HEMOGLOBIN
INTERNATIONAL JOURNAL FOR HEMOGLOBIN RESEARCH

Taylor & Francis
Taylor & Francis Group

Hemoglobin
international journal for hemoglobin research

ISSN: 0363-0269 (Print) 1532-432X (Online) Journal homepage: http://www.tandfonline.com/loi/ihem20

# First Report of a Coincidental Discovery of Hb Shimonoseki [α54(E3)Gln→Arg, *HBA2*: c.164A > G (or *HBA1*)] in a Greek Family

**Stamatia Theodoridou, Evangelia Delaki, Evangelia Skatharoudi, Olga Karakasidou, Timoleon-Achilleas Vyzantiadis, Theodoros Theodoridis & Panagiota Chalkia**

**To cite this article:** Stamatia Theodoridou, Evangelia Delaki, Evangelia Skatharoudi, Olga Karakasidou, Timoleon-Achilleas Vyzantiadis, Theodoros Theodoridis & Panagiota Chalkia (2018) First Report of a Coincidental Discovery of Hb Shimonoseki [α54(E3)Gln→Arg, *HBA2*: c.164A>G (or *HBA1*)] in a Greek Family, Hemoglobin, 42:4, 281-282, DOI: 10.1080/03630269.2018.1513368

**To link to this article:** https://doi.org/10.1080/03630269.2018.1513368

Published online: 17 Jan 2019.

HEMOGLOBIN
2018, VOL. 42, NO. 4, 281–282
https://doi.org/10.1080/03630269.2018.1513368

Taylor & Francis
Taylor & Francis Group

SHORT COMMUNICATION



# First Report of a Coincidental Discovery of Hb Shimonoseki [α54(E3)Gln→Arg, *HBA2*: c.164A > G (or *HBA1*)] in a Greek Family

Stamatia Theodoridou[a], Evangelia Delaki[b], Evangelia Skatharoudi[a], Olga Karakasidou[a], Timoleon-Achilleas Vyzantiadis[c], Theodoros Theodoridis[d] and Panagiota Chalkia[a]

[a]Haemoglobinopathy Prevention Unit, Hippokration Hospital of Thessaloniki, Thessaloniki, Greece; [b]Thalassaemia National Centre of Greece, Laikon General Hospital of Athens, Athens, Greece; [c]First Department of Microbiology, Medical School, Aristotelion University of Thessaloniki, Thessaloniki, Greece; [d]First Department of Obstetrics and Gynaecology, Aristotelion University of Thessaloniki, Thessaloniki, Greece

**ABSTRACT**

The rare Hb Shimonoseki [α54(E3)Gln→Arg, *HBA2*: c.164A > G (or *HBA1*)] has been reported in Western Japan. Hb Shimonoseki seems to be an innocuous variant and few published data are available. Heterozygous carriers have no clinical or hematological findings. The abnormal hemoglobin (Hb) was detected by high performance liquid chromatography (HPLC) and classic electrophoresis or capillary electrophoresis (CE), but confirmation of the variant is based on molecular studies. This is the first description of Hb Shimonoseki heterozygosity in a Greek family.

**ARTICLE HISTORY**
Received 7 July 2018
Revised 5 August 2018
Accepted 6 August 2018

**KEYWORDS**
Genetic counseling; Hb Shimonoseki; pre pregnancy counseling; pregnancy; thalassemia

Hb Shimonoseki [α54(E3)Gln→Arg, *HBA2*: c.164A>G (or *HBA1*)] was first described by Yamoaka *et al.* [1, 2] in Western Japan. No clinical or hematological abnormalities are associated with the presence of Hb Shimonoseki. The oxygen equilibrium function of this variant is the same as Hb A, and the oxygen affinity and Bohr effect of the variant are normal [3].

Hb Shimonoseki seems to be an innocuous variant and few published data are available [4]. We report the first cases of heterozygous carriers of Hb Shimonoseki in three family members coming from a small town in the region of Macedonia, Northern Greece.

A 32-year-old woman was referred for pre conception screening for hemoglobinopathies with her husband, as their ethnic and regional backgrounds were at high risk for thalassemia. Carrier identification is carried out at all Thalassaemia Prevention Units in Greece following a standard scheme that includes the tests mentioned below.

The hematological data of the young woman were as follows: hemoglobin (Hb) level of 13.2 g/dL, red blood cell (RBC) count of $4.35 \times 10^{12}$/L, mean cell volume (MCV) 90.4 fL, mean cell Hb (MCH) 30.3 pg; high performance liquid chromatography (HPLC) analysis showed a Hb $A_2$ level of 2.7%, Hb F of 1.0% and Hb S window 23.0% (Figure 1), with negative sickle test and inclusion bodies, while her ferritin level was 55.0 ng/mL. The blood film was normal. Classic electrophoresis at acid and alkaline pH showed electrophoretic properties of Hb D (Figure 2) and capillary electrophoresis (CE) showed an abnormal variant of 21.0% in zone 5 (Figure 3).

As her husband came from the same region, he was also screened and his blood test showed an Hb level of 15.4 g/dL, RBC count of $5.07 \times 10^{12}$/L, MCV 92.5 fL, MCH 30.4 pg; HPLC analysis showed a Hb $A_2$ level of 3.3% and Hb F of 2.0% with negative sickle test and inclusion bodies, while his ferritin level was 20.0 ng/mL. His blood film was normal. Family screening as well as molecular study (direct sequencing) of the variant was performed for identification and further genetic counseling. Surprisingly, we were faced with a coincidental discovery of this rare heterozygosity for Hb

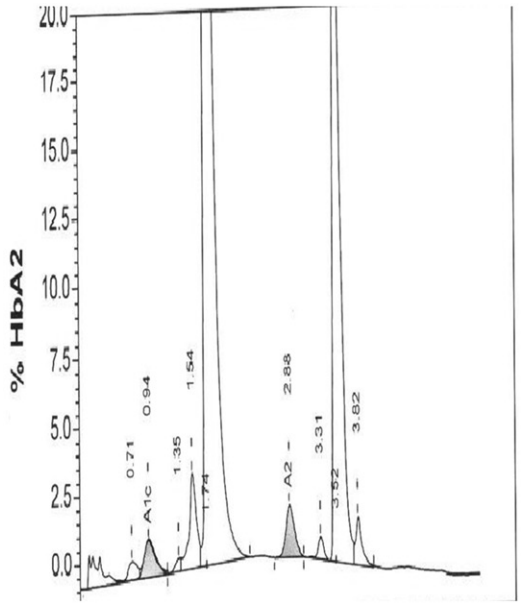
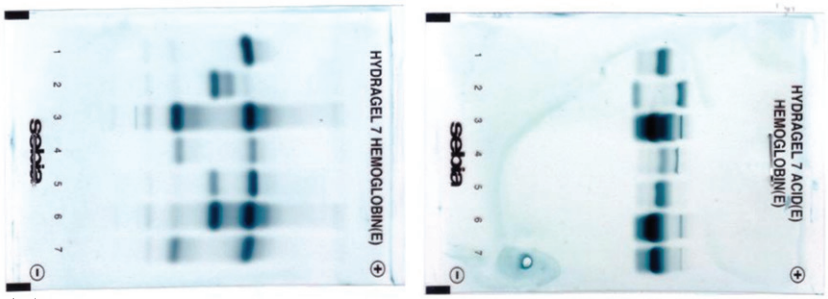



**Figure 1.** High performance liquid chromatography (VARIANT II™ analysis; Bio-Rad Laboratories).

**CONTACT** Stamatia Theodoridou hmesogiaki@ippokratio.gr Haemoglobinopathy Prevention Unit, Hippokration Hospital of Thessaloniki, Konstantinoupoleos 48, 54649 Thessaloniki, Greece.




1. A
2. S/F
3.A/O
4.AO
5. AX= Hemoglobin Shimonoseki
6. AD
7 AE

**Figure 2.** Classic electrophoresis at acid and alkaline pH.

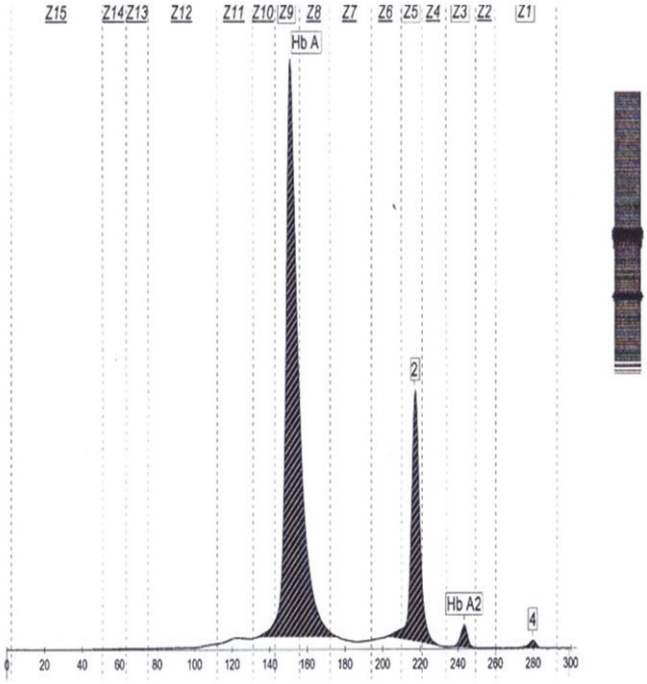



**Figure 3.** Capillary electrophoresis (Sebia).

Shimonoseki (*HBA2*: c.164A>G), that to the best of our knowledge, has never been reported before in Greece. Subsequently, in order to further investigate the inheritance pattern, study of the proband's family showed the same variant in her sister and her mother (Table 1). No further genetic analysis was performed on her husband as they were not at risk of having a thalassemic offspring.

As has already been reported [5], several Hb variants may behave like Hb S (*HBB*: c.20A>T) in analytical systems, and a combination of methods is needed to recognize Hb S with certainty and thus avoid a false positive diagnosis of sickle cell trait or disease. DNA sequencing documents different variants of Hb, many of them with no clinical significance, since most individuals who carry these variants in a heterozygous state have completely normal hematological findings [6]. In Greece, a country of approximately 11 million people, hemoglobinopathies are the most frequent genetic diseases [7]. The spectrum of thalassemia determinants in Greece is variable, the relative incidence being approximately 5.0–10.0%. This is the first description of Hb Shimonoseki heterozygosity in a Greek family.

**Table 1.** Hematological and molecular findings in the studied family members.

| Parameters | Proband | Father | Mother | Sister |
|---|---|---|---|---|
| Sex-age (years) | F-32 | M-64 | F-56 | M-34 |
| RBC ($10^{12}$/L) | 4.35 | 4.87 | 4.59 | 3.83 |
| Hb (g/dL) | 13.2 | 14.9 | 14.1 | 12.4 |
| MCV (fL) | 90.4 | 90.4 | 90.7 | 96.7 |
| MCH (pg) | 30.3 | 30.7 | 30.6 | 32.5 |
| Hb $A_2$ (%) | 1.9 | 3 | 1.9 | 2.7 |
| Hb X (S window) (%) | 23 | 0 | 22.5 | 23.3 |
| CE zone 5 (%) | 21.6 | 0 | 21 | 22 |
| α Genotype | $\alpha^{\text{codon 54(A>G)}}/\alpha^{A}$ | $\alpha^{A}/\alpha^{A}$ | $\alpha^{\text{codon 54(A>G)}}/\alpha^{A}$ | $\alpha^{\text{codon 54(A>G)}}/\alpha^{A}$ |

RBC: red blood cell count; Hb: hemoglobin; MCV: mean corpuscular volume; MCH: mean corpuscular Hb.

## Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

## References

[1] Yamaoka K, Kawamura K, Hanada M, *et al.* Studies of abnormal hemoglobins. Jap J Hum Genet 1960;5:99–111.
[2] Hanada M, Rucknagel DL. The characterization of Hemoglobin Shimonoseki. Blood 1964;24(5):624–635.
[3] Imai K, Morimoto H, Kotani M, *et al.* Studies on the function of abnormal hemoglobins. II. Oxyzen equilibrium of abnormal hemoglobins: Shimonoseki, Ube II, Hikari, Gifu and Agenogi. Biochim Biophys Acta 1970;200(2):197–202.
[4] Bain B, Wild B, Stephens A, *et al.* Variant Haemoglobins. A Guide to Identification. Oxford (Oxfordshire, UK): Wiley Blackwell, 2010.
[5] Moradkhani K, Riou J, Wajcman H. Pitfalls in the genetic diagnosis of Hb S. Clin Biochem 2013;46(4-5):291–299.
[6] Wajcman H, Moradkhani K. Abnormal haemoglobins: detection & characterization. Indian J Med Res 2011;134:538–546.
[7] Loutradi-Anagnostou A. Prevention of thalassemia in Greece: 25 year experience. Presented at The 8th International Conference on Thalassaemia and Haemoglobinopathies, October 18-21 2001, Athens, Greece. Athens (Greece): Abstract Book 16–18.