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Assessment Of Quality-Of-Life Improvement In Severe Haemophilia-A With Inhibitor Patients Receiving Emicizumab Prophylaxis – Hospital Based Prospective Observational Study - Original Research Article

Dr. P Anil Kiran [1], Dr. A Vijaya Jyothi [2], Dr. BK Niranjan [3], Dr. Y Vamseedhar [4], Dr. K Lakshmi Sai Pooja [5]

[1]Associate Professor, Dept of Paediatrics, Government medical college, Kadapa*
[2]Associate Professor, Dept of Pathology, Government Medical College, Kadapa
[3]Associate Professor, Dept of Paediatrics, Government Medical College, Kadapa
[4]Professor & Head of Department, Dept of Paediatrics, Government Medical College, Kadapa
[5]Post graduate, Dept of Paediatrics, Government Medical College, Kadapa

Abstract – To assess Quality of Life Improvement following Emicizumab prophylaxis in severe Haemophilia- A patients
To evaluate the impact on ABR and functional independence in hemophilia A patients. To assess the quality-of-life improvement in severe hemophilia patients on Emicizumab prophylaxis for the period of 6 months

Introduction –
Haemophilia is a rare X-linked recessive genetic disorder characterized by poor blood coagulation. It is also known as Royals disease.[1] Haemophilia A is caused by deficiency of clotting factor VIII resulting in frequent bleeding episodes. Joint haemorrhage is frequently observed in people with severe HA. [2,3] In Haemophilia A: Defective or absent FVIII → Impaired formation of the tenase complex (FVIIIa–FIXa). Decreased conversion of Factor X to Xa → Reduced thrombin formation. Poor fibrin clot stability → Prolonged bleeding. Approximately 1 in 5000 males have haemophilia with an incidence of around 1 in 1333 male live births.[4] Over 1 million women were estimated to be affected worldwide.[5] Haemophilia Federation of India in 2019 in their annual report there are 21,800 patients have been registered with haemophilia.[6] Routine replacement therapy with standard or extended half- life FVIII concentrates, or other non-factor-based therapies is frequently used to treat HA. The recommended course of treatment for severe HA is routine prophylaxis, which attempts to reduce musculoskeletal problems and spontaneous bleeding to move patients toward a moderate phenotype.[7] FVIII prophylaxis is to keep FVIII activity at or above 1 IU/dL in order to prevent bleeding, however because of its brief half-life (around 12 hours), frequent intravenous infusions are required (three to four times per week).[8] Emicizumab (Hemlibra®) is a recombinant, humanized, bispecific (i.e., it binds two distinct targets concurrently) monoclonal antibody that links factor IXa to factor X to mimic the action of activated FVIII, allowing for efficient haemostasis in HA patients, It is authorized for prophylactic use in patients with HA in 2018 by the European Medicines Agency and the US Food and Drug Administration, both with and without FVIII inh
ibitors. Emicizumab has been authorized for usage in India since April 2019 and is prescribed for HA patients with or without inhibitors. Regardless of FVIII inhibitors, emicizumab restores haemostasis because its sequences are not like those of FVIII Hence, this study retrospectively evaluates the impact of emicizumab prophylaxis on bleeding rates, joint health, functional ability, and quality of life among patients with severe HA.

Subject & Methods – Study design - Hospital-based, Prospective, non-interventional observational study

Study period -Period of 6 months from January 2025 to June 2025
Study setting - Department of Paediatrics, Government medical college hospital, Kadapa Sampling methods

& Sample size -By convenience sampling method, A total of 20 patients under review & treatment

Inclusion & Exclusion criteria –
Patients with severe HA (FVIII <1%) with inhibitors who had been on emicizumab prophylaxis for at least six months included & Patients with other bleeding disorders, prior thromboembolic events excluded.
Ethical consideration -Approval by Institutional Ethics Committee of Government Medical College Kadapa under approval IEC NO: 001/GMC/KDP/2024 on 16 December 2024.
Data collection Methods -Patient's Medical routinely maintained both in patient's individual files and department official record register.
Statistical Analysis -Analysis of data has been done by using SPSS 26 software.
Results – A total of n = 20 children diagnosed with Hemophilia A were included in the study.
Majority of participants were male, with ages ranging from 2 to 13 years with Mean age group of 9 years. All the cases were with severe hemophilia, positive family history of hemophilia was reported in 45% of the study participants, all children were inhibitor positive and were receiving Emicizumab at the time of data collection The presence of target joints was noted in 70% of the participants, indicating chronic joint involvement due to repeated bleeding episodes prior to prophylaxis. There is no history of any viral infections among the study participants.

Table 1: Socio-demographic and clinical characteristics of the study population

S.no	Characteristics	Category	Total n = 20 (%)
1	Age group	1-5years 6-10 years 10-15 years	2(10%) 11(55%) 7(35%)
2	Sex	Male Female	19(95%) 1(5%)
3	Type A/B	Hemophilia A Hemophilia B	20 (100%) 0
4	Severity	Mild Moderate Severe	0 0 20 (100%)
5	Family History	Yes No	9(45%) 11(55%)
6	Target joint	Yes No	14(70%) 6(30%)
7	**Inhibitors**	**Yes** **No**	**20 (100%)** **0**
8	Viral infection	Yes No	0 20 (100%)

Figure 1: pie chart for age group

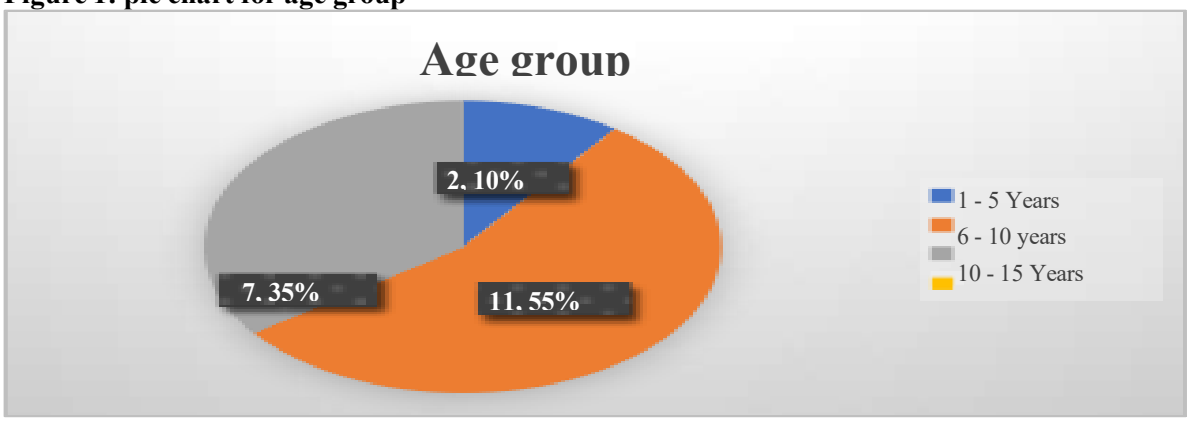

Table 2: Comparative analyses of FISH at pretreatment and post-treatment 6 months

FISH	Pretreatment	Post-treatment (6 months)
8 – 16	12	0
16 – 24	8	5
24 - 32	0	15
Mean	14.00	25.95
S.D	5.46	5.01
t- statistic	15.133	
P value	< 0.001 (Statistically significant)	

Before initiation of Emicizumab prophylaxis, the mean FISH total score among severe Hemophilia A patients was 14.00 ± 5.46, indicating moderate functional limitation in daily activities such as walking, self-care, and performing routine tasks.

The relatively low baseline scores reflect the degree of physical dependence and restricted mobility common in patients with recurrent bleeding episodes and joint arthropathy. After initiation of Emicizumab prophylaxis, the mean FISH total score significantly increased to 25.95 ± 5.01, demonstrating a clear improvement in physical independence and activity performance. Patients exhibited enhanced ability to perform daily activities such as walking, climbing stairs, and self-care without external assistance. The mean improvement in FISH score was 11.95 which was found to be statistically significant ($t = 15.13$, $p < 0.001$) using a paired t-test.

Table 3: Comparative analyses of ABR at pretreatment and post-treatment 6 months

ABR	Pretreatment	Post-treatment (6 months)
Mean	32.20	0.35
S.D	10.58	0.88
t- statistic	−13.21	
P value	< 0.001 (Statistically significant)	

The mean ABR decreased from 32.20 ± 10.58 before Emicizumab to 0.35 ± 0.88 after treatment, showing a mean reduction of 31.85 bleeding episodes per year. The paired t-test revealed there is significant difference ($t = -13.21$, $p < 0.001$), indicating that Emicizumab prophylaxis effectively reduced bleeding frequency in severe Hemophilia A patients. Clinically, this reflects a near-complete control of spontaneous and traumatic bleeds, highlighting the strong efficacy of Emicizumab as a preventive therapy.

Table 4: Comparative analyses of EQ-5D-5L at pretreatment and post-treatment 6 months

EQ-5D-5L	Pretreatment	Post-treatment (6 months)
Mean	45.45	73.20
S.D	10.54	8.73
t- statistic	23.866	
	< 0.001 (Statistically significant)	

EQ-5D-5L score showed significant improvement by 6 months. The mean score increased from (mean ± SD 45.45 ± 10.54) to (mean ± SD 73.20 ± 8.73) after treatment. The mean improvement in EQ-5D-5L score was 27.7 which was found to be statistically significant ($t = 23.866$, $p < 0.001$) using a paired t-test. showing improvement in QoL. The therapy not only reduced bleeding-related events but also enhanced mobility, independence, pain control, and mental well-being, these findings confirm that Emicizumab substantially improves the quality of life among patients with severe Hemophilia A.

Conclusion – Compared to traditional factor VIII prophylaxis requiring frequent intravenous infusions, Emicizumab's subcutaneous route and extended half-life (≈26.8 days) provide better adherence and lower treatment fatigue. In this study, ABR showed a >98% reduction, FISH scores improved by 85% indicating

restored mobility, EQ-5D-5L scores improved by 27.7% reflecting substantial QoL gain. No adverse events or thrombotic complications were reported during the study

Discussion -- This study evaluated the impact of Emicizumab prophylaxis on annualized bleeding rate (ABR), functional independence (FISH score), and quality of life (EQ-5D-5L) in children with severe Haemophilia A with inhibitors over a 6-month period. Before initiation of Emicizumab, participants exhibited a high annualized bleeding rate (mean ABR 32.2 ± 10.58) with marked functional limitations (mean FISH 14.0 ± 5.46). After six months of prophylaxis, mean ABR declined dramatically to 0.35 ± 0.88, representing a reduction of over 98%in bleeding frequency ($p < 0.001$). These findings are like global multicentre studies such as the Oldenburg et al., 2017 HAVEN 1 and Mahlangu et al., 2018 HAVEN 3 trials[11,12], which demonstrated similar reductions in bleeding rates among both inhibitor and non-inhibitor patients showing near-zero annualized bleeding rates. Functional independence improved substantially, as evidenced by a mean FISH score increase from 14.0 to 25.95 ($p < 0.001$). This indicates a significant restoration of musculoskeletal function and daily activity performance.

Santagostino et al.[13] (2020) in their study also has similar findings there is enhanced joint outcomes and decreased hemarthrosis incidence following Emicizumab initiation. Quality of life, assessed through the EQ-5D-5L instrument, improved from a mean score of 45.45 ± 10.54 to 73.20 ± 8.73 ($p < 0.001$), reflecting better physical, psychological, and social well-being.

Young et al., 2020[14] Comparable outcomes were reported in the HAVEN 2 pediatric trial where caregivers of children receiving Emicizumab noted dramatic improvements in physical activity, emotional stability, and family functioning.

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