Reviewer's report

Title: Metabolic and Endocrinologic complications in Beta-thalassemia major: A Multicenter Study in Tehran

Authors:

Dr Alireza A Shamshirsaz (alirezashamshirsaz@yahoo.com)
Mir R Bekheirnia (rezabkh@hotmail.com)
Mohammad Kamgar (m_kamgar@yahoo.com)
Dr Nima Pourzahedgilani (nimapg@yahoo.com)
Navid Bouzari (nbouzari@yahoo.com)
Mohammad R Habibzadeh (mrezahabibzadeh@yahoo.com)
Seyed R Hashemi (r_hashemi@hotmail.com)
Amir H Shamshirsaz (shamshir_a1978@yahoo.com)
Shahriar S Aghakhani (agakhani@parsonline.net)
Dr Hooman H Homayoun (emrc@sina.tums.ac.ir)
Dr Bagher B Larijani (emrc@sina.tums.ac.ir)

Version: 1 Date: 1 Jul 2003

Reviewer: Anne Yardumian

Level of interest: not specified

Advice on publication: Other (see below)

Firstly, in answer to the specific questions posed:

1) although the question posed by the authors in not new, in that very similar studies have been undertaken in other groups of thalassaemia patients, I am not aware of a similar study being reported in a group of Iranian patients. There is likely to be variation between complication rates in patients managed in different countries, there being possible genetic and dietary differences between different population groups which might contribute. As well as being of importance to the ongoing management of patients in Tehran, therefore, difference highlighted might help lead to better understanding of causation. I think the study is therefore valid and interesting; and as always one has the greatest respect for doctors managing such large patient populations, and what they can teach us. In the UK we manage about 800 patients with major thalassaemia syndromes, minuscule compared to the 20,000 in Iran!

2) the methods are appropriate and reasonably well described, I have some suggestions about the methods section under the detailed, page-referenced comments below.

3) The data seem sound, no control was included as this is an observational study about prevalence of certain complications in a cohort of patients. I am uncertain about the selection of patients to include - it is stated they were 'randomly selected' but with no indication how that was done.

4) Relevant standards for reporting are met.

5) The discussion / conclusion sections are adequate, with a few minor comments detailed below.

6) The title is appropriate, the abstract does not include all the factors measured and reported on, I
have listed those which I think should be included.

7) there are a couple of places (mentioned below) where I did not quite understand what was being said, as the phrasing is not quite correct, these just need clarifying.

Overall I think this is an interesting and worthwhile study which deserves to be published, but in my opinion a few amendments should first be made, as noted below.

Specific comments / questions are as follows:
(I have starred * those that I think really must be noted / amended)

a. Abstract, last sentence of 'Background' - ...to determine the prevalence of prominent thalassaemia complications and their relationship.. - relationship to what? To each other? To extent of iron loading?

b. From the 'Methods' section of the abstract, some things are missing eg that you took menstrual history, undertook clinical examination including height and weight measurement and pubertal status, also that you measured glucose levels.

c. * page 4, main paper, Background, line 3 - globin, not globulin, chains.

d. From immediately after ref [4], until the end of the next para, ending ref [9] - I think all this section really belongs in the discussion, not at this point.

e. end of that section - I'd suggest omitting ... 'in a period of life when disturbance ...later in life'. It doesn't really add anything, I feel.

f. * start of methods section - in what way were the patients 'randomly' selected? This is important as many seemingly random methods do bias the group selected.

g. * 5th line same section - the diagnosis was based on peripheral blood evaluation and Hb electrophoresis - from sample taken when? Of course not at entry to study as, if truly thalassaemia major, just about all the peripheral blood would be donor, transfused blood so would not give useful results.

h. You need to include in the methods section what you did, in the order 'history, clinical examination, laboratory tests' otherwise it does not read smoothly. Could this be re-ordered?

i. Reference ranges should not be included in the methods, but in the results section, so your patients results can be compared to reference range. Likewise the definition of osteopenia, and hypogonadism etc - my preference would be for all this to go to results section.

j. * You have defined hypogonadism, and primary and secondary amenorrhoea, but not the term 'impaired puberty' which you use at start of Results and Discussion sections. Also - as half your patients were under 15 years of age at the time of study - it would not be possible to assess puberty properly in many, and 'hypogonadism' as defined only in the few which were 16 or over. Do these
%'s therefore relate to a relevant sub-group?

k. bottom of p9, 16% of patients had family history of type I diabetes - was that 16% of all patients or just of those who themselves had diabetes?

l. regarding thyroid function, calcium levels etc - it would be interesting and useful to note if / how frequently you monitor for these as a matter of routine when following up these patients?

m. I'd exclude the Thyroid function test results at top of p10 - presume these are on treatment?

n. Discussion - line 4 - 'Three of [how many] postmenarchal patients...

o. You note higher rates of 'impaired puberty' but lower rates of hypogonadism in your study compared to some others. Isn't the first a precursor of the second, but many of your study group had not yet reached the age for formal diagnosis of hypogonadism?

p. the sentence before ref [16] I do not understand what you imply by saying ' considering our study was not longitudinal'.

q. p 13 , a couple of expressions which I found hard to understand and could possibly be reworded.... 2nd para, 'Short stature which may be a remarkable finding to predict our patients' growth status' and start of next para 'High endocrine abnormalities...'

r. towards end of p 14 - re possible high prevalence of deficiency of zinc and copper in Iranian general population - are there any references about this, or is it just surmising?

**Competing interests:**

None declared.