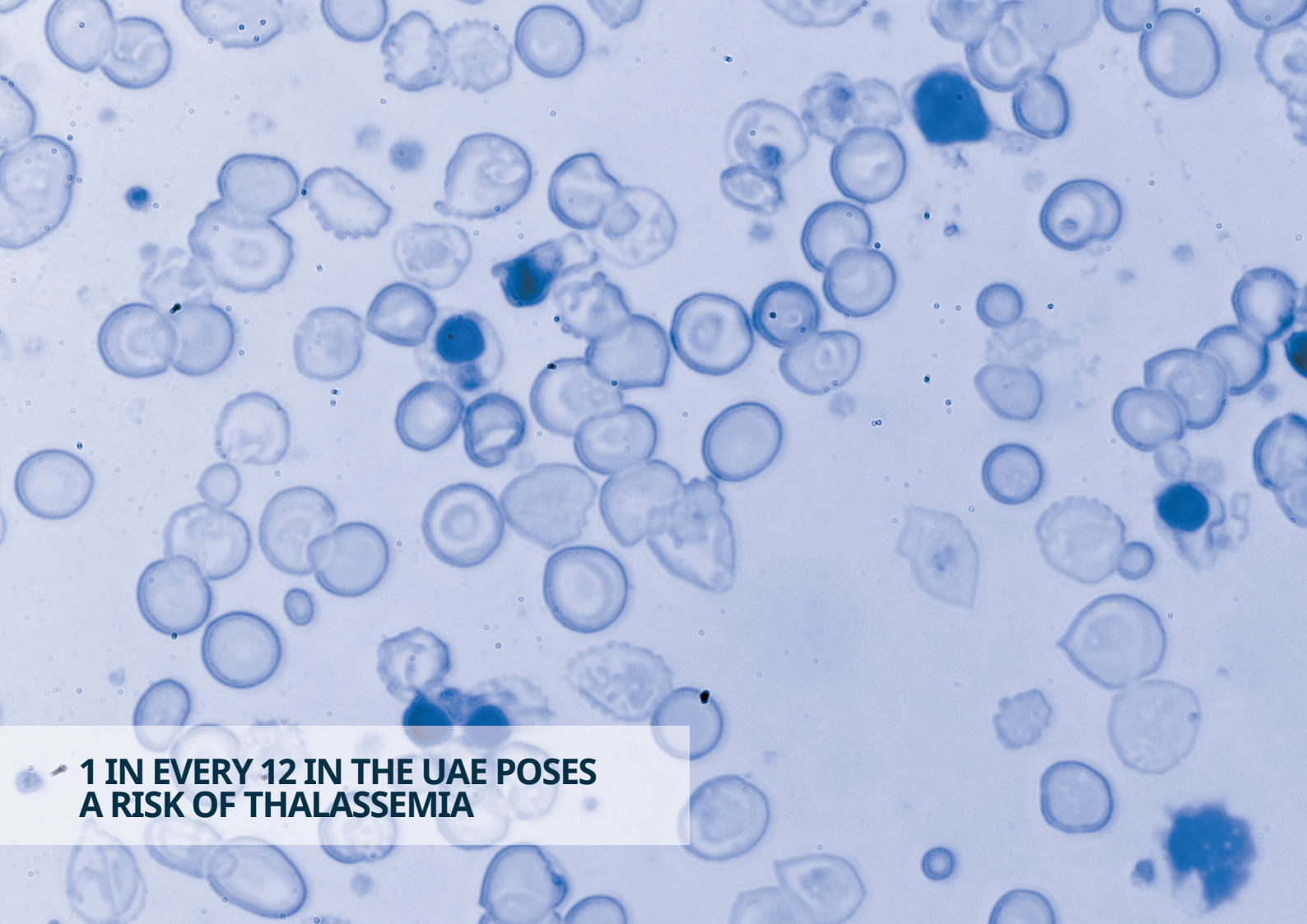
المختبر المرجعي الوطني
National Reference Laboratory
A Mubadala Health Partner

TOGETHER, LET'S MAKE A DIFFERENCE

Alpha-thalassemia affects many lives.
Change begins with one step.



1 IN EVERY 12 IN THE UAE POSES A RISK OF THALASSEMIA

TOGETHER, LET'S ALERT THEM.

Many families in the region are unaware of the fact that alpha-thalassemia has no prevalent symptoms during the initial stages. The ideal way to stay safe is to get tested. We believe that together we can join forces and provide the people of our region, the best of both worlds – expertise and technology. Let's begin with spreading the word.

Alpha-Thalassemia in brief

Alpha-thalassemia is one of the most common blood disorders worldwide. Highly prevalent in South East Asia, Africa and the Mediterranean region, alpha-thalassemia cases can also be found in different countries due to migration [1].

HBA1 and HBA2 Genes Decoded

In healthy adults, hemoglobin is comprised mainly of hemoglobin A (Hb A), which consists of two α - globin and two β-globin polypeptide chains.

The α-polypeptide chains are typically encoded by two copies of each HBA1 and HBA2 genes for giving a total of four functioning α-globin genes (α,α/α,α).

HBA1 and HBA2 adjacent genes are normally located on each of the two copies of chromosome 16. Pathogenic variants in these genes cause a decrease in the production of α-globin chains relative to β-globin chains, thus causing alpha-thalassemia [2].

Approximately 90% of α-globin gene loss is due to deletions and around 10% of cases is due to non-deletion sequence variants. The table ahead summarizes the various types of alpha-thalassemia and their associated genotypes & clinical characteristics [2, 3].

1. Harteveld, C. L. and Higgs, D. R. 2010. α-thalassemia. Orphanet J Rare Dis. 5:13
2. Galanello R. & Cao A. 2011. Alpha-Thalassemia. Genetics in Medicine. 13:83–88
3. Origa R. and Moi P. 2016. Alpha-Thalassemia. Gene Reviews https://www.ncbi.nlm.nih.gov/books/NBK1435/

THERE'S MORE TO THALASSEMIA THAN THEY KNOW.

TOGETHER, LET'S SIMPLIFY THEIR LIFE.

Hearing about alpha-thalassemia is one thing and knowing about it in detail is another. We believe that together we can encourage people to know about alpha-thalassemia and the effect it can have in their lives.

Types of alpha-thalassemia and their Associated Genotypes and Clinical Characteristics

α-thalassemia type	Genotype	Clinical features
α-thalassemia silent carrier	-,α/α,α	• Typically, asymptomatic • May have normal or slightly reduced hematological indices like α-thalassemia trait • Normal HbA2 and HbF
α-thalassemia trait	-,-/α,α or -,α/-,α	• May have borderline anemia, but commonly asymptomatic • Microcytosis and hypochromia is typically present, with slightly reduced hematological parameters such as MCV and MCH • Normal HbA2 and HbF

α-thalassemia type	Genotype	Clinical features
Hemoglobin H (HbH) disease	-,-/-,a	• Disease severity varies greatly from mild to severe • Onset of disease ranges from first year of life to adulthood • Microcytic hypochromic hemolytic anemia • Splenomegaly and mild jaundice • Thalassemia causes bone changes in some cases • Some patients are blood transfusion dependent • Some patients may suffer from acute episodes of hemolysis in response to oxidant drugs and infections • Some older patients may have iron overload
Hemoglobin Bart, hydrops fetalis syndrome	-,-/-,-	Most severe lethal type with fetal onset of: • Generalized edema • Pleural and pericardial effusions • Severe hypochromic anemia • Significant hepatosplenomegaly • Some of the maternal complications may include preeclampsia, polyhydramnios, and premature delivery • Most affected fetuses will be delivered as stillborn or die shortly after birth some rare cases will survive after intrauterine, and frequent afterbirth transfusions


KIDS INHERIT MANY THINGS FROM THEIR PARENTS.
LET IT NOT BE THALASSEMIA CAUSING GENES.

TOGETHER, LET'S PROTECT THEM.

With the provision of reliable, timely and informative services, we endeavour to change the dynamics of alpha-thalassemia in the region. Together, we can safeguard our people, ensuring a healthy life.

Normally everyone inherits two α-globin genes from each parent. When both parents are carriers of alpha-thalassemia, they will be at risk of having children with either alpha-thalassemia trait, HbH disease or Hb Bart syndrome, depending on the number of missing/non-functional
α-globin genes which are inherited [3].

There are eight common deletions that take out either one α-globin gene (α3.7 & α4.2), two α-globin genes (--SEA, --MED, --FIL, and --THAI), and those that remove one α-globin gene and only part of the other gene (-(α)5.2, -(α)20.5). These common deletions account for about 85% of all α-globin gene pathogenic alterations [3-5].

Less frequently, alpha-thalassemia is caused by non-deletion sequence variants. These variants include single nucleotide variants, causing nonsense, missense, or splice site mutations, in addition to smaller insertions or deletions in critical regions of the α-globin gene.

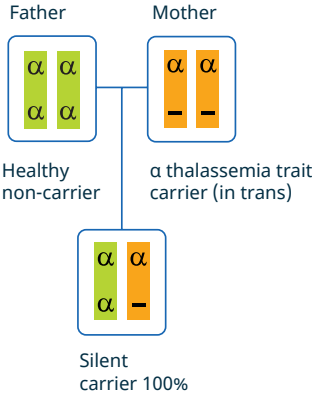
The most common non-deletion variant, which is frequently reported in South East Asia, is Hb Constant Spring (HbCS). This variant is caused by a mutation in the stop codon of HBA2 gene. Alpha-thalassemia disease caused by non-deletion variants is usually more severe than types caused by deletions [1, 3].

1 Harteveld, C. L. and Higgs, D. R. 2010. α-thalassaemia. Orphanet J Rare Dis. 5:13.
3 Origa R. and Moi P. 2016. Alpha-Thalassemia. Gene Reviews. https://www.ncbi.nlm.nih.gov/books/NBK1435/
4 Harteveld C. L. 2014. State of the art and new developments in molecular diagnostics for hemoglobinopathies in multiethnic societies. Int. Jnl. Lab. Hem. 36: 1–12
5 Higgs D. R. 2013. The Molecular Basis of α –Thalassemia. Cold Spring Harb Perspect Med. 3:a011718

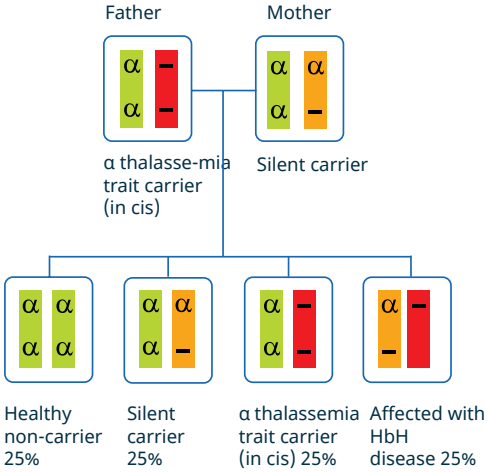
THERE ARE MANY WAYS TO BE AFFECTED. AWARENESS IS THE KEY TO MOVING FORWARD.

Inheritance patterns for alpha-thalassemia

(A) One partner is alpha-thalassemia trait carrier (in trans) and the other is a healthy non-carrier



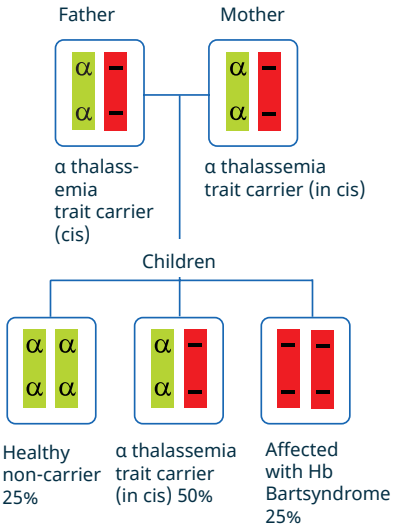
(B) One partner is a silent carrier and the other is alpha-thalassemia trait carrier (in cis)



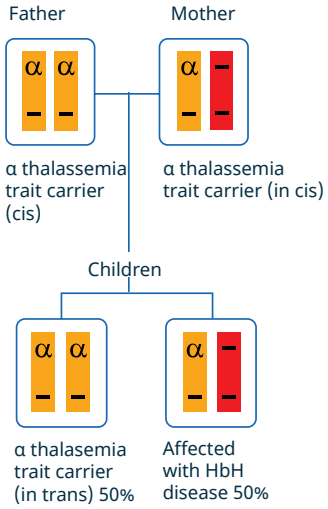
TOGETHER, LET'S RAISE AWARENESS

We aspire to conduct more campaigns across the region to spread the word about thalassemia. Your support will help us move closer to our goals and nurse the nation back to health.

(C) Both partners are alpha-thalassemia trait carriers (in cis)



(D) One partner is alpha-thalassemia trait carrier (in trans) and the other is affected with HbH disease.




HISTORY CAN AFFECT THE FUTURE.
WHY NOT ACT IN THE PRESENT?

TOGETHER, LET'S SECURE THEIR HEALTH – TODAY AND TOMORROW.

At NRL, we care for our people's future and hence, we take the onus of securing them today by inspiring them to take up the test for Thalassemia. We would be glad to have you by our side and make our society a healthier place to live in.

Indications for testing

- Healthy individuals with a family history of the disease or for those of South East Asian, Mediterranean, Middle Eastern, and African descent.
- Individuals with microcytosis, decreased hemoglobin with undetected iron deficiency.
- To confirm a diagnosis of alpha-thalassemia disease in patients with HbH disease or Hb Bart, hydrop fetalis syndrome.

TESTING FOR ALPHA-THALASSEMIA. TRUSTED RESULTS.

TOGETHER, LET'S DO IT.

Being the largest CAP accredited referral laboratory network in the Middle East, we have the latest technology in place and an automated lab that meets the international standards of quality.

Sample type	Volume/concentration	Container	Transport temperature
Peripheral blood	Adults & older children: 5-10 ml Infants (<2yrs): 2-3 ml Children (>2yrs):3-5 ml	EDTA (purple top) tube OR ACD (yellow top) tube.	Room temperature*
DNA	5µg of purified DNA, with a concentration of at least 100ng/µl.	Screw cap tube OR Eppendorf (safe lock)	Room temperature*

* Store blood samples at room temperature or refrigerate at 4oC until the time of shipment. Do not freeze the blood samples. In case of hot weather, use an insulated container with ice packs and make sure to place a thin material like a paper towel between the sample and the ice packs to prevent freezing.

METHODOLOGY – HOW DO WE DO IT

Deletion/Duplication analysis of the α-globin locus is performed by Multiplex Ligation-Dependent Probe Amplification (MLPA) assay.

The assay will detect, in principle, all genomic deletions and duplications involving aforementioned locus within the boundaries of the region which is interrogated by the assay.

It will also detect Constant Spring point mutation. Any partial exonic deletions and duplications outside of the region of interest cannot be detected.

The analysis does not detect other point mutations within α-globin locus. The presence of a rare mutation cannot be entirely ruled out [4].

4- Harteveld C. L. 2014. State of the art and new developments in molecular diagnostics for hemoglobinopathies in multiethnic societies. Int. Jnl. Lab. Hem. 36: 1–12

TOGETHER, LET'S BRING THE CHANGE.

ABU DHABI

National Reference Laboratory,
Corporate Headquarters,
Block-A, Ground Floor SH-2,
ICAD 1, P.O. Box 92323
Abu Dhabi, UAE.

DUBAI

National Reference Laboratory,
Dubai Science Park Laboratory Complex,
Um Suqeim Road, Al Barsha South 2,
Ground Floor, Lab Number 0013,
P.O. Box 2087, Dubai, UAE.

+971 800-NRL (675) | customercare@nrl.ae | www.nrl.ae

المختبر المرجعي الوطني

National Reference Laboratory

A Mubadala Health Partner

+971 800-NRL (675) | customercare@nrl.ae | www.nrl.ae