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Sidra Asad Ali

Natasha Ali  
*Aga Khan University*

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# A Rare Haemoglobin Variant Identified as K Woolwich in a Pakistani Male

Sidra Asad Ali and Natasha Ali

## ABSTRACT

Haemoglobin (Hb) K Woolwich is a rare Hb variant which was first described in a family from West Indies and its occurrence was later reported mainly in Black families from many African countries. We report a case of a young male who came for evaluation of anemia. His complete blood count showed hypochromic, microcytic anemia and his serum ferritin was low. Hb electrophoresis done as part of initial workup showed an abnormal band which moved faster than HbA. For further evaluation, Hb analysis by high performance liquid chromatography was subsequently performed and revealed Hb K Woolwich. This is a rare Hb variant recognized in Pakistani population for the first time through careful interpretation of the chromatographic behavior of the Hb.

**Key Words:** Haemoglobin K Woolwich. High performance liquid chromatography. Haemoglobin electrophoresis.

## INTRODUCTION

The inherited disorders of Haemoglobin (Hb) are the most common single gene disorders with approximately 7% of the world's population being carriers.<sup>1</sup> Hb variants are abnormal Hbs that in most cases are produced as a result of single point mutation of the amino acid sequence. Over 1100 of these mutant Hbs have been described according to database of human Hb variants and more than 800 of them involve beta chain.<sup>2</sup>

Hb K Woolwich is a result of substitution of lysine by glutamine in beta chain ( $\beta$ 132 Lys-Gln) at codon 132. It was first described by Cabannes and Buhr as fast variant of normal adult Hb.<sup>3</sup> The family in which this Hb K was first observed came from West Indies and was of African ancestry. It was noted at Woolwich, England and hence named as Hb K Woolwich.<sup>4</sup> Subsequently reports from Nigeria, Ghana and Ivory Coast were described.<sup>4-6</sup>

## CASE REPORT

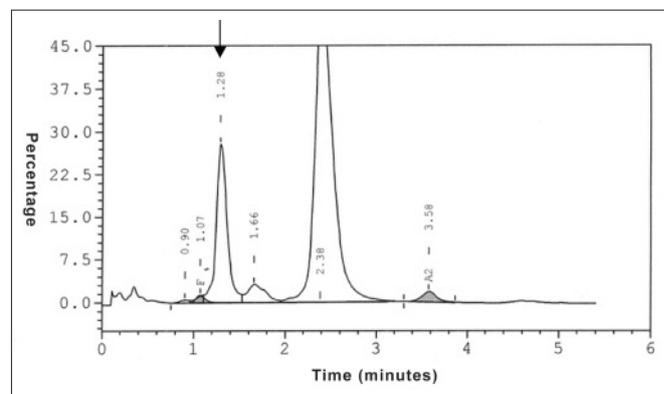
We present a case of 32-year old male who came to haematology clinic for evaluation of anemia. He had complains of weakness, epigastric pain and easy fatigability for past 3 months. His personal history was significant for beetle nut chewing while past history and family history was otherwise unremarkable. Examination revealed pallor only. Complete blood count showed haemoglobin 6.1 g/l, Mean Corpuscular Volume (MCV) 57.7 fl Mean Corpuscular Haemoglobin (MCH) 16.4 pg,

white blood cell count,  $9.1 \times 10^9/l$  and platelets  $325 \times 10^9/l$ . Peripheral smear showed hypochromic, microcytic erythrocytes and pencil cells while thrombocytes and white blood cells were normal on film. Considering the peripheral film findings, his serum ferritin was done and it was 3.1 ng/ml.

Hb gel electrophoresis done as a part of initial workup of anemia showed an abnormal band moving faster than HbA and was reported as Hb H performed outside our institution and was not confirmed on High Performance Liquid Chromatography (HPLC).

Hence for further evaluation, we performed Hb analysis by HPLC on BIORAD VARIANT II and a peak at P2 region with retention time of 1.28 minutes was identified which comprised 22.1% of total Hb (Figure 1). The findings were suggestive of Hb K Woolwich. However, amino acid sequencing and nucleic acid sequencing could not be performed due to non-availability of these tests at our setup.

HPLC of his father was subsequently performed and it also showed peak at same region with retention time of



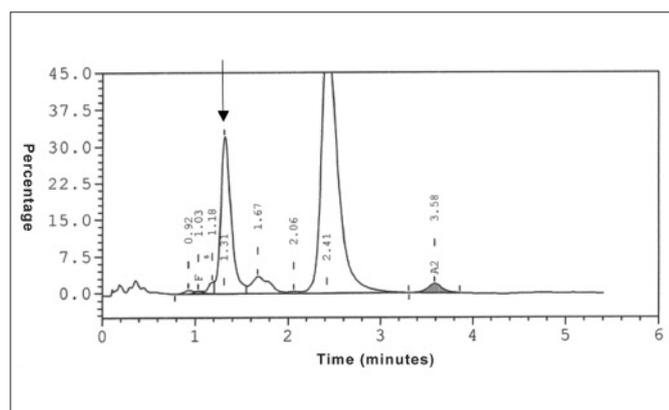
**Figure 1:** Haemoglobin analysis of patient by HPLC showing a peak at retention time of 1.28 minutes (indicated by arrow) which comprised 22.1% of total haemoglobin and was identified as Hb K Woolwich.

Department of Pathology and Laboratory Medicine, The Aga Khan University, Karachi.

Correspondence: Dr. Natasha Ali, Assistant Professor, Section of Hematology, Department of Pathology and Laboratory Medicine/Oncology, The Aga Khan University, Stadium Road, Karachi-74800.

E-mail: natasha.ali@aku.edu

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**Figure 2:** Haemoglobin analysis of patient's father by HPLC showing a peak at same region with retention time of 1.31 minutes (indicated by arrow) comprising 24.8% of total haemoglobin.

1.31 minutes comprising 24.8% of total Hb (Figure 2). Quality Control (QC) of HPLC is maintained through LJ chart by running daily controls and calibrators which are provided by the vendor. The patient was started on Tab. Ferrous Sulphate 200 mg twice a day to which he responded and his Hb improved 10.7 g/dl.

## DISCUSSION

Hb K Woolwich is a stable beta chain variant which occurs in people of the Akan group in West Africa and it is predominant in the Attie subgroup. In 1974, Lang *et al.* suggested that the  $\beta$ -K Woolwich gene behaved as a  $\beta^+$ -thalassaemia gene, on the basis of results from a family of elevated levels of HbA<sub>2</sub> in heterozygotes and the reduced synthesis rate of the  $\beta^{KW}$  chains in relation to the  $\beta^A$  chains in one case.<sup>7</sup> However, later Cabannes *et al.* described a family with 6 heterozygotes and single homozygote who had no clinical and haematological abnormality.<sup>6</sup> This subject remains controversial and no other study of globin chain synthesis was reported till 1986 when Zago *et al.* presented haematological characterization of a Brazilian Negro family with 6 Hb K Woolwich heterozygotes, and the measurement of the rate of globin chain synthesis as well which proved to be normal and their results demonstrated that there was no globin chain synthesis imbalance.<sup>8</sup>

It is a silent abnormality with no clinical manifestation and is found in combination with Hb S<sup>9</sup>, Hb C<sup>10</sup>, alpha-, and beta<sup>+</sup>-thalassaemia. The expression of Hb K Woolwich with other beta chain variants also does not produce any symptoms in an affected individual.

The use of Hb electrophoresis by conventional gel technique may falsely label fast moving Hbs as Hb H and miss the diagnosis leading to underreporting of rare Hb variants as was the case in our patient.

Literature review has revealed that studies or case reports from this part of the world have not been reported yet and the prevalence of Hb K Woolwich in our population needs to be accredited. Reports like this may act as an awareness tool for physicians regarding abnormal variants which may be important in haemoglobinopathy screening program. It may also act as database for future studies in the region.

This case emphasizes the importance of identifying abnormal Hb variants, which may be missed by conventional gel technique of Hb electrophoresis. The recognition of Hb abnormalities is of anthropological interest given their ethnic specificity.

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