Table SVI. *In silico* analysis of variants detected in the present study.

Location	Gene	Amino acids change	PolyPhen-2	Mutation Taster	REVEL (>0.5)	M-CAP	MaxEntScan	BDGP	NetGene2
chr14:81558933	*TSHR*	p.C176R	PROBABLY DAMAGING	Disease causing	0.718	Possibly Pathogenic			
chr14:81609751	*TSHR*	p.R450H	PROBABLY DAMAGING	Disease causing	0.943	Possibly Pathogenic			
chr14:81609984	*TSHR*	p.R528S	BENIGN	Disease causing	0.303	Possibly Pathogenic			
chr14:81610254	*TSHR*	p.K618*		Disease causing					
chr15:45404068	*DUOX2*	p.D137E	PROBABLY DAMAGING	Disease causing	0.53	Possibly Pathogenic			
chr15:45402093	*DUOX2*	p.R376W	PROBABLY DAMAGING	Disease causing	0.421	Possibly Pathogenic			
chr15:45401791	*DUOX2*	p.E389K	BENIGN	Polymorphism	0.111	Likely Benign			
chr15:45401737	*DUOX2*	p.V407F	PROBABLY DAMAGING	Disease causing	0.37	Possibly Pathogenic			
chr15:4538	*DUOX*	p.G1521*		Disease					

6434	*2*			causing		
chr15:4540	*DUOX*	p.R432H	PROBABLY	Disease	0.296	Possibly
1090	*2*		DAMAGING	causing		Pathogenic
chr15:4540	*DUOX*	p.R434*		Disease		
1085	*2*			causing		
chr15:4540	*DUOX*	p.R434_S440de		Disease		
1064	*2*	l		causing		
chr15:4539	*DUOX*	p.K530*		Disease		
9648	*2*			causing		
chr15:4539	*DUOX*	p.F591S	PROBABLY	Disease	0.691	Possibly
9089	*2*		DAMAGING	causing		Pathogenic
chr15:4539	*DUOX*	p.G624fs		Disease		
8800	*2*			causing		
chr15:4539	*DUOX*	p.R625*		Disease		
8798	*2*			causing		
chr15:4539	*DUOX*	p.V779M		Disease	0.079	
6563	*2*		BENIGN	causing		
chr15:4539	*DUOX*	p.T803fs		Disease		
6491	*2*			causing		
chr15:4539	*DUOX*	p.E879K	PROBABLY	Disease	0.793	Possibly
6177	*2*		DAMAGING	causing		Pathogenic
chr15:4539	*DUOX*	p.R885L	PROBABLY	Disease	0.22	Possibly

6158	*2*		DAMAGING	causing		Pathogenic			
chr15:45391946	*DUOX2*	p.R1110Q	PROBABLY DAMAGING	Disease causing	0.91	Possibly Pathogenic			
chr15:45389889	*DUOX2*	p.A1206T	PROBABLY DAMAGING	Disease causing	0.381	Possibly Pathogenic			
chr15:45389811	*DUOX2*	IVS28+1G>T					8.72/0.22	0.91/-	0.82/-
chr15:45387285	*DUOX2*	p.Y1415C	PROBABLY DAMAGING	Disease causing	0.913	Possibly Pathogenic			
chr15:45408396	*DUOXA2*	p.R94C	PROBABLY DAMAGING	Polymorphism	0.222	Possibly Pathogenic			
chr15:45409472	*DUOXA2*	p.Y246*		Disease causing					
chr19:18004669	*SLC5A5*	p.Q639*		Polymorphism					
chr2:1480963	*TPO*	p.S309P	BENIGN	Polymorphism	0.351	Possibly Pathogenic			
chr2:1481120	*TPO*	p.R361L	PROBABLY DAMAGING	Disease causing	0.311				
chr2:1491708	*TPO*	p.S571R	BENIGN	Polymorphism	0.146	Possibly Pathogenic			
chr2:15004	*TPO*	p.E757fs		Disease					

18				causing		
chr2:15206 72	*TPO*	p.R846W	PROBABLY DAMAGING	Polymorphi sm	0.215	Possibly Pathogenic
chr2:15443 94	*TPO*	p.P883S	BENIGN	Polymorphi sm	0.317	Likely Benign
chr5:17742 1297	*PROP1*	p.G51V	BENIGN	Polymorphi sm	0.166	Possibly Pathogenic
chr7:10730 3808	*SLC26 A4*	p.Y78H	PROBABLY DAMAGING	Disease causing	0.96	Possibly Pathogenic
chr7:10733 4884	*SLC26 A4*	p.A434T	BENIGN	Disease causing	0.602	Possibly Pathogenic
chr7:10734 1570	*SLC26 A4*	p.Y578H	PROBABLY DAMAGING	Disease causing	0.507	Possibly Pathogenic
chr8:11010 0245	*TRHR*	p.I168M	BENIGN	Polymorphi sm	0.068	Likely Benign
chr8:13388 5463	*TG*	p.N212S	BENIGN	Polymorphi sm	0.065	Possibly Pathogenic
chr8:13390 0739	*TG*	p.R896Q	PROBABLY DAMAGING	Disease causing	0.325	Possibly Pathogenic
chr8:13390 6036	*TG*	p.E955fs		Disease causing		
chr8:13395	*TG*	p.V1738I	BENIGN	Polymorphi	0.078	Likely Benign

3766				sm		
chr8:13398 0087	*TG*	p.S1912N	BENIGN	Polymorphi sm	0.071	Likely Benign
chr8:13398 0143	*TG*	p.I1931V	BENIGN	Polymorphi sm	0.361	Likely Benign
chr8:13403 1903	*TG*	p.L2282fs		Disease causing		
chr8:13404 2211	*TG*	p.I2394M	PROBABLY DAMAGING	Disease causing	0.397	Possibly Pathogenic
chr8:13412 5846	*TG*	p.R2585W	PROBABLY DAMAGING	Disease causing	0.117	Possibly Pathogenic

PolyPhen-2, MutationTaster, REVEL and M-CAP were used to predict the effects of missense and indel mutations; MaxEntScan, BDGP, and NetGene-2 were used to predict the damaging effects of splicing mutations with a wild-type/mutant score; – means depletion of the 5′ splice site. PolyPhen-2, Polymorphism Phenotyping v2; REVEL, Rare Exome Variant Ensemble Learner; M-CAP, Mendelian Clinically Applicable Pathogenicity; BDGP, Berkeley Drosophila Genome Project; NA: not available.