Original Article

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Factors associated with diagnostic delays in Peruvian patients with rare diseases

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SUMMARY: Rare diseases affect fewer than 1 in 2,000 individuals. Patients often encounter barriers to specialist care and prompt diagnosis, hindering effective disease management and access to appropriate treatments. This study aimed to identify determinants of diagnostic delay among patients with rare diseases affiliated with Peruvian associations in 2024. A descriptive cross-sectional design was employed in 2024, enrolling patients with rare diseases or their caregivers from Peruvian associations. Data collection utilized an expert-validated survey encompassing sociodemographic characteristics, medical history, and diagnostic challenges. The primary outcome was diagnostic delay, defined as the interval from symptom onset to confirmed diagnosis. Data analysis included descriptive and inferential statistical methods. A total of 236 participants responded, with the majority being women (61.4%). A diagnosis was received within a year of symptom onset for 54.7% of participants, and 46.2% reported difficulties accessing healthcare. Major barriers identified included prolonged wait times for appointments or treatment (52.3%) and geographic limitations impeding access (37.6%). The median diagnostic delay was longer for women (63.1 months) compared to men (26.9 months). Limited access to healthcare was associated with an average delay of 21.8 months, whereas consulting more than ten general practitioners was associated with a 42.6-month delay. In summary, over half of the patients with rare diseases in Peru included in this study received a diagnosis within one year. However, the most significant delays were observed in non-genetic rare diseases. Key contributors to prolonged diagnostic timelines included limited access to healthcare and consultations with multiple general practitioners.

Keywords: rare diseases, delayed diagnosis, risk factors, developing countries

1. Introduction

A rare disease (RD) is traditionally defined as a condition affecting fewer than 1 in 1,500 to 1 in 10,000 individuals (*1,2*). The European Union (EU) defines a rare disease as any genetic or acquired condition that is life-threatening or chronically disabling (*3*). Rare diseases are low-prevalence, highly complex conditions that can pose life-threatening risks or lead to long-term disability. While most of these diseases have a genetic origin, some arise from autoimmune, toxic, or infectious factors. The clinical manifestations of rare diseases are highly varied and may include rare cancers, unusual physical traits, neurodevelopmental disorders, and congenital anomalies (*3,4*).

According to the World Health Organization (WHO), there are approximately 7,000 rare diseases that collectively affect around 7% of the global population (*5*). The European Organization for Rare Diseases (EURORDIS) estimates that there are between 6,000 and 8,000 rare diseases affecting 6% to 8% of the population within the European Union (*4*). In Peru, it is estimated that more than 2.5 million people are living with a rare disease (*6*).

Individuals with rare diseases face significant diagnostic challenges that impede timely access to appropriate treatments and limit research opportunities. Additional barriers include limited access to specialized healthcare centers, high medical costs, and insufficient social and financial support. Furthermore, the general lack of awareness regarding these conditions can lead to social isolation and inadequate information about the disease (*4*). The diagnosis of rare diseases remains problematic due to the vast diversity of conditions, their often poorly defined nature, and the limited availability of information on their overall burden (*7*).

An important issue with rare diseases is that their low prevalence results in limited awareness among healthcare professionals. Symptoms are often confused with those of more common conditions, leading to

delays in diagnosis and reduced accuracy. Diagnostic confirmation frequently requires specialized testing, which — especially in low- and middle-income countries — is only available in a limited number of centers (*8*).

Reducing the diagnostic odyssey is crucial for the effective management of rare diseases, influenced by factors such as income level and healthcare system performance. In Spain, the average time to diagnosis is estimated at 6.18 years. More than half of the patients (56.4%) experience diagnostic delays of over one year, which can be categorized into three main groups: 19% wait between 1 and 3 years, 16.7% between 4 and 9 years, and 20.9% experience delays exceeding 10 years (*9*).

The objective of this study was to identify the factors contributing to diagnostic delays in Peruvian patients with rare diseases.

2. Patients and Methods

2.1. Study design

This study is a descriptive, cross-sectional analysis. Data were collected in 2024 through surveys distributed electronically by representatives of 14 Peruvian rare disease patient associations and the Peruvian Federation of Rare Diseases. The survey included both closed- and open-ended questions, allowing for the collection of both quantitative and qualitative data regarding patient experiences and access to healthcare services, from the onset of symptoms to the time of diagnosis.

2.2. Participants

Inclusion criteria: Patients were eligible if they: *i*) provided informed consent, *ii*) had a confirmed diagnosis of a rare disease established in a Peruvian healthcare facility (clinical, biochemical, or molecular), and *iii*) were able to complete the questionnaire either directly or with the support of a caregiver.

Exclusion criteria: We excluded participants who had incomplete questionnaires, unverified diagnoses, or who were unable to recall essential information regarding the diagnostic timeline (*e.g.*, approximate dates of first symptoms, first medical consultation, or final diagnosis).

2.3. Variables

The following variables were collected: age, sex, age at diagnosis, specific diagnosis, educational level, monthly family income, place of origin, and religion. Additionally, the time elapsed from symptom onset to diagnosis and the number of general practitioners and specialists consulted were recorded. We identified the initial healthcare facility (where the patient first sought care) and the final facility (where the diagnosis was ultimately made). These facilities were then classified by their level of care complexity (Levels I, II, or III) according to the RENIPRESS (*Registro Nacional de Instituciones Prestadoras de Servicios de Salud*, National Registry of Health Service Provider Institutions) database. We identified the patient's health system affiliation. Patients were categorized as belonging to: the Ministry of Health (*Ministerio de Salud*, MINSA), which covers the uninsured population; the Social Security system (*Seguro Social de Salud*, EsSalud), which covers formal employees; the private sector; or the Armed Forces health system. Perceived access to the healthcare facility where the diagnosis was made was categorized as either easy or difficult. The perceived difficulty in accessing healthcare was assessed as a subjective patient-reported measure. It was evaluated across three dimensions: waiting time for medical consultation, geographic distance to specialized care, and structural barriers within the healthcare system. Participants rated the degree of difficulty based on their personal experience.

The method of diagnosis was classified as clinical, laboratory-based, imaging, or molecular. Patient perceptions regarding the complexity of the diagnostic examination were also recorded. Finally, diseases were subclassified as genetic or non-genetic based on their etiology, and diagnoses were categorized as either clinical or clinically supported by additional testing.

2.4. Data collection method

Data were obtained using an online survey that comprehensively covered all study variables. To reduce potential response bias and maintain the integrity of self-reported information, participants (patients or caregivers) completed the survey independently and at their own convenience.

2.5. Sample size

The sample size included 236 patients or caregivers, calculated using the following formula (*10*):

n = [EDFF*Np(1-p)]/ [(d2/Z21-α/2*(N-1) + p*(1-p)]; where
N: Population size
p: Expected proportion
z: 1.96

2.6. Statistical methods

A descriptive analysis was conducted by calculating measures of central tendency (mean or median) and dispersion (standard deviation or interquartile range) for quantitative variables, while absolute frequencies and percentages were calculated for qualitative variables. Differences in means or medians were assessed through bivariate analysis using the student's *t*-test, Mann–Whitney

U test, ANOVA, or Kruskal–Wallis test, as appropriate. Additionally, an exploratory multiple linear regression analysis was performed to evaluate diagnostic delay as a continuous variable (in months), reporting β coefficients and 95% CIs, and a multiple logistic regression model was also fitted using a ≥ 12-month delay as a dichotomous outcome (reporting adjusted odds ratios). Both analyses were exploratory, and the sample size was not powered to detect small effects. Data processing was carried out using Stata v.18 and Microsoft Excel. Statistical significance was set at $P < 0.05$, and 95% confidence intervals (CI) were calculated for all estimators.

2.7. Ethical Approval

The study was reviewed and approved by the Institutional Review Board of Universidad Ricardo Palma (Nº PG 012 2024-A). The survey ensured participant anonymity and involved no foreseeable risks. Although personal identification was not possible, the confidentiality of both participants and the data collected was strictly maintained. The study followed the ethical principles outlined in the Declaration of Helsinki, the Belmont Report, and the Code of Ethics of the Peruvian Medical Association, upholding autonomy, beneficence, non-maleficence, and justice.

3. Results

3.1. Participants

A total of 241 patients or caregivers participated in the survey, all of whom provided informed consent. Five participants were excluded due to incomplete responses or inability to recall key dates required to estimate diagnostic delay.

3.2. Demographic characteristics

The sample consisted of 145 women (61.4%), with a median age of 23 years. Most participants resided in Lima (71.6%). Among the participants, Catholicism was the most prevalent religion (84.7%). In terms of educational attainment, 20.8% had not any grade of education, while 25.4% had completed an undergraduate degree.

The median age at diagnosis was 12 years, and the median diagnostic delay — from symptom onset to confirmed diagnosis — was 12 months.. Patients reported a median of three consultations with general practitioners and two consultations with specialists. The median monthly household income was 2,000 Peruvian soles (Table 1).

3.3. Characteristics of the process at the onset of symptoms

The analysis of participants revealed that the majority, 54.7% (n = 129), received their diagnosis in less than 1 year, while the remaining 45.3% (n = 107) were diagnosed after more than 1 year. Concurrently, there was a near-even split regarding access to their health center: a slight majority of participants, 53.8% (n = 127), reported having easy access, compared to 46.2% (n = 109) who reported having difficult access. Most patients consulted fewer than nine general practitioners (92.4%) and fewer than nine specialists (94.5%). The first facility visited was most often a Ministry of Health (MINSA) hospital (31.8%) or an EsSalud hospital (25.5%). Based on the RENIPRESS classification of institutional complexity, 24.1% of patients received care at a level III-1 facility (Table 2).

3.4. Diagnostic characteristics

Most diagnoses were made at national institutes (31.4%) and EsSalud hospitals (26.7%). In terms of institutional complexity, level III-2 facilities predominated (53.3%). Most cases were diagnosed through clinical evaluation combined with laboratory tests (50.4%) or additional imaging studies (23.7%). Additionally, when assessing the use of advanced diagnostic tests, a significant majority of participants, 69.1% (n = 163), reported they had not undergone such testing, whereas 30.9% (n = 73) confirmed the use of advanced diagnostic procedures, with biopsy (45.2%) and exome/genome sequencing (16.4%) being the most used methods. Among imaging modalities, magnetic resonance imaging (33.3%) and

Table 1. General characteristics of patients with rare diseases affiliated with patient associations in Peru

Variable	Median	IQR
Age (years)	23	36.15
Socioeconomic level (Monthly income in soles)	2,000	2500
Age at diagnosis (years)	12	29
Diagnosis time (months)	12	44
Number of doctors they saw	3	4
Number of specialists they saw	2	2
Sex	*n*	%
Female	145	61.4%
Male	91	38.6%
Origin		
Lime	169	71.6%
Province	67	28.4%
Religion		
Catholic	200	84.7%
Evangelical	15	6.4%
Jehovah's Witness	6	2.5%
Others	15	6.4%
Level of education		
None	49	20.8%
Incomplete primary education	27	11.4%
Completed primary education	12	5.0%
Incomplete secondary education	19	8.1%
Completed secondary education	29	12.3%
Incomplete tertiary education	41	17.4%
Complete undergraduate degree	59	25.0%

IQR, Interquartile Range.

Table 2. Diagnostic journey of patients with rare diseases from Peruvian patient associations

Variable	*n*	%
Difficulty		
Waiting time for a medical appointment	57	52.3%
Distance	41	37.6%
Structural	11	10.1%
General practitioners who visited		
≤ 9 doctors	218	92.4%
≥ 10 doctors	18	7.6%
Specialists who visited		
≤ 9 specialists	223	94.5%
≥ 10 specialists	13	5.5%
Establishment that came for the first time		
MINSA Hospitals	75	31.8%
EsSalud Hospitals	55	23.3%
Health Posts	29	12.3%
Private hospitals	25	10.6%
National Institutes	22	9.3%
Multi-specialty clinic	16	6.8%
Hospital of the Armed Forces and Police	8	3.4%
Private practice	6	2.5%
The level of complexity they first went to		
Level of care I-1	7	3.0%
Level of care I-2	8	3.4%
Level of care I-3	31	13.1%
Level of care I-4	9	3.8%
Level of care II-1	16	6.8%
Level of care II-2	54	22.9%
Level of care II-E	10	4.2%
Level of care III-1	57	24.1%
Level of care III-2	40	16.9%
Level of care III-E	4	1.7%

ultrasound (25.9%) were the most frequently employed (Table 3).

3.5. Frequency of rare diseases

In the study population, the most prevalent diagnosis was systemic lupus erythematosus (25.4%), followed by hemophilia A (7.6%) and Ehlers–Danlos syndrome (5.1%). Other notable diagnoses included myasthenia gravis (4.7%), sensorineural hearing loss (3.8%), and cystic fibrosis (3.4%). However, most conditions had a low frequency (≤ 2.5%) (Supplementary Figure S1, *https://www.irdrjournal.com/action/getSupplementalData.php?ID=277*).

3.6. Characteristics of the process at the onset of symptoms

Women experienced a significantly longer time to receive a definitive diagnosis compared to men (63.1 *vs.* 26.9 months). A paradoxical trend was observed regarding educational attainment: those with completed undergraduate degrees took a longer time for diagnosis. Participants with no schooling reported a median diagnostic delay of 6 months, whereas those with undergraduate completed degrees reported a median delay of 36 months (Table 4).

Table 3. Diagnostic setting, complexity level, and diagnostic tools in patients with rare diseases in Peru

Variable	*n*	%
The establishment where diagnosis was made		
National Institutes	74	31.4%
EsSalud Hospitals	63	26.7%
Private Hospitals	43	18.2%
MINSA Hospitals	42	17.8%
Private practice	6	2.5%
Hospital of the Armed Forces and Police	5	2.1%
Multi-specialty clinic	3	1.3%
The Level of complexity at which the diagnosis was made		
Level of care I-1	6	2.5%
Level of care I-3	3	1.3%
Level of care I-4	2	0.9%
Level of care II-1	8	3.4%
Level of care II-2	27	11.4%
Level of care II-E	17	7.2%
Level of care III-1	43	18.2%
Level of care III-2	125	53.0%
Level of care III-E	5	2.1%
Type of diagnostic test		
Clinical evaluation + clinical laboratory tests	119	50.4%
Clinical evaluation + clinical laboratory tests +imaging tests	56	23.7%
Clinical evaluation + imaging tests	52	22.0%
Clinical evaluation	7	3.0%
Others	2	0.9%
Type of laboratory diagnosis		
Biopsy	45	45.2%
Exome/Genome Sequencing	12	16.4%
Karyotype	9	2.8%
Genetic panel	3	4.1%
Neonatal screening	2	2.8%
Others	12	16.4%
Type of diagnostic imaging		
Magnetic resonance imaging	35	33.3%
Computed tomography	23	21.9%
Radiography	11	10.5%
Electromyography	11	10.5%
Ultrasound	10	9.5%
Auditory evoked potentials	6	5.7%
Echocardiogram	5	4.8%
Electroencephalogram	1	0.9%
Others	3	2.9%

No significant differences in the time to diagnosis were observed based on place of origin, religion, or perceived ease of access to healthcare. However, significant differences were noted among participants who experienced barriers such as long wait times for medical appointments and those who reported distance-related obstacles (Table 4).

An increase in patient age at diagnosis was associated with a 3.1-month delay in the time to diagnosis. Additionally, patients who consulted ten or more general practitioners experienced a delay of 142.6 months in receiving a diagnosis. Lastly, the diagnosis of non-genetic rare diseases was delayed by 54 months compared to genetic rare diseases (Table 5).

Greater difficulty in accessing healthcare services was linked to an increased risk of delayed diagnosis.

Table 4. Sociodemographic and clinical factors associated with diagnostic delay in patients with rare diseases in Peru

Variable	Mean ± SD	CI (95%)	*p*-value
Sex			
Male (*n* = 91)	26.92 ± 55.80	15.3–38.5	0.0034
Female (*n* = 145)	63.12 ± 118.36	43.7–82.6	
Origin			
Lima (*n* =169)	49.76 ± 105.14	33.8–65.73	0.4422
Province (*n* = 67)	47.65 ± 88.22	26.1–69.1	
Religion			
Catholic (*n* =200)	48.11 ± 99.36	34.25–61.96	0.3522
Non-Catholic (*n* = 36)	55.03 ± 107.53	18.64–91.41	
Access to the health center			
Easy (*n* = 127)	33.55 ± 79.06	19.67–47.44	0.0048
Difficult (*n* = 109)	67.35 ± 119.49	44.86–89.95	
Level of complexity of the establishment visited for the first time			
Level of care I-II (*n* = 108)	36.30 ± 82.46	20.57–52.03	0.0353
Level of care III (*n* = 128)	60.02 ± 112.60	40.32–79.71	
Establishment that came for the first time			
State (*n* = 187)	46.96 ± 93.87	34.03–59.89	0.1937
Private (*n* = 49)	63.73 ± 137.3	13.36–114.10	
Level of complexity of the diagnostic establishment			
Level of care I-II (*n* = 57)	62.03 ± 115.68	31.33–92.73	0.1338
Level of care III (*n* = 179)	45.06 ± 95.08	31.04–59.09	
Establishing a diagnosis			
State (*n* = 187)	43.08 ± 93.29	29.62–56.54	0.0346
Private (*n* = 49)	72.37 ± 122.36	37.22–107.52	
Diseases			
Genetics (*n* = 123)	44.61 ± 82.02	29.97–59.25	0.2345
Non-genetic (*n* = 113)	54.11 ± 117.45	32.22–76.01	
Type of exams			
Clinical examination (*n* = 7)	56.85 ± 80.18	-17.29–131.01	0.4188
Clinical examination + complementary tests (*n* = 229)	48.93 ± 101.13	35.76–62.10	
Level of education	Median	IQR	0.0006*
None	6	13	
Incomplete primary education	7	16	
Completed primary education	9	52	
Incomplete secondary education	15	20.7	
Completed secondary education	12	16	
Incomplete tertiary education	24	126	
Completed undergraduate degree	36	78	
Difficulty			
Distance	24	42	0.4811*
Structural	12	178	
Waiting time for a medical appointment	24	62	

*Mann-Whitney *U* test. IQR, Interquartile Range.

Likewise, patients who had consulted more than ten general practitioners had more than a fivefold increased risk of receiving a diagnosis more than twelve months after symptom onset (Supplementary Table S1, *https://www.irdrjournal.com/action/getSupplementalData.php?ID=277*).

4. Discussion

Timely diagnosis of rare diseases is critically important due to its impact on the quality of life for both patients and their families. In this study, a diagnostic delay of 12 months or more was observed in 45.3% of cases.

The female predominance noted in this study aligns with previous reports from Spain, which documented similar proportions ranging from 56% to 58.8% (*9,11*). This predominance may be explained by the high proportion of patients with systemic lupus erythematosus in the sample, a condition known to have a female prevalence of up to 90% (*12*).

Most patients in this study were from the department of Lima (71.6%). This high frequency, compared to other regions of the country, could be attributed to potential underreporting in those areas, as clinical suspicion and definitive diagnosis of rare diseases are often more challenging outside the capital. This challenge may be partly due to the lower concentration — or even absence — of rare disease specialists in regions beyond Lima (*13*). However, a prior study conducted in Peru on economic evaluations reported that 70% of patients came from departments outside Lima. This finding may have been influenced by the small sample size in that study (*14*).

Published data indicate that between 71.9% and 80% of patients with rare diseases have a genetic etiology,

Table 5. Association between diagnostic delay in rare diseases and factors related to healthcare access, income level, hospital type, and etiology, Peru

Variable	Coef. β	*p*-value	95% CI
Age (years)	-0.083	0.098	-1.82–0.16
Socioeconomic level (Monthly income in soles)	-0.0003	0.509	-0.001–0.001
Age at diagnosis (years)	3.182	**< 0.001**	2.04–4.33
Number of doctors they saw	-1.834	0.618	-9.07–5.40
Number of specialists they saw	6.154	0.14	-2.03–14.34
Sex			
Male	-21.01	0.086	-45.01–2.99
Religion			
Not Catholic	-10.26	0.494	-39.77–19.24
Place of residence			
Province	11.667	0.349	-12.85–36.18
Access to the health center			
Difficult	21,860	0.052	-0.17–43.89
General practitioners visited			
≥ 10 physicians	142.62	**< 0.001**	72.15–213.10
Specialists who visited			
≥ 10 specialists	-16.50	0.690	-97.82–64.82
Establishment that came for the first time			
Private	13.542	0.484	-24.52–51.60
Level of complexity of the establishment visited for the first time			
Level of care I and II	-93.208	0.433	-32.69–14.05
Establishment where the diagnosis was made			
Private	-14.514	0.455	-52.76–23.73
Level of complexity of the establishment where the diagnosis was made			
Level of care I and II	-12.884	0.470	-47.98–22.22
Type of exams			
Clinical examination + tests complementary	24	0.454	-39.23–87.45
Diagnosis			
Non-genetic	54	**< 0.001**	25.96–82.01

with 69.9% presenting exclusively in childhood (*15*). The study found that 52.1% of the participants had genetic diseases. This discrepancy could be due to the sample size in the current study, which reflects a higher proportion of non-genetic rare disease diagnoses, including infectious, immunological, degenerative, or proliferative conditions (*3*). Another possible explanation is the lack of implementation of technologies in Peru, such as tandem mass spectrometry for expanded newborn screening, and genomic testing methods like next-generation sequencing and chromosomal microarray analysis (*16-18*). The existing gap in the diagnosis of rare diseases largely stems from the wide range of genetic tests currently available, which enable early and accurate identification of numerous genetic conditions. These tools have revolutionized diagnostic processes by facilitating timely and precise detection. In contrast, non-genetic rare diseases pose greater diagnostic challenges, as most lack specific tests for direct identification, often leading to delays in diagnosis and treatment (*19*).

The median time to diagnosis was 12 months, though the range was quite broad. In contrast, studies conducted in Spain and across the European Union reported mean diagnostic delays of 6.18 and 4.7 years, respectively (*9,20*). This discrepancy may result from the clinical heterogeneity of rare diseases. In our setting, some patients likely exhibit more evident clinical manifestations, facilitating earlier recognition and diagnosis, in line with the differences observed across this group of disorders (*21*). Conversely, individuals with milder or atypical presentations may experience significant delays in diagnosis (*22*). Another possible explanation is the presence of autosomal dominant inheritance diseases, which tend to manifest more frequently in multiple family members, allowing for earlier identification and evaluation of patients (*3*).

Patients who perceived easier access to health centers had a shorter average time to diagnosis compared to those who reported difficulties in accessing care. This finding aligns with existing evidence indicating that barriers such as limited appointment availability, geographic distance, or structural constraints can significantly contribute to diagnostic delays (*23*). This may be due to the lower density of specialists and subspecialists in our area, which hinders access to health services and contributes to delays in care.

A significant difference in diagnosis time was also observed between individuals who faced challenges obtaining medical appointments and those who dealt with geographic distance issues. These obstacles prevent timely evaluations, thereby extending the interval between symptom onset and diagnostic confirmation (*24*).

We found a paradoxical pattern regarding educational

level: participants with a completed undergraduate degree exhibited longer diagnostic delays. This may be explained by the fact that individuals with lower socioeconomic resources — who often have lower educational attainment — are more likely to seek care within the public healthcare system, where access to molecular diagnostic services is more consolidated (*15*).

Regarding the frequency of visits to general practitioners, a diagnostic delay of over one year was more frequently noted among patients who consulted more than ten general practitioners. This finding is consistent with previous reports indicating that when patients see specialist physicians more than ten times, it is associated with significant diagnostic delays (OR = 5.19; 95% CI: 2.6–5.15) (OR = 5.19; 95% CI: 2.6–5.15) (*11,20*). This situation may be explained by the fact that patients consulting more specialists often have a subtle disease presentation. This makes clinical suspicion challenging and prompts families or patients to seek multiple medical opinions. Similarly, the time to diagnosis does not appear to be shortened when patients undergo a combination of clinical evaluations and complementary tests. This contrasts with a study conducted in Spain, where genetic testing — while effective in confirming diagnoses — was associated with a longer time to diagnosis (OR = 1.3; 95% CI: 1.2–1.5) (*11*). Additionally, this difference may be attributed to the limited training or experience that general practitioners typically have in managing rare diseases compared to specialists. This gap in clinical knowledge may hinder the early recognition of uncommon signs and symptoms, prolonging the diagnostic process.

When examining the type of rare disease, individuals with non-genetic conditions reported a significantly longer time to diagnosis compared to those with genetic disorders. Consistent with previous studies conducted in Spain, individuals with nervous system diseases were found to have a higher risk of diagnostic delay (OR = 1.4; 95% CI: 1.0–1.8), whereas those with ocular and adnexal conditions had a lower risk (OR = 0.7; 95% CI: 0.5–0.9) (*11*). This discrepancy may be due to the absence of specific diagnostic tests for many of these diseases and the variability in their phenotypic manifestations (*2*). Furthermore, despite significant advances in disease diagnosis, their impact remains limited unless effectively integrated into the academic training and continuing education of healthcare professionals. Proper recognition of rare diseases requires ongoing updates and effective dissemination of scientific knowledge to medical personnel (*25,26*).

This study has certain limitations inherent to addressing a topic that remains underexplored. First, potential inconsistencies in the collected data may arise from the lack of standardized clinical documentation, variability in diagnostic criteria across healthcare facilities, or patients' difficulty in accurately recalling the time to diagnosis or the tests performed. Additionally, the low frequency of individual pathologies limited disease-specific analyses and restricted the ability to establish robust associations between diagnostic and therapeutic factors. Moreover, recruitment was carried out through patient associations, which may introduce selection bias. Individuals engaged in these organizations are often more informed about their condition and actively involved in advocacy activities, whereas those who are not part of such networks may have different levels of disease awareness or healthcare-seeking behaviors. Consequently, diagnostic delays and knowledge indicators reported in this study may not fully represent the broader population of affected individuals. Finally, diagnostic times were based on self-reported information, introducing the possibility of recall bias, as participants may not accurately remember the sequence or timing of consultations and diagnostic procedures. As this is a descriptive study, the findings should be viewed as an initial approximation, intended to serve as a foundation for future research aimed at enhancing our understanding of these processes in the context of rare diseases.

In the specific context of Peru, the population affected by rare diseases remains largely unidentified, posing a significant challenge for patient outreach and the collection of representative data (*6*). Moreover, the absence of consolidated registries may have influenced sample selection and affected the accuracy of the results. Similarly, the limited awareness and training among healthcare professionals regarding these conditions could have contributed to underreporting or misdiagnosis. A study conducted in Peru on the level of knowledge about rare diseases revealed that more than half of the participants demonstrated an impoverished understanding (*2*).

This research shows that diagnostic delays are common for individuals with rare diseases in Peru and highlights how health-system organization shapes patients' diagnostic journeys. The absence of unified registries, limited specialist awareness, and uneven access to molecular testing all lead to prolonged diagnostic pathways.

Improving primary-care training, establishing structured referral networks, expanding tele-genetics support, and creating a national registry are realistic steps that could shorten diagnostic delays and promote fair access to specialized care. Emphasizing these measures would meaningfully enhance early detection and overall care for people living with rare diseases in Peru.

Despite its limitations, the main strength of this study lies in its reflection of patient perceptions and its status as the first to quantify diagnostic delays while identifying modifiable factors that could optimize earlier detection.

5. Conclusion

Nearly half of the patients included in the study received a definitive diagnosis more than twelve months after

symptom onset, with such delays being more frequent in rare, non-genetic diseases. No significant associations were found between time to diagnosis and demographic or structural variables, including socioeconomic status, sex, religion, place of residence, type of healthcare facility, level of complexity, or type of diagnostic test. These findings suggest that barriers to timely diagnosis are multifactorial and may be influenced by factors that have yet to be identified or systematically studied.

However, a trend toward longer diagnostic delays was observed among patients who reported difficulties accessing health centers and those who consulted more than ten general practitioners. These findings highlight the need to improve access to specialized services and to strengthen the training of healthcare professionals in the recognition and management of rare diseases, particularly at the primary care level, in order to reduce diagnostic delays and optimize care for this vulnerable population.

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