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Original Research

Exploratory Study on Genetic Variants Related to Hydatidosis Susceptibility and Albendazole Pharmacogenetics in the Cusco Region in Peru

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Abstract

Background: Hydatidosis, caused by *Echinococcus granulosus*, is a neglected zoonotic disease with significant public health implications in endemic regions, such as in Cusco, Peru. Genetic factors influencing susceptibility to infection and responses to albendazole, the primary treatment, remain unclear. Thus, this study aimed to investigates genetic polymorphisms associated with hydatidosis susceptibility and albendazole metabolism in the Cusco region. **Methods**: Hence, a cross-sectional study was conducted using 20 individuals from endemic areas. Peripheral blood samples were collected for genomic DNA extraction, followed by single-nucleotide polymorphism (SNP) genotyping using the Illumina Global Screening Array. Polymorphisms in genes related to immunity (interleukin 10 (*IL10*), interleukin 17A (*IL17A*), vitamin D receptor (*VDR*), interferon gamma (*IFNG*), forkhead box P3 (*FOXP3*), interleukin 4 (*IL4*), tumor necrosis factor (*TNF*), toll-like receptor 4 (*TLR4*), cytotoxic T-lymphocyte antigen 4 (*CTLA4*), mannose-binding lectin 2 (*MBL2*), interleukin 12B (*IL12B*), and transforming growth factor-beta 1 (*TGFB1*)) and drug metabolism genes (cytochrome P450 family 3 subfamily A member 4 (*CYP3A4*), cytochrome P450 family 2 subfamily B member 6 (*CYP2B6*), cytochrome P450 family 1 subfamily A member 2 (*CYP1A2*), ATP-binding cassette subfamily B member 1 (*ABCB1*), solute carrier organic anion transporter family member 1B1 (*SLCO1B1*), and cytochrome P450 family 2 subfamily E member 1 (*CYP2E1*)) were analyzed. **Results**: High-frequency alleles were identified in six SNPs associated with susceptibility to *Echinococcus granulosus*: *IL10* rs1800896 (77.5%), *IL17A* rs2275913 (97.5%), *IFNG* rs2779249 (92.5%), *FOXP3* rs11568821 (97.5%), *TGFB1* rs1800469 (80.0%), and *VDR* rs2228570 (87.5%). Likewise, elevated allele frequencies were observed for two SNPs potentially involved in albendazole metabolism: *CYP3A4* rs2740574 (87.5%) and *CYP2B6* rs2266780 (97.5%). A comparative analysis with other populations revealed significant differences in SNP frequencies in the Cusco population, both in SNPs related to susceptibility (*IL17A* rs2275913, *VDR* rs2228570, and *TGFB1* rs1800469; $p < 0.001$) and pharmacogenetic-related SNPs (*CYP2B6* rs2266782, *SLCO1B1* rs4149056, and *CYP2E1* rs8330; $p < 0.05$), suggesting the existence of unique local genetic patterns. **Conclusion**: These findings underscore the importance of pharmacogenetic screening to optimize albendazole therapy and support precision medical approaches for hydatidosis management in endemic regions. Further studies with larger cohorts are required to confirm these associations.

Keywords: hydatidosis; genetic susceptibility; *Echinococcus granulosus*; pharmacogenetics; SNPs; albendazole

1. Introduction

Hydatidosis is a zoonotic parasitic disease caused by *Echinococcus granulosus*, a cestode that leads to the formation of hydatid cysts in various organs, primarily the liver and lungs [1]. This disease presents a significant public health burden, particularly in regions where livestock farming and close human-animal interactions facilitate its transmission [2]. Endemic areas, such as Cusco, Peru, continue to report high infection rates due to environmental, socioeconomic, and cultural factors that sustain the parasite's life cycle [3].

Despite advances in diagnosis and treatment, hydatidosis remains a major cause of morbidity, often requiring complex medical or surgical interventions [4]. Albendazole, the primary pharmacological treatment, demonstrates variable efficacy across individuals, which has been linked to genetic factors influencing drug metabolism and immune response [5]. Studies have highlighted the role of genetic predisposition in both susceptibility to infection and response to pharmacological therapy [6]. Genome-wide association studies (GWAS) have identified several candidate genes involved in immune modulation and drug metabolism, providing insights into inter-individual differences in disease susceptibility and treatment efficacy [7].

This genetic susceptibility may influence the host's response to infection, determining the severity of the clinical presentation and the effectiveness of treatment in hydatidosis. Among the genes implicated in modulating the immune

response to this disease are interleukin 10 (*IL10*), *IL17A*, tumor necrosis factor (*TNF*), toll-like receptor 4 (*TLR4*), cytotoxic T-lymphocyte antigen 4 (*CTLA4*), mannose-binding lectin 2 (*MBL2*), vitamin D receptor (*VDR*), interferon gamma (*IFNG*), Forkhead box P3 (*FOXP3*), and transforming growth factor-beta 1 (*TGFB1*), all of which are involved in inflammatory pathways and immune tolerance mechanisms [8–11].

Pharmacogenetics has emerged as a crucial field in understanding how genetic variations influence drug metabolism, efficacy, and toxicity [12]. Enzymes such as cytochrome P450 family 3 subfamily A member 4 (CYP3A4) and CYP2C19 are essential to albendazole metabolism, influencing its bioavailability and therapeutic impact [13]. Genetic polymorphisms in these enzymes have been associated with altered drug response, potentially leading to treatment failure or adverse effects [14]. Likewise, polymorphisms associated with the metabolism of albendazole, the main drug used in the treatment of hydatidosis, have been reported. Genes such as *CYP3A4*, *CYP1A2*, *CYP2B6*, *CYP2E1*, ATP-binding cassette subfamily B member 1 (*ABCB1*), and solute carrier organic anion transporter family member 1B1 (*SLCO1B1*) have been linked to the bioavailability, therapeutic efficacy, and toxicity profile of albendazole [13,15]. By investigating the pharmacogenetic profile of individuals receiving albendazole, this study aims to contribute to the optimization of treatment regimens, minimizing variability and improving clinical outcomes [16].

The prevalence of genetic variations that may be linked to albendazole metabolism and hydatidosis susceptibility in people from endemic areas in Cusco, Peru, is examined in this exploratory investigation. The goal of the study is to find biologically significant variations that might merit more research in subsequent association studies, even though no phenotypic or clinical outcome data were gathered. Through single nucleotide polymorphism (SNP) genotyping using the Illumina Global Screening Array, we aim to identify genetic markers that may influence both disease susceptibility and therapeutic response [17]. This research has implications for the development of personalized medicine strategies, which could lead to more effective disease management in endemic populations.

2. Materials and methods

2.1 Study Design and Population

This study employed a cross-sectional design to investigate the prevalence of genetic susceptibility to hydatidosis and pharmacogenetic response to albendazole. Participants were recruited from three endemic localities in Cusco, Peru, with a study population of 20 individuals selected from regional healthcare centers and the local community. Participants were between the ages of 18 and 60, lived in Cusco's endemic districts, and gave written informed consent. Exclusion criteria included current or prior antiparasitic treatment, chronic infections (e.g., HIV or tuberculosis), autoimmune diseases, or refusal to provide a blood sample.

2.2 Sample Collection and DNA Extraction

Peripheral blood samples (3 mL) were collected in ethylenediaminetetraacetic acid (EDTA) tubes and stored at –80 °C until processing. Genomic DNA was extracted using the PureLink Genomic DNA Mini Kit (K182001, Invitrogen, Carlsbad, CA, USA), following the manufacturer's protocols. DNA purity and concentration were evaluated using a NanoDrop Lite spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA), and DNA integrity was assessed by agarose gel electrophoresis.

2.3 Genotyping and SNP Selection

Genome-wide SNP genotyping was performed using the Illumina Global Screening Array (GSA) (Illumina Inc., San Diego, CA, USA), which includes pharmacogenetically relevant and disease-associated polymorphisms. SNPs selected for analysis focused on genes involved in immune regulation, inflammation, pathogen defense, and immune tolerance (*IL10*, *IL4*, *IL17A*, *TNF*, *TLR4*, *CTLA4*, *VDR*, *TGFB1*, *MBL2*, *IFNG*, *FOXP3* and *IL12B*) and drug metabolism (*CYP3A4*, *CYP1A2*, *CYP2B6*, *ABCB1*, *SLCO1B1* and *CYP2E1*). This study also presents a comparative analysis of risk allele frequencies among the Cusco population and other populations, including Peru, Colombia, Mexico, and global data. Allele frequency information for external populations was obtained from the 1000 Genomes Project and the Ensembl Genome Browser (GRCh37/hg19 release). Data analysis was conducted using whole-genome association analysis toolset (PLINK) v1.9 (Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA). Standard QC limits were met by all individual samples, with call rates over 98% and no heterozygosity outliers found. Concordance rates could not be determined since duplicate genotyping was not carried out due to the small sample size. There were no differences in the distribution of genotypes by sex. Less than 2% of SNPs were eliminated because of poor call rates, and none were eliminated because of deviation from Hardy-Weinberg Equilibrium ($p < 0.05$). These exclusions had little bearing on the study of the target polymorphisms.

2.4 Statistical Analysis

For genotypic and allelic frequencies, 95% confidence intervals were calculated. Data analysis was carried out using Stata 15 program (StataCorp. 2016. Stata Statistical Software: Release 15. College Station, TX, USA).

3. Results

The allele frequency analysis of genetic variants related to hydatidosis susceptibility and albendazole metabolism in the Cusco population (Table 1) showed that

Table 1. Allele frequencies of gene polymorphisms associated with susceptibility to hydatidosis and albendazole metabolism in a Cusco population.

	Gene	SNP	Position	Substituted aminoacid	Allele frequency (95% CI)
Susceptibility	*IL10*	rs1800896	–1082 A/G	–	0.775 (0.645–0.904)
		rs1800871	–819 T/C	–	0.275 (0.136–0.413)
		rs1800872	–592 A/C	–	0.275 (0.136–0.413)
	IL4	rs2243250	–590 C/T	–	0.375 (0.224–0.525)
	IL17A	rs2275913	–197 G/A	–	0.975 (0.926–1.023)
	TNF	rs1800629	–308 G/A	–	0.025 (0.023–0.073)
	TLR4	rs4986790	+896 A/G	D299G	0.000
		rs4986791	+1196 C/T	T399I	0.000
	CTLA4	rs231775	+49 A/G	T17A	0.250 (0.115–0.384)
	MBL2	rs1800450	+230 G/A	G54D	0.375 (0.224–0.525)
		rs1800451	+239 A/G	G57E	0.000
		rs5030737	+221 C/G	R52C	0.000
	VDR	rs2228570	+2 C/T	M1I	0.875 (0.772–0.977)
		rs731236	+352 T/C	–	0.100 (0.007–0.192)
		rs1544410	intron 8	–	0.100 (0.007–0.192)
		rs7975232	intron 8	–	0.250 (0.115–0.384)
	IFNG	rs2779249	–1616 T/C	–	0.925 (0.843–1.006)
	FOXP3	rs11568821	–3279 A/C	–	0.975 (0.926–1.023)
	TGFB1	rs1800469	–509 C/T	–	0.800 (0.676–0.923)
	IL12B	rs3212227	+1188 A/C	–	0.475 (0.320–0.629)
Pharmacogenetic	*CYP3A4*	rs2740574	–392 A>G	–	0.875 (0.772–0.977)
		rs2242480	–298 G>A	–	0.400 (0.248–0.551)
	CYP1A2	rs762551	–163 C>A	–	0.225 (0.095–0.354)
	CYP2B6	rs2266780	516 G>T	Q172H	0.975 (0.926–1.023)
		rs2266782	785 A>G	K262R	0.100 (0.007–0.192)
	ABCB1	rs1045642	3435 C>T	–	0.325 (0.179–0.470)
		rs1128503	1236 C>T	–	0.425 (0.271–0.578)
		rs2032582	2677 G>A	A893T	0.325 (0.179–0.470)
	SLCO1B1	rs4149056	521 T>C	V174A	0.325 (0.179–0.470)
	CYP2E1	rs8330	–333 T>C	–	0.100 (0.007–0.192)

ABCB1, ATP-binding cassette subfamily B member 1; *CTLA4*, cytotoxic T-lymphocyte antigen 4; *FOXP3*, forkhead box P3; *IFNG*, interferon gamma; *IL10*, interleukin 10; *MBL2*, mannose-binding lectin 2; *SLCO1B1*, solute carrier organic anion transporter family member 1B1; SNP, single nucleotide polymorphism; *TGFB1*, transforming growth factor-beta 1; *TLR4*, toll-like receptor 4; *TNF*, tumor necrosis factor; *VDR*, vitamin D receptor; *CYP1A2*, cytochrome P450 family 1 subfamily A member 2; *CYP3A4*, cytochrome P450 family 3 subfamily A member 4; *CYP2B6*, cytochrome P450 family 2 subfamily B member 6; *CYP2E1*, cytochrome P450 family 2 subfamily E member 1.

the *IL10* rs1800896 (–1082 A/G) polymorphism had a G allele frequency of 0.775 (95% CI: 0.645–0.904), while the *IL17A* rs2275913 (–197 G/A) polymorphism exhibited an A allele frequency of 0.975 (0.926–1.023). Other polymorphisms evaluated included *VDR* rs2228570 (M1I C/T), which presented a T allele frequency of 0.875 (95% CI: 0.772–0.977), and *IFNG* rs2779249 (–1616 T/C), where the C allele was observed at a frequency of 0.925 (95% CI: 0.843–1.006). Additionally, *FOXP3* rs11568821 (–3279 A/C) showed a high C allele frequency of 0.975 (95% CI: 0.926–1.023), and *TGFB1* rs1800469 (–509 C/T) exhibited a T allele frequency of 0.800 (95% CI: 0.676–0.923). The *CYP2B6* rs2266780 (Q172H G>T) polymorphism exhibited a T allele frequency of 0.975 (95% CI: 0.926–1.023), while the *CYP3A4* rs2740574 (–392 A>G) polymorphism showed a G allele frequency of 0.875 (95% CI: 0.772–0.977); both polymorphisms are involved in drug metabolism.

The genotypic distribution of the studied polymorphisms is summarized in Table 2. The most frequently observed heterozygous genotype was *CYP3A4* rs2242480, with a GA frequency of 0.600 (95% CI: 0.360–0.799). This was followed by *MBL2* rs1800450, *IL12B* rs3212227 and *ABCB1* rs1045642, each with genotype frequencies of 0.550 (95% CI: 0.317–0.762) for the GA, AC, and CT genotypes, respectively. Non-heterozygous genotypes was observed in *TLR4* (rs4986790, rs4986791) and *MBL2* (rs1800451, rs5030737). In terms of non-wild type homoz-

Table 2. Frequencies of immune-related and pharmacogenetic gene polymorphisms associated with susceptibility to hydatidosis and albendazole metabolism in a Cusco population.

	Gene	SNP	Position	Wild-type frequency (proportion, 95% CI)	Heterozygote frequency (proportion, 95% CI)	Homozygote frequency (proportion, 95% CI)
Susceptibility	*IL10*	rs1800896	–1082 A/G	AA: 0.050 (0.005–0.322)	AG: 0.350 (0.164–0.595)	GG: 0.600 (0.360–0.799)
		rs1800871	–819 T/C	TT: 0.600 (0.360–0.799)	TC: 0.250 (0.099–0.502)	CC: 0.150 (0.043–0.403)
		rs1800872	–592 A/C	AA: 0.600 (0.360–0.799)	AC: 0.250 (0.099–0.502)	CC: 0.150 (0.043–0.403)
	IL4	rs2243250	–590 C/T	CC: 0.400 (0.200–0.639)	CT: 0.450 (0.237–0.682)	TT: 0.150 (0.043–0.403)
	IL17A	rs2275913	–197 G/A	GG: 0.000	GA: 0.050 (0.005–0.322)	AA: 0.950 (0.677–0.994)
	TNF	rs1800629	–308 G/A	AA: 0.950 (0.677–0.994)	GA: 0.050 (0.005–0.322)	GG: 0.000
	TLR4	rs4986790	+896 A/G	AA: 1.000	AG: 0.000	GG: 0.000
		rs4986791	+1196 C/T	CC: 0.000	CT: 0.000	TT: 1.000
	CTLA4	rs231775	+49 A/G	AA: 0.550 (0.317–0.762)	AG: 0.400 (0.200–0.639)	GG: 0.050 (0.005–0.322)
	MBL2	rs1800450	+230 G/A	GG: 0.350 (0.164–0.595)	GA: 0.550 (0.317–0.762)	AA: 0.100 (0.001–0.230)
		rs1800451	+239 A/G	GG: 1.000	GA: 0.000	AA: 0.000
		rs5030737	+221 C/G	GG: 1.000	GA: 0.000	AA: 0.000
	VDR	rs2228570	+2 C/T	CC: 0.000	CT: 0.250 (0.099–0.502)	TT: 0.750 (0.497–0.900)
		rs731236	+352 T/C	TT: 0.800 (0.546–0.930)	TC: 0.200 (0.069–0.453)	CC: 0.000
		rs1544410	intron 8	TT: 0.800 (0.546–0.930)	TC: 0.200 (0.069–0.453)	CC: 0.000
		rs7975232	intron 8	TT: 0.650 (0.404–0.835)	TC: 0.200 (0.069–0.453)	TT: 0.150 (0.043–0.403)
	IFNG	rs2779249	–1616 T/C	TT: 0.000	TC: 0.150 (0.043–0.403)	CC: 0.850 (0.596–0.956)
	FOXP3	rs11568821	–3279 A/C	AA: 0.000	AC: 0.050 (0.005–0.322)	CC: 0.950 (0.677–0.994)
	TGFB1	rs1800469	–509 C/T	CC: 0.000	CT: 0.400 (0.200–0.639)	TT: 0.600 (0.360–0.799)
	IL12B	rs3212227	+1188 A/C	AA: 0.250 (0.099–0.502)	AC: 0.550 (0.317–0.762)	CC: 0.200 (0.069–0.453)
Pharmacogenetic	*CYP3A4*	rs2740574	–392 A>G	AA: 0.050 (0.005–0.322)	AG: 0.150 (0.043–0.403)	GG: 0.800 (0.546–0.930)
		rs2242480	–298 G>A	GG: 0.300 (0.130–0.549)	GA: 0.600 (0.360–0.799)	AA: 0.100 (0.001–0.230)
	CYP1A2	rs762551	–163 C>A	CC: 0.550 (0.317–0.762)	CA: 0.450 (0.237–0.682)	AA: 0.000
	CYP2B6	rs2266780	516 G>T	GG: 0.000	GT: 0.050 (0.005–0.322)	TT: 0.950 (0.677–0.994)
		rs2266782	785 A>G	AA: 0.800 (0.546–0.930)	AG: 0.200 (0.069–0.453)	GG: 0.000
	ABCB1	rs1045642	3435 C>T	CC: 0.400 (0.200–0.639)	CT: 0.550 (0.317–0.762)	TT: 0.050 (0.005–0.322)
		rs1128503	1236 C>T	CC: 0.350 (0.164–0.595)	CT: 0.450 (0.237–0.682)	TT: 0.200 (0.069–0.453)
		rs2032582	2677 G>A	GG: 0.500 (0.276–0.723)	GT: 0.350 (0.164–0.595)	TT: 0.150 (0.043–0.403)
	SLCO1B1	rs4149056	521 T>C	TT: 0.450 (0.237–0.682)	TC: 0.450 (0.237–0.682)	CC: 0.100 (0.001–0.230)
	CYP2E1	rs8330	–333 T>C	TT: 0.800 (0.546–0.930)	TC: 0.200 (0.069–0.453)	CC: 0.000

ygous genotypes, *TLR4* rs4986791 had all TT frequency (100%), followed by *IL17A* rs2275913, *FOXP3* rs11568821 and *CYP2B6* rs2266780, each with genotype frequencies of 0.950 (95% CI: 0.677–0.994) for the AA, CC, and TT genotypes, respectively.

Table 3 presents a comparative analysis of risk allele frequencies between the Cusco population and other populations, including Peru, Colombia, Mexico, and global data from the 1000 Genomes Project. The *TGFB1* rs1800469 T allele frequency in Cusco (80.0%) was notably higher than in Peru (57.06%), Colombia (43.62%), Mexico (39.84%) and global population (36.80%) ($p < 0.001$). The *VDR* rs2228570 T allele frequency in Cusco (87.5%) was considerably higher than the reported frequencies for Peru (69.41%), Colombia (40.96%), Mexico (48.44%), and the global population (32.85%) ($p < 0.001$). In contrast, the *IL17A* rs2275913 G allele frequency in Cusco (2.5%) was the lowest among all populations analyzed ($p < 0.001$), highlighting a potential distinctive immune-related genetic profile in this high-altitude population. In case of impact drug metabolism, *CYP2B6* rs2266782 G allele frequency in Cusco (90.0%) was slightly upper than the reported frequencies for Peru (70.00%), Colombia (71.81%), and Mexico (67.19%) and global population (65.22%) ($p = 0.003$). The *SLCO1B1* (rs4149056) and *CYP2E1* (rs8330) allele frequency varied among these populations ($p = 0.001$ and $p = 0.041$ respectively).

4. Discussion

This study provides crucial insights into the genetic basis of hydatidosis susceptibility and the pharmacogenetics of albendazole treatment. The identification of high-prevalence SNPs in *IL10*, *IL17A*, *VDR*, *IFNG*, *FOXP3*, and *TGFB1* highlights the role of immune and metabolic pathways in infection outcomes. Similar to findings in other parasitic diseases, *IL10* polymorphisms influence immune suppression and parasite persistence, while *IL17A* variants impact inflammatory responses and resistance to infection [18,19]. Studies from different regions confirm the role of *VDR* polymorphisms in modulating macrophage activity and parasite clearance, while *IFNG* variants have been linked to immune activation and disease severity [20,21].

Additionally, the regulatory functions of *FOXP3* and *TGFB1* are essential in determining immune tolerance and inflammation during *E. granulosus* infection. Polymorphisms in *FOXP3* affect Treg cell activity, influencing susceptibility and disease progression, with similar findings reported in Turkish and Indian populations [22,23]. *TGFB1* polymorphisms, associated with immune suppression and tissue remodeling, parallel observations in schistosomiasis and leishmaniasis, reinforcing the cytokine's role in modulating helminthic infections [24,25]. These findings emphasize the genetic complexity of hydatidosis and align with global studies, supporting the need for personalized treatment approaches.

For example, because IL17A is involved in neutrophil recruitment and pro-inflammatory responses to parasites [26], the low frequency of the *IL17A* rs2275913 A variant in Cusco (2.5%) may suggest a unique immunological profile. Similarly, immunological suppression and chronic infection may be encouraged by the high frequency of the *TGFB1* rs1800469 T allele, which is associated with higher TGFB1 expression. Changes in macrophage activity have been linked to the common *VDR* rs2228570 T allele [27]. Despite the lack of clinical data, these results point to population-specific genetic patterns that need more functional research.

Analysis revealed that high-prevalence SNPs in *CYP3A4* and *CYP2B6* could affect albendazole treatment outcomes. By altering enzyme activity, genetic variations in CYP3A4, specifically CYP3A4*1B (rs2740574), may have an impact on albendazole metabolism [28,29]. To keep things focused, only the variants examined in our dataset are discussed, even if other variants have been described. These results offer a preliminary understanding of the population's baseline pharmacogenetic profiles, which need further functional and clinical verification. These findings highlight the need for pharmacogenetically guided dosing to improve albendazole treatment outcomes and minimize adverse effects.

Polymorphisms in *CYP2B6*, such as *CYP2B66* (rs3745274) and *CYP2B69* (rs28399499), affect albendazole metabolism, potentially altering its therapeutic efficacy in hydatidosis [30,31]. Studies on other antiparasitic drugs suggest that *CYP2B6* variants contribute to interindividual variability in drug clearance, reinforcing the need for pharmacogenetic screening to optimize albendazole dosing and enhance treatment response [32,33]. Further research is needed to establish personalized dosing strategies based on *CYP3A4* and *CYP2B6* genetic profiles, ensuring better therapeutic outcomes and reduced toxicity in hydatidosis patients.

The genetic variability observed in the Cusco population compared to other Latin American populations highlights differences in immune regulation and drug metabolism. The higher *TGFB1* rs1800469 T allele frequency may influence inflammatory responses, while variations in *VDR* rs2228570 could affect immune function and disease susceptibility [34,35]. These findings emphasize the importance of population-specific genetic studies to understand disease risk and treatment outcomes [36,37]. Regarding pharmacogenetics, the elevated *CYP2B6* rs2266782 G allele frequency suggests potential differences in drug metabolism, impacting albendazole efficacy and other treatments [38,39]. Variability in *SLCO1B1* (rs4149056) and *CYP2E1* (rs8330) further highlights the need for pharmacogenetic screening to optimize drug dosing and minimize adverse effects in this population [40,41].

The variability observed in treatment responses highlight the necessity for personalized medicine approaches

Table 3. Comparison of hydatidosis risk alleles and pharmacogenetically relevant SNPs for albendazole metabolism in the studied peruvian population and various human populations (percent).

	Gene	SNPs	Risk allele	Population				All populations	*p* value*
				Cusco	Peru	Colombia	Mexico		
Susceptibility	*IL10*	rs1800896	G	22.50	24.71	32.98	32.03	27.22	0.737
		rs1800871	T	27.50	37.06	29.79	42.19	43.47	0.131
		rs1800872	A	27.50	37.06	29.79	42.19	43.49	0.131
	IL4	rs2243250	T	37.50	48.24	35.64	44.53	46.98	0.404
	IL17A	rs2275913	G	2.50	11.76	26.06	24.22	29.27	0.000
	TNF	rs1800629	A	2.50	5.88	6.91	5.47	9.03	0.281
	TLR4	rs4986790	G	0	0.59	5.32	3.13	5.99	0.183
		rs4986791	T	0	0	6.38	3.13	4.07	0.578
	CTLA4	rs231775	G	75.00	62.94	44.68	42.97	42.73	0.001
	VDR	rs2228570	T	87.50	69.41	40.96	48.44	32.85	0.000
		rs731236	C	10.00	11.76	25.53	20.31	27.66	0.026
		rs1544410	G	90.00	87.65	75.00	80.47	70.41	0.016
		rs7975232	C	75.00	78.24	49.47	59.38	48.46	0.007
	TGFB1	rs1800469	T	80.00	57.06	43.62	39.84	36.80	0.000
	IL12B	rs3212227	C	47.50	45.88	24.47	39.84	35.90	0.286
Pharmacogenetic	*CYP3A4*	rs2740574	G	12.50	3.53	10.11	7.03	23.08	0.242
		rs2242480	A	60.00	57.65	28.72	39.06	42.17	0.082
	CYP1A2	rs762551	A	77.50	86.47	73.40	73.44	62.98	0.147
	CYP2B6	rs2266780	T	97.50	94.12	91.49	91.41	90.85	0.281
		rs2266782	G	90.00	70.00	71.81	67.19	65.22	0.003
	ABCB1	rs1045642	T	32.50	37.65	44.15	47.66	39.52	0.526
		rs1128503	T	42.50	32.94	42.55	46.88	41.61	1.000
		rs2032582	A	32.50	29.41	41.49	40.63	33.43	1.000
	SLCO1B1	rs4149056	C	32.50	14.12	18.09	7.81	8.77	0.001
	CYP2E1	rs8330	C	90.00	78.24	78.19	79.69	74.50	0.041

* Chi square test for Cusco vs All population.

in endemic populations. By integrating pharmacogenetic screening into clinical practice, clinicians may optimize albendazole dosing and predict treatment efficacy based on genetic profiles. Personalized medicine strategies have been successfully implemented for other antiparasitic drugs, demonstrating improved patient outcomes and reduced drug resistance [42,43].

The statistical power and precision of allele frequency estimations are severely limited by the small sample size (n = 20), despite the fact that this study offers insightful genetic information about the endemic population of Cusco. These results are quite uncertain, as evidenced by the broad confidence intervals found, for as for *IL10* rs1800896 (G allele frequency: 0.775; 95% CI: 0.645–0.904). These restrictions hinder the capacity to establish strong genetic connections and limit the generalizability of our findings. Consequently, it is appropriate to consider the outcomes as exploratory and hypothesis-generating. Additionally, gene-environment interactions should be explored, considering the impact of dietary, microbiome, and immune factors on disease progression and drug metabolism [44,45].

This study offers early proof of genetic variability associated with albendazole metabolism and hydatidosis that is specific to a group. The results are used to generate hypotheses, despite being based only on genotypic data with no clinical link. In order to enable precision medicine in endemic settings, future research should investigate multi-omic techniques and validate these findings in larger cohorts with phenotypic and pharmacokinetic data.

5. Conclusions

Our study concludes by offering important initial insights into the genetic diversity of candidate genes that may be connected to albendazole metabolism and hydatidosis risk. The identification of key SNPs in *IL10*, *IL17A*, *VDR*, *IFNG*, *FOXP3*, and *TGFB1* reinforces the role of immune regulation in infection outcomes, with parallels observed in other parasitic diseases. Additionally, genetic variability in *CYP3A4* and *CYP2B6* highlights the potential impact of polymorphisms on albendazole metabolism, emphasizing the need for pharmacogenetic-guided dosing strategies to enhance therapeutic efficacy and minimize adverse effects. Differences in allele frequencies between the Cusco population and other Latin American groups further emphasize the importance of population-specific genetic studies to refine treatment approaches.

As hydatidosis remains a persistent health challenge in endemic regions, the application of precision medicine approaches could significantly impact disease management by enabling more effective and personalized treatment strategies. Future research should focus on expanding genomic databases, incorporating multi-ethnic populations, and exploring gene-environment interactions to refine our understanding of host-parasite dynamics and optimize therapeutic interventions. These advancements could pave the way for a more individualized approach to hydatidosis treatment, ultimately improving patient outcomes and contributing to more efficient disease control efforts in affected regions.

Abbreviations

ABCB1, ATP-binding cassette subfamily B member 1; CI, Confidence interval; CTLA4, Cytotoxic T-lymphocyte antigen 4; CYP, Cytochrome P450; DNA, Deoxyribonucleic acid; EDTA, Ethylenediaminetetraacetic acid; FOXP3, Forkhead box P3; GSA, Global Screening Array; GWAS, Genome-wide association study; IFNG, Interferon gamma; IL, Interleukin; MBL2, Mannose-binding lectin 2; PLINK, Whole-genome association analysis toolset; SLCO1B1, Solute carrier organic anion transporter family member 1B1; SNP, Single nucleotide polymorphism; TGFB1, Transforming growth factor-beta 1; TLR, Toll-like receptor; TNF, Tumor necrosis factor; VDR, Vitamin D receptor.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

Study design: LJV. Performed the experiments: LJV, MYGP. Analyzed the data: LJV, MYGP, DL, SJS, RC. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Our study was approved by the Ethics in Research Committee of the Universidad Continental of Peru (N°047-2024-CIEI-UC) and follows the principles of the Declaration of Helsinki. Written informed consent was obtained from all the participants.

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Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT in order to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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