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| Table S3 :Summary of the shared variants identified in 24 CHD patients through whole exome sequencing (WES) analysis | | | | | | | | | | | | | | | | | |
| Patient ID | Cardiac Phenotype | Extra Cardiac phenotype | Age | Gender | Country of origin | Gene | Protein change | Nucleotide change | Gemini  segregation | Zygosity | Inheritance | ClinVar | ACMG/AMP classification | ACMG/AMP Sub classification | Reported in other studies | Reported cases country of origin | *References* |
| Cardio-2.A | TOF | None | 6 months | F | Qatar | *TTN* | p.Asn32797Ser | c.98390A>G | CH | Heterozygous | Paternal | Conflict interpretation | Likely benign | BP1, BP6, PP3 | Late onset progressive distal myopathy | European | [1] |
| Cardio-5.A | ATS | None | 2 months | M | Yemen | *SLC2A10* | p.Ser81Arg | c.243C>G | AR | Homozygous | Both parents | Pathogenic | Likely pathogenic | PM1,PM2,PP3,PP5 | ATS | Qatari, KSA | [2, 3] |
| Cardio-11.A | ASD | Squint, polydactyly | 3 months | F | India | *PRR12* | p.Gly1813Arg | c.5437G>A | AR | Homozygous | Both parents | None | US | PM1,BP1 | none | - | - |
| Cardio-12.A | multiple CHD | Failure to thrive | 20 days | F | Sri Lanka | *KMT2D* | p.Pro3665Ala | c.10993C>G | CH | Heterozygous | Maternal | Conflicting interpretation | US | BP1 | Kabuki syndrome | Unknown | [4] |
| Cardio-15.A | Shone's complex (hypoplastic transverse arch, VSD, PDA) | None |  | F | Pakistan | *FLT1* | - | c.1437-6delT | *de novo* | Heterozygous | None | None | none | - | none | - | - |
| 7 days | *CCDC141* | p.Val1457Ile | - | AR | Homozygous | Both parents | Likely Benign | Likely benign | BS1,BP6 | Reported  (unknown condition) | - | [4] |
| Cardio-16.A | TOF | None |  | M | Sudan | *SORBS2* | p.Phe1188Leu | c.3564C>A | Could not be identified | Heterozygous | Not reported \* | None | US | PM1 | none | - | - |
| 9 months | *DYNC2H1* | p.Val1899Ile | c.5695G>A | CH | Heterozygous | Maternal | Conflicting interpretation | US | PM1,PM2 | Short rib Thoracic dysplasia | Multiple submitters(unknown ethnicities) | [5] |
|  | *BMP10* | p.Thr200Ser | c.599C>G | *de novo* | Heterozygous | None | None | US | PM1,BS1 | none | - | - |
|  | *KYNU* | p.Thr25Met | c.74C>T | *de novo* | Heterozygous | None | Benign | US | PM1,PM2,BP6 | none | - | - |
|  | *PLCD4* | p.Val364Met | c.1090G>A | *de novo* | Heterozygous | None | None | US | PM1,BP4 | none | - | - |
|  | *MLIP* | p.Pro459Arg | c.1376C>G | *de novo* | Heterozygous | None | None | US | PM1 | none | - | - |
|  | *PBX3* | p.His401Gln | c.1203T>A | *de novo* | Heterozygous | None | None | US | PM1,PM2 | none | - | - |
|  | *OR51E1* | p.Ala156Thr | c.466G>A | *de novo* | Heterozygous | None | None | US | PM1 | none | - | - |
| Cardio-18.A | Aortic stenosis & insufficiency, mild LVH, frequent PACs | none |  | M | Qatari | *CMYA5* | p.Ser2012Phe | c.6035C>T | AR | Homozygous | One copy was maternally inherited( all siblings are carrriers)\*\* | Benign | likely benign | BS1,BP6 | Reported (unknown condition) | Unknown | [6] |
| 18 years | *CMYA5* | p.Glu584Ala | c.1751A>C | AR | Homozygous | One copy was maternally inherited( all siblings are carriers)\*\* | Benign | likely benign | PM1,PM2 | Reported (unknown comnditon) | Unknown | [7] |
| Cardio-27.A | TOF | Prolonged QT interval, hearing loss |  | F | Yemen | *CHD7* | p.Arg2098\* | c.6292C>T | *de novo* | Heterozygous | none | Pathogenic | Pathogenic | PVS1,PM2,PP3,PP5 | Immune deficiency, CHARGE syndrome | China | [8, 9] |
| Cardio-31.A | HLH | None |  | F | Sudan | *DNAH11* | c.9946-7T>C | - | AR | Homozygous | One copy paternally inherited \*\*\* | None | None | PM2 | none | - | - |
|  | *DNAAF3* | p.Val536Met | c.1606G>A | AR | Homozygous | One copy paternally inherited \*\*\* | Benign/likely benign | Likely Bening | PM1,BS1,BP1,BP4,BP6 | Hypertrophic cardiomyopathy, Dilated Cardiomyopathy, Recessive, Familial restrictive cardiomyopathy, Primary ciliary dyskinesia | - | - |
| 6 years | *DNAAF3* | p.Trp44Leu | c.131G>T | AR | Homozygous | One copy paternally inherited \*\*\* | Benign | likely benign | PM1,BS1,BP1,BP6 | Primary ciliary dyskinesia | - | - |
|  | *COL5A2* | p.Arg956Pro | c.2867G>C | CH | Heterozygous | Paternal | Benign | Likely benign | PM1,BS1,BP6 | Ehler Danlos Syndrome, cardiovascular phenotype | Unknown | [10] |
|  | *SMYD4* | p.Tyr295Cys | c.884A>G | AR | Homozygous | One copy paternally inherited \*\*\* | None | US | PM1 | none | - | - |
| Cardio-36.A | TOF | None |  | F | Sudan | *IFT172* | p.Val1204Leu | c.3610G>C | CH | heterozygous | Maternal | Benign /likely benign | US | BP6 | Retinitis pigmentosa 71,Short-rib thoracic dysplasia 10 with or without polydactyly | Unknown | [11] |
| 5 months | *IFT172* | p.Arg1134Leu | c.3401G>T | CH | Heterozygous | Paternal | Benign/likely benign | Likely benign | BS1,BP6 | Retinitis pigmentosa 71,Short-rib thoracic dysplasia 10 with or without polydactyly | Unknown | [11] |
|  | *SLC24A4* | p.Gln22His | c.66A>T | CH | Heterozygous | Paternal | None | US | PM1,PM2 | none | - | - |
|  | *ATP10D* | p.Arg266His | c.797G>A | AD | Heterozygous | Maternal(brother is also carrier) | None | US | PM1,PM3 | none | - | - |
|  | *CDH20* | p.Gln371Arg | c.1112A>G | AR | homozygous | Both parents | None | US | PM1,BS1 | none | - | - |
|  | *PLEC* | p.Ala1545Val | c.4634C>T | CH | Heterozygous | Maternal | Benign | US | PM1,PM2 | Limb-girdle muscular dystrophy, type 2Q.Epidermolysis bullosa simplex with muscular dystrophy | Unknown | [12] |
| Cardio-38.A | Poly Valvular disease, Mitral valve prolapse | None | 11 years | M | Qatar | *LRRC56* | p.Pro305His | c.914C>A | Could not be identified | Heterozygous | Not reported \* | None | US | - | none | - | - |
| cardio-40.A | Tricuspid Atresia, restrictive VSD,Large PDA | None | 5 months | F | India | *DNAH9* | p.Arg1517Gln | c.4550G>A | CH | Heterozygous | Maternal | None | US | PM1 | Crisponi/CISS1-like and Bohring-Opitz like syndrome | Turkish | [13] |
| *SAAL1* | p.Pro95Leu | c.284C>T | CH | Heterozygous | Paternal | None | US | PM1 | none | - | - |
| Cardio-41.A | Fontan,Right isomerism,Interrupted IVC, mitral atresis, DORV,Large VSD, severe PS | None | 16 years | F | Yemen | *DYNC2H1* | p.Leu592Phe | c.1774C>T | AD | Heterozygous | Maternal | Uncertain significant | US | PM2,PP3 | Intellectual disability, Jeune thoracic dystrophy, Short-rib thoracic dysplasia 3 with or without polydactyly | Unknown | [14] |
| Cardio-42.A | TOF | None | 6 months | M | Kuwait | *DNAH5* | p.Asn1420Asp | c.4258A>G | CH | Heterozygous | Paternal | VUS | US | PM1,PM2 | Primary ciliary dyskinesia | Unknown | [15] |
| Cardio-47.A | TGA | None | 15 days | M | Egypt | *INPP5F* | p.Leu131Met | c.391C>A | CH | Heterozygous | Paternal | None | US | PM1,PM2 | None | - | - |
| Cardio-48.A | HLH | None |  | F | Pakistan | *SHROOM3* | p.Gln1623Lys | c.4867C>A | AR | Homozygous | Both parents | None | US | PM1 | None | - | - |
|  | *SCN10A* | p.Ser470Tyr | c.1409C>A | CH | Heterozygous | Maternal | None | US | BP4, BP1, BS1, PP3 | None | - | - |
| 20 days | *PDE4DIP* | p.Gly1542Arg | c.4624G>A | CH | Heterozygous | Paternal | Likely benign | US | PM2 | None | - | - |
| Cardio-49.A | DILV, TGA | None |  | F | Pakistan | *NUP210* | p.Pro1742Arg | c.5225C>G | CH | Heterozygous | Maternal | None | US | PM2 | None | - | - |
| 22 days | *COL6A2* | p.Arg784His | c.2351G>A | CH | Heterozygous | Maternal | Benign /likely benign | US | PM1,PM2,BP6 | None | - | - |
| Cardio-50.A | TOF | None | 4 months | M | India | *GLA* | p.Asp313Tyr | c.937G>T | UPD | Homozygous | Maternal | Conflicting interpretations of pathogenicity | US | BP6, PP3 | Hypertrophic cardiomyopathy, Fabry disease, Angiokeratoma corporis diffusum,sudden unexplained death, cardiac variant | Unknown | [16] |
| Cardio-53.A | COA | None | 3 months | M | Morocco | *KARS* | p.Glu120Gln | c.358G>C | CH | Heterozygous | Maternal | None | US | PM1,PM2 | None | - | - |
|  | *PLEC* | p.Gln2111His | c.6333G>C | CH | Heterozygous | Maternal | None | US | PM1,PM2,PP3 | none | - | - |
|  | *ANKS6* | p.Pro736Ala | c.2206C>G | CH | Heterozygous | Maternal | None | US | PM1,PM2,PP3,BP6 | None | - | - |

-Abbreviations:

TOF: tetralogy of Fallot, CHD: congenital cardiac defects.: HLH: hypoplastic left heart syndrome, ASD: atrial septal defect, ATSL arterial tortuosity syndrome, VSD: ventricular septal defect, PDA: patent ductus arteriousus,TAPVD: total anomalous pulmonary venous defect,DORV: double outlet right ventricle,TGA: transposition of great artery,DILV: double inlet left ventricle,COA: cortication of aorta F: female, M: Male, XLR: X-linked recessive, CH: compound heterozygous , AD: Autosomal dominant, AR: autosomal recessive,US: uncertain significance, UPD: uniparental disomy.

-ACMG/AMP sub-classification:

PM1: Located in a mutational hot spot and/or critical and well-established functional domain (e.g. active site of an enzyme) without benign variation

PM2: Absent from controls (or at extremely low frequency if recessive in Exome Sequencing Project, 1000 Genomes or ExAC

PM5: Novel missense change at an amino acid residue where a different missense change determined to be pathogenic has been seen before

BS1: Allele frequency is greater than expected for disorder

BP1: Missense variant in a gene for which primarily truncating variants are known to cause disease

BP4: Multiple lines of computational evidence suggest no impact on gene or gene product (conservation, evolutionary, splicing impact, etc)

BP6: Reputable source recently reports variant as benign but the evidence is not available to the laboratory to perform an independent evaluation

PVS1: Null variant (nonsense, frameshift, canonical +/−1 or 2 splice sites, initiation codon, single or multi-exon deletion) in a gene where loss of function (LOF)  
is a known mechanism of disease

PS2: De novo (both maternity and paternity confirmed) in a patient with the disease and no family history

PP2: Missense variant in a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease

PP3: Multiple lines of computational evidence support a deleterious effect on the gene or gene product (conservation, evolutionary, splicing impact, etc)

PP5: Reputable source recently reports variant as pathogenic but the evidence is not available to the laboratory to perform an independent evaluation

\*: number of enrolled family member is not enough to identify the source of the variant.

\*\*: father was not enrolled, could not identify the source of the other variant copy.

\*\*\*: Mother was not enrolled, could not identify the source of the other variant copy.

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