

## Plasma viscosity in patients with Waldenstrom macroglobulinaemia

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### Introduction

Hyperviscosity is a potentially life-threatening clinical syndrome. Measurement of plasma viscosity (PV) may support the diagnosis. Traditionally it is considered rare to develop hyperviscosity syndrome in those with PV < 3 mPa. We evaluated the outcomes of patients with high PV in our cohort of patients with Waldenstrom macroglobulinaemia.

### Methods

We retrospectively examined records of patients with IgM associated disorders who had a PV  $\geq$  3mPa recorded between 2018-2025 at University College London Hospitals. Statistical analyses were conducted using Stata v19 (StataCorp, Texas).

### Results

155 patients with an IgM associated disorder were identified with PV  $\geq$  3mPa from 707 recordings. Nine were excluded due to having another non-Hodgkin lymphoma, leaving 146 with Waldenstrom macroglobulinaemia (91 male, 55 female). At diagnosis, median age was 61 years (IQR 54-69) and IgM monoclonal protein (M-protein) 29g/L (IQR 16-42). MYD88 was mutated in 75/78 (96%) and CXCR4 mutated in 9/13 (69%) of tested cases; a concurrent cryoglobulin was identified in 34/140 (24%). Median PV was 3.6 mPa (IQR 3.2-4.5): 53 (36%) were >4 mPa; 23 (16%) >5 mPa and 9 (6%) >6 mPa. Hyperviscosity symptoms were documented in 70 (48%) and all underwent plasma exchange, at a median of 58 months (IQR 8-101) from diagnosis. PV did not significantly differ between symptomatic and asymptomatic patients (3.7 [IQR 3.2-4.9] v 3.5 [IQR 3.2-4.3],  $p=0.17$ ). Prior to plasma exchange, median M-protein was 41 g/L (IQR 33-48) and PV 4.5 mPa (IQR 3.8-6.5). Plasma exchange achieved a median 27% (IQR 15-35%) reduction in paraprotein and 43% (IQR 24-57) reduction in PV. At a median follow-up of 110 months (IQR 50-172) from diagnosis, 30 patients died during follow-up, 19 of whom had undergone plasma exchange. Five-year overall survival from diagnosis was 93% (95% CI 87-97) and 5-year survival from first exchange was 66% (95% CI 50-77). Survival from diagnosis did not differ significantly between symptomatic and asymptomatic patients (HR 1.62, 95% CI 0.77-3.40,  $p = 0.21$ ). Between 3-5 mPa, PV discriminated poorly between symptomatic and asymptomatic cases (overall AUC 0.57, 95% CI 0.47-0.66), however symptoms were more frequent at higher PV: 65% >5 mPa ( $p = 0.07$ ) and 8/9 (89%) >6 mPa ( $p = 0.014$ ). A threshold of >6 mPa was highly specific (99%) but insensitive (11%). PV > 6 mPa identified those with symptoms (8/9) and higher mortality (4/9) (log rank  $p < 0.001$ ).

## **Conclusion**

Symptomatic hyperviscosity occurred across the range of PV above 3 mPa consistent with a non-linear relationship in WM. There is no single threshold discriminatory for clinical symptoms however a PV > 6 mPa is strongly predictive of symptoms and poorer outcome. PV may support clinical assessment in management of hyperviscosity.

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