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ORIGINAL ARTICLE

Bibliometric analysis on trends and future direction of facioscapulohumeral muscular dystrophy research

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ABSTRACT

Objectives: This study aimed to provide comprehensive overview of the evolution of the field of facioscapulohumeral muscular dystrophy (FSHD), a rare muscle disorder of genetic origin that affects individuals worldwide.

Materials and methods: The Web of Science database was searched on July 21, 2023, for studies on FSHD published since 1971. Bibliometric analysis of 1,493 articles was conducted to highlight publication trends and their connection with other topics. Descriptive, performance, network, and science mapping analyses were performed using CiteSpace (6.3.R1) to identify influential factors, including keywords, most cited articles, productive authors, and journals.

Results: Bibliometric analysis revealed that the FSHD literature expanded significantly over the past half century, particularly after 4,000 citations in 2015. There was growing interest in FSHD within its own field and other fields, including sports medicine, ophthalmology, molecular biology, and genetics. The most prominent topic was hearing loss in previous years, then focus shifted to myogenic differentiation and prevalence. The largest keyword cluster was gene location, while the most active study cluster was *DUX4* expression. The most cited article was: "A unifying genetic model for facioscapulohumeral muscular dystrophy." Clusters neuromuscular morphogenesis and inheritable neuromuscular disorder were found crucial for linking progression of disease with muscle dysfunction.

Conclusion: This study included a large number of studies published since 1971 and provided broad perspective of the FSHD field. The results suggest that new research may emerge and progress on different grounds, contributing to treatment development.

Keywords: Bibliometric analysis, bibliometry, CiteSpace, facioscapulohumeral muscular dystrophy, FSHD.

Facioscapulohumeral muscular dystrophy (FSHD) is a prevalent form of dystrophy with no available treatment, and the prevalence of the disease is approximately 1 in 10,000 individuals.[1] The onset is around second and third decades of life. The commonly affected muscles are the face, shoulder blades, and upper limbs. The dystrophy is asymmetrical and progressive, with the involvement of lower muscle groups, resulting in wheelchair-bound dystrophy in the later stages.[2] Although FSHD can be easily diagnosed by a trained eye, the clinical presentation is highly variable.[3] The heterogeneity of clinical courses among individuals complicates unified standard for clinical studies. *In vitro* models also exhibit a high degree of variability. Consequently, publications in this field yield a wide range of outcomes.

Facioscapulohumeral muscular dystrophy can be inherited in an autosomal dominant, autosomal recessive, or digenic inheritance pattern, which are classified as FSHD1 and FSHD2 at the molecular level, with no discernible clinical differences.[4] Based on linkage studies, FSHD is associated with D4Z4 repeat region on chromosome 4qter.[5] This region consists of one to 10 repeats in patients classified as FSHD1, while healthy individuals

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carry >11 repeats.[5] Each repeat consists of 3,300 bases containing the *DUX4* transcription factor.[5] Contraction of the repeat unit leads to the loss of repression causing the expression of *DUX4* mRNA. With the qA sequence located on 4qter, the expressed *DUX4* mRNA can be stabilized, which is toxic to muscle cells and causes dystrophy.[6] Another mechanism leading to FSHD is the hypomethylation of the D4Z4 repeats. Mutations in the *SMCHD1*,[7] *DNMT3B*,[8] and LRIF1[9] genes have been found to be responsible for this hypomethylation. Patients carrying these mutations with the D4Z4 repeat contraction are classified as FSHD2.

A bibliometric study examining the intellectual structure of the field has not yet been conducted, and a comprehensive overview of the FSHD field is required to guide future studies. Hence, this study aimed to provide a comprehensive overview of the themes, the trends, and the evolution of the research on FSHD. Therefore, we provided an overview of the main works and topics of FSHD studies by using both descriptive and network bibliometric analyses.[10,11] Using a specific analytical approach, this article on FSHD aimed to address the following points: *(i)* the growth trends in FSHD-related publications and the key features of the FSHD research field; *(ii)* the trends and themes belonging to main research and keywords; *(iii)* the connections between studies; *(iv)* critical transitions that could be milestones in the development of the field; *(v)* journals, countries/regions, institutions, and authors that were influential and highly productive.

MATERIALS AND METHODS

The study data were downloaded from Web of Science (WoS), which includes scientific journals with high-impact factors worldwide, on July 21, 2023. The selection criteria were Facioscapulohumeral* or FSHD. To specify FSHD, we used the keyword "facioscapulohumeral muscular dystrophy," but not "muscular dystrophy," to exclude other muscle diseases such as Duchenne muscular dystrophy and myotonic dystrophy. Relevant research was identified based on a "topic" search, which included title, abstract, Keywords Plus, and author keywords, and 2,245 publications were found. For the second step, we limited the type of articles and reviews written in English beginning from the first publication in 1971. After these selections, article number decreased to 1,536. The documents listed after this step underwent independent examination by two researchers. For interrater agreement, publications were examined by considering qualitative criteria, such as content and journal scope. A consensus was reached by obtaining the final opinion of a field expert. After completing all necessary selection steps, a total of 1,493 studies were identified as compatible data (Supplementary Figure 1). The ratio of document types was as follows: articles, 88.08% (n=1,315); reviews, 11.92% (n=178). Downloaded studies were in Excel file format for descriptive statistics and plain text format for CiteSpace analysis. The data was not provided separately in the study as it was downloaded from a publicly accessible database.

The study attempted to present an overview of the fundamental studies and issues that drive the field, as well as to evaluate the global distribution, collaborations, knowledge structures, and trends. To this end, bibliometric analysis enabled work with a large dataset of 1,494 publications and 34,792 references listed after the selection steps. This study's bibliometric analyses included descriptive statistics, performance analysis, co-citation network analysis, co-occurrence, and science mapping. The CiteSpace (6.3.R1) Advanced software (updated on February 12, 2024; software available at https://citespace.podia.com/) was used. CiteSpace was used to analyze the academic studies in the dataset and the references cited in these studies, helping track changes and identify new areas for expansion. Ethical approval was not applicable for this study since it was based solely on bibliometric analysis of the published literature.

First, descriptive statistics and performance analysis for FSHD-related research data were performed. Research topics, hot spots, and future trends were identified through keyword analysis. Co-citation and cluster analysis were conducted to identify knowledge structures. To highlight the research frontiers over time, a burst detection analysis of countries/regions, authors, keywords, and references was conducted.[12]

A document co-citation analysis (DCA) examined the links between documents. The nodes, which are the analytical elements of CiteSpace, were analyzed separately according to references, authors, journals, keywords, and countries. Network metrics were used to enrich the evaluation of the bibliometric analysis. Betweenness centrality value and sigma were used as network metrics. Betweenness centrality was measured by calculating the total number of shortest paths

through a given node ($\delta_{v,w}$ *[u]*) and dividing that by the total number of shortest paths in the entire network ($\delta_{v,w}$). The sigma value was obtained by evaluating the citation burst, and intermediate centrality corresponded to the level of innovation and influence of a node in the network.[13]

Scientific studies likely to point to new ideas exhibited a high sigma value (>0.1). A dual-map overlay was used to analyze journal evolution and interdisciplinary relationships. Blondel's algorithm was used to identify journal clusters and their highly modularity partitions.[12] This algorithm was chosen for its ability to identify partitions with high modularity.

Descriptive statistics and performance analysis were performed for the most productive journals, countries, and authors, and citation network analysis was performed to identify influential publications. Clustering, a more advanced bibliometric analysis enrichment technique, was used to create thematic clusters. Cluster analysis is a common statistical method that involves grouping similar observations together clusters. The resulting cluster visualization was generated with a log-likelihood ratio (LLR) based on keyword synchronous image matching and clustering labels.

Algorithms based on modularity optimization were used to measure the strength of dividing a network into clusters.[14] The modularity Q index was used to express the degree of divisibility of a network into smaller components, the mean silhouette score was used to measure the quality of clusters and the homogeneity of clusters.[15] If the modularity Q value was >0.3, the cluster structure was defined as significant. If the silhouette values were >0.5, the cluster structure was considered homogeneous. If the silhouette values were >0.7, the cluster structure was considered reliable. Finally, the timeline view showed the evolution of the clusters over time and whether improvements continued over the years.

RESULTS

Distribution of publications on facioscapulohumeral muscular disorder by year

The distribution of the studies on FSHD over the years (Figure 1) indicated a growing literature in FSHD publications, with an increasing number of studies and citations, demonstrating that the field remained up-to-date. The first publication in the WOS database dates to 1971. From 1971 to 2023, the first peak of publications was in 1,995. The second peak, in both publications and citations, was in 2021, with the highest number of citations in 2021 (n=4,923).

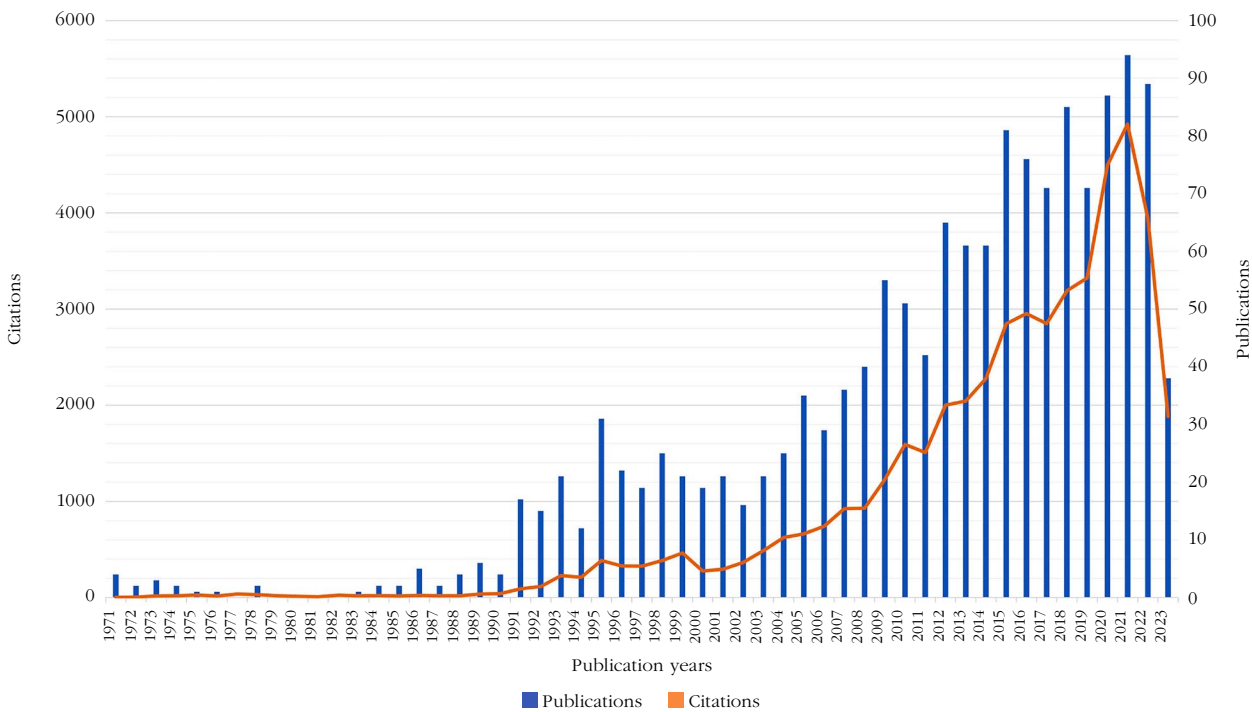

Figure 1. The distribution of publications (blue bars) and citations (orange line) from 1971 to 2023.

The projected average annual growth rate of publications until 2023 was approximately 6.15%. There was a strong, positive, relationship between the number of publications and the number of citations (r=0.957 [correlation was considered significant at 0.01] and r^2=0.916).

The expected average annual growth rate for citations of FSHD studies until 2023 was approximately 17.26%. The increase in the number of citations was greater than the increase in the number of publications, indicating a growing interest to FSHD across various fields.

A total of 1,493 publications were cited 49,284 times, including self-citations. On average, each publication received 33.01 citations, demonstrating that FSHD is an effective, developing, and current field attracting attention.

Keyword co-occurrence clustering analysis

High-frequency keywords provide insight into the research hotspots and the direction of research progress. We conducted bibliometric keyword analysis to conceptualize the evolution and the dynamics of studies. This process included setting the node type to keyword, running CiteSpace, and obtaining the keyword visualization graph for FSHD research (Figure 2). Each node in the figure represented a keyword. The size of the node increased as the number of articles containing the keyword increased. The most frequently cited keywords, with the highest the centrality values representing the greatest ability to link other keywords, were "facioscapulohumeral muscular dystrophy," "muscular dystrophy," and "FSHD" (Table 1).

The CiteSpace software utilizes a detection algorithm to identify the most significant citation words. In the FSHD field, this algorithm detected 37 citation bursts started with hearing loss, coats syndrome, deletions, and localization in 1990, then shifted to human chromosome 4q35, myogenic differentiation, and prevalence in recent years (Supplementary Table 1).

To identify the domains of the articles, we organized keywords in a hierarchical manner through the clustering network. Nodes corresponded to different co-occurrence keywords, and clusters corresponded to different majors

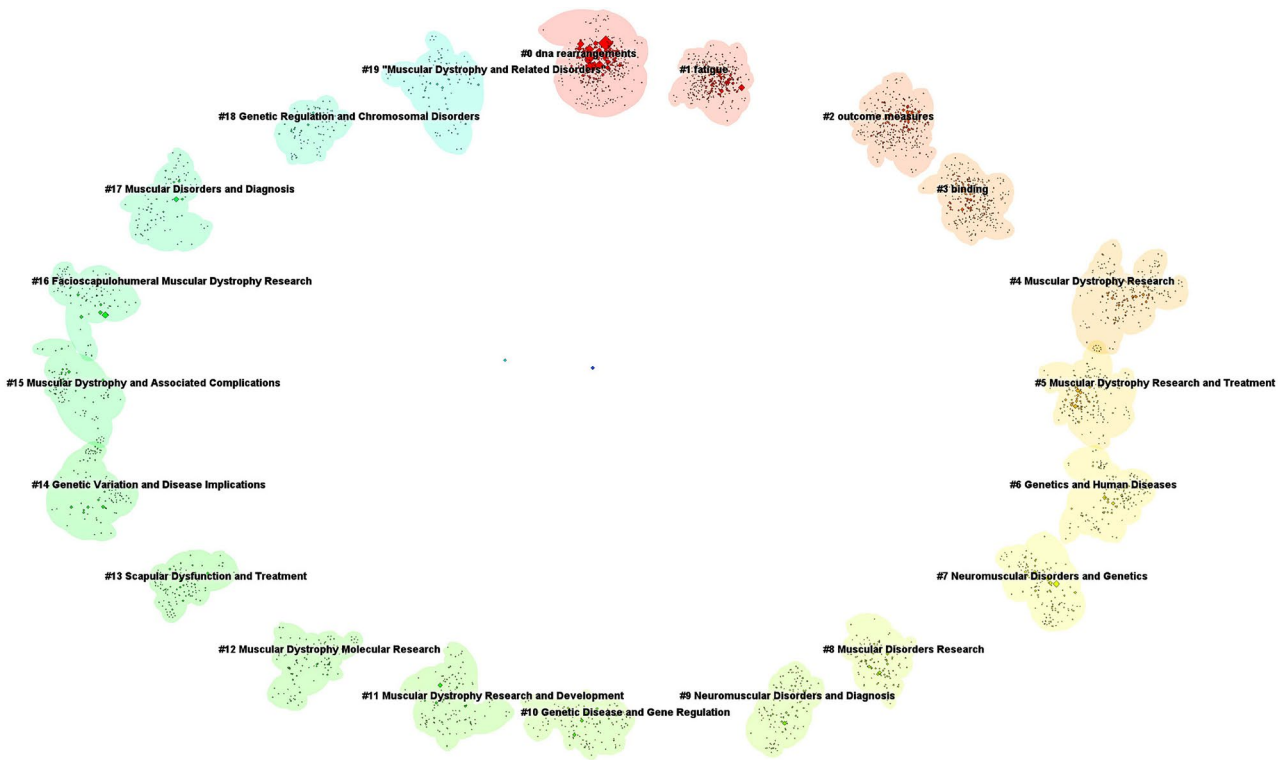

Figure 2. Keyword science mapping, and visualization of the keywords as clusters. Clusters are numbered starting from 0, and the size of the clusters decreases as the number increases. The network consists of 4,298 nodes and 25,295 connections. Red nodes represent the citation burst.

TABLE 1
The 20 most frequently used keywords ranked by betweenness centrality values

Rank	Counted	Centrality	Year	Keywords	Rank	Counted	Centrality	Year	Keywords
1	595	0.00	1991	Facioscapulohumeral muscular dystrophy	11	94	0.04	1992	Family
2	266	0.00	1991	Muscular dystrophy	12	91	0.02	1991	Diagnosis
3	226	0.00	1993	FSHD	13	87	0.01	1991	Myotonic dystrophy
4	219	0.00	1994	DNA rearrangements	14	86	0.01	1998	Skeletal muscle
5	182	0.01	1991	Gene	15	82	0.01	1991	Muscle
6	180	0.01	1996	D4Z4	16	81	0.00	2008	Candidate gene
7	170	0.02	1992	Expression	17	75	0.00	2004	Phenotype
8	124	0.01	1991	Locus	18	72	0.03	1999	Model
9	118	0.02	1992	Facioscapulohumeral dystrophy	19	70	0.01	1991	Mutations
10	115	0.02	1991	Disease	20	62	0.02	1993	4q35

FSHD: Facioscapulohumeral muscular dystrophy; DNA: Deoxyribonucleic acid.

or topics. Cluster analysis was calculated with a modularity Q index of 0.6725 and a weighted mean silhouette of 0.849. Clusters were numbered starting from 0, and the size of the clusters decreased as the number increased.[16] As a result of the analysis, the network consisted of 4,298 nodes and 25,295 connections, with red nodes representing citation bursts. Clusters 0 (DNA rearrangement) and 1 (fatigue) had red nodes, which reflected citation bursts (Figure 2, Supplementary Table 2).

Document co-citation analysis

A DCA was first conducted to examine the links between scientific studies in which two documents are co-cited.[17] The number of

TABLE 2
The most cited references of the documents

Citation counts	Authors	Title	Year
202	Lemmers et al.[6]	A unifying genetic model for facioscapulohumeral muscular dystrophy	2010
185	Lemmers et al.[7]	Digenic inheritance of an *SMCHD1* mutation and an FSHD-permissive D4Z4 allele causes facioscapulohumeral muscular dystrophy type 2	2012
141	Geng et al.[37]	*DUX4* Activates Germline Genes, Retroelements, and Immune Mediators: Implications for Facioscapulohumeral Dystrophy	2012
138	Snider et al.[38]	Facioscapulohumeral dystrophy: incomplete suppression of a retrotransposed gene	2010
137	Deenen et al.[1]	Population-based incidence and prevalence of facioscapulohumeral dystrophy	2014
120	van den Boogaard et al.[8]	Mutations in *DNMT3B* Modify Epigenetic Repression of the D4Z4 Repeat and the Penetrance of Facioscapulohumeral Dystrophy	2016
100	Wallace et al.[39]	*DUX4*, a candidate gene for facioscapulohumeral muscular dystrophy, causes p53-dependent myopathy *in vivo*	2011
98	Lemmers et al.[43]	Inter-individual differences in CpG methylation at D4Z4 correlate with clinical variability in FSHD1 and FSHD2	2015
97	Rickard et al.[44]	Endogenous *DUX4* expression in FSHD myotubes is sufficient to cause cell death and disrupts RNA splicing and cell migration pathways	2015
95	Dixit et al.[45]	*DUX4*, a candidate gene of facioscapulohumeral muscular dystrophy, encodes a transcriptional activator of PITX1	2007

DUX4: Double homeobox 4; *DNMT3B*: DNA methyltransferase 3 beta; FSHD1: Facioscapulohumeral muscular dystrophy type 1.

references in the 1,493 articles related to FSHD studies was 34,792, and the mean citation per publication was 23.3.

The article with the highest number of citations was the study by Lemmers et al.,[6] with 202 citations, followed by Lemmers et al.'s[7] study, with 185, and Geng et al.'s[18] study, with 141. The 10 most cited articles are summarized in Table 2.

The network obtained for the DCA was composed of 10,729 nodes and 45,270 links. The clusters we obtained for DCA showed a modularity Q index of 0.9592 and a weighted mean silhouette of 0.9787. Thus, the nodes formed a network that could be divided into clusters, each of which was homogeneous (Supplementary Table 2).

The structure of the cluster network is given in Figure 3. This method identified the most cited publications and their links by grouping them into different research clusters where publications regularly shared similar ideas.[19] Similarity does not mean that the findings of the publications are consistent and compatible with each other; publications that belong to the same cluster due to subject similarity may have conflicting viewpoints. This is an important tool in understanding trends, interactions, and potential collaborations in science.

The main cluster (Cluster 0) "gene location" by LLR comprised 455 members, and the silhouette value was 0.959. The primary article citing in this cluster was (1996) "Neuro muscular disorders: gene location." The most cited members of this cluster were Edwards et al.,[20] Ben Othmane et al.,[21] and Liu et al.[22] These studies mainly identified the chromosomal locations of specific genes and the muscle diseases with which they were associated (Figure 3).

The second main cluster (Cluster 1), "inheritable neuromuscular disorder," by LLR comprised 307 members, and the silhouette value was 0.955. The major citing article of the cluster was that of Greenberg and Walsh.[23] The most cited member of this cluster was the study of Upadhyaya et al.[24] (Figure 3).

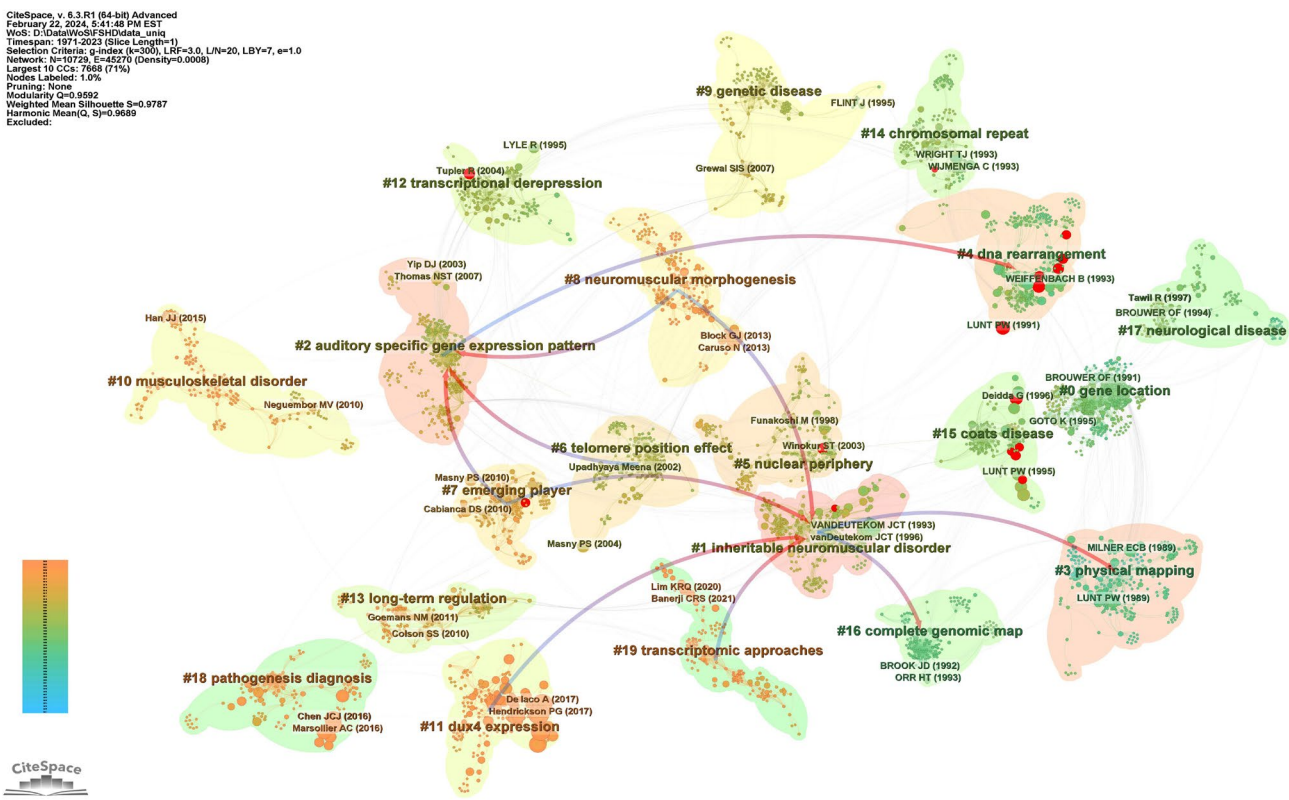

Figure 3. Cluster network of documents generated through the DCA.

*Nodes in the map represent references. The lines between clusters show "cluster dependencies", reflecting the relationships and connections between different clusters. Thicker connecting lines indicate stronger relationships between clusters. Red nodes indicate citation bursts. DCA: Document co-citation analysis.

The ninth largest cluster (Cluster 8), "neuromuscular morphogenesis," by LLR had 185 members, and the silhouette value was 0.98. The major citing article of the cluster was by Banerji and Zammit.[25] The most cited members within this cluster were Grolimund et al.,[26] Geisler and Paro,[27] and Bachasson et al.[28] (Figure 3).

Cluster 11, "*DUX4* expression," was an active cluster. The major citing article of the cluster was the study of Mocciaro et al.[29] (Figure 3).

The 20th largest cluster (Cluster 19), "transcriptomic approaches," by LLR had 142 members, and the silhouette value was 0.98. The major citing article of the cluster was the study of Coppedè et al.[30] (Figure 3).

Citation burst, which refers to a sudden increase in the number of citations received by a particular publication or author (Table 3),[31] was observed predominantly in Cluster 4 (DNA rearrangement) and Cluster 15 (Coats disease). This may signify an increase in visibility or that an influential, groundbreaking study has attracted the attention of numerous researchers. Nevertheless, it is essential to acknowledge that the citation explosion may also result from artificial manipulations. Sigma metrics provides a numerical score that represents the level of association between two documents in a co-citation network.[16] The top ranked item by sigma was "Telomere position effect in human cells"[32] in Cluster 8 (neuromuscular morphogenesis; sigma value: 1.45). The second was "Efforts toward understanding the molecular basis of facioscapulohumeral muscular dystrophy"[33] in Cluster 4 (DNA rearrangement; sigma value: 1.37). The third was "D4F104S1 deletion in facioscapulohumeral muscular dystrophy: phenotype, size, and detection",[34] in Cluster 21 (prenatal diagnosis; sigma value: 1.26).

Intellectual landscape of facioscapulohumeral muscular disorder publications

This section summarized the intellectual landscape. Research interests, thoughts, and trends related to FSHD publications were identified and visualized.

Journal dual map

A dual-map overlay performs a base map of the citations made by journals (citing journals) with a base map of cited journals. It can show the disciplinary relationship between the articles through citation relationships.[35] The curve is a citation association line from outside to the right, explaining the flow of knowledge and connections between different fields. The dual-map overlay consists of lines representing the citation frequency for each publication, and the thickness of each line is scaled according to the Z-score (Figure 4). The Z-score standardizes data, allowing objective evaluation of the impact and relevance

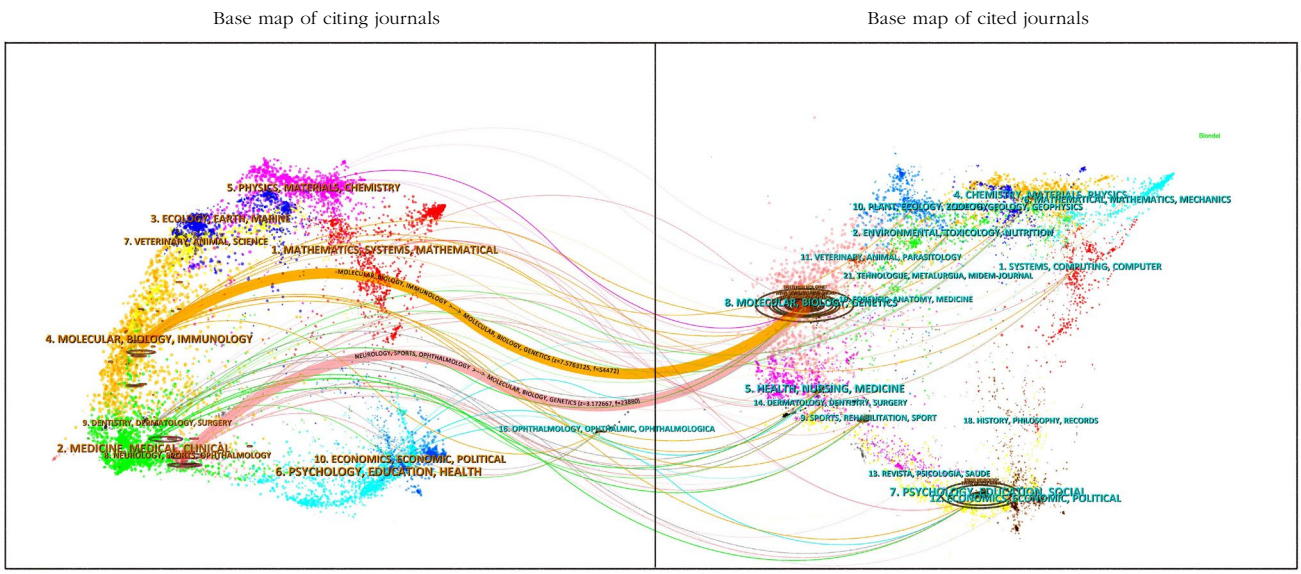

Figure 4. Dual-map overlay of journals in FSHD research. The visualization is divided into two parts: citing journals on the left and cited journals on the right. Two main citation paths are shown in orange and pink. The curve represents citation association line from outside to the right with the flow corresponding of knowledge and connections.

FSHD: Facioscapulohumeral muscular dystrophy.

of publications within and across fields. As shown in Figure 4, the left side, where the orange and pink paths begin, references of studies focused on molecular, biology, immunology, neurology, sports, and ophthalmology, and the right side, where the path reaches, disciplines of molecular, biology, and genetics.

The most influential journal

A total of 1,493 publications were published in 471 different journals. To identify the leading journals in the field of FSHD, we first analyzed the distribution of the publications in the journals. With 99 publications, the journal that published the most of the FSHD related articles was Muscle & Nerve (impact factor=3.4; 2022). The most cited journal was Neurology (impact factor=9.9; Table 4).

Contribution of countries/regions

Data was analyzed by country to identify the distribution of 1,493 studies in the world. The contribution of the USA was in the first place with 593 publications, followed by the Netherlands. It is noteworthy that the Leiden University in the Netherlands was the most productive institution in the field and holds a key position in this field. The betweenness centrality was another analysis investigating collaboration of countries. Countries with high betweenness centrality values were, respectively, France (0.27), the Netherlands (0.23), and the USA (0.20; Supplementary Table 3).

Analysis of the co-authorship and the most influential authors

Authors play a crucial role in assessing the scope and the development of the research field. With an average of 4 (exact number 3.85) authors per publication, 5,747 different authors were involved in the creation of the FSHD literature. In addition to authors with good publishing skills, it is important to identify core authors who have made major contributions and promoted the development of the field.[36] The most active and cited authors were van der Maarel SM and Lemmers RJ (Supplementary Table 4).

DISCUSSION

To observe the overall picture of the literature, bibliometric studies have begun to come to the fore in the subfields of neurology.[37] In this study, we investigated the FSHD literature from

TABLE 3
Top 20 references with the strongest citation bursts

References	Year	Strength	Begin	End	1971-2023
Wijmenga et al.[46]	1990	40.02	1991	1997	
Wijmenga et al.[47]	1991	30.69	1991	1998	
Sarfarazi et al.[48]	1992	37.17	1992	1999	
Wijmenga et al.[49]	1992	51.68	1993	1999	
Vandeutekom et al.[50]	1993	37.93	1994	2000	
Gabellini et al.[51]	2002	46.47	2003	2009	
Jiang et al.[52]	2003	30.49	2004	2010	
Tawil et al.[53]	2006	36.86	2007	2013	
Gabellini et al.[54]	2006	35.91	2007	2013	
Dixit et al.[45]	2007	43.42	2008	2014	
Kowaljow et al.[55]	2007	36.3	2008	2014	
Bosnakovski et al.[56]	2008	33.4	2009	2015	
Snider et al.[57]	2009	30.06	2009	2016	
Zeng et al.[58]	2009	34.06	2010	2016	
Lemmers et al.[6]	2010	77.03	2011	2017	
Snider et al.[38]	2010	53.4	2011	2017	
Geng et al.[37]	2012	44.91	2012	2019	
Wallace et al.[39]	2011	34.35	2012	2018	
Lemmers et al.[7]	2012	66.65	2013	2019	
Deenen et al.[1]	2014	39.86	2015	2021	

TABLE 4
The top 10 journals of relevant literature on FSHD and the metrics of cited journals. The metrics of the journals were obtained from the Scimago Journal & Country Rank on July 28, 2023

Journals published on FSHD				Cited journals			
Journals	Counted	Quartile	h-index	Cited Journals	Counted	Quartile	h-index
Muscle & Nerve	99	Q2	159	Neurology	959	Q1	396
Neuromuscular Disorders	91	Q1	109	Neuromuscular Disorders	865	Q1	109
Neurology	65	Q1	396	Human Molecular Genetics	853	Q1	294
Human Molecular Genetics	63	Q1	294	Muscle & Nerve	822	Q2	159
Plos One	39	Q1	404	Nature Genetics	817	Q1	621
Journal of Medical Genetics	36	Q1	185	American Journal of Human Genetics	726	Q1	321
Journal of Neurology	33	Q1	152	Annals of Neurology	724	Q1	321
American Journal of Human Genetics	26	Q1	321	Science	602	Q1	1283
Skeletal Muscle	18	Q1	53	Journal of Medical Genetics	577	Q1	185
Journal of the Neurological Sciences	16	Q2	149	PNAS	549	Q1	838

FSHD: Facioscapulohumeral muscular dystrophy; PNAS: Proceedings of the National Academy of Sciences.

a bibliometric perspective. Literature on FSHD followed a path from studies related to gene location and progressed to more detailed research topics. The first notable increase in citations occurred in 1995 (Figure 1), which might be associated with publication of linkage studies in the years 1994 to 1995.

The different naming of the disease were the most recurring keywords suggesting lack of standardization. Consensus on a uniform naming is needed. Other commonly used keywords included molecular genetic terms: DNA rearrangement, gene, D4Z4, expression, locus, model, mutations, and 4q35 (Table 1). Keywords DNA rearrangement (Cluster 0) and fatigue (Cluster 1) hold significance within the research field (Figure 2).

A review of the most cited studies revealed a study by Lemmers et al.,[6] which proposed a genetic model for FSHD. The second study was also by Lemmers et al.,[7] defining the FSHD2 subtype and related the *SMCHD1* gene with the methylation status of the FSHD locus. Third and fourth most cited studies, elucidate the functions of *DUX4* (Table 2).[18,38]

In DCA, Cluster 1 was "gene location." Studies cited in this cluster provided an understanding of the genetic basis and molecular diagnosis of muscle diseases.[20-22] Studies in Cluster 2, "inheritable neuromuscular disorder," contributed to the molecular diagnosis of neuromuscular diseases (Figure 2, Supplementary Table 2).

Another cluster of interest in the field was "neuromuscular morphogenesis," providing mechanistic explanations. Most cited studies in this cluster offered aspects to the molecular and physiological basis of neuromuscular diseases. Banerji and Zammit[25] focused on the role of PAX7, another transcription factor that functions in a reverse direction with *DUX4*; Geisler and Paro[27] revealed Trithorax and Polycomb group-dependent epigenetic regulation; and Grolimund et al.[26] put forth telomer associated peptides (Figure 2, Supplementary Table 2).

Cluster 11, "*DUX4* expression," was the most active cluster. This is not surprising because FSHD is characterized by the abnormal expression of the *DUX4* gene, leading to series of cellular events that result in muscle degeneration.[6,25,38,39] Understanding the *DUX4* pathway is crucial, as its activity is a key driver of the disease process in FSHD, making it a primary target for therapeutic interventions (Figure 2, Supplementary Table 2).

Another key cluster was Cluster 19, "transcriptomic approaches." In the context of FSHD, transcriptomics is used to identify differential gene expression patterns, including the misregulation of the *DUX4* gene. By comprehensively analyzing RNA profiles, researchers can pinpoint aberrantly

expressed specific transcripts in FSHD compared to healthy individuals. This helps elucidating the downstream effects of *DUX4* expression, including the impact on muscle atrophy and degeneration. Furthermore, transcriptomic studies facilitate the discovery of biomarkers for FSHD and the development of targeted therapies by revealing the complex network of gene interactions and pathways disrupted in the disease (Figure 2, Supplementary Table 2).

The relationship between "neuromuscular morphogenesis" (Cluster 8) and "inheritable neuromuscular disorder" (Cluster 1) was crucial for linking the progression of the disease with muscle dysfunction. The genetic background of FSHD disrupts the development and formation of muscle cells and neuromuscular junctions, leading to muscle weakness. Therefore, the strong dependence of Cluster 8 on Cluster 1 (Figure 3) highlighted the importance of this relationship in understanding the nature of the disease and developing treatments.

The fact that Cluster 1, "inheritable neuromuscular disorder," was inactive indicated that this cluster was no longer being studied. We believe that after the establishment of broad theoretical structure, studies in this field shifted to active areas, such as *DUX4* expression (Figure 2, Supplementary Table 2).

The sigma score reflects the structural and temporal importance of an article. Node's sigma score analysis revealed studies focused on molecular genetic base of FSHD with a particular focus on telomeres.[32-34] We can infer that FSHD studies in different fields are progressing based on molecular genetics.

Top references with strongest citation bursts can be defined as the corner stones of the FSHD field. Geng et al.[18] investigated specifically gene expression changes in skeletal muscles. Wallace et al.[39] provided detailed information on the clinical features and genetic underpinnings of FSHD, aiding to understand phenotypic diversity. Lemmers et al.[7] provided critical information on the genetic etiology by examining the genetic variations and its impact on the clinical course of the disease. Deenen et al.[1] investigated the epidemiology, prevalence, and demographic characteristics of FSHD (Table 3).

The journal dual map revealed that the relation of FSHD to neurology, sports medicine, and ophthalmology comprised many aspects of molecular biology and genetics. A collaboration between these areas might be essential for the comprehensive understanding of FSHD. Researchers and healthcare professionals can work together to improve patient care, identify potential treatments, and advance our understanding of this complex neuromuscular disorder by combining knowledge of neurology, sports medicine, ophthalmology, molecular biology, and genetics.

Cited journal analysis revealed that Muscle & Nerve, Neurology, and Neuromuscular Disorders were effective journals shaping the FSHD era. The most cited journals were well-established and high quality (Q1, Q2) journals (Table 4). Leading countries in FSHD research were determined as the USA, the Netherlands, Italy, France, and England.

Lemmers RJLF was the most cited author, and van der Maarel SM was the most productive author, with 135 publications elucidating the fundamental mechanisms underlying FSHD.[6] Some of their studies are still used as the main source for FSHD diagnosis and subtyping.[7] Frants[34,46,50] and Padberg[40] were also key researchers who played important roles to start up FSHD research in Leiden University: the most productive institution. Tawil and Van Der Maarel[41] was the second most active and cited author that contributed to the FSHD era by bringing together new developments in review articles as well as in clinical studies. Smith et al.,[42] another key researcher, made significant contributions and actively participated in central studies most of which elucidate *DUX4*-related molecular mechanisms, including *DUX4*'s relationship with cancer (Supplementary Table 4).

This study had some limitations. The dataset was derived from the WoS Core Collection. Although this collection is widely recognized for its high-quality indexing, it may not cover all relevant publications, particularly those indexed in other databases such as Scopus, Google Scholar, or regional repositories. The types of publications included in the study were research articles and reviews; therefore, bibliometric analysis of the present study did not include the data shared in other types of publications, such as congress abstracts and letters to the editor. Only articles published in English were included in the study, which may have excluded some potentially relevant studies published in other languages. Future studies may benefit by combining multiple databases and multilingual datasets.

In conclusion, FSHD is one of the most common forms of dystrophy. A bibliometric analysis of the FSHD literature revealed that FSHD was an active field with a high rate of citations from other fields. The majority of the early FSHD studies and the most cited articles with a high centrality profile were on *(i)* the identification of the genetic locus responsible for the disease and *(ii)* the role of *DUX4*. There is still no cure, and clinical trials related to treatment continue at various stages. Most of these are based on modulation of the key molecule: *DUX4*. Regulation of epigenetic mechanisms represents another recent approach to treatment options. There are still many unexplained clinical and molecular points in FSHD. Results of the present bibliometric analysis suggests that future molecular and clinical studies might focus on the *(i)* the development of diagnostic tools, *(ii)* in-depth elucidation of pathophysiological mechanisms, and *(iii)* the development of new treatments in light of newly discovered data.

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