living well with thalassaemia

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IS IT TRUE THAT THE DIAGNOSIS OF THALASSAEMIA IS THE SAME FOR EVERYONE?

FALSE. The thalassaemia syndromes are all very different from each other both for the type of genetic defect present in the red blood cells and, above all, for the clinical manifestations and the severity of the different forms!

The thalassaemia syndromes are a group of inherited genetic diseases that are transmitted by parents to their children through their genes. These diseases are not transmitted through blood, air or water, or through physical or sexual contact. In the thalassaemia syndromes, the normal production of haemoglobin is either partly or completely suppressed because of a defect in the synthesis of one or more of the globin chains that represent the components of haemoglobin.

There are different globin chains: alpha, beta, gamma or delta.

Sometimes, the defect involves more than one chain at the same time, as in the case of the delta or beta-thalassaemias.

Beta-thalassaemias. The beta-thalassaemias are determined by alterations in the gene for the beta chain. The following cases can be observed:

- alterations of both gene copies (both maternal and paternal), with an almost complete absence of the beta chain in thalassaemia major or Cooley's disease. This leads to cases of severe anaemia due to the early destruction of the red blood cells in the bone marrow. If this anaemia goes untreated, skeletal changes take place because the bone marrow, where the red blood cells are produced, increases in volume to try and compensate for the loss. The red blood cells that are produced are poor in haemoglobin and are quickly destroyed causing also spleen size to increase (splenomegaly). If it is not treated, thalassaemia major can lead to death before the patient reaches 20 years of age;

- minor and/or silent mutations of the gene of the beta globin chains in a homozygote or double heterozygous state, result in thalassaemia intermedia, the less severe form of the thalassaemias, that presents in an extremely wide variety of ways. Typical symptoms are anaemia, increased spleen size and biliary stones;

- the alteration of one copy of the gene (heterozygotes) of the beta globin chains leads to beta-thalassaemia minor that does not usually cause any symptoms or at least very mild symptoms (mild microcytic anaemia). People with this type of alteration are usually healthy carriers of the disease.

Alpha-thalassaemias. The alpha-thalassaemias are hereditary disorders characterised by reduced or suppressed production of the alpha globin chains. There are four human alpha globin genes. These are found in the following forms:

- the alterations of all four genes for the alpha globin chains leads to the serious condition of foetal hydrops. This is often lethal for the foetus or for the newborn infant immediately after birth.

However, immediate standard blood transfusions will allow the newborn child who survives to have a disease course through life similar to that of patients with beta-thalassaemia;

- in the so-called haemoglobin H disease, there is an alteration is due in three genes for the alpha globin chains and a microcytic anaemia is observed (low haemoglobin levels and small red blood cells) often associated with an enlarged spleen (splenomegaly). The disease usually presents during childhood or early adulthood;

- also in the case of alpha-thalassaemia, a mutation involving only one gene or only two of the four alpha genes results in thalassaemia minor (respectively of type 2 or type 1), the so-called "silent" forms, without any symptoms at all.

When the diagnosis of a mild form becomes important: the case of delta thalassaemia.

From haematological point of view, the delta thalassaemia is an innocuous condition since it involves the A2 haemoglobin (containing of delta chains), that represents 2-3 % of the adult normal haemoglobin. Diagnosing the delta thalassaemia is however very important, because this can mask the diagnosis of the healthy carrier of beta-thalassaemia. In this condition there is an increase of the Hb A2. However, if together with beta thalassaemia there is also a mutation resulting from the presence of a delta thalassaemia, the value of Hb A2 will be reduced to normal levels, making the diagnosis of beta-thalassemia difficult. This is important for the genetic counseling because a child, born to parents who are both carriers of beta thalassemia, has one out of four possibility of inheriting the thalassaemia major, but if the HbA2 is normal that risk will not be recognised.