

# Pain and bone disease: a patient's view

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## Abstract

Pain in thalassemia proves to be an emergent issue even if it is not possible to correlate it definitely to bone disease, but we strongly believe that a multidisciplinary approach, may be as decisive in this case as it was in the struggle against thalassemia. In fact, we strongly believe that the involvement of various specialists such as endocrinologists, orthopedist, anesthesiologist, in a close team coordinated by a specialist in thalassemia is absolutely necessary for achieving our aims. First of all, we need to implement clinical trials to identify the mechanisms of disease, to find the optimal management of the problem in order to provide new therapeutic methods for preventing the thalassemia-induced osteoporosis and to reduce the presence of very disabling pain for patients. Patients' expectations for the future are to continuously improve the quality of life. To do that it is needed to identify pathways to prevent all the complications of thalassemia that cause widespread pain, above all osteoporosis. Although we have seen that osteoporosis is not the sole cause of pain for thalassemia patients, it is true that this seems to have a great incidence in thalassemia patients and it gives a significant contribute to an increased pain.

## Introduction

This work aims to present a patient's view on a subject very sensitive for the thalassemia patients: the pain and the bone disease. For the purpose we summarized the results reported from several interesting works published over the last years. Maybe it could be considered a little bit technical but we believe it's important that the patients have an idea of the large incidence of this problem.

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Key words: pain, bone disease.

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Thalassemia Reports 2011; 1(s2):e24  
doi:10.4081/thal.2011.s2.e24

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*Parts of this work were presented at the "12th International Conference on Thalassemia and Hemoglobinopathies", Antalya (Turkey), 11-14 May 2011.*

Of course it's astonishing for us to discuss this issue because since few years ago it would be considered out of any imagination to speak about osteoporosis, a problem usually correlated to the old age of human being, for patients affected from thalassaemia.

The improvement in life expectancy of Thalassemia patients thanks to developments in diagnostic and therapeutic approaches achieved in the last twenty years has shifted the focus on monitoring and on management of complications.

The main complication for patient's survival expectations is the iron overload on the liver and on heart due to blood transfusion treatment, it has been investigated for years. This led to a significant improvement in both quality of life and life expectancy for patients.

Today we can rely on several therapeutic solutions able to prevent heart's failure, the main cause of death for thalassemia patients, or to face the arise heart's disease in order to avoid worst problems.

We can also delay for a long time the liver complications and fight the endocrine problems.

We cannot say that everything is fine yet, but the advances made are undoubtedly very significant.

This is true, unfortunately, only for thalassemia living in most developed countries where the health system is more developed.

A lot of undeveloped countries, actually, are sustaining big efforts in order to reach acceptable standards of treatment for their patients. In the last decade some countries have significantly improved in their treating to thalassemia. Even though the optimum is not achieved yet.

To maintain acceptable levels of quality of life, when it is not possible to improve it, it becomes necessary to draw attention to those complications which, although not a matter of life and death, have strong social consequences for patients and do not allow to them to carry out a normal social life.

Amongst the secondary complications of thalassemia is osteoporosis, a complication related to a deficiency in the balance of bone turnover.

Adult thalassemia patients report with increasing frequency the presence of pain and complain, in some cases, the presence of fractures due to osteoporosis.

This issue, actually, reflects a problem reported also from the general population, in fact the incidence of pain in the whole population is in a range within 38% - 45%, so it is difficult for physicians to define a differential diagnosis between a thalassemia patient and a non-thalassemia one.

However, recent studies, greatly demanded by the patients, seem to confirm that the presence of pain should be considered as an emergent issue even in thalassemia.

A study on quality of life achieved at the Thalassemia Centre in Genoa, Italy, in 2001 revealed that a large number of patients suffered from a widespread pain mainly concentrated in the back.

According to this study, approximately 40% of patients with Thalassemia Major and 15% with Thalassemia Intermedia reported a constant back pain and a widespread state of malaise due to the presence of pain.

As reported the percentage of patients that suffered from back pain was perfectly within the range above mentioned. Therefore, the ques-

tion is how much the presence of thalassemia affects the presence of pain.

Indeed, the conclusions reported that the state of malaise due to the presence of a widespread pain was the main factor of the scarce perception the patients had on an acceptable level of quality of life.

According to more recent studies this percentage, among thalassemia population, rises significantly; up to 69% would be affected by rather strong pain and at least 28% report a pain of moderate in intensity. It's needed to underline this numbers: 97% of the patients report pain, this is a big problem that require specific attention.

The pain increases in intensity and frequency with increasing the age of the patients especially for the over 35. Pain in children has been investigated too, with no significance results.

Therefore, It seems that the age is one of the most important factors for evaluating the incidence of pain in thalassemia because with increasing the age of patients the percentage rises up to 97%, much more than in general population. Probably, the presence of a chronic disease, such as thalassemia, is crucial to an increased presence of pain among the patients in comparison with the normal population.

This issue is especially important, because it could hamper normal daily activity; in fact the pain severely limits mobility and functionality of the affected, it compromises the performance of work and it has also serious repercussions on the psychological sphere for people trying to go over the difficulties imposed by their condition.

The conclusion of this stud, carried out in USA by the Thalassemia Clinical Research Network, is that over 50% of patients report a high degree of interference with work and about 25% a level slightly more moderate. Here, we have to consider once more the numbers: 75% of patients report that pain has a relevant incidence on our lives.

Furthermore, according to another study, some patients, seem to suffer, as a percentage higher than the control group, from the early degeneration of the lumbar discs. This is another possible cause of strong and widespread pain with severely impaired mobility which can lead to a surgical treatment.

It's obvious that these factors have also negative effects from an economic point of view because of the amount of working days lost.

The back seems to be the place where the pain is more aggressive, 24%, followed by the knees, 15%, and head / neck, 10%, fewer patients complained of pain in other locations. No pain is attributable to previous trauma.

The available therapeutic responses are not always adequate, for different reasons but mainly due to the fact that the therapies usually administered are simply anti-inflammatory ones, sporadic, and in any case, too bland and not very effective to control the pain adequately.

It must also be said that the therapeutic approaches adopted from thalassemia centers for facing this kind of pain were often very conservative because the administration of more specific drugs for a better control of the pain was strongly advised against not to compromise the liver function, already the target organ of iron overload.

We have also to keep in mind that the pain was not associated before to the thalassemia such as for sickle cell, so the conservative approach adopted to the pain had some good explanation.

So many questions are requiring a prompt answer: Is it clear if the presence of the pain is strictly correlated to the presence of osteoporosis? Could the osteoporosis in a chronic disease with hormone deficiencies contribute to an increased presence of pain?

There have been many speculations about it but no definite answer has been identified yet.

It seems that there are no close correlations with the level of Hb, nor with a lack of vitamin D or with hormone deficiencies or other typical aspects of thalassemia but the pain described, as already mentioned, it is very debilitating, especially for older patients.

Even if it is not clear whether the presence of the pain is strictly cor-

related to the presence of osteoporosis, undoubtedly, the osteoporosis in a chronic disease with hormone deficiencies can contribute to an increased presence of pain.

It must be said that there is a marginal effect due to the use of chelating agents, for direct experience of patients, it appears that the Deferioxamine is more easily associated with the presence of pain than Deferasirox, which allows a reduction of pain perception with increasing dose of administration. Furthermore 3% of patients that are under treatment with Deferiprone suffer from arthropathies.

However, the scientific community is always sensitive to the continuous demands of patients who require to focus on the treatment of complications, so in the hope of giving a response to the pain syndrome that accompanies the condition of osteoporosis.

Several clinical trials have been activated in order to verify if some families of drugs, already used to treat osteoporosis-affected non-thalassemia patients, can give a positive response and to ensure the containment of the problem also in thalassemia.

More recent knowledge seems to indicate that containing osteoporosis could also help to reduce the presence of pain or, better, to give a lower perception of it.

Today the use of bisphosphonates, the most widely used family of drugs, proves to be only partially effective, this is a personal patient's view, probably because of subjective response to treatment. A couple of studies were recently published, which seem to show a good efficacy of both zoledronic acid, even if this it has been done on a small sample of patients and requires confirmation, and neridronate.

However, it's essential to further investigate the problem because these therapies are effective if administered regularly, over long time but they do not seem able to give a timely response to pain that causes the worsening in quality of life.

However, according to another study, always conducted in Genoa in 2009, the use of these drugs acted to improve the situation. Indeed, preliminary results seem to indicate a reduction in the presence of pain and a general improvement in patients' perception of their health status.

Obviously, this difference in perception cannot be exclusively related to the introduction of therapies to fight osteoporosis, but even thanks to the availability of new drugs useful for general treatment of thalassemia that undoubtedly contribute to improving the physical and psychological condition of patients. Furthermore, the more accurate controls of complications reflects positively on the life-style of patients and this factor is decisive for assuring them a better perception of their general health.

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