Analysis of outcomes of hemophilia care over 50-year span reveals progress, disparities

March 16 2016

Despite significant advances in hemophilia therapies and increased access to integrated treatment centers over the last half century, men with severe forms of this disease still experience physical limitations and disability, according to new research published online today in *Blood*, the Journal of the American Society of Hematology (ASH). The incidence of joint bleeding also remains higher than expected, even among a subset of men with mild hemophilia.

"Our analysis provides a snapshot of how improvements in care have translated into outcomes across different generations of men with hemophilia," said Paul E. Monahan, MD, Professor of Hematology/Oncology in the Department of Pediatrics at The University of North Carolina-Chapel Hill, and one of the study's authors. "While there is reason to be pleased with the progress we've made, our data show some surprising deficits and suggest that efforts are needed to more consistently apply the integration of standard of care multidisciplinary services and preventive blood clotting factor treatments to further normalize the lives of men living with hemophilia."

Hemophilia is a genetic bleeding disorder that prevents the blood from clotting normally, leading to a high risk of excessive internal and external bleeding and complications in the joints, muscles, and organs. Because the disease is inherited through a defect in the X chromosome, it is more common in males than females. Hemophilia affects roughly 1 in 5,000 males each year, according to the Centers for Disease Control and Prevention (CDC).

Dr. Monahan and his team analyzed data for 7,486 men with hemophilia collected prospectively by the CDC and 130 federally supported Hemophilia Treatment Centers (HTC) between 1998 and 2011, which represents the largest database of men living with hemophilia. They grouped the men into four birth cohorts to evaluate how outcomes—access to care, physical and social functioning, complications, and mortality—have changed over the last 50 years. While incremental advances in care have led to today's effective at-home bleeding prevention treatments, there have also been devastating setbacks, most notably the contamination of transfused blood clotting factor concentrates with HIV and hepatitis C (HCV) in the 1980s.

Researchers further analyzed the data to compare the experience of 4,899 men with severe hemophilia with those of 2,587 men living with mild hemophilia to control for outcomes like aging or environment that would be expected to similarly impact all men within each birth cohort, independent of the severity of the clotting deficiency.

Based on their analysis, researchers discovered that men with severe hemophilia were three times as likely to report limitations in their activities or be disabled compared to those with mild hemophilia, regardless of when they were born. These men were also more likely to report missing 10 days of work or school during the previous year.

Somewhat surprisingly, frequent bleeding was common even among men with severe hemophilia in the youngest birth cohort—access to effective, safe clotting therapies and multidisciplinary care has been available throughout the lifetime of men in this era. In this group of men with severe hemophilia, 1 in 3 report having more than five bleeding events in six months, and 1 in 4 has a joint affected by recurrent bleeding.

"Clear disparities remain in terms of frequent bleeding and disability between men with severe hemophilia and mild hemophilia across every

decade of adult life," said Dr. Monahan. "We thought the difference in functional outcomes would have narrowed over the years; that is, men with severe hemophilia should look more like those with mild disorder given improved therapeutics and access to care, but this wasn't the case."

He added, "What needs examination is why—despite widespread availability of preventive and on-demand therapies for home use—we still see disparities. It speaks to the need for continued disease surveillance to monitor and inform hemophilia interventions and outcomes."

Moreover, a subset of men with mild blood clotting factor deficiency was found to nevertheless report frequent joint bleeding. This reinforces the need for focused studies to appropriately identify and understand this subpopulation amongst those who would be expected to be mild by laboratory measurement, but are expressing an exaggerated frequency of bleeding, according to Dr. Monahan.

Importantly, liver failure has surpassed bleeding issues and HIV as the leading cause of death among U.S. men with hemophilia, which researchers say underscores the need to swiftly evaluate and treat HCV infections.

"Liver disease worsens bleeding, so eradicating hepatitis C infections needs to be a priority, especially as we now have remarkably effective therapies," said Dr. Monahan.

Researchers also found that men in the youngest two birth cohorts—those born between 1976 and 1993—are most likely to be uninsured, which is especially concerning if they don't have ready access to clotting factor or HTC services.