	17 (8.4)	0
I try to know more about PID	61 (30)	82 (40.4)	56 (27.6)	4 (2)	0

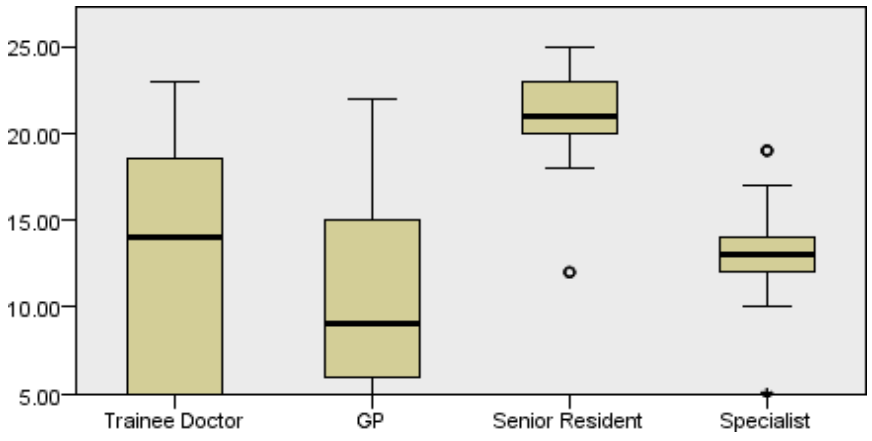

Figure 1: Mean distribution of knowledge indicators (KI) among specialties.

DISCUSSION:

Primary immune deficiency is a group of diseases that are difficult to be diagnosed, and lead to long term sequelae in patients especially in pediatric age groups. Enhancing knowledge of physicians for early diagnosis and management of PID would improve patients' outcomes. [10] In this study, more than half of physicians graduated before 2010 which indicated that they are still fresh in their practice and there were 5.4% trainee doctors, 33.5% senior residents, 29.1% general practitioners, and 32% specialist doctors, that would be a good distribution to identify all the gaps per each specialty. Regional and global studies assessed the specialized doctors like pediatricians, internists and so on, and this could be an area of further research.[11, 12] The majority of participants worked at PHCCs (67%) and this gave us an opportunity to identify the knowledge gaps there. Warning signs are essential and important to identify patients with PID. Most of participants (95.6%) knew that the recurrent infection is a clue for PID, and only 46.3% knew that the eczema and subcutaneous bleeding is a clue for PID, while only 14.3% of participants believed that all 10 given information for clues of PID are true. Two thirds (62%) of participants knew more than 5 clues for PID. These results are lower in comparison to other studies that conducted in Kuwait [13], in which 67% of their participants have good knowledge regarding the clues for PID, and this pointed out that many of physicians in our study did not have enough knowledge about the warning signs of PID disease. This could be explained by the fact that there is no clear continuous education program to educate physicians about the PID. Knowledge scores were significantly higher among trainee doctors, senior residents, and specialist doctors in comparison to general practitioners. Also, trainee doctors and senior residents knew more clues in comparison to specialist doctors. These results come in line with other studies that showed there was a significant lower knowledge of PID among GPs in comparison to specialized doctors[74], while a study conducted in Ukraine by Hariyan showed that there was no difference between GPs and specialized doctors. [11]Physicians working at TIs knew the warning signs significantly more in comparison to physicians working at PHCCs. This in turn pointed out the lack of knowledge among physicians working at PHCCs. This observation is in line with other studies that demonstrated similar results.[14]The mean of knowledge about the associated syndromes with PID was nearly 50%, and it is in line with other studies that showed a lot of physicians not aware about Wiskott Aldrich Syndrome, Chediak Higashi Syndrome, and Ataxia Telangectasia [8,12], and a lot of programs have been implanted there to increase awareness among physicians, while in our study there was high frequency of knowing regarding all syndromes associated with PID among senior resident and it was significantly higher among them in comparison to other specialties, and this could be attributed to the continuous education in TIs that increase their knowledge about specified syndromes. The clues to support the diagnosis of PID are very important to be familiar with by physicians who are in contact with suspected cases of PID to refer them to specialized doctors. In studies conducted in United State at 2016 among family medicine doctors, high number of them showed difficulties in the diagnosis, which in turn reflect the small number of patients followed by them [15]. In our study, the lack of diagnostic clue was significantly higher among GP and even among specialized doctors who worked at PHCCs which is in line with other study conducted in United States at 2010 showed that family physicians have the lowest odd ratio for diagnosis of PIDs [16]. Lack of disease knowledge has a major impact on the diagnosis of disease itself. Vaccines like BCG and OPV should not be given for patients with PIDs; however, there were higher percentages of trainee doctors and senior residents who agreed to these vaccinations for PID patients, while high percentage of specialists and GP physicians did not agree to do so. This fact may be related to close contact of GPs and specialists with immunization programs and gave them the knowledge and better informed for vaccinations. Attitude could play an important role to identify physician's area of development. Collectively, the response toward attitude was driven by senior resident while GPs and specialists had some controversy to some of attitude parts. Attitude is proved to be a very important part for right management of patients and could impact it a lot with bad attitude.[17] For the practice, also GPs and specialists showed controversy toward referral of PID patients to specialists. They have some disagreement about trying to learn more.

This could be affected by the knowledge of such physicians about PID. To test the effect of knowledge and attitude on practice, we calculated the indicator for each parameter, the KI was highest value (21 ± 3) for senior residents and the lowest value observed (11 ± 5) was for GPs. In Dantas's study [14], he calculated that too and the KI was higher among pediatricians in comparison to other specialties. Also, in our study, TIs worker have better KI than PHCCs physicians. For AI both specialists and senior residents have a mean of 3 ± 1 while trainees and GPs have a mean of 2±1, and again, GPs have lower attitude for PID which was the same observation in other global studies.[12,14] In multiple linear regressions, the effect of independent variables (KI) and (AI) significantly affect the practice, and this observation was demonstrated in other studies[13, 14, 18] and our explanation to that, in fact the knowledge could play an essential role to enhance both attitude and practice.

CONCLUSIONS & RECOMMENDATIONS:

We concluded that PID diseases are still underestimated by physicians regarding awareness and diagnosis with deficiencies in knowledge among some physicians especially those working at PHCCs regarding prophylactic treatment and vaccination of children with PID. GP doctors lack a lot of knowledge for PID that affects their attitude and practice. We recommend increasing awareness among PHCCs physicians especially GP doctors for PID warning signs and diagnostic tips and implant CME sessions to enhance the educational level.

REFERENCES:

1. Modell V, Knaus M, Modell F, Roifman C, Orange J, Notarangelo LD. Global overview of primary immunodeficiencies: a report from Jeffrey Modell Centers worldwide focused on diagnosis, treatment, and discovery. Immunol Res. 2014; 60:132–44.
2. Bousfiha AA, Jeddane L, Ailal F, Benhsaien I, Mahlaoui N, Casanova JL, et al. Primary immunodeficiency diseases worldwide: more common than generally thought. J Clin Immunol. 2013;33:1–7.
3. Boyle JM, Buckley RH. Population prevalence of diagnosed primary immunodeficiency diseases in the United States. J Clin Immunol. 2007;27:497–502.
4. Espinosa-Rosales FJ, Condino-Neto A, Franco JL, Sorensen RU. Into action: Improving access to optimum care for all primary immunodeficiency patients. J Clin Immunol. 2016;36:415–17.
5. Joshi AY, Iyer VN, Hagan JB, St Sauver JL, Boyce TG. Incidence and temporal trends of primary immunodeficiency: a population-based cohort study. Mayo Clin Proc. 2009;84:16–22.
6. Modell V, Quinn J, Ginsberg G, Gladue R, Orange J, Modell F. Modeling strategy to identify patients with primary immunodeficiency utilizing risk management and outcome measurement. Immunologic research. 2017;65:713-20.
7. Mohammadzadeh I, Moazzami B, Ghaffari J, Agha mohammadi A, Rezaei
8. N. Primary immunodeficiency diseases in Northern Iran. Allergologia et immunopathologia. 2017 ;45:244-50.
9. Boyarchuk O, Lewandowicz-Uszyńska A, Kinash M, Haliyash N, Sahal I, Kovalchu k T. Physicians' awareness concerning primary immunodeficiencies in the Ternopil Region of Ukraine. Pediatria Polska—Polish Journal of Paediatrics. 2018;93:221–28.
10. Boyarchuk O, Kinash M, Hariyan T, Bakalyuk T. Evaluation of knowledge about primary immunodeficiencies among postgraduate medical students. Archives of the Balkan Medical Union. 2019;54:11–19.
11. Nourijelyani K, Aghamohammadi A, Salehi Sadaghiani M, Behniafard N, Abolhassani H, Pourjabar S, et al. Physicians awareness on primary immunodeficiency disorders in Iran. Iran J Allergy Asthma Immunol. 2012;11:57–64.
12. Wood P, Stanworth S, Burton J, Jones A, Peckham D, Green T, et al. UK Primary Immunodeficiency Network. Recognition, clinical diagnosis and management of patients with primary antibody deficiencies: a systematic review. Clin Exp Immunol. 2007;149:410–23.
13. Hariyan T, Kinash M, Kovalenko R, Boyarchuk O. Evaluation of awareness about primary immunodeficiencies among physicians before and after implementation of the educational program: A longitudinal study. PLoS One.2020 May 29;15:1-10.

14. Al-Herz, W., Zainal, M.E., Salama, M. *et al.* Primary Immunodeficiency Disorders: Survey of Pediatricians in Kuwait. *J Clin Immunol. 2008*; 28:379– 83.

15. Dantas EO, Arandaa CS, Rêgo AM, Tavares FS, Severo Ferreira JF, de Quadros MA,etal.Doctors' awareness concerning primary immuno deficiencies in Brazil. Allergol Immunopathol (Madr). 2015; 43:272–78.

16. Orange JS, Seeborg FO, Boyle M, Scalchunes C, Hernandez-Trujillo V. Family Physician Perspectives on Primary Immunodeficiency Diseases. Front Med (Lausanne). 2016;3:12.

17. Waltenburg R, Kobrynski L, Reyes M, Bowen S, Khoury MJ. Primary immunodeficiency diseases: practice among primary care providers and awareness among the general public, United States, 2008. Genetics in Medicine. 2010;12:792-800.

18. Mahlaoui N, Warnatz K, Jones A, Workman S, Cant A. Advances in the Care of Primary Immunodeficiencies (PIDs): from Birth to Adulthood. JClin Immunol. 2017;37:452-60.

19. Sullivan KE. Pathogenesis of pediatric rheumatologic diseases. Pediatric Clinics. 2018;65:639-55.