Scientometric Study on Dyslipidaemia

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Authors’ contributions

This work was carried out in collaboration among all authors. Author RP wrote the first draft of the manuscript, designed the paper and explored the available literature and research work already done in the field. Author VD guided about the whole study, edited the draft and contributed by giving valuable inputs to make the paper impactful. Author GP managed the literature searches, helped in designing the study and gave valuable inputs in relation to ayurveda literature. All authors read and approved the final manuscript.

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ABSTRACT

Dyslipidaemia an ever increasing menace emerging out of present lifestyle, is one of the major risk factors for developing Cardio-vascular abnormalities like Coronary Artery Disease (CAD), Myocardial infarction (MI), Cardiac arrest and is often associated with other metabolic disorders. Clinicians across the globe are trying hard to combat it. We have presented a Scientometric analysis of dyslipidaemia which includes Ayurvedic perspective also.

Objective: In this study we intended to study detailed Scientometric and Bibliometric study on dyslipidaemia literature.

Materials and methods: The data was collected using databases of Science-direct and Scopus, using the keywords ‘Dyslipidaemia’, ‘Dyslipidaemia in Ayurveda’, ‘Dyslipidaemia in India’, ‘Medoroga in Ayurveda’ and ‘Medoraga in India’.
Results: A total of 85,500 items were retrieved from ‘science direct’ website, where majority of them were research articles and maximum publications were from the last decade indicating the recent enhancement in prevalence and awareness. A volley of research papers have come up with multiple approaches which include modern pharmacological measures, Ayurveda remedies and other herbal medicines along with non-pharmacological approaches like Yoga and Pranayama. Newer therapeutic agents like Ezetimibe, proprotein convertase subtilisin/kexin type 9 (PCSK9) monoclonal antibodies, PCSK9 small interference RNA (siRNA), and bempedoic acid, when added to the commonly used statin therapy have shown additional improvement to CV outcomes. Recent advances have come up with hepatocyte-specific targeting modifications and have shown promising lipid lowering effects.

Conclusion: Our study was probably the first such kind of work in field of dyslipidaemia which includes publications related to Ayurveda and other herbal remedies also. It shows the ever rising trends in the publications related to dyslipidaemia and its relation to other metabolic disorders in recent years. The major concern is the progression in cases of dyslipidaemia and its cardiovascular outcomes despite of having substantial research work and awareness in different streams of medicine. We must focus on the multifactorial approach encouraging behavioural, dietary and pharmacological control of cholesterol and sensitize the masses about its serious consequences. A cumulative approach including modern advances with much safer herbal remedies and practice of Yogasana and Pranayama is the need of hour and may probably bring the best solution.

Keywords: Ayurveda; dyslipidaemia; medoroga; atherosclerosis; lifestyle disorder.

1. INTRODUCTION

Dyslipidaemia is a group of disorders of lipoprotein metabolism, which includes overproduction or deficiency of lipoproteins or both. Hyperlipidaemia is the more common type [1]. Abnormality in the level of lipoproteins is increasing with rapid pace among the Indian population in recent times. Dyslipidaemia is a major contributor to cardiovascular mortality in developed countries. Males are more commonly affected and incidence is high in sixth decade of life. Studies show increasing mean cholesterol levels in Indian population. Prevalence of high cholesterol is reported to be as high as 25-30% in urban and 15-20% in rural subjects. Low HDL cholesterol, borderline high LDL cholesterol and high triglyceride levels are commonly found in Indians. The study in the paediatric population having poorly controlled type-1 diabetes mellitus, shows a prevalence of 47.2% in which abnormality of LDL cholesterol was most common. This study highlights that poor glycaemic control and high TSH values were important predictors of chances of dyslipidaemia [2]. Coronary events like CAD are significantly associated with raised Apo-lipoprotein A, LDL cholesterol, total cholesterol and non-HDL cholesterol according to recent studies [3]. Dyslipidaemia makes a patient more prone to cardiovascular diseases like MI, Coronary artery disease, cardiac arrest, peripheral arterial disease, comorbidities like dyspnoea, lethargy, tiredness, weight gain, loss of appetite, PCOD, Hypertension, Hypothyroidism, infertility, atherosclerosis or even cardiovascular death. High income countries have more prevalence rates [1]. Up to 2020, 93 million U.S adults aged 20 or more have higher range of total cholesterol levels(more than 200 mg/dl) and 7% of children and adolescents(6 to 9 years of age) have high total cholesterol level [4]. Major Ayurvedic texts have all described various aspects of obesity and dyslipidaemia under the broad umbrella of Sthaulya, Medoroga and Dhamani pratichyaya. They have explained causative factors, clinical implications and complications, beneficial diets, aggravating factors as well as preventive aspects [5,6]. Meda (lipids) has been categorised as badhham (fixed or consolidated) and abaddham (non-compact or free-flowing), that can be understood as Visceral adipose tissues and free form of lipids in circulation respectively [7]. Atisthaulya (obesity) which is the outcome of medodhatu agni dushti (impaired lipid metabolism), is considered as one of the eight most condemned pathological categories. Lack of physical activities, sedentary lifestyle, sleeping in day time, excessive intake of fatty and alcoholic drinks, sweet foods, over-eating, water intake immediately after meals, genetic predisposition etc., are explained as major causes of lipid derangement and obesity [8,9]. The patients having deranged lipid metabolism are predisposed to shorter life span, face problems like difficulty in doing daily activities like walking, sexual intercourse etc., over sweating, foul body odour, breathlessness, excessive
hunger and thirst, lethargy and over-weight [5]. The beneficial diet to decrease fats and to improve metabolism includes old rice (aged), Indian grains and herbs like Kodrava (Paspalum scrobiculatum), Syamaka (a cultivated millet-Panicum frumentaceum), Priyangu (Aglagia elaeagnoida), barley. Grams, kulatha (horse gram), honey, lentil, mudga (Vigna radiate L.), pigeon peas, poppy of paddy, edibles and juices having bitter taste, buttermilk, cingata variety of fishes, fried brinjal, Triphla, Guggul, Lauh bhasm, Trikatu, mustard oil, cardamom, sesame oil, leafy vegetables, warm water, shilajatu (asphaltum) etc.[9,10]

2. MATERIALS AND METHODS

The data of this study was collected from website of ‘Science Direct’, which is a website of Dutch publisher Elsevier and the database of ‘Scopus’. Science Direct contains a large Bibliographic database of medical and scientific publications [11]. Scopus is a source-neutral abstract and citation database which contains 25,100 titles from 5000 plus global publishers, thus presents most comprehensive overview of research output globally, in different scientific fields including the field of medicine [12]. The keywords used were ‘Dyslipidaemia’, ‘Dyslipidaemia in Ayurveda’, ‘Dyslipidaemia in India’, ‘Dyslipidaemia in Ayurveda, India’, ‘Hyperlipidaemia in India’, ‘Hyperlipidaemia in Ayurveda’, ‘Medoroga in Ayurveda’ and ‘Medoraga in India’. Items published during the period of 1998-2021 were included.

3. RESULTS

3.1 Number of Published Documents and Major Subject Areas

A total of 85,500 items were retrieved from ‘science direct’ website, out of which the research articles were in majority and maximum results were from publications in the last decade. A total of 61,509 results were from the period 2010-2021. The details covering the articles types and major subject areas have been shown in Table 1. On exploring Scopus database, only 84 results were found. Out of which 13 were webpages, 69 books and two were journals. The two journals were American journal of preventive cardiology and Journal of Clinical Lipidology.

3.2 Publications Related to India

On searching for keyword- ‘Dyslipidaemia in India’, 5,036 items were retrieved. Out of them Research articles were 2232, Review articles 885, followed by 802 conference abstracts and 402 book chapters. Rest of the findings can be seen in Table 1. On searching for ‘Hyperlipidaemia in India’, 4,687 results were found. Out of them 1988 were research articles, 866 were reviews and 640 were book chapters.
3.3 Number of Documents Published Related to Ayurveda

‘Dyslipidaemia in Ayurveda’ revealed just 216 items. 82 research articles, 38 review articles, 45 book chapters and 12 conference abstracts were found. ‘Dyslipidaemia in Ayurveda, India’ yielded 172 results including 44 open access papers. ‘Hyperlipidaemia in Ayurveda, India’ has shown 268 results including 43 open access publications were found. Keyword ‘Medoroga in Ayurveda’ showed 8 results only. There were no results found for word ‘Medoroga’ on searching Scopus database. The summary of research findings related to Ayurveda and other herbal medicines is as follows-

CQR-300 (Cissus quadrangularis extract) inhibited the differentiation of 3T3-L1 adipocytes by regulating adipogenesis-related genes and proteins and could inhibit lipid accumulation in these adipocytes without causing cell cytotoxicity [13].

The results of study conducted on atherosclerotic rats suggested that anti-atherosclerotic activity of hydroalcoholic extract (HAE) of root bark of P. integrifolia Linn., was found due to its modulatory activity on metabolic pathway of lipid through a key enzyme HMG-CoA reductase along with the maintenance of collagen and calcium contents, which plays an integral role in atherosclerosis [14].

Plumbagin possessed an advantage over Orlistat in that it not only ameliorated hepatic steatosis but also exerted antioxidant, anti-inflammatory and anti-fibrotic effects which are beneficial in protecting against NASH. It also reduced liver injury, suppressed lipogenesis and stimulated fat oxidation. Plumbagin reduced the gene expression of SREBP-1c and increased that of PPAR-α, reduced body weight gain, BMI and abdominal obesity, insulin resistance and lowered serum glucose and also improved the dyslipidaemia in rats [15].

Study evaluating the short-term effect of Lemon honey juice fasting (LHJF) on lipid profile and body composition in healthy individuals showed significant reduction in weight, body mass index (BMI), fat mass (FM), free FM (FFM), and total serum triglycerides (TSTGs) with insignificant reduction in fat percentage and total serum cholesterol compared to baseline [16].

Herbal Formulation for Obesity (HFO-02) that consists of Triphala, Trinad, Guggul and Vrikshamla, did not show reduction in weight, however a significant decrease in the body circumference and skin fold was demonstrated [17].

Administration of Dhanwantaram Kashayam in diabetic rats increased the activity levels of antioxidant enzymes and reduced the levels of total cholesterol, phospholipids and triglycerides. Outcome of this study points to the possibility of developing Dhanwantaram Kashayam as a dietary supplement that can alleviate the complications associated with diabetes or prevent them altogether [18].

This study undertaken to investigate the effects of GEF (Garcinol enriched fraction) against hyperlipidemia in diet induced hyperlipidemic C57BL/6 mice showed a dose dependent amelioration of hyperlipidemia and also modified the underlying pathological mechanisms namely oxidative stress and inflammation. Thus this can be a promising measure to combat and prevent atherosclerosis [19].

ERE (standardized Embelia ribes ethanol extract) showed a preventive effect on body weight gain, visceral fat accumulation and elevated blood pressure. Furthermore, it decreased the myocardial lipid peroxidation, improved insulin and leptin sensitivity and increased antioxidant levels in obese rats [20].

Assessment of results of a study on lipid lowering effect of extract of a plant named Nepeta hindostana, in experimentally induced dyslipidaemia indicate that antidyislipidemic effect of the plant extracts was mediated through the inhibition of biosynthesis, absorption and secretion of lipids [21].

The combination of powdered sprouted mung bean (green gram ) and yam powder (Amorphophallus paeoniifolius) have significantly reduced the serum lipid levels as well as the atherogenic indices in albino rats in comparison to the, bile acid sequestering agent, Cholestyramine as standard. Thus use of this combination could help in reducing high CAD risk among Asians [22].

C. pluricaulis methanolic extract (CPME) significantly ameliorate the lipid abnormalities in experimental rats but did not show hypoglycemic effects [23].
Anti-hyperglycemic, anti-hyperlipidemic effect of *Arjunarishta* may be mediated by decreased TNF-α and increased PGC-1α and IRS-1, in High-fat diet fed (HFD) Wistar rats [24].

A case report concludes that lifestyle change by integration of specific non-drug Yoga and Naturopathic intervention is useful in the management of Metabolic Syndrome and can effectively decrease the need of pharmacological measures [25].

The people with dominant *Kapha dosha* (*K*) exhibit more risk towards metabolic syndrome like cardiovascular disorders, dyslipidaemia and obesity [26]. This could be due to increased visceral adipose tissue that further elevates TG-VLDL secretion and impairs glucose tolerance, insulin resistance etc [27,28].

The findings of another study suggests that yoga practices can improve lipid metabolism in specific constitutional types where, *Pitta-Kapha* group need yoga practices of moderate intensity as compared to *Vata-Pitta* group, to improve lipid metabolism with balanced ratio of low to high density lipoproteins. This is of importance, as it would be beneficial to differentiate mode of yoga intervention as per the constitutional type [29].

### 3.4 Journals/ Publication Titles

For the keyword ‘Dyslipidaemia’, the title with maximum publications was *Atherosclerosis* (3,743) followed by ‘Atherosclerosis supplements’ (2887). Afterwards Journal of American college of Cardiology was followed by International journal of cardiology, Metabolism and journal of clinical Lipidology. Other notable journals were– Diabetes research and clinical practice, Gastroenterology and American Heart Journal. In Ayurveda, Journal of Ayurveda and Integrative medicine was most productive journal with 19 publications. Other notable contributors were– journal of ethno-pharmacology, Biomedicine and Pharmacotherapy, journal of neurological sciences, journal of traditional and complementary medicine and other journals which contributed are mentioned in Table 1.

![Chart 2. Comparison of publications in ayurveda to the overall publications in India](chart.png)
Table 1. Document types, Number of publications and total percentage

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<td>4. The American Journal of Cardiology</td>
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<td>5. International Journal of Cardiology</td>
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<td>7. Journal of Clinical Lipidology</td>
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<td>8. Diabetes Research and Clinical Practice</td>
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<td>9. Gastroenterology</td>
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<td>10. American Heart Journal</td>
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### 3.5 Progression of Publications

2020 was the most productive year with 7,614 publications regarding dyslipidaemia, followed by 6,422 in 2018, 6,293 in 2019 and 5,684 publications in 2016. Total 61,509 results were found in last decade from the period of 2010-2021. This indicates the steep rise in the cases of dyslipidaemia and therefore increasing concern of researchers towards this challenge.

### 3.6 Current Trends in Research on Dyslipidaemia

For last many years Statins have been the backbone of lipid lowering therapy and have substantial low density lipoproteins cholesterol (LDL-C) lowering effect. But around 40% of total number of patients receiving statins experience cardiovascular disease [30,31]. They have some other notable side effects like insulin resistance and myopathy or myalgia [32]. Studies show Rosuvastatin is more efficacious in improving lipid profile, atherogenic index and modulation of inflammatory biomarkers in dyslipidemic T2D patients compared with Atorvastatin. However, both statins are equivalent as cardioprotective agents in dyslipidemic T2D patients [33]. In another study, the combination of Fimasartan and rosvastatin was shown to have effects on target diseases like hypertension and dyslipidaemia, but there was no synergistic effect. They had even lower rate of concurrent control in patients having high risk for cardiovascular diseases. More active treatment is therefore required in high-risk patients [34].

Recently statins have been used with Ezetimibe or proprotein convertase subtilisin- kexin type 9 (PCSK-9) inhibitors to reduce LDL-C levels further but still a significant residual risk of CVD exist [35]. The protein named as Niemann-Pick C1-like 1 protein plays a key role in cholesterol absorption from the intestines and it is targeted upon by Ezetimibe [32]. Co-administration of ezetimibe with statins in a study on hypercholestaemia patients significantly decreased CRP and insulin levels, increased adiponectin levels and insulin sensitivity, and reduced visceral fat and blood pressure [36]. New therapeutic agents like peroxisome proliferator-activated receptor a (PPAR-a) agonists and Omega-3 fatty acids, have shown
promising results for lowering triglycerides (TG), TG- rich lipoproteins (TRL) and lipoprotein-a [LP(a)]. Novel approaches like small interference RNA (siRNA) and Antisense oligonucleotide (ASO) effectively reduce the expression of target genes. With recentheen revolutionary advances like hepatocyte- specific targeting modifications, drugs can directly be delivered to hepatic cells where lipid metabolism takes place mainly and doses of cumulative drugs can also be lowered. A substance called triantennary N-acetylgalactosamine (GalNAc) has been designed to deliver the drug specifically to liver cells and thus reduce the side effects and also improve the efficacy of drugs. They are used in conjugation with drugs like ASOs and siRNA e.g. IONIS-APO (a) and Inclisiran respectively. This is a revolutionary advancement that promises to reduce the required doses, make the drugs safer and to improve the outcome of treatment [32].

4. DISCUSSION

Scientometrics is known as the science of measuring and analysing science. Biometrics is measurement of impact of publication. Bibliometrics is often used to do scientometric studies. These both terms are used interchangeably quite often [37]. Both of them are methodological approaches in which the scientific literature itself becomes a subject of analysis. They could be considered as ‘science of science’ [38]. The use of term Bibliometrics was first done in 1969 by Pritchard and Campbell was first to perform a bibliometric study in 1896 [39]. The foremost definition of scientometric literature in research was given by Nalimov and Mulchenko. Only a few studies using scientometrics and bibliometrics, have been done related to field of Alternative and Complimentary medicine. Maximum of these were related to acupuncture field [40]. China was found to be leading country (47.4%) followed by USA (17.5%) and UK (8.2%) in a study done by Ma et al. on analysis of acupuncture literature (PubMed) [41]. Only three results were shown in Elsevier’s database, for Complimentary therapies in clinical practice. Total six papers related to Ayurveda and other complimentary medicines including Leech therapy, Homeopathy evolution, Apitherapy and Cancer & Ayurvedic drugs [42,43,44,45]. One paper on Ayush and meta-research was published in J-AIM [46]. On searching for the Scientometric study related papers, a total of 271 results were found in the field of Medicine and Dentistry including 153 research and 26 review articles. Total 2025 results related to Bibliometric study were found in the field of Medicine and Dentistry, including 982 research and 279 review articles. The review of a vast literature on dyslipidaemia has shown multi-dimensional work related to this field. Researchers have tried to find out the causative factors, clinical implications, its relation with other co-morbidities and various treatment approaches. As far as modern medicine is concerned, statins had been the mainstay of treatment in last many years despite of often resulting in side effects and not being able to prevent cardiovascular diseases. To overcome this problem it is now being advised to be used in conjugation with newer safer drugs like Ezetimibe, PCSK9 inhibitors etc. Findings of the study done to investigate the effects of early and advanced dyslipidaemia on angiotensin II induced contraction, show the early phase of dyslipidaemia may be the most favourable moment for effective athero-protective therapeutic interventions [47]. Therefore it’s better to intervene as early as possible in dyslipidaemia management. Therefore effective screening of high-risk groups and earlier management is the key to prevent complications. Recent advancements in delivering drugs to the target hepatocytes directly have revolutionised the modern approach and is believed to change the present scenario. Complementary and alternative medicines like Ayurveda and other herbal medicines have come up with many potent, cheaper and safer options. Ayurvedic medicines like Cissus quadrangularis, Premna integrifolia, Plumbago zeylanica, Arjunarisht, Dhanwantram Kashayam, Garcinol, Embil Ribes, Convolvulus pluricaulis etc. have proven benefits in hyperlipidaemia and are much safer natural options. Considering the concept of Ayurveda which explains the more pre-disposition of Kapha prakriti (a type of body constitution) people [48] to have metabolic disorders like dyslipidaemia, obesity, diabetes etc., can aid in early screening of such people and thus helpful in preventing the pathologies by making necessary changes in dietary habits and lifestyle of them. This concept can be beneficial in sensitising the general public about knowledge of their body constitution and required preventive measures to remain healthy. This can also be helpful in tackling all other lifestyle disorders and non-communicable diseases. Indian traditional practices like regular performance of Yogasana and Pranayam, following traditional lifestyle are the key to prevent the disease and to effectively deal with already existing cases. The research papers also re-validate their effectiveness.
Therefore they should be warmheartedly encouraged in clinical management of dyslipidaemia. Multi-dimensional approach is the best way to combat this ever-increasing global problem.

To the best of our knowledge, this study is a novel work done in this particular sphere of bibliometric/ scientometric study on dyslipidaemia which also includes work done in field of Ayurveda. This study has the limitation as we have retrieved data from Science Direct and Scopus only, which are among the leading and reliable databases for scientific publications. Other databases may further be explored to go for a wider applicable study.

5. CONCLUSION

This study brings forward the useful researches on management of deranged lipids from western medicine, Ayurveda and other herbal remedies. It also highlights the importance of early screening by analysis of body constitution to find out the vulnerable people (Kapha predominant constitution) and taking preventive measures accordingly. Timely intervention through lifestyle changes, physical therapies and suitable pharmacological agents is foremost requirement. The ever emerging cases of dyslipidaemia and its association with other metabolic disorders, creates the dire need to take more effective steps and multi-dimensional approach to encourage behavioural, dietary and pharmacological control of cholesterol. The current trends in finding potent and target oriented approach to hepatocytes promise to be a boon in terms of safety and efficacy, although the clinical outcomes of the novel therapeutics are yet to be proven. There is still a lot of scope for further research in field of Ayurveda and other complementary systems to find out better outcomes to tackle this entity, as their strength lies in the management of Lifestyle related disorders and the approach is more nature-friendly.

CONSENT

As per international standard or university standard written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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