



Universiteit  
Leiden  
The Netherlands

## **$\beta$ -Thalassemia intermedia: morbidity uncovered**

Musallam, K.M.S.; Taher, A.T.

### **Citation**

Musallam, K. M. S., & Taher, A. T. (2012, June 21).  *$\beta$ -Thalassemia intermedia: morbidity uncovered*. Retrieved from <https://hdl.handle.net/1887/19124>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/19124>

**Note:** To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/19124> holds various files of this Leiden University dissertation.

**Author:** Musallam, Khaled Mousa Saleh and Taher, Ali Taher

**Title:**  $\beta$ -Thalassemia intermedia : morbidity uncovered

**Issue Date:** 2012-06-21

*“The knowledge of anything, since all things have causes, is not acquired or complete unless it is known by its causes.”*

**Ibn Seena (Avicenna)**



# **$\beta$ -Thalassemia Intermedia**

## ***Morbidity Uncovered***

**Khaled M. Musallam**

**&**

**Ali T. Taher**



**-Thalassemia Intermedia**  
*Morbidity Uncovered*

**Proefschrift**

ter verkrijging van  
de graad van Doctor aan de Universiteit Leiden,  
op gezag van Rector Magnificus prof.mr. P.F. van der Heijden,  
volgens besluit van het College voor Promoties  
te verdedigen op vrijdag 21 juni 2012

te klokke 13.45 uur

door

**Khaled Mousa Saleh Musallam**

geboren te Amman, Jordanië in 1982

en te klokke 15.00 uur

door

**Ali Taher Taher**

geboren te Tyre, Libanon in 1960

## **PROMOTIECOMMISSIE**

**Promotor:** Prof. Dr. F.R. Rosendaal

**Copromotor:** Dr. F. Peyvandi  
(Universiteit van Milaan)

**Overige leden:** Prof. Dr. H.R. Büller  
(Universiteit van Amsterdam)  
Prof. Dr. W.E. Fibbe  
Prof. Dr. P.H. Reitsma  
Dr. P. Giordano

The work described in this thesis was performed at the Department of Internal Medicine of the American University of Beirut Medical Center in Beirut, Lebanon (Khaled M. Musallam and Ali T. Taher) and the Department of Medicine and Medical Specialties, IRCCS Ca' Granda Foundation Maggiore Policlinico Hospital, Milan, Italy (Khaled M. Musallam).

Part of the work described in this thesis was funded through unrestricted educational grants from Novartis Pharmaceuticals.

## CONTENTS

<b>Chapter 1</b>	<b>INTRODUCTION</b>	<b>13</b>
<b>Chapter 2</b>	<b>INEFFECTIVE ERYTHROPOIESIS</b>	<b>25</b>
	Levels Of Growth Differentiation Factor-15 Are High And Correlate With Clinical Severity In Transfusion- independent Patients With Thalassaemia Intermedia <i>Blood Cells, Molecules &amp; Diseases 2011;47:232-234</i>	<b>27</b>
	Fetal Hemoglobin Levels And Morbidity In Untransfused Patients With $\alpha$ -thalassaemia Intermedia <i>Blood 2012;119:364-367</i>	<b>33</b>
<b>Chapter 3</b>	<b>IRON OVERLOAD</b>	<b>41</b>
	Levels Of Non-transferrin-bound Iron As An Index Of Iron Overload In Patients With Thalassaemia Intermedia <i>British Journal of Haematology 2009;146:569-572</i>	<b>43</b>
	Elevated Liver Iron Concentration Is A Marker Of Increased Morbidity In Patients With Thalassaemia Intermedia <i>Haematologica 2011;96:1605-1612</i>	<b>49</b>

	Magnetic Resonance Evaluation Of Hepatic And Myocardial Iron Deposition In Transfusion-independent Thalassemia Intermedia Compared To Regularly Transfused Thalassemia Major Patients <i>American Journal of Hematology 2010;85:288-290</i>	<b>63</b>
	Absence Of Cardiac Siderosis Despite Hepatic Iron Overload In Italian Patients With Thalassemia Intermedia: An MRI T2* Study <i>Annals of Hematology 2010;89:585-589</i>	<b>69</b>
	Glomerular Hyperfiltration And Proteinuria In Transfusion-independent Patients With -thalassemia Intermedia	<b>77</b>
<b>Chapter 4</b>	<b>VASCULAR DISEASE</b>	<b>107</b>
	Splenectomy And Thrombosis: The Case Of Thalassemia Intermedia <i>Journal of Thrombosis &amp; Haemostasis 2010;8:2152-2158</i>	<b>109</b>
	Risk Factors For Pulmonary Hypertension In Patients With Thalassemia Intermedia <i>European Journal of Internal Medicine 2011;22:607-610</i>	<b>119</b>

	Asymptomatic Brain Magnetic Resonance Imaging Abnormalities In Splenectomized Adults With Thalassemia Intermedia <i>Journal of Thrombosis &amp; Haemostasis 2010;8:54-59</i>	<b>125</b>
	Brain Magnetic Resonance Angiography In Splenectomized Adults With $\alpha$ -thalassemia Intermedia <i>European Journal of Haematology 2011;87:539-546</i>	<b>133</b>
	Brain Positron Emission Tomography In Splenectomized Adults With $\alpha$ -thalassemia Intermedia: Uncovering Yet Another Covert Abnormality <i>Annals of Hematology 2012;91:235-241</i>	<b>143</b>
<b>Chapter 5</b>	<b>HEALTH-RELATED QUALITY OF LIFE</b>	<b>153</b>
	Health-related Quality Of Life In Adults With Transfusion-independent Thalassaemia Intermedia Compared To Regularly Transfused Thalassaemia Major: New Insights <i>European Journal of Haematology 2011;87:73-79</i>	<b>155</b>
<b>Chapter 6</b>	<b>MANAGEMENT</b>	<b>165</b>
	Age-related Complications In Treatment-naïve Patients With Thalassaemia Intermedia <i>British Journal of Haematology 2010;150:486-489</i>	<b>167</b>

Overview On Practices In Thalassemia Intermedia Management Aiming For Lowering Complication Rates Across A Region Of Endemicity: The OPTIMAL CARE Study <i>Blood 2010;115:1886-1892</i>	<b>173</b>
Optimal Management Of Thalassaemia Intermedia <i>British Journal of Haematology 2011;152:512-523</i>	<b>183</b>
<b>Summary / Samenvatting</b>	<b>197</b>
<b>Acknowledgments</b>	<b>211</b>
<b>Curriculum Vitae</b>	<b>215</b>