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Ethnic association in primary systemic vasculitis: A systematic review

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Abstract

Background: Literature described wide disparities in incidence and prevalence between different types of vasculitis. There were no comprehensive studies on ethnic or racial associations in all types of primary systemic vasculitis (PSV) in any published article, until this review commenced in 2020. The purpose of the review is to synthesize the evidence regarding the relation of ethnicity and the incidence and/or prevalence of different types of PSV.

Methods: A total of 52 selected articles which include Clinical trials, cohorts, cross-sectional studies, case series, and case studies and have been published within the last 10 years in the human population, were reviewed by searching The Medline, PubMed, and Google Scholars databases using predefined keywords. The PRISMA diagrams were followed to identify relevant articles. The methodological qualities of the studies were assessed using the EPHPP tool. Finally, a summary of the evidence on the association between ethnic origin and PSV was painstakingly compiled.

Results: The connection between ethnicity and different types of PSV has been found to be significantly diverse in this research such as vasculitis is more common in Asians and Scandinavians, Kawasaki disease and periarteritis nodules are more prevalent in Japanese and Alaska-natives, ANCA-associated vasculitis is more frequent in Caucasians, whereas Henoch-Schonlein purpura and Cogan syndrome more usual in Caucasians and Asians. Furthermore, Behçet's disease more commonly occurs on the "Silk Road", especially in Turkey.

Conclusion: Genetic susceptibility and environmental elements could be the contributing factors to the global variation in the incidence and prevalence of primary systemic vasculitis.

Keywords: Vasculitis; Ethnic; Racial; Association; Incidence and Prevalence

1. Background

Vasculitis is a rare heterogeneous group of disorders that may occur independently, such as (i) primary systemic vasculitis (PSV), eg, granulomatosis with polyangiitis (GPA) or (ii) secondary to other diseases such as lupus and

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rheumatoid arthritis. The word "vasculitis" means inflammation of the blood vessels [1]. Vasculitis is usually a systemic disease, although it may be localized to a single organ or vascular bed and may sometimes be of no clinical significance [1]. The pathological consequence of inflammation observed in histopathology is vascular wall destruction, and fibrinoid necrosis [1]. Although the cause of vasculitis is unknown, several factors such as ethnicity, genetic affiliation, sex, and environment including infections, toxins, ultraviolet rays, medications, smoking, and substances have been identified those cause allergies to influence the manifestation of the disease [1]. As terms, "vasculitis", and "arteritis", include about 20 different types of vasculitis [2]. Vasculitides are classified according to vessel size and the presence of anti-neutrophil cytoplasmic antibodies (ANCA) in the serum. However, the nomenclature of Chapel Hill Consensus 2012 (CHCC2012) is generally considered for classification of vasculitis [3]. According to CHCC2012, Takayasu's arteritis (TAK) and giant cell arteritis (GCA) belongs to the group of large vessel inflammatory diseases. Moderate vasculitis includes periarterial nodal inflammation (PAN) and Kawasaki disease (KD). Small-vessel-vasculitis are (a) ANCA-associated vasculitis (AAV) including (i) microscopic polyangiitis (MPA), (ii) granulomatosis with polyangiitis (GPA), and (iii) eosinophilic granulomatosis with polyangiitis (EGPA), and (b) immunocomplex vasculitis including (i) anti-glomerular basement membrane disease (Anti-GBM), (ii) cryoglobulinemia (CV) vasculitis, (iii) Henoch-Schoenlein purpura (HSP) and (iv) complement deficiency urticarial vasculitis (HUV). In addition, the European Medicines Agency (EMA) vasculitis classification algorithm was recently developed to reconcile the differences between the ACR and CHCC classifications for GPA, MPA, EGPA, and PAN [1].

The incidence of vasculitis, especially ANCA-induced vasculitis, has increased significantly over the past 10 years for a variety of reasons including better knowledge of these diseases, but it remains rare with less than 30 new cases per million population per year [1]. Sufficient evidence establishes that giant cell arteritis (GCA) is a heterogeneous disorder of the elderly in terms of clinical features such as fatigue, weight loss, low-grade fever; immunopathology, and its response to treatment [4]. The estimated incidence of GCA varies from 1.4 to 20 per 100,000 people over 50 years of age [5]. According to Crow et al. (2009), the median survival time for GCA is estimated to be 3.7 years [6]. Takayasu's arteritis (TA) is the most common childhood vasculitis and the most common cause of renal vascular hypertension in children. The 5 and 10-year TA-related mortality rates have been estimated at 1.9 and 3.9 per 100 cases, respectively, with higher mortality rates among Caucasians and smokers [7]. The annual incidence of Takayasu's arteritis is about two per million of the population [8]. The prevalence of periarteritis nodules has decreased over the past decades, as has the rate of hepatitis B virus (HBV) infection, but cutaneous periarteritis remains fairly common [1]. Kawasaki disease (KD) is the most common moderate inflammatory acute vasculitis in infants and young children that may get complicated by coronary aneurysms in 1 in 4 untreated cases [9]. Cases of KD have been described as the leading cause of acquired heart disease worldwide in children of developed countries. The prevalence of Kawasaki disease varies widely between 5 and 265 per 100,000 children under 5 years of age [10]. The annual incidence of periarteritis nodule (PAN) varies from 8 to 31 cases per million [11]. The overall incidence of ANCA-associated vasculitis (AVV) ranges from 46 to 184 per million [12]. Among AAVs, the annual incidence of MPA, GPA, and EGPA ranged from 1 to 8; 10 to 95; and <1 to 14 per million respectively (Hoang and Park, 2020). The annual incidence of HSP ranges from 13 to 127 per million people [11].

The risk factors for vasculitis are also diverse [11]. Demirkaya and colleagues found that ethnicity, genetic predisposition, age, and environmental factors as common risk factors for PSV [13, 14]. Among people of European ancestry, the HLA DP6-inherited population was approximately 4 times more likely to develop vasculitis compared with the control population, while SEPINA1*14 gene-positive individuals showed altered 50% lower change in the development of vasculitis compared with the control population [14]. According to Brogan and Eleftheriou (2017), the detection of biomarkers such as proteinase-3 myeloperoxidase (MPO), circulating microparticles, neutrophil extracellular trap (NET), and CD163 in urine promote the growing understanding of the pathogenesis of PSV and its prognosis [15]. PAN is associated with the absence of adenosine deaminase type 2 (DADA2) [15]. The clinical features of vasculitis have been shown to vary between different ethnic groups and geographical regions [16, 17]. For example, the incidence of myeloperoxidase-positive microangiopathy (MPO) and anti-cytoplasmic antibody (ANCA) is higher in Asian countries. On the other hand, Northern Europe and the United States (US) have a higher incidence of proteinase-3 (PR3) ANCA-associated granulomatosis with polyangiitis (GPA) [17]. Pearce and colleagues found large differences in the incidence of ANCA-associated vasculitis (AAV) among eight different ethnic groups in their multicenter observational study including 1217 patients with AAV at 133 locations from September 2014 to March 2016 [18]. The incidence and prevalence of AAV have increased over the past decade [19]. In recent years, environmental and genetic factors have been found to contribute largely to the increased risk of PSV [19].

To the knowledge of the authors, and after extensive research, no comprehensive studies regarding the association between ethnicity or race and the incidence and/or prevalence of primary systemic vasculitis (PSV) are available in a single article before starting this review. Synoptic information regarding ethnic influence in primary vasculitis has the potential to greatly assist epidemiologists, clinical researchers, and clinicians in their practice. This review was planned to answer the questions related to the evidence of the relation between ethnicity and PSV. The objectives of the review were (i) to synthesize evidence regarding an ethnic association in different types of PSV, and (ii) to determine the incidence and/or prevalence of the different types of PSV. The authors present clinical trials, cohort studies, cross-sectional studies, case series, and case studies. This review appears to be an appropriate approach to evidence dissemination, with the primary goal of more clearly answering the question of prevalence and ethnicity in PSV.

1.1. Search strategy to identify studies

Available evidence was systematically searched in Medline, PubMed, and Google Scholars using the keywords 'vasculitis', 'vasculitides', 'risk factors', 'ethnicity', population race, 'race' and 'racial association', as well as Boolean expressions where appropriate. Articles published in English literature within the past 10 years were considered for this review and all other articles were automatically excluded. The search was completed on October 31, 2020.

2. Method of Review

PRISMA diagrams were followed to identify relevant articles. A total of 182 articles were found in English literature by searching through a search engine using predefined keywords (shown in the PRISMA diagram, Figure 1). Finally, 52 articles [18, 20-70] were selected for this review obeying the selection criteria (shown in Table 1). Then, the methodological quality of the selected articles was assessed using the Effective Public Health Practice Project (EPHPP) – a quality assessment tool for quantitative studies in this review shown in Table 2. Thus, the frequency, incidence, and prevalence of PSV among different ethnic/racial groups were extracted from selected articles according to the selection criteria. All extracted data were then summarized in Table 1 showing the author's name, year of publication, country, and reported types of vasculitis. Effect sizes and results are reported in articles and saved in spreadsheets in Microsoft Excel 2016. Extracted data were aggregated and analyzed using the same Microsoft Excel 2016. Finally, a synopsis of evidence was made meticulously.

Table 2 Summary of extracted data of the selected articles

Sl No.	Author	Year	Study design	Sample Size	Country	Types of vasculitis
1	Nair et al. [20]	2018	Case Control study	104	India	Takayasu's arteritis
2	Takamura et al. [21]	2012	Case Control study	96	Japan	Takayasu's arteritis
3	Terao et al. [22]	2013	Cohort study	379	Japan	Takayasu's arteritis
4	Gudbrandsson et al. [23]	2016	Cohort study	2800000	Norway	Takayasu's arteritis
5	Bilge et al. [24]	2012	Cross Sectional study	22	Turkey	Takayasu's arteritis
6	Gruener et al. [25]	2019	Cohort study	586	USA	Giant cell arteritis
7	Brekke et al. [26]	2017	Cohort study	792	Norway	Giant cell arteritis
8	Tan et al. [27]	2019	Cross Sectional study	92	UK	Giant cell arteritis
9	Pereira et al. [28]	2015	Cross Sectional study	38	USA	Giant cell arteritis
10	Wang et al. [29]	2019	Case control study	1155	China	Kawasaki disease
11	Kuo et al. [30]	2011	Case control study	381	Taiwan	Kawasaki Disease
12	Yeter et al. [31]	2016	Case control study	8748	USA	Kawasaki Disease
13	Kim et al. [32]	2017	Case series	6	USA	Kawasaki disease

14	Amano et al. [33]	2019	Clinical trial	82	Japan	Kawasaki Disease
15	Nagelkerke et al. [34]	2019	Cohort study	4000	UK	Kawasaki disease
16	Boudiaf et al. [35]	2016	Cross Sectional study	133	Algeria	Kawasaki Disease
17	Fernandez-Cooke et al. [36]	2019	Cross Sectional study	625	Spain	Kawasaki Disease
18	Holman et al. [37]	2011	Cross Sectional study	528	USA	Kawasaki disease
19	Ghimire et al. [38]	2019	Cross Sectional study	10486	USA	Kawasaki disease
20	Manlhiot et al. [39]	2017	Cross Sectional study	1373	Canada	Kawasaki disease
21	Nakamura et al. [40]	2011	Cross Sectional study	23337	Japan	Kawasaki disease
22	Makino et al. [41]	2015	Cross Sectional study	26691	Japan	Kawasaki disease
23	Makino et al. [42]	2018	Cross Sectional study	31675	Japan	Kawasaki disease
24	Park et al. [43]	2011	Cross Sectional study	9039	Korea	Kawasaki disease
25	Karadag et al. [44]	2018	Cohort study	93	UK and Turkey	Polyarteritis Nodosa
26	Jelusic et al. [45]	2012	Cross sectional study	12	Croatia	Polyarteritis Nodosa
27	Pearce et al. [18]	2017	Cross sectional study	1217	UK	ANCA Associated Vasculitis
28	Berti et al. [46]	2017	Cross Sectional study	58	USA	ANCA associated vasculitis
29	Wu et al. [47]	2015	Case Control study	176	China	ANCA Associated Vasculitis
30	Fujimoto et al. [48]	2011	Case control study	136	Japan, UK	ANCA Associated Vasculitis
31	Cao et al. [49]	2011	Case control study	137	USA	ANCA associated vasculitis
32	Enkhmaa et al. [50]	2015	Case control study	267	USA	ANCA Associated Vasculitis
33	Ahn et al. [51]	2012	Cohort study	55	Korea	ANCA Associated Vasculitis
34	Li et al. [52]	2018	Cross Sectional study	43,677,829	China	ANCA Associated Vasculitis
35	Faurschou et al. [53]	2013	Cross Sectional study	7	Denmark	ANCA Associated Vasculitis
36	Terrier et al. [54]	2017	Cross Sectional study	760	France	ANCA Associated Vasculitis

37	Nesher et al. [55]	2016	Cross Sectional study	619	Israel	ANCA Associated Vasculitis
38	Wada et al. [56]	2012	Cross Sectional study	62	Japan	ANCA Associated Vasculitis
39	Pearce et al. [57]	2016	Cross sectional study	107	UK	ANCA Associated Vasculitis
40	Ortiz-Fernadez et al. [58]	2016	Cohort study	404	Spain	Behcet’s disease
41	Saleh et al. [59]	2012	Cross Sectional study	6134	USA	Behcet’s disease
42	Li et al. [60]	2012	Case Control study	722	China	Behcet’s disease
43	Hou et al. [61]	2013	Case Control study	738	China	Behcet’s disease
44	Wu et al. [62]	2014	Case Control study	1086	China	Behcet’s disease
45	Bonyadi et al. [63]	2014	Case Control study	69	Iran	Behcet’s disease
46	Shahneh et al. [64]	2012	Cohort study	290	Iran	Behcet’s disease
47	Shi et al. [65]	2014	Case control study	1617	China	Behcet's Disease
48	Li et al. [66]	2014	Case control study	1626	China	Behcet’s disease
49	Montes-Cano et al. [67]	2013	Case control study	304	Spain	Behcet's disease
50	Savey et al. [68]	2014	Cross Sectional study	769	France	Behcet’s disease
51	Jiang et al. [69]	2016	Case control study	384	China	Behcet’s disease
52	Kawasaki et al. [70]	2010	Cross sectional study	120	Japan	Henoch-Schonlein purpura
	Total Participants			**46616166**		

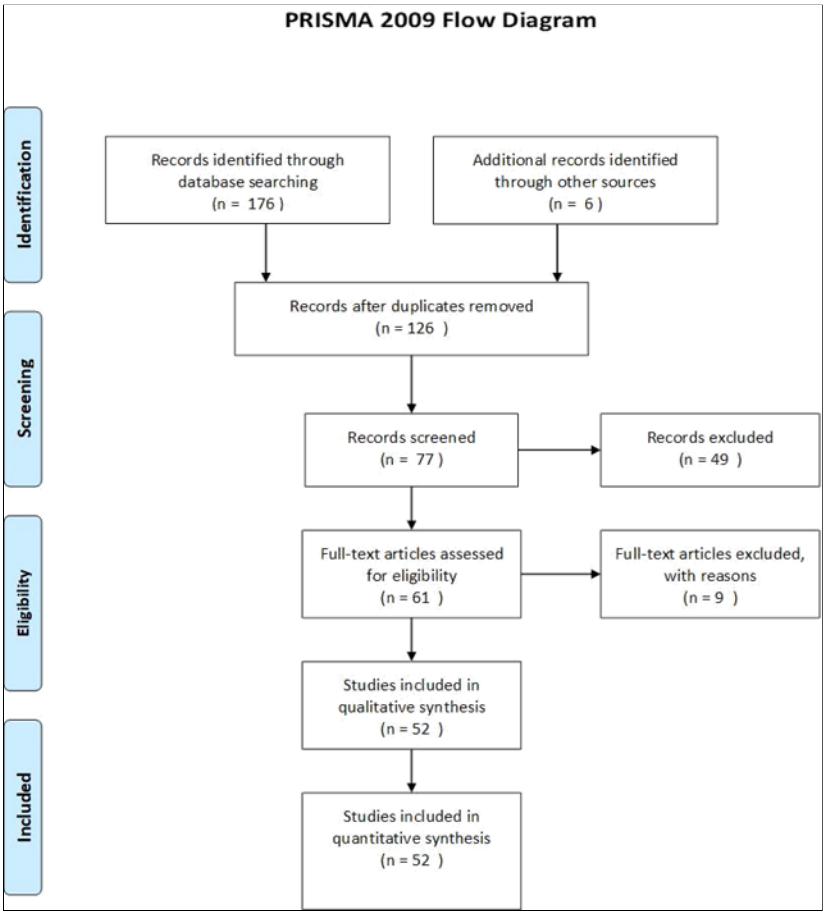

Figure 1 PRISMA diagram flowchart for selection of the articles included in this review

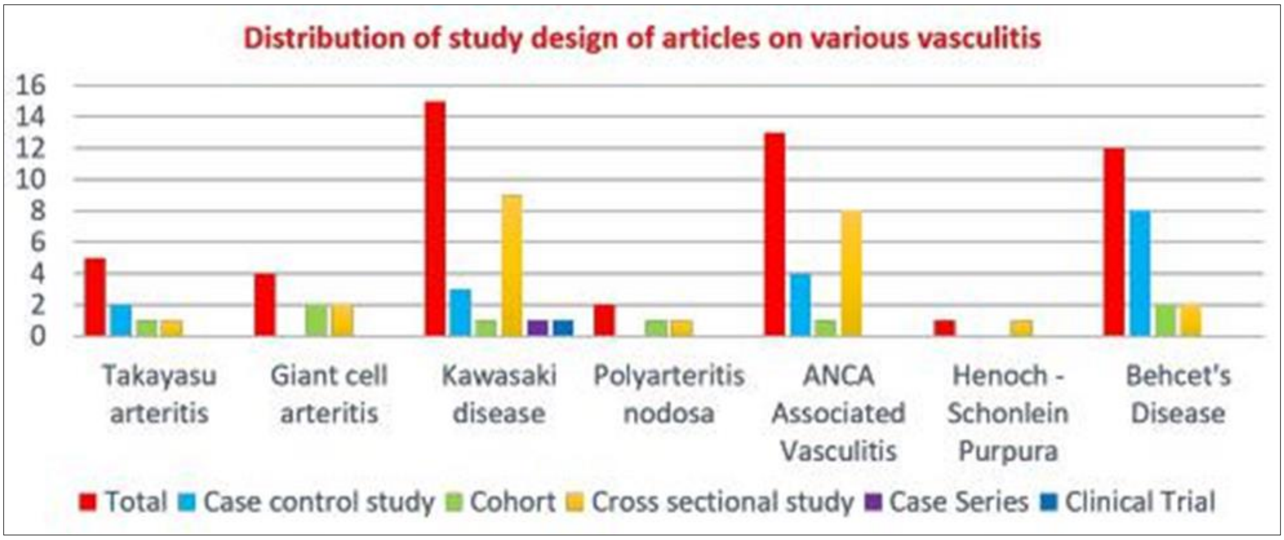

Figure 2 Bar chart illustrating the distribution of the number of study designs of articles various vasculitis

3. Results

In this review, 52 publications with 46616166 participants were included (Table 1). A cross-sectional design was used in 46.2% of the included articles as the most common study design (24 out of 52). Case-control designs were used in

32.7% of research, followed by cohort studies in 17.3% of cases, and case series designs in the remaining studies. The USA, Japan, and China, respectively, contributed 19.2%, 17.3%, and 17.3% of the articles. Among all enlisted articles, the most frequent articles were around Kawasaki disease 15 (28.9%), taken after by ANCA-related vasculitis 13 (25%), and Behcet's illness 12 (23.1%) individually. The conveyance of articles agreeing to distinctive consideration plans concerning different sorts of vasculitis was displayed within the figure-2. The affiliation of ethnicity and distinctive types of PSV widely varies, appeared in Table 3. Takayasu disease and giant cell arteritis are ~~more~~ predominant among Asians and Scandinavians individually. The prevalence of Kawasaki disease and Polyarteritis nodosa are more among people of the Japanese and native Alaskan populace. ANCA-related vasculitis is more common among Caucasians in Minnesota, USA. Henoch-schonlein purpura and Cogan's syndrome occurs more among Caucasians and Asians. Other than that, Behcet's disease is more predominant within the 'Silk-road', particularly in Turkey. On the other hand, Takayasu disease and giant cell arteritis are less frequent among Jews and Japanese respectively. Kawasaki disease and polyarteritis nodosa are less common among native Australians and European children, and south Sweden respectively. ANCA-associated vasculitis is less prevalent among black sub-Saharans. Behcet's disease is less frequent among native British.

Table 1 Effective Public Health Practice Project (EPHPP) - Quality assessment tool for quantitative studies

	Particulars of the Studies				EPHPP Components						
Sl No.	**Author**	**Year**	**Journal**	**Study Design**	**Selection Bias**	**Study design**	**Confounders**	**Blinding**	**Data Collection Method**	**Withdrawal and Dropout**	**Global Rating**
1	Nair et al. [20]	2018	International Journal of Rheumatic Diseases	Case Control study	M	W	M	NA	S	NA	Moderate
2	Takamura et al. [21]	2012	Circulation Journal	Case Control study	M	W	S	NA	S	NA	Moderate
3	Terao et al. [22]	2013	The American Journal of Human Genetics	Cohort study	S	W	NA	NA	M	M	Moderate
4	Gudbrandsson et al. [23]	2016	Arthritis Care & Research	Cohort study	S	W	S	NA	S	S	Moderate
5	Bilge et al. [24]	2012	Rheumatology International	Cross Sectional study	W	W	NA	NA	M	NA	Weak
6	Gruener et al. [25]	2019	JAMA Ophthalmology	Cohort study	S	W	NA	NA	S	S	Moderate
7	Brekke et al. [26]	2017	Arthritis Research & Therapy	Cohort study	M	W	NA	NA	M	M	Moderate
8	Tan et al. [27]	2019	Eye	Cross Sectional study	W	W	NA	NA	S	NA	Weak
9	Pereira et al. [28]	2015	British Journal of Ophthalmology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
10	Wang et al. [29]	2019	Bioscience Reports	Case control study	W	W	NA	W	S	M	Weak

11	Kuo et al. [30]	2011	Journal of Human Genetics	Case control study	W	W	W	W	S	M	Weak
12	Yeter et al. [31]	2016	International Journal of Environmental Research and Public Health	Case control study	W	W	M	W	S	M	Weak
13	Kim et al. [32]	2017	PLoS ONE	Case series	W	W	W	W	S	S	Weak
14	Amano et al. [33]	2019	Pediatric Rheumatology	Clinical trial	W	M	M	W	S	S	Weak
15	Nagelkerke et al. [34]	2019	Frontiers in Immunology	Cohort study	M	W	S	NA	M	M	Moderate
16	Boudiaf et al. [35]	2016	Journal of Tropical Pediatrics	Cross Sectional study	W	W	NA	NA	S	NA	Weak
17	Fernandez-Cooke et al. [36]	2019	PLoS ONE	Cross Sectional study	W	W	NA	NA	S	NA	Weak
18	Holman et al. [37]	2011	Hawaii Medical Journal	Cross Sectional study	W	W	NA	NA	S	NA	Weak
19	Ghimire et al. [38]	2019	Cardiology in the Young	Cross Sectional study	W	W	NA	NA	S	NA	Weak
20	Manlhiot et al. [39]	2017	Canadian Journal of Cardiology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
21	Nakamura et al. [40]	2011	Journal of Epidemiology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
22	Makino et al. [41]	2015	Journal of Epidemiology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
23	Makino et al. [42]	2018	Pediatrics International	Cross Sectional study	W	W	NA	NA	S	NA	Weak
24	Park et al. [43]	2011	Pediatrics International	Cross Sectional study	W	W	NA	NA	S	NA	Weak
25	Karadag et al. [44]	2018	Rheumatology International	Cohort study	M	W	M	NA	M	M	Moderate
26	Jelusic et al. [45]	2012	Rheumatology International	Cross sectional study	W	W	NA	NA	S	NA	Weak
27	Pearce et al. [18]	2017	Rheumatology	Cross sectional study	W	W	NA	NA	S	NA	Weak

28	Berti et al. [46]	2017	Arthritis & Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
29	Wu et al. [47]	2015	International Journal of Rheumatic Diseases	Case Control study	W	W	S	W	S	M	Weak
30	Fujimoto et al. [48]	2011	Rheumatology	Case control study	W	W	M	W	S	M	Weak
31	Cao et al. [49]	2011	Journal of the American Society of Nephrology	Case control study	W	W	S	W	S	M	Weak
32	Enkhmaa et al. [50]	2015	Atherosclerosis	Case control study	W	W	S	W	S	M	Weak
33	Ahn et al. [51]	2012	Rheumatology International	Cohort study	M	W	M	NA	M	M	Moderate
34	Li et al. [52]	2018	Arthritis Research & Therapy	Cross Sectional study	W	W	NA	NA	S	NA	Weak
35	Faurschou et al. [53]	2013	Clinical and Experimental Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
36	Terrier et al. [54]	2017	Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
37	Nesher et al. [55]	2016	The Journal of Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
38	Wada et al. [56]	2012	The Journal of Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
39	Pearce et al. [57]	2016	Rheumatology	Cross sectional study	W	W	NA	NA	S	NA	Weak
40	Ortiz-Fernadez et al. [58]	2016	Clinical and Experimental Rheumatology	Cohort study	M	W	M	NA	M	M	Moderate
41	Saleh et al. [59]	2012	Ocular Immunology and Inflammation	Cross Sectional study	W	W	NA	NA	S	NA	Weak
42	Li et al. [60]	2012	Human Genetics	Case Control study	W	W	M	NA	S	NA	Weak
43	Hou et al. [61]	2013	Human Genetics	Case Control study	W	W	S	NA	S	NA	Weak

44	Wu et al. [62]	2014	Clinical and Experimental Rheumatology	Case Control study	W	W	W	NA	S	NA	Weak
45	Bonyadi et al. [63]	2014	International Journal of Dermatology	Case Control study	W	W	W	NA	S	NA	Weak
46	Shahneh et al. [64]	2012	Pakistan Journal of Biological Sciences	Cohort study	W	W	M	NA	M	M	Weak
47	Shi et al. [65]	2014	PLoS ONE	Case control study	W	W	S	W	S	M	Weak
48	Li et al. [66]	2014	PLoS ONE	Case control study	W	W	S	W	S	M	Weak
49	Montes-Cano et al. [67]	2013	Arthritis Research & Therapy	Case control study	W	W	S	W	S	M	Weak
50	Savey et al. [68]	2014	Orphanet Journal of Rare Diseases	Cross Sectional study	W	W	NA	NA	S	NA	Weak
51	Jiang et al. [69]	2016	Scientific Reports	Case control study	M	W	S	NA	S	M	Moderate
52	Kawasaki et al. [70]	2010	International Urology and Nephrology	Cross sectional study	W	W	NA	NA	S	NA	Weak

S=STRONG, M=MODERATE, W=WEAK, and NA=NOT APPLICABLE
GLOBAL RATING: STRONG (no WEAK ratings), MODERATE (one WEAK rating), WEAK (two or more WEAK ratings)

Table 2 Effective Public Health Practice Project (EPHPP) **-** Quality assessment tool for quantitative studies

	Particulars of the Studies				**EPHPP Components**						
Sl No.	**Author**	**Year**	**Journal**	**Study Design**	**Selection Bias**	**Study design**	**Confounders**	**Blinding**	**Data Collection Method**	**Withdrawal and Dropout**	**Global Rating**
1	Nair et al. [20]	2018	International Journal of Rheumatic Diseases	Case Control study	M	W	M	NA	S	NA	Moderate
2	Takamura et al. [21]	2012	Circulation Journal	Case Control study	M	W	S	NA	S	NA	Moderate
3	Terao et al. [22]	2013	The American Journal of	Cohort study	S	W	NA	NA	M	M	Moderate

			Human Genetics								
4	Gudbrandsson et al. [23]	2016	Arthritis Care & Research	Cohort study	S	W	S	NA	S	S	Moderate
5	Bilge et al. [24]	2012	Rheumatology International	Cross Sectional study	W	W	NA	NA	M	NA	Weak
6	Gruener et al. [25]	2019	JAMA Ophthalmology	Cohort study	S	W	NA	NA	S	S	Moderate
7	Brekke et al. [26]	2017	Arthritis Research & Therapy	Cohort study	M	W	NA	NA	M	M	Moderate
8	Tan et al. [27]	2019	Eye	Cross Sectional study	W	W	NA	NA	S	NA	Weak
9	Pereira et al. [28]	2015	British Journal of Ophthalmology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
10	Wang et al. [29]	2019	Bioscience Reports	Case control study	W	W	NA	W	S	M	Weak
11	Kuo et al. [30]	2011	Journal of Human Genetics	Case control study	W	W	W	W	S	M	Weak
12	Yeter et al. [31]	2016	International Journal of Environmental Research and Public Health	Case control study	W	W	M	W	S	M	Weak
13	Kim et al. [32]	2017	PLoS ONE	Case series	W	W	W	W	S	S	Weak
14	Amano et al. [33]	2019	Pediatric Rheumatology	Clinical trial	W	M	M	W	S	S	Weak
15	Nagelkerke et al. [34]	2019	Frontiers in Immunology	Cohort study	M	W	S	NA	M	M	Moderate
16	Boudiaf et al. [35]	2016	Journal of Tropical Pediatrics	Cross Sectional study	W	W	NA	NA	S	NA	Weak
17	Fernandez-Cooke et al. [36]	2019	PLoS ONE	Cross Sectional study	W	W	NA	NA	S	NA	Weak

18	Holman et al. [37]	2011	Hawaii Medical Journal	Cross Sectional study	W	W	NA	NA	S	NA	Weak
19	Ghimire et al. [38]	2019	Cardiology in the Young	Cross Sectional study	W	W	NA	NA	S	NA	Weak
20	Manlhiot et al. [39]	2017	Canadian Journal of Cardiology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
21	Nakamura et al. [40]	2011	Journal of Epidemiology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
22	Makino et al. [41]	2015	Journal of Epidemiology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
23	Makino et al. [42]	2018	Pediatrics International	Cross Sectional study	W	W	NA	NA	S	NA	Weak
24	Park et al. [43]	2011	Pediatrics International	Cross Sectional study	W	W	NA	NA	S	NA	Weak
25	Karadag et al. [44]	2018	Rheumatology International	Cohort study	M	W	M	NA	M	M	Moderate
26	Jelusic et al. [45]	2012	Rheumatology International	Cross sectional study	W	W	NA	NA	S	NA	Weak
27	Pearce et al. [18]	2017	Rheumatology	Cross sectional study	W	W	NA	NA	S	NA	Weak
28	Berti et al. [46]	2017	Arthritis & Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
29	Wu et al. [47]	2015	International Journal of Rheumatic Diseases	Case Control study	W	W	S	W	S	M	Weak
30	Fujimoto et al. [48]	2011	Rheumatology	Case control study	W	W	M	W	S	M	Weak

31	Cao et al. [49]	2011	Journal of the American Society of Nephrology	Case control study	W	W	S	W	S	M	Weak
32	Enkhmaa et al. [50]	2015	Atherosclerosis	Case control study	W	W	S	W	S	M	Weak
33	Ahn et al. [51]	2012	Rheumatology International	Cohort study	M	W	M	NA	M	M	Moderate
34	Li et al. [52]	2018	Arthritis Research & Therapy	Cross Sectional study	W	W	NA	NA	S	NA	Weak
35	Faurschou et al. [53]	2013	Clinical and Experimental Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
36	Terrier et al. [54]	2017	Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
37	Nesher et al. [55]	2016	The Journal of Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
38	Wada et al. [56]	2012	The Journal of Rheumatology	Cross Sectional study	W	W	NA	NA	S	NA	Weak
39	Pearce et al. [57]	2016	Rheumatology	Cross sectional study	W	W	NA	NA	S	NA	Weak
40	Ortiz-Fernadez et al. [58]	2016	Clinical and Experimental Rheumatology	Cohort study	M	W	M	NA	M	M	Moderate
41	Saleh et al. [59]	2012	Ocular Immunology and Inflammation	Cross Sectional study	W	W	NA	NA	S	NA	Weak
42	Li et al. [60]	2012	Human Genetics	Case Control study	W	W	M	NA	S	NA	Weak
43	Hou et al. [61]	2013	Human Genetics	Case Control study	W	W	S	NA	S	NA	Weak

44	Wu et al. [62]	2014	Clinical and Experimental Rheumatology	Case Control study	W	W	W	NA	S	NA	Weak
45	Bonyadi et al. [63]	2014	International Journal of Dermatology	Case Control study	W	W	W	NA	S	NA	Weak
46	Shahneh et al. [64]	2012	Pakistan Journal of Biological Sciences	Cohort study	W	W	M	NA	M	M	Weak
47	Shi et al. [65]	2014	PLoS ONE	Case control study	W	W	S	W	S	M	Weak
48	Li et al. [66]	2014	PLoS ONE	Case control study	W	W	S	W	S	M	Weak
49	Montes-Cano et al. [67]	2013	Arthritis Research & Therapy	Case control study	W	W	S	W	S	M	Weak
50	Savey et al. [68]	2014	Orphanet Journal of Rare Diseases	Cross Sectional study	W	W	NA	NA	S	NA	Weak
51	Jiang et al. [69]	2016	Scientific Reports	Case control study	M	W	S	NA	S	M	Moderate
52	Kawasaki et al. [70]	2010	International Urology and Nephrology	Cross sectional study	W	W	NA	NA	S	NA	Weak

S=STRONG, M=MODERATE, W=WEAK, and NA=NOT APPLICABLE
GLOBAL RATING: STRONG (no WEAK ratings), MODERATE (one WEAK rating), WEAK (two or more WEAK ratings)

Table 3 Association between ethnicity and different types of primary systemic vasculitis

Vessels Size	Vasculitis type	Global Scenario	Ethnic Association			
			Most Common		Least common	
			Ethnic origin	Incidence or Prevalence	Ethnic origin	Incidence or Prevalence
Large sized vessels	Takayasu arteritis [Gudbrandsson et al., 2016; Russo and Katsicas, 2018]	Prevalence: 1-2 per million	Asians	Prevalence: 108 per million	Jews	Prevalence: <1.0 per million
	Giant Cell Arteritis [Richards, March and Gabriel, 2010;	Prevalence: 0.4 to 300 per million	Scandinavians	Prevalence 200 to 320 per million population	Japanese	Prevalence: 1.47 per 10 million population

		Kobayashi and Fujimoto, 2013]			aged over 50 years		aged over 50 years
Medium sized vessels		Polyarteritis nodosa [Ungprasert, Koster, Thongprayoon and Warrington, 2016)	Annual incidence: 2 to 30 cases per million	Native Alaskan	Prevalence: 77 per million	South Sweden	Annual incidence 1.6 cases per million
		Kawasaki Disease [Makino et al., 2018; Dietz et al., 2017; [Marchesi et al., 2018]	Annual incidence 34 to 2186 cases per million	Japanese children	Annual incidence: >3000 per million	Native Australian and European children	Annual incidence: 28 to 50 cases per million
Small sized Vessels	ANCA Associated (AAV)	AAV [Pearce et al., 2017; [Berti et a., 2017]	Overall annual incidence: 12-20 per million	Caucasians in Minnesota	Prevalence >400 per million	Hispanic	Annual incidence: 5-15 cases per million
		Granulomatosis with polyangiitis [Greco et al., 2015; Berti et a., 2017; Pierini et al, 2019; Terrier et al., 2017]	Overall prevalence in Europe 50 per million	Caucasians in Minnesota	Prevalence 218 per million	Black sub-Saharans	Annual incidence: 2 to 8 cases per million
		Microscopic polyangiitis [Berti et a., 2017]	Overall Prevalence: 10 to 30 per million	Caucasians in Minnesota	Prevalence 184 per million	Black sub-Saharan	Prevalence: 5 to 10 per million
		Eosinophilic Granulomatosis with polyangiitis (EGPA) [Gokhale et al., 2019; [Berti et a., 2017; Fujimoto et al., 2011]	Overall prevalence in USA 3.2 to 5.9 per million	Caucasians in Minnesota	Prevalence 18 per million and Annual incidence: 4 per million	Unknown	
	Immunocomplex, IgA vasculitis	Henoch-Schonlein Purpura	Annual incidence- Children: 100- 220 cases per million (Piram, Maldini and Mahr, 2012]	Caucasian and Asian children	Annual incidence: 200-250 cases per million	African children	Annual incidence: 2-7 cases per million
Variable sized vessels		Behcet's syndrome [Davatchi et al., 2016]	Annual incidence 5-4200 cases per million	'Silk road' Especially Turkey	Annual Incidence:	United kingdom	Annual incidence: 6.4 cases per million

				200 to 4200 cases per million		
	Cogan's syndrome	No data found				

4. Discussion

The incidence and prevalence of vasculitis vary greatly by ethnic group and geographic location. Genetic and environmental factors such as infections, exposure to toxins, and smoking also influence the incidence and prevalence of primary systemic vasculitis.

4.1. Takayasu's arteritis (TA)

TA is a chronic systemic vasculitis affecting large arteries such as the aorta, its major branches, and occasionally coronary and pulmonary arteries [71]. The name "Takayasu disease" was first suggested by Minoru Nakajima in 1921 in the name of great ophthalmologist professor Mikito Takayasu [72]. In succession, several other names have been proposed such as (i) avascular disease, (ii) aortic arch syndrome, and (iii) obstructive-producing arteritis [73]. The annual global incidence of TA is estimated at two per million population [8,21]. Russo and co-workers found a higher prevalence of TA in Central and South America, Africans, Indians, and Russians, whereas a rare incidence in Jews [8]. According to Takamura et al. (2012), a higher prevalence of TA has been observed in Southeast Asians, the Indian subcontinent, Brazilians, Chileans, and Argentines compared with other regions of the globe [21]. In the southeast Norwegian cohort of 2.8 million population, the point prevalence of Takayasu's arteritis was estimated at 22.0 per million in Northern Europeans, compared with 78.1 per million in Asian whites and 108.3 per million in Africans [23]. An association between TAK and HLA-B52 has been observed in several HLA-B52 ethnic populations [20-24]. Therefore, it is speculated that the higher rate of TAK in Asians may be reflected by the increased frequency of HLA-B52 in this ethnic group. Takamura and colleagues found a positive association of HLA B67 and HLA B52 of approximately 5-fold and 4-fold, respectively, in Japanese patients with Takayasu's arteritis compared with controls [21]. The fundamental role of IL12B in the pathogenesis of HLA-B52-associated TA has been described [22]. The increased rate of TA in Asians may reflect a higher frequency of HLA-B52 in this population [24]. For example, the frequency of HLA-B52 in the Japanese population is estimated to be 10%, and the prevalence of TAK is estimated to be 40 per million of the population in Japan. While the frequency of HLA-B52 is estimated to be 2% in the European population, and the incidence of TAK is much lower than in Japan [20-24].

4.2. Giant cell arteritis

The most common primary systemic vasculitis in adults over 50 years of age is giant cell arteritis (GCA), which affects medium to large arteries and is affected more often in women than in men [74, 75]. In Europe and North America, giant cell arteritis (GCA) is the most common type of vasculitis [76]. GCA is considered a disease of the elderly mainly between the ages of 61 and 80 years with a male-to-female ratio of about 1:2 [76]. Geographic variations, cyclical patterns, and seasonal fluctuations have been observed in the incidence of GCA [77]. A correlation between the peak incidence of GCA and the outbreak of viral infection was identified [77]. Geographic variations in the incidence of GCA are due to a combination of genetic and environmental variables [77]. GCA is more common in Caucasians, especially Scandinavians, with an annual incidence of 20 to 32.0 per 100,000 population, whereas GCA is rare in African Americans over 50 years of age [78]. According to Tan and colleagues, among 92 patients with GCA, Caucasian Britons, descendants of the Indian subcontinent, black British, and other citizens were 66.30, 16.30, 9.78, and 2.17% respectively [27]. Gruener and colleagues studied the ethnic association of GCA in their 10-year cohort where the temporal biopsy was performed in 586 individuals with GCA in the United States [25]. In this cohort, 65.2, 28.5. 1.4, 1.2, and 3.8% of participants were White, Black, Hispanic, Asian, and of unknown ethnic origin respectively; while among biopsy-proven GCA, 81.5, 15.2, and 2.3% were White, Black, and unknown ethnic origin respectively [25]. The biopsy-proven annual incidence of GCA was estimated at 36 and 31 cases per million, respectively, in whites and blacks in this cohort [25]. In addition, Brekke et al. (2017) found a mean crude incidence of 16.7 and a biopsy-proven incidence of 11.2 per 100,000 Scandinavian patients aged more than 50 years in their retrospective cohort study of 40 years' hospital records [26]. In the UK, patients under 65 years of age have the highest number of deaths in the first year after diagnosis [79]. Genetic susceptibility may be related to racial/ethnic differences in the incidence and prevalence of GCA. The HLA-DR4 polymorphism is less common in the Japanese population [79]. HLA-DRB04 genetic association was observed in GCA. The association of GCA is two to four times more frequent in individuals with positive HLA-DR4 polymorphisms [80].

4.3. Polyarteritis nodosa (PAN)

Kussmaul and Maier were the first to classically describe PAN in 1866 [44]. PAN is a moderate inflammatory vasculitis of small blood vessels that is characterized by necrosis and nodules of aneurysms along the vessel wall. Although PAN is relatively rare in children, it is the third most common vasculitis after Henoch-Schonlein purpura and Kawasaki disease in children. The highest prevalence in males with a peak occurring in ages 7-11 [81]. PAN was observed to be the least common vasculitis among primary systemic vasculitis in a large multinational vasculitis observational study (DCVAS - Diagnostic criteria and classification of vasculitis) [82, 83]. The annual worldwide incidence of PAN is 2 to 30 per million population [84]. The overall annual incidence is estimated to be between 2 and 9 cases per million population in Europe and the United States [81]. The highest incidence of PAN has been estimated at 77 per million Alaska natives [82]. The annual incidence is estimated to be 1.6 parts per million in the south [84]. In Jerusalem, the average annual incidence of PAN has been recorded as 3.6 per million adults [55]. The prevalence of PAN was estimated at 30.7 per million inhabitants in Paris in 2000. The overall incidence in European descendants was twice that of non-European ancestry in Paris [85]. The overall annual incidence has decreased in Poland. The annual incidence rates were estimated at 3.3 and 1.9 cases per million population in 2008 and 2013 in Poland, respectively [86]. The downward trend may be the result of a decrease in the prevalence of hepatitis B during this period in Poland. However, PAN may recur in one-third of cases, and case mortality is estimated to be 4% in the United Kingdom [87]. The frequency of PAN was only 3.8% in PSV in Croatian children [45]. The link between geographic location, ethnicity, and NAP development is not clear. Karadag and colleagues (2018) found a younger age at the onset of PAN in the Turkish population than in the British in their group [44]. The risk of recurrence is higher in children with severe gastrointestinal lesions and the duration of remission is prolonged in such cases [86]. The Mediterranean fever gene (MEFV) mutation is an important underlying factor found in Turkey to create an inflammatory environment and demonstrates an uncanny response to streptococcal infections, ultimately leading to PAN [88].

4.4. Kawasaki Disease

Kawasaki disease (KD) was named after a great Japanese physician, Dr. Tomisaku Kawasaki, who first described the disorder well in 1961 [89]. KD was first described in Japan and it is now labeled worldwide [90]. The cause of Kawasaki disease (KD) is still unknown. Among infants in the developing world, KD is the leading cause of acquired heart disease and it mainly affects small and medium-sized blood vessels [91]. KD is more common in Japanese children [42]. The annual incidence of Kawasaki disease (KD) in Japanese children aged 0–4 years was estimated at 3030 and 3080 per million in 2013 and 2014 respectively [42]. A higher frequency of KD has been found in children of Asian descent in the United States [38]. Holman et al (2010) described a higher susceptibility of children of Japanese ancestry in Hawaii, where the highest prevalence of KD (2105 per million) was observed in children of Japanese ancestry under 5 years old; while the lowest incidence (137 per million) was observed in white children of the same age [37]. The overall incidence in US children under 5 years of age has been estimated at 250 per million from hospital data. According to Manlhiot et al., 2017, the annual incidence of KD in Canada is 19.6 per 100,000 children under 5 years of age [39]. East Asian children are 10 to 20 times more likely to develop KD than children living in the West [31]. In Korea, the annual incidence of KD is estimated at 113.1 per 100,000 children and this rate is increasing day by day [43]. Negelkerke and colleagues found strong, weak, and absent linkage disequilibrium (LD) among Europeans, Africans, and Asian descendants respectively in their cohort including 1028 individuals with KD in the UK [34]. There is a linear association in KD risk across ethnicities, especially among Asian, African, Caucasian, and Hispanic children, and exposure to mercury and cadmium from seafood in particular [31]. The recurrence rate of KD in Japan is estimated to be 3% [9]. The recurrence of KD was greater than five episodes per thousand patient-years of follow-up in Japan, and the most frequent relapses were observed during the first two years of disease onset [9]. The relative risk of KD is a 10-fold increase in individuals with a positive family history compared with the general Japanese population [91]. The recurrence rate of KS in Canada has been estimated at 2.9 episodes per thousand patient-years of follow-up, with recurrence occurring on average 1.5 years after the first episode with similar clinical features [92]. Evidence for genetic factors for vulnerability to KD includes the following such as (i) observed higher incidence in Japanese children and children of living Japanese ancestry Outside of Japan, (ii) the prevalence of KD is higher in children with a history of KD in their parents, and (iii) the prevalence of KD is higher in siblings and twins of the same parent [9]. Single nucleotide polymorphisms in six genes or genomic regions such as (i) FcyR2a, (ii) caspase 3 (PASP3), (iii) human leukocyte antigen (HLA) class II, (iv) B-cell lymphoid kinase (BLK), (v) inositol 1,4,5 triphosphate kinase-C (ITPKC) and (vi) CD40 have been described in genome-wide association and family studies [9]. In children of European ancestry, a higher risk of the coronary aneurysm was associated with variants of the TGFβ2, TGFβR2, and SMAD3 genes [9]. An association between the HLA determinant and susceptibility to KD was observed in Japanese and Taiwanese children. Nonetheless, no association between HLA determinants and susceptibility to KD was found in children of European ancestry [9]. Higher KD occurrence was found in winter and spring compared with fall and there is a strong association between first- and second-degree relatives with KD history [36]. Seasonal peaks of KD are observed in winter in the tropical northern hemisphere, on the other hand, low numbers are observed in autumn and summer. However, no seasonal variation of KD was observed in the tropical and extratropical south hemispheres [9].

4.5. ANCA-Associated Vasculitis (AAV)

ANCA-associated vasculitis (AAV) has been well recognized since 1948 [93]. ANCA-associated vasculitis (AAV) is a group of primary systemic vasculitis that affects small blood vessels and causes vascular necrosis in the presence of ANCA in the blood. AAV is classified into three types (i) microscopic polyangiitis (MPA), (II) granulomatosis with polyangiitis (GPA), and (iii) Eosinophilic granulomatosis with polyangiitis (EGPA) [93]. The overall annual incidence of ANCA-associated vasculitis was estimated at 23.1 per million in the UK cohort [57]. The annual incidence of AAV was 25.8 per million in whites, whereas 8.4/1000 in blacks and minority ethnic (BME) populations [57]. The annual incidence of AAV among Jews is estimated at 8 per million population [55]. Fujimoto and coworkers found no difference between the UK and Japan with annual incidence rates estimated at 21.8 and 22.6 per million adults in the UK and Japan, respectively [48]. The overall prevalence of AAV has been reported to be 42.1 per 100,000, with an average annual incidence of 3.3 per 100,000 population in Minnesota, USA. An incidence of AAV was found in 0.25% of Dong, Zhuang, and Li Chinese ethnic populations with a positive correlation between carbon monoxide exposure and AAV development [52]. Furthermore, the overall incidence of AAV has been estimated at 131–183, 198, 137, and 209 per 10 million people per year in Spain, the United Kingdom, Australia, and Sweden, respectively. GPA is more common than MPA in northern Europe, and MPA is more common than GPA in southern Europe [94,95]. In the United Kingdom, the combined annual incidence of GPA and MPA was estimated at 1.5 cases per million cases in the 1980s [96]. The overall prevalence of AAV ranges from 30 to 218 cases per million population worldwide [96]. The literature suggests that the prevalence of AAV has increased in recent years as both survival and incidence of AAV have increased [96]. For example, AAV prevalence in northern and southern Germany was 74 per million in 1994 and 149 per million in 2006, only doubling in 12 years. Katsuyama and co-workers reported ANCA positive for MPO was higher in Japan (83.7%) than in the UK (30.0%) [17]. On the other hand, PR3-positive AAV was reported to be lower in Japan (7.0%) compared to the UK (58.0%) [17]. The estimated annual incidence of total AAV in children was reported at 0.22 to 0.45 per million and 3.2 per million in French and Sweden [96]. Pearce and colleagues reported that people from Northern Europe, Turkey, and the Indian subcontinent had higher PR3-ANCA-associated vasculitis [57]. Japanese and Chinese have a 60-fold and 7-fold higher risk of developing MPO-ANCA-associated vasculitis compared with northern Europeans [48]. A higher likelihood of MPO-AAV is also observed in Caucasian Americans, Turks, and Southern Europeans compared to Northern Europeans. A higher proportion of MPO-positive AAV patients compared with PR3-positive AAV has also been reported in Asian countries such as China and Taiwan [48]. Sreihet and colleagues reviewed disease severity in Caucasian and Hispanic patients with AAV in 2014 [12]. Hispanic patients have been reported to exhibit more severe disease activity and greater organ involvement compared to Caucasians residing in the same geographic area [12, 97]. Both type I and type II HLA genes are predisposed to developing AAV. HLA-B*08, HLA-A*01, and HLA-DRB1*03 have been reported to be genetically susceptible to AAV, especially GPA [98]. The relationship between HLA class II genes and clinically apparent disorders or ANCA archetypes fluctuates between ethnicity and geographic location. HLA-DRB1*13 was found to be protective against PR3-ANCA-positive Dutch GPA and German GPA patients [98]. While HLA-DRB1*04 was found to be associated with Dutch GPA patients and German GPA-positive ANCA PR3 patients with an increased risk of developing end-stage renal disease (ESRD) [98]. In addition, among British and German patients with GPA, HLA-DBP1*04 was reported more frequently. In Caucasians, the HLA-DBP1 polymorphism, rs3117242(G) has been reported to confer genetic susceptibility to the development of GPA, especially PR3-ANCA-positive GPA [98]. Among African Americans and Chinese, the genetic factors HLA-DRB1*15 and HLA-DBR1*1202 have been reported to be susceptible to PR3-ANCA-positive vasculitis, respectively. Japanese patients with MPA-positive AAV and MPO have been reported to have an association with HLA-DRB1*0901 and its haplotype [98]. Prognosis and disease severity are also associated with HLA polymorphisms. Poor prognosis and poor response to treatment have been reported in HLA-DRB1*0405-positive patients, while higher mortality has been reported in Chinese AAV patients with HLA-DRB1*0403 [98]. Interestingly, the HLA-DPB1/RXRB*0301/01 haplotype was associated with a lower risk of GPA, while the HLA-DPB1/RXRB*0401/03 haplotype was associated with a higher risk of GPA. The RXRB rs6531 polymorphism was commonly found in patients with a positive mean GPA score for ANCA. Ring finger protein-1 (RING) polymorphisms such as rs213210, rs213209, and rs213208 are associated with GPA patients in Germany [98]. Severe symptoms of GPA were observed in white Europeans compared with sub-Saharan Africans and Afro-Caribbeans (hazard ratio 1.96) [54]. The prevalence of GPA increased from 28.8 to 64.8 per million UK population in 2020 [96]. In southern Sweden, the prevalence of GPA was reported to be 160 per million, which was much higher than in the UK. Similarly, in the United States, a survey of insurance claims databases found the prevalence of GPA to be 30.5 per million adults aged 18 to 65 [99]. However, the highest prevalence of her GPA in the United States (218 per million) was reported in his 20-year study conducted at the Mayo Clinic in the United States [46]. Methodological differences between studies may be a possible reason for this large variation in the prevalence of GPA in the United States. Alike USA, the prevalence is also on the rise in Norway [85]. In 1988 his GPA was 30.4 per million, while in 1998 he was 95.1 per million in Norway [85].

This is a more than three-fold increase in prevalence during his ten years in Norway [85]. In New Zealand and Australia, the prevalence of GPA is estimated at 112 and 95 per million, respectively [99]. Similar to total AAV, a trend of increasing incidence of GPA has been observed worldwide [99]. Eosinophilic granulomatosis with polyangiitis (EGPA) also known as Churg-Strauss disease, was developed by two physicians, Dr. Churg and Dr. Strauss, who described EGPA in detail in 1951 as eosinophil-rich necrotic granulomatous inflammation of small to medium-sized vessels. EPGA commonly affects the airways and is associated with the presence of asthma. The coexistence of glomerulonephritis and ANCA is common in EGPA. EGPA has the highest prevalence in Australia, estimated at 22.3 per million population [96]. The prevalence of EGPA was given as 10.7, 13, 14, and 18 cases per million population in Paris, Norway, Sweden, and the United States respectively [46, 96]. The annual incidence of EGPA in children aged 0 to 17 years is estimated at 0.4 cases per million in Sweden [96].

4.6. Immune complex microvasculitis (ISVV)

It is the deposition of immunoglobulins and/or complement components in the walls of small vessels in ISVV [3]. Immune complex vasculitis includes (i) Henoch-Schönlein purpura (HSP/IgA vasculitis), (ii) anti-glomerular basement membrane (anti-GBM) disease, (iii) cryoglobulinemia vasculitis, and (iv) hypocomplementaemic urticaria vasculitis (HUV/anti-C1q vasculitis) [3]. The most common form of vasculitis in children is Henoch-Schönlein purpura (HSP), also known as immunoglobulin A vasculitis (IgAV) [100]. IgAV usually presents as an acute nonthrombocytopenic vasculitis affecting small blood vessels before the age of 10 years, with peak onset between 4 and 6 years of age and a slight predominance in males. However, IgAV is very rare in infants. The global incidence of IgAV has been estimated at 30–270 cases per million children per year [100]. In most ethnic groups in Europe, the annual incidence is estimated at 220 per million population under the age of 14 [16]. Though, Asian ethnic groups, especially Korean and Japanese children, are strongly affected by her IgAV compared to African ancestry [100]. The average annual incidence of HSP nephritis in Japan is estimated at 34–36 per million of the pediatric population [70]. However, HSP is less than one-third in black children compared to Asian or white children [16]. Moreover, hospitalization rates have been reported among various ethnic groups such as 1.9 Hispanics, 1.6 Whites, and 0.9 Blacks per 100,000 children in the United States [101]. Because IgAV can be caused by viral infections, seasonal variations in outbreaks have been shown [100]. In South Korea, the seasonal variation of IgAV in 16,000 children was studied, with fewer cases in summer than in winter and autumn [101]. HSP susceptibility is strongly associated with HLA-DRB1*0103 [102]. However, HSP susceptibility and disease severity can also be influenced by non-HLA genetic markers [102].

4.7. Anti-Glomerular Basement Membrane (Anti-GBM) Diseases

Anti-GBM disease or 'Goodpasture's disease' has been described as a rare type of PSV that affects renal and/or pulmonary capillaries. The overall annual incidence of the anti-GBM disease is estimated to be less than 1 per million European population. In Ireland, the estimated incidence of the disease was 1.6 per million population per year. Anti-GBM disease was well recognized among Asians and Caucasians but was considered a rare disease in Africa [103]. The literature describes seasonal variations and outbreaks, particularly the temporal and spatial accumulation of disease. Anti-GBM disease is caused by environmental factors such as influenza infection and smoking [103]. Genetic factors that predispose to anti-GBM disease may be triggered in the presence of environmental factors. The HLA-DR2 haplotype is estimated to be inherited 80% of the time. HLA-DBR1 alleles, specifically HLA-DRB1*1501, and HLA-DRB1*0401, have been reported to be positively associated with this disease, whereas HLA-DRB1*07 is associated with this disease and showed a protective effect. HLA-DRB1*1501 associations have been reported in Asian populations [103]. In addition, susceptibility to diseases of non-HLA gene polymorphisms has also been reported. Non-HLA genes encoding Fcy receptors and COL4A3 polymorphisms have been described in disease manifestation [103].

4.8. Cryoglobulinemia

Cryoglobulinemia is characterized by the constant presence of abnormal immunoglobulins (Ig) in the serum, which accelerates at low temperatures and decays again with warming [1]. Cryoglobulinemia consists of (i) type I cryoglobulinemia- consisting of monoclonal immunoglobulin (Ig), (ii) type II cryoglobulinemia- consisting of monoclonal Ig binding to polyclonal heavy chains, and (iii) III Type cryoglobulinemia - is divided into three types consisting of polyclonal immunoglobulins. Cryoglobulinemia is a rare disease in the general population of Europe and the United States. The overall prevalence of cryoglobulinemia is estimated at <5 per 10,000 populations in the United States and Europe [105]. However, a higher prevalence has been reported in the Mediterranean region. Mixed cryoglobulinemia, especially type II, can be caused by hepatitis-C virus (HCV) infection. Despite geographical differences, HCV infection is widespread in Central Asia, East Asia, and Northeast Africa, and is estimated to infect more than 184 million people worldwide. The estimated prevalence of HCV in the above regions ranged from 15 to 35 per 1,000 population, with a prevalence of less than 1/2 in Western Europe, the United Kingdom, Asia Pacific, North America, and Latin America [105]. It is estimated at 10-20 in the Mediterranean region and 25-30 per 1,000 inhabitants in Eastern Europe [105]. Several studies have reported that cryoglobulinemia occurs in 10-60% of HCV infected cases. [104 -106]. A genome-wide association study (GWAS) shows a significant association between cryoglobulin-associated vasculitis (CryVas) and a single nucleotide polymorphism (SNP, rs9461776) near NOTCH4 and HLA-DRB1 and HLA-DQA1 on chromosome 6 reported [106].

4.9. Hypocomplement urticaria-like vasculitis (HUV/anti-C1q vasculitis)

HUV is a form of immune complex small vessel vasculitis, characterized by urticaria and hypocomplemententemia for at least 6 months, accompanied by (i) arthralgia, (ii) glomerulonephritis, (iii) uveitis, and/or (iv) characterized by comorbid systemic symptoms such as recurrent abdominal pain [107]. In addition, chronic obstructive pulmonary disease (COPD) is commonly found in his HUV and is the leading cause of HUV mortality and morbidity. Global incidence and prevalence have not been reported to date. However, the annual incidence in Sweden is estimated at 7 per 10 million people. His estimated point prevalence of HUV in Sweden in 2015 was 9.5 per million. In addition, 57 cases of HUV were recorded in the French national database [107].

4.10. Behcet's disease

Behcet's disease (BD) or Adamantiades-Behcet's disease is an idiopathic, chronic, recurrent vasculitis that can involve the mucocutaneous, joints, blood vessels, eyes, gastrointestinal tract, and central nervous system (CNS) affecting by variable vessel vasculitis, including arteries, veins, arterioles, venules, and capillaries [3]. Mortality and morbidity are significantly higher in BD. It primarily affects young adults due to its specific geographic distribution known as the "Silk Road", corresponding to ancient routes between the Middle East, Mediterranean, and the Far East. BD has the highest prevalence in Turkey, 3700 per million population. The prevalence of BD in Japan is estimated at 160 per million people, and more than 20,000 patients sought medical help in Japan in 2014 [108]. Low incidence and prevalence have been reported in Europe and North America. A small number of cases have also been reported from Brazil, Africa, and Australia. Interestingly, the incidence of BD is lower among Armenians living in Istanbul, Turkey [1]. Phenotypic representation among different ethnic groups can vary in BD. Patients with BD in sub-Saharan Africa have been reported to have greater central nervous system involvement, higher mortality, and lower frequencies of the HLA-B51 allele compared with those in North Africa and Europe, respectively. [68]. A genetic association has been reported in BD [108, 109]. Significant associations of HLA-B5, HLA-B35, HLA-51, HLA-B52, and HLA-CW4 in BD patients have been reported in the Iranian Azerbaijani population [64, 109]. However, while there is no statistically significant association between the PTPN22 gene and BD in the Spanish population [56], there is a significant association between the PTPN2 polymorphism and BD in the Han population [62]. Nonetheless, no significant association of his MDR1C3435T polymorphism was found between a BD patient and his Turkish healthcare manager in Azerbaijan, Iran [63]. The rs9494885 TC genotype is common twice in BD patients compared with controls [60]. However, HLA-B51 is found in 15% of the Japanese population, whereas one-third of Behcet's disease is not associated with HLA-B51 [108].

4.11. Cogan Syndrome

Cogan syndrome (CS) is a rare autoimmune vasculitis [110]. The main features of Cogan's syndrome are eye inflammation and sensorineural hearing loss. Young adults are more commonly affected, but people of all ages can suffer from the disease. Anti-Hsp70 antibodies are associated with CS. It can occur in individuals of any race or ethnic group but is more common in Caucasians [111]. Cogan's syndrome is one of the rarest PSVs, has no gender predominance, and affects only young adults with a peak age of 29 years [112]. Approximately 250 cases have been reported so far, most of them Caucasian [112]. In expert opinion, the actual number of cases of CS is dwarfed by (i) idiopathic recurrent keratitis, (ii) idiopathic deafness, and (iii) underdiagnoses or lack of diagnosis as an autoimmune inner ear disease. It has been explained that there may be more cases than published [112].

4.12. Single Organ Vasculitis (SOV)

Instead of "focal vasculitis", the term "single organ vasculitis" (SOV) is considered more appropriate. SOV is self-evident vasculitis confined to a single organ such as the skin, central nervous system, or reproductive tract. SOV is classified into three subclasses: (i) focal single-organ vasculitis, (ii) multiple single-organ vasculitis, and (iii) diffuse single-organ vasculitis [113]. However, SOV has an inherent risk of conversion to systemic vasculitis and continuous follow-up for at least 6 months should be considered and implemented. Primary central nervous system vasculitis (CNS) is the most commonly reported form of SOV. Approximately 500 cases of primary CNS vasculitis have been reported [113]. The estimated incidence of primary CNS vasculitis in the United States is estimated at 2.4 cases per million population per year. Nonsystemic vasculitic neuropathy (NSVN), limited renal vasculitis, pulmonary Takayasu disease, retinal vasculitis, thoracic vasculitis, vasculitis of genitourinary structures, gallbladder vasculitis, and aortic vasculitis are described in case reports [113]. However, no data were found on ethnic associations in occurrence in geographical locations.

5. Conclusion

Although evidence for an association between ethnicity and different types of vasculitis is limited, the prevalence and incidence of PSV vary widely among different ethnic and/or racial groups worldwide. Genetic susceptibility and environmental factors also contribute to the incidence and prevalence of primary systemic vasculitis.

Limitation

Articles related to PSV published in the last 10 years are included in this review. In addition, a systematic search of English literature was conducted in the PubMed and Google Scientist databases. Therefore, some published articles may not be included in this review. Due to differences in study design, we were unable to perform a meta-analysis. Therefore, pooled prevalence and incidence of primary systemic vasculitis were not estimated for any ethnic group in this review.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

None of the authors has any conflict of interest including financial involvement in the organization or company.

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