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PATIENT REPORT

Patient Age/Sex: Female

Specimen Collected: 09-Feb-26 11:02

Beta Globin (HBB) Deletion/Duplication **|Received: 09-Feb-26 11:04** **Report/Verified: 09-Feb-26 11:05**

Procedure	Result	Units	Reference Interval
Beta Globin (HBB) Del/Dup Specimen	Whole Blood		
Beta Globin (HBB) Del/Dup Interp	See Note [f1 i1]		

Result Footnote

f1: Beta Globin (HBB) Del/Dup Interp

RESULT
One pathogenic variant was detected in the beta-globin gene cluster.

DNA VARIANT
Classification: Pathogenic
Gene: HBB
Nucleic Acid Change: HBB full-gene deletion; Heterozygous
Commonly Known As: Filipino deletion
Variant Phenotype: Beta(0) Thalassemia (absence of beta-chain synthesis)

INTERPRETATION
One copy of a pathogenic deletion of the HBB gene was detected by deletion/duplication analysis of the beta- globin gene cluster and its locus control region. This result is consistent with beta-thalassemia trait. Individuals heterozygous for this deletion are predicted to have microcytic, hypochromic anemia and elevated levels of Hb F. The clinical presentation may vary due to other genetic modifiers or coexisting conditions. A more severe disorder is possible if a second HBB pathogenic variant is present on the opposite chromosome that is not detected by this assay.

Evidence for variant classification: The Filipino deletion is a common pathogenic deletion found among individuals from the Phillipines, Malaysia, and Indonesia, particularly in individuals with beta-thalassemia trait or beta-thalassemia major (Eng, 1993; Thong, 1999; HbVar ID: 989). In the heterozygous state, it is associated with beta-thalassemia trait (Eng, 1993), but in the homozygous state or in trans to a pathogenic HBB variant, this deletion has been observed in numerous individuals with beta-thalassemia major (Eng, 1993; Thong, 1999; HbVar database). This deletion removes the entire HBB coding sequence and extends downstream into a cluster of olfactory receptor genes, though it does not delete the HBD gene upstream of HBB (Waye, 1994; Van Ziffle, 2011). Based on available information, the Filipino deletion is considered to be pathogenic.

RECOMMENDATIONS
Medical management should rely on clinical findings and family history. Carrier screening should be offered to this individual's reproductive partner. Family members should be offered testing for the identified pathogenic variant (Beta Globin (HBB) Deletion/Duplication by MLPA, ARUP test code 3019786). Genetic consultation is recommended.

COMMENTS
Reference sequences for beta-globin gene cluster: GenBank # NG_000007.3

REFERENCES
Link to HbVar database: https://globin.bx.psu.edu/hbvar/menu.html

Eng B, et al. Identification of two novel beta zero-thalassemia mutations in a Filipino family: frameshift codon 67 (-TG) and a beta-globin gene deletion. Hum Mutat. 1993;2(5):375-9. PMID: 8257991.

Waye JS, et al. Filipino beta-thalassemia due to a large deletion: identification of the deletion

Result Footnote

f1: Beta Globin (HBB) Del/Dup Interp

endpoints and polymerase chain reaction (PCR)-based diagnosis. Hum Genet. 1994 Nov;94(5):530-2. PMID: 7959690.

Thong MK, et al. A single, large deletion accounts for all the beta-globin gene mutations in twenty families from Sabah (North Borneo), Malaysia. Mutation in brief no. 240. Online. Hum Mutat. 1999;13(5):413. PMID: 10338100.

Van Ziffle J, et al. Homozygous deletion of six olfactory receptor genes in a subset of individuals with Beta- thalassemia. PLoS One. 2011 Feb 24;6(2):e17327. PMID: 21390308.

This result has been reviewed and approved by [redacted]

Test Information

i1: Beta Globin (HBB) Del/Dup Interp

BACKGROUND INFORMATION: Beta Globin (HBB)
Deletion/Duplication

CHARACTERISTICS: Beta thalassemia is caused by decreased or absent synthesis of the hemoglobin beta-chain resulting in variable clinical presentations ranging from mild anemia to transfusion dependence. Hereditary persistence of fetal hemoglobin (HPFH) is a clinically benign condition caused by variants within the beta globin gene cluster that alter normal hemoglobin switching and result in persistent fetal hemoglobin (Hb F) production.

INCIDENCE: Varies by ethnicity.

INHERITANCE: Usually autosomal recessive, infrequently autosomal dominant.

CAUSE: Pathogenic variants within the HBB gene or variants involving the beta globin gene cluster and its regulatory elements.

CLINICAL SENSITIVITY: Varies by ethnicity.

METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the beta globin gene cluster (HBB, HBD, HBG1, HBG2, HBE1) and its locus control region.

ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.

LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. HBB single base pair substitutions, small deletions/duplications, deep intronic and promoter variants will not be detected. Breakpoints of large deletions/duplications will not be determined; therefore, the precise clinical phenotype associated with a particular deletion (e.g., HPFH vs. delta-beta thalassemia) may not be known. Single exon deletion/duplications may not be detected based on the breakpoints of the rearrangement. Intragenic deletions in the beta globin cluster genes, other than HBB, may not be detected. This assay does not assess for sequence variants within the coding or regulatory regions of HBB, HBD, HBG1, HBG2 or HBE1. Apparent copy

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number changes detected solely in the HBG1-HBG2 region will not be reported as they can result from benign sequence variants or gene conversion events. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Certain gene therapies may impact the performance of this test and interpretation of this result; the presence or absence of variants, zygosity, and HBB gene copy number may not be determined in such cases.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.