# Prevalence of hemoglobin disorder based on Hb A1c capillary electrophoresis assay: experience from a laboratory in France

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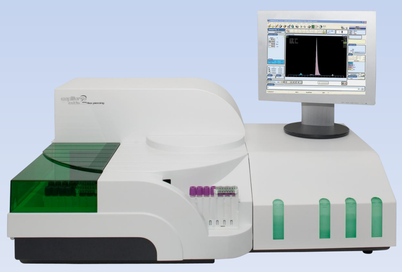
## Background

Hemoglobinopathies are now common worldwide due to migration. At least 5.2% of the world population carry an hemoglobin (Hb) variant and around 1.1% of couples are at risk for having children with an hemoglobin disorder[1]. Thus, genetic counseling for these couples is essential. In France, there is no systematic screening and all laboratories do not routinely realize hemoglobin studies. We evaluated the possibility to use Hb A1c measurement by capillary electrophoresis (CE), much used in routine, to incidentally discover hemoglobinopathies and calculated their prevalence in our recruitment area.



A CAPILLARYS 2
Flex Piercing instrument
(Sebia, France)

## Material & Methods

Prevalence study: A retrospective study was carried out over an 8-day period. A total of 3,233 patient samples were received for diabetes screening and follow-up. All samples were analyzed by CE on the CAPILLAYS 2 Flex Piercing (Sebia, France), with the "HbA1c" kit. Profiles showing Hb variants, Beta-thalassemia (Hb A2 > 3%) or elevated Hb F (> 2%) were counted up.

Sensitivity study: A prospective study was performed over an 3-day period. All patient samples presenting an Hb variant (n=75) (as identified previously by CE on the CAPILLAYS 2 Flex Piercing (Sebia, France), with the "HbA1c" kit) were analyzed by CE on the CAPILLAYS 2 Flex Piercing (Sebia, France) with the "Hemoglobin(e)" kit, in order to confirm the presence of the Hb variants.

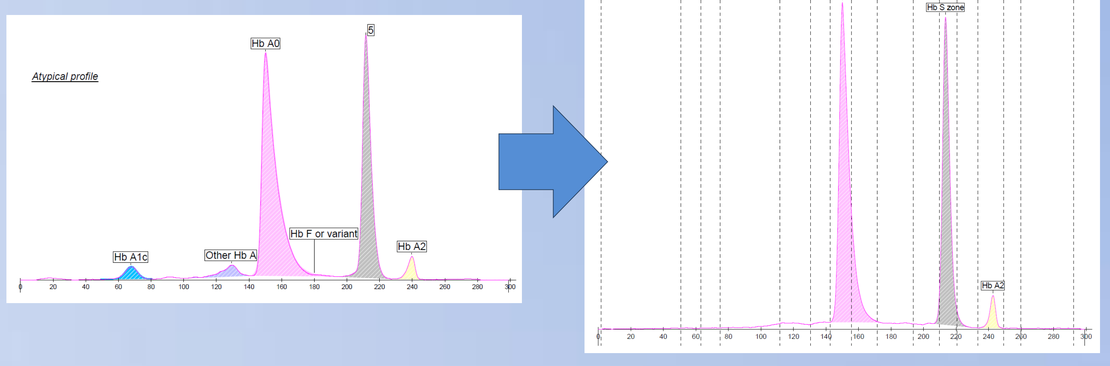



**Figure 1:** HbA1c (left) and Hb (right) capillary electrophoresis profiles on CAPILLARYS 2 Flex Piercing.
*Same patient sample, presenting an Hb S.*

## Conclusion

**The detection of undiagnosed hemoglobinopathies during Hb A1c capillary electrophoresis assay is not rare. Beyond the Hb A1c measurement, around 10-20 cases of hemoglobin disorders are found per day in our laboratory, representing a prevalence of 3.74% in the population studied.**

**These incidental observations avoid us to report misleading Hb A1c results for such patients as their RBC lifespan can be decreased[2]. Furthermore, HbA1c capillary electrophoresis can be used as a massive screening test. All hemoglobin disorders should be reported to the clinicians and must lead to further investigations (e.g. Hb testing by CE) and genetic counseling for the individuals.**

1. Modell B. and Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bulletin of the World Health Organization. http://www.who.int/bulletin/volumes/86/6/06-036673/en/
2. Ji L, Yu J, Zhou Y, *et al*. Erroneous HbA1c measurements in the presence of β-thalassemia and common Chinese hemoglobin variants. Clin Chem Lab Med. 2015 Jan 13.

## Results

Prevalence study:

Our 57 collecting centers are located in 6 departments around Paris and cover more than 500 km$^2$ and 988.000 inhabitants. This region is prone to an multiethnic mixing. We use capillary electrophoresis for Hb and Hb A1c, both assays allowing to highlight hemoglobin abnormalities in clear-cut and precise profiles **(Figure 1)**.

Regarding the amount of tests in our laboratory, HbA1c CE assay represents 98% whereas Hb CE assay only 2%. As there is no systematic screening for hemoglobinopathies in France, HbA1c CE assay appears to be a good option to screen the population. A total of 121 hemoglobinopathies were found among the 3,233 patients samples analyzed: prevalence can be considered equal to 3.74%, which is compatible with ones previously calculated for European population[1].

Among these hemoglobinopathies, 23 Beta-thalassemias were found, 87 Beta variants, 7 Delta variants and 3 Alpha variants and one hemoglobinopathy leading to an Hb F increase **(Figure 2)**. These hemoglobin disorders have a prevalence of 0.71%, 2.69%, 0.22%, 0.09% and 0.03%, respectively, in the population studied.

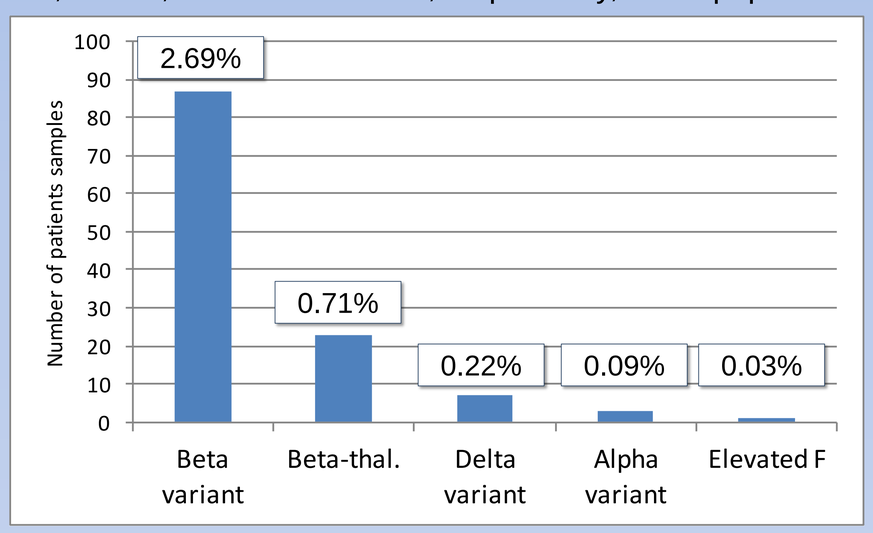



**Figure 2:** Number of patients samples presenting an hemoglobinopathy and discovered during HbA1c CE analysis.
*In square: prevalence of the condition related to the population studied (n=3,233)*

Among the Beta variants, Hb S-like variants are the most common of the discovered Beta variants (64.4%, with 2 homozygous cases). Interestingly, no Hb D-like were found **(Figure 3)**.

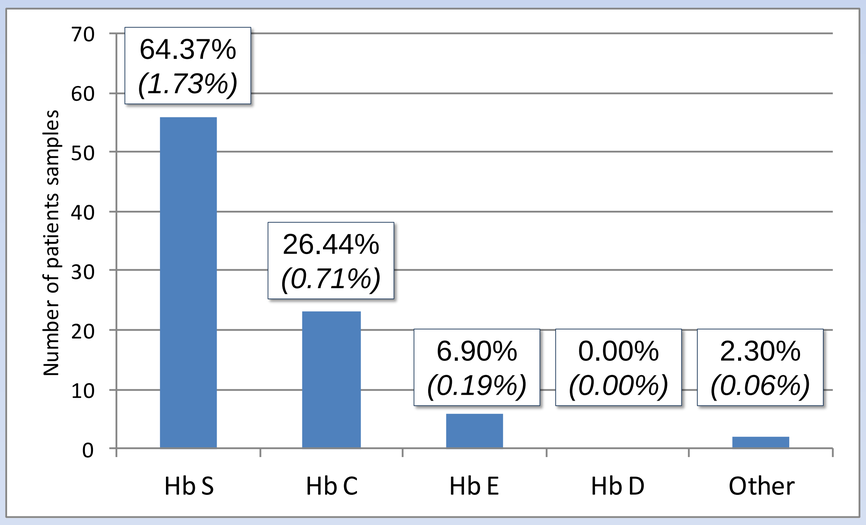



**Figure 3:** Number of patients samples presenting a Beta variant and discovered during HbA1c CE analysis.
*In square: prevalence of the condition related to the total of Beta variants found (n=87) and to the population studied (into bracket).*

Sensitivity study:

Patients samples containing Hb variants detected during the HbA1c CE technique were analyzed by Hb CE technique. Presence of abnormalities was confirmed in all the samples processed (without discrepancy with the initial findings), indicating that the HbA1c CE technique has 100% sensitivity and is suitable for hemoglobinopathies screening.